



Effective Health Care Program

Technical Brief
Number 6

Stereotactic Body Radiation Therapy



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Number 6

Stereotactic Body Radiation Therapy

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

This EPC evidence report is a Technical Brief. A Technical Brief is a rapid report, typically on an emerging medical technology, strategy or intervention. It provides an overview of key issues related to the intervention—for example, current indications, relevant patient populations and subgroups of interest, outcomes measured, and contextual factors that may affect decisions regarding the intervention. Although Technical Briefs generally focus on interventions for which there are limited published data and too few completed protocol-driven studies to support definitive conclusions, the decision to request a Technical Brief is not solely based on the availability of clinical studies. The goals of the Technical Brief are to provide an early objective description of the state of the science, a potential framework for assessing the applications and implications of the intervention, a summary of ongoing research, and information on future research needs. In particular, through the Technical Brief, AHRQ hopes to gain insight on the appropriate conceptual framework and critical issues that will inform future comparative effectiveness research.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome comments on this Technical Brief. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.hhs.gov.

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Peer Reviewers

We wish to acknowledge individuals listed below for their review of this report. This report has been reviewed in draft form by individuals chosen for their expertise and diverse perspectives. The purpose of the review was to provide candid, objective, and critical comments for consideration by the EPC in preparation of the final report. Synthesis of the scientific literature presented here does not necessarily represent the views of individual reviewers.

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Stereotactic Body Radiation Therapy

Structured Abstract

Objectives. Conduct a systematic literature scan for published data for the treatment of stereotactic body radiation therapy (SBRT) and provide a broad overview of the current state of SBRT for solid malignant tumors.

Data Sources. Ovid, MEDLINE, EMBASE, the Cochrane Database, and the Health Technology Assessment Database from January 2000 to December 2010. We also searched www.ClinicalTrials.gov, www.fda.gov, and gray literature within *Windhover*, *Current HC News*, *Gray Sheet*, *The Wall Street Journal*, *Clinica*, and the Google search engine.

Review Methods. Clinical studies of any design, published in English that delivered SBRT in 10 or fewer fractions, and enrolled at least three patients with solid malignant tumors in the body (excluding head and spine) were included. Two reviewers abstracted information on study design, patients, and reported outcomes. We synthesized the following variables if reported: cancer type, patient inclusion criteria, type of radiation, instrumentation, and algorithms used, study design and size, comparators, concurrent and/or prior treatments, length of followup, outcomes measured, and adverse events.

Results. Our searches identified a total of 124 relevant prospective and retrospective single group studies. The bulk of the studies examined SBRT for tumors of the lung/thorax ($k = 68$). We found 27 studies of tumors located in the pancreas, liver, colon, and fewer than 10 studies each for sites within uterus, pelvis, sacrum, kidney, prostate, and thyroid. There were 10 studies that included multiple treatment sites within the study. Study designs for SBRT include prospective and retrospective single group studies. Study size varied from 3 (minimum acceptable for inclusion in this review) to 398 patients. None of the published trials were comparative studies. Reported patient inclusion criteria include inoperable tumors, patients refusing surgery, biopsy proven disease, life expectancy, no prior radiation therapy (RT) or prior RT received in a particular time frame prior to SBRT, and required performance levels on the Karnofsky or World Health Organization/Eastern Cooperative Oncology Group scales. Several studies reported the use of modified linacs ($k = 47$), CyberKnife ($k = 39$), Novalis Shaped Beam or Clinac ($k = 16$), Body GammaKnife ($k=1$), Tomotherapy Hi-Art ($k = 2$), FOCAL unit ($k = 1$), and Synergy systems ($k = 6$). Typically, inverse treatment planning algorithms; pencil beam algorithms for dose calculation; and tissue maximum ratio calculation algorithms were reported. Prior treatments reported include surgery, radiation therapy (e.g., intensity-modulated radiation therapy (IMRT), brachytherapy), pharmaceuticals (e.g., tamoxifen), and/or chemotherapy. We calculated an overall mean and median for the length of followup for each cancer type. The shortest mean and median followup was within the multiple site category (12.9 and 8.2 months [1-95 months] respectively). Studies of the tumors involving the pelvis, sacrum, and uterus had the longest mean/median followup (31 and 33 months [range 2-77 months]). The reported outcomes include tumor control/response, toxicity, and overall survival. Most studies used four criteria to measure tumor control/tumor response: complete response, partial response, stable disease, and progression of disease. The most frequently reported adverse events include pain, fatigue, nausea, bleeding, and diarrhea.

Conclusions. In brief, SBRT appears to be widely disseminated for treatment of a variety of cancer types, although a majority of studies have only focused on treatment of thoracic tumors. None of the currently available studies include comparison groups. Comparative studies are needed to provide evidence that the theoretical advantages of SBRT over other radiotherapies actually occur in the clinical setting. Currently, there is only one small ongoing trial doing so. Consequently, a full systematic review of the current literature cannot answer questions on the effectiveness and safety of SBRT compared to other radiotherapy interventions.

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Executive Summary

Background

The development of stereotactic body radiation therapy (SBRT) began in the early 1990s at the Karolinska Institute (Stockholm, Sweden) with researchers Ingmar Lax and Henric Blomgren and was derived from the techniques and procedures of stereotactic radiosurgery (SRS). Researchers in Japan and North America helped develop this treatment during this same time in the 1990s. The American College of Radiology (ACR) and the American Society for Radiation Oncology (ASTRO) define SBRT as “an external beam radiation therapy method used to very precisely deliver a high dose of radiation to an extracranial target within the body, using either a single dose or a small number of fractions.”¹ SBRT combines multiple finely collimated radiation beams and stereotaxy (3D target localization). The multiple radiation beams intersect to deliver an accurate, high dose of radiation to a carefully defined location.

There are several terms that have been used interchangeably for SBRT. These terms include “stereotactic radiotherapy,” “fractionated stereotactic radiosurgery,” “hypofractionated stereotactic radiosurgery,” and “staged radiosurgery.” Consensus does not exist for the definition of SBRT with respect to a maximum number of radiation fractions, the minimum radiation dose per fraction, or the maximum number and diameter of lesions to be treated.²

SBRT is characterized by patient immobilization, limiting normal tissue exposure to high-dose radiation, preventing or accounting for organ motion (e.g., respiratory motion), the use of stereotaxy, and the subcentimeter^{3,4} accuracy of the delivered dose. The key components of a SBRT procedure are target delineation,⁵ treatment planning, and treatment delivery. The treatment team includes a radiation oncologist, medical physicist, radiation therapist, and depending on the body site and indication, a diagnostic radiologist, nurse, anesthetist, and dosimetrist as needed.⁶ Medical professionals, such as surgeons, may also play a role in the treatment team.

Scope

The goal of this Technical Brief is to provide a broad overview of the current state of SBRT for solid malignant tumors. The first draft included a review of SRS and SBRT treatment for all sites within the body (including spine and head) excluding the brain. However, based on the feedback of external reviewers and current working definitions of SRS and SBRT, the scope of this Technical Brief has been adjusted to focus on SBRT.

The definition of SRS developed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the American Society for Radiation Oncology (ASTRO) is as follows:

Stereotactic radiosurgery is a distinct discipline that utilizes externally generated ionizing radiation in certain cases to inactivate or eradicate (a) defined target (s) in the head or spine without the need to make an incision. The target is defined by high-resolution stereotactic imaging. To assure quality of patient care the procedure involves a multidisciplinary team consisting of a neurosurgeon, radiation oncologist, and medical physicist.

Stereotactic radiosurgery (SRS) is typically performed in a single session, using a rigidly attached stereotactic guiding device, other immobilization technology and/or a stereotactic image-guidance system, but can be performed in a limited number of sessions, up to a maximum of five.

Technologies that are used to perform SRS include linear accelerators, particle beam accelerators and multisource Cobalt 60 units. In order to enhance precision, various devices may incorporate robotics and real time imaging.⁷

The American Medical Association (AMA) has common procedural terminology (CPT) codes for SRS and SBRT that are recognized by the Centers for Medicare and Medicaid Services (CMS). According to the CPT codes, SRS treatment is delivered to a cranial lesion or spinal lesion consisting of one session (CPT codes: 77371, 77372, 77432, 63620); while SBRT has two applicable codes (77373 and 77435) with treatment delivery not to exceed five fractions within the body.⁸

This Technical Brief reports on the current technologies available to deliver SBRT; the types and locations of tumors that have been treated with SBRT; the possible advantages and disadvantages of the technology; the extent of diffusion of the technology; and provide information about advances in the technology that are currently in development. This Technical Brief does not assess the quality of the retrieved studies or come to any conclusions about the reported results and adverse events.

Methods

Literature Searches

ECRI Institute's biomedical engineers and medical physicists suggested confining our searches to the past five to eight years given the changes in the technology over time. Consequently, our search strategy for published studies involved Ovid, MEDLINE, EMBASE, the Cochrane Database, and the Health Technology Assessment Database from January 2000 to December 2010. The full search strategy can be found in Appendix A: Literature Search Methods.

We also searched the Internet for gray literature applicable to the Background section, Guiding Question 1 and Guiding Question 2. We performed the Internet searches in the Google search engine, and visited relevant links within the first 10 pages of search results. Gray literature was also searched within *Windhover*, *Current HC News*, *Gray Sheet*, *The Wall Street Journal*, and *Clinica*. We also visited association and organization Web sites (e.g., International RadioSurgery Association), and Web sites posted within each organization's site. Information for instrumentation was captured by a search of the manufacturers' Web sites and a search of the Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) (<http://www.fda.gov/cdrh/>). Instrumentation information can be found in Appendix F: Currently Marketed Devices for SBRT. Additional information on device specifications and compatible accessories was obtained through interviews with manufacturers (Appendix N).

Study Eligibility

Eligible studies were clinical studies of any design, published in English, with patient population of at least 3 patients, the use of SBRT, and with treatments delivered in 10 or fewer fractions. Studies not eligible for data extraction included treatment planning (e.g., dosing),

treatment delivery (e.g., accuracy), nonmalignant tumors, the use of more than 10 treatment fractions, and fewer than 3 patients.

Guiding Questions and Findings of This Technical Brief

Guiding Question 1.

1a. For which cancers has stereotactic body radiation therapy been used?

Based on our literature search, SBRT has been used for tumors located in the lung/ thorax, thyroid, pancreas, liver, colon, uterus, pelvis, sacrum, kidney, prostate, and thyroid. The bulk of the studies identified in our searches were for tumors of the lung/thorax (k = 68).

1b. What are the theoretical advantages and disadvantages of stereotactic body radiation therapy compared to other radiation therapies that are currently used for cancer treatment?

Theoretically, SBRT's most important features and reported advantages compared to other forms of external beam radiation therapy (EBRT) are the use of high-dose radiation, the delivery of one to five fractions within a few days (e.g., 2–3 days), decreasing the overall length of treatment, and an improved treatment response.⁵ Standard fractionated radiotherapy (e.g., 2D-CRT, 3D-CRT, intensity-modulated radiation therapy (IMRT)) are typically delivered in 25–50 fractions, 5 days per week, for approximately 5 to 10 weeks. SBRT can be difficult to administer because of interfraction or intrafraction movements within the body (e.g., respiratory movements) and movements of the body.⁵

1c. What are the potential safety issues and harms of the use of stereotactic body radiation therapy?

As with other radiation treatments, geographic misses of the targeted tumor cause damage to surrounding healthy tissues. However, because each SBRT radiation fraction is a higher dose compared to other forms of EBRT, the potential for radiation injury is also higher.⁹ An essential part of SBRT is maintaining the delivery of the prescribed dose by strict quality control of the tumor images and the regular verification of the image sets.

Guiding Question 2.

2a. What specialized instrumentation is needed for stereotactic body radiation therapy and what is the FDA status of this instrumentation?

SBRT can be delivered by dedicated and nondedicated linear accelerators. Advanced patient positioning, patient immobilization, multi-leaf collimators (MLCs) and micro-MLCs, x-ray tracking (stereotactic), advanced control systems, and treatment planning software are requirements for linear accelerator (linac) modification when performing an SBRT treatment. Nondedicated systems are capable of performing conventional radiation therapy, IMRT, along with SBRT, while dedicated systems are geared for SBRT treatments alone. SBRT can be delivered via a step and shoot method or dynamic delivery.⁵ Step and shoot delivery turns the radiation beam off when the gantry rotates to the next planned delivery angle. The use of dynamic delivery enables continuous delivery of the radiation beam by adjusting the MLC as the gantry rotates. Advantages of dynamic delivery include a decrease in treatment time, less organ

movement during the treatment session, and an increase in patient throughput.^{5,10} SBRT devices are regulated by the FDA under the 510(k) process. To date there are 12 commercially available systems with identifiable features delivering SBRT treatments.

2b. What is an estimate of the number of hospitals that currently have the capability for stereotactic body radiation therapy in the United States?

We identified 384 facilities in the United States capable of performing SBRT in September 2009. An overall listing of these facilities, including specific body sites treated and devices employed can be found in Appendix J: Facilities Performing SBRT for Solid Tumors.

2c. What instrumentation technologies are in development?

The Gyro Knife, manufactured by GammaStar Medical Group Ltd., is commercially available in the European Union having recently received the Conformité Européenne (CE) certification for European Union, medical devices.¹¹ The device, featuring a Cobalt 60 radioactive source and two vertical rotating gyroscopes, currently awaits clearance by the FDA. It appears that this device has two configurations, linac-based x-rays or Cobalt (gamma) and has the potential to treat any organ in the body.

Guiding Question 3.

Conduct a systematic literature scan for studies on the use and safety of SBRT in cancer, with a synthesis of the following variables:

3a. Type of cancer and patient inclusion criteria

The bulk of the studies examined SBRT for tumors of the lung/thorax (k = 68). We found 27 studies of tumors located in the pancreas, liver, colon, and fewer than 10 studies each for sites within uterus, pelvis, sacrum, kidney, prostate, and thyroid. There were 10 studies that included multiple treatment sites within the study. Patient inclusion criteria commonly used in multiple studies across the different cancer types include inoperable tumors or patients refusing surgery; biopsy proven disease; a particular patient's life expectancy; no prior RT or prior RT received in a particular time frame prior to SBRT; and a required level of performance on the Karnofsky or World Health Organization (WHO)/Eastern Cooperative Oncology Group (ECOG) scales.

3b. Type of radiation and instrumentation and algorithms used

Photon radiation was used in all included studies for SBRT treatment. The instrumentation reported in all studies included modified linacs (k = 47), CyberKnife (k = 39), Novalis Shaped Beam or Clinac (k = 16), Body GammaKnife (k = 1), Tomotherapy Hi-Art (k = 2), FOCAL unit (k = 1), and Synergy systems (k = 6). Algorithms are used to plan and deliver treatment. The studies reported inverse treatment planning algorithms; pencil beam algorithms for dose calculation; and tissue maximum ratio calculation algorithms. Most of the studies described the device and photon energy, radiation beam angles, collimation technique, body immobilization technique, treatment planning imaging, treatment planning system/algorithm, tumor tracking, respiratory tracking/control, and image guidance during treatment. For more information, see Appendix M: Literature Results Device Specifications.

3c. Study design and study size

Study designs for SBRT include prospective and retrospective single group studies. Study size varied from 3 (minimum acceptable for inclusion in this review) to 398 patients.

3d. Comparator used in comparative studies

None of the published trials were comparative studies. We identified 50 ongoing SBRT trials (see Appendix K: Ongoing Clinical Trials). Only one of these trials involved a direct comparison of SBRT to a different form of radiation therapy. This trial commenced in April 2009 in France (NCT00870116), and is a nonrandomized comparison of SBRT delivered by CyberKnife versus SBRT delivered by linac versus conformational RT for treatment of non-small cell lung cancer (NSCLC). There are three other comparative trials which plan to use historical controls, one for metastatic breast cancer (NCT00167414), one in NSCLC (NCT00727350) and one in pancreatic cancer (NCT00350142). A lung cancer trial, based in the Netherlands (ClinicalTrials.gov identifier: NCT00687986), is a randomized trial comparing SBRT with primary resection of the tumor. The primary outcomes are local control, regional control, quality of life, and treatment costs. The enrollment target was 960 patients, and completion was expected in December 2013; however, the trial was terminated in April 2011 because of poor recruitment. Another trial being conducted in China (NCT00840749) will compare SBRT to surgical resection in NSCLC. The enrollment target is 1030 patients, with planned completion in 2013. Another trial (NCT00843726) being conducted in Roswell, NY, will randomize 98 patients to either one or three fractions of SBRT for treatment of NSCLC.

3e. Concurrent and/or prior treatments used

Prior treatments reported include surgery, radiation therapy (e.g., IMRT, brachytherapy), pharmaceuticals (e.g., tamoxifen), and/or chemotherapy. Some studies specified that prior radiation therapy or chemotherapy had to be completed within a certain timeframe before SBRT (e.g., 12 weeks). Chemotherapy was the concurrent treatment most often reported within the studies.

3f. Length of followup

We have calculated an overall mean and median for the length of followup for each cancer type. The shortest mean and median followup was within the multiple site category (12.9 and 8.2 months [1-95 months] respectively). Studies of the tumors involving the pelvis, sacrum, and uterus had the longest mean/median followup (31 and 33 months [range 2-77 months]).

3g. Outcomes measured

The outcomes measured typically included tumor control or tumor response, toxicity, and overall survival. Overall cause-specific survival rates, overall survival, and disease-free survival rates were typically calculated using the Kaplan-Meier method. Most studies used the following four criteria to measure tumor control or tumor response: complete response, partial response, stable disease, and progression of disease.

3h. Adverse events, harms, and safety issues reported

Some of the most frequently reported adverse events include pain, fatigue, nausea, bleeding, and diarrhea. Some of the patients in these studies had prior cancer treatment and received SBRT for recurring cancers, and some patients had comorbidities.

Remaining Issues and Future Research Needs

Based on our literature searches, the studies published after 2000 were single-group prospective or single-group retrospective studies. We found 27 studies for tumors located in the pancreas, liver, colon, and fewer than 10 studies each for sites within the uterus, pelvis, kidney, prostate, and thyroid. These sites of treatment can be difficult to target, as there may be periodic (e.g., respiratory movement) or irregular (e.g., peristalsis) movement, or shrinkage of the tumor between fractionated treatments.

We did not identify any published randomized controlled trials (RCTs). Prospective controlled/comparative trials, preferably RCTs, are essential for establishing the relative safety and efficacy of SBRT in comparison to other methods of treatment. Considerations for selection of appropriate treatment candidates include prior radiation history of the treatment tissues, treatment volume, organ function, capacity for recovery, number of sites of disease, and many other individual cancer-related factors.⁹ Future studies may help to determine the optimal number of radiation fractions, the minimum and maximum dose per fraction, the maximum number and diameter of lesions for various locations, and efficacy of SBRT treatment.

References

1. American College of Radiology (ACR). Practice guideline for the performance of stereotactic body radiation therapy. Reston VA: American College of Radiology (ACR);2009:8.
2. Fuss M, Thomas Jr. CR. Stereotactic body radiation therapy: an ablative treatment option for primary and secondary liver tumors. *Ann Surg Oncol* 2004 Feb;11(2):130-138. PMID: 14761915.
3. Smink KA, Schneider SM. Overview of stereotactic body radiotherapy and the nursing role. *Clin J Oncol Nurs* 2008 Dec;12(6):889-893. PMID: 19064382.
4. Read PW. Stereotactic body radiation therapy: 2007 Update. *Community Oncol* 2007 Oct;4(10):616-620.
5. Miyamoto C. (Chairperson & Professor, Department of Radiation Oncology, Temple University School of Medicine). Personal Communication; 2010 Feb 23:51.
6. American College of Radiology (ACR). Practice guideline for the performance of stereotactic body radiation therapy. Reston VA: American College of Radiology (ACR);2004:8.
7. Barnett GH, Linskey ME, Adler JR, et al. Stereotactic radiosurgery—an organized neurosurgery-sanctioned definition. *J Neurosurg* 2007 Jan;106(1):1-5. PMID: 17240553.
8. Stereotactic radiotherapy (SRS)/stereotactic radiation therapy (SBRT) for Medicare plans. Policy # SURGERY 058.1 T3. Trumbull CT: Oxford Health Plans, LLC; January 2009. Available at: <https://www.oxhp.com>. Accessed September 3, 2009.
9. Meyer JL, Verhey L, Xia P, et al. New technologies in the radiotherapy clinic. *Front Radiat Ther Oncol* 2007;40:1-17. PMID: 17641499.
10. Chen JC, Rahimian J, Girvigian MR, et al. Contemporary methods of radiosurgery treatment with the Novalis linear accelerator system. *Neurosurg Focus* 2007;23(6):E4. PMID: 18081481.
11. GammaStar's Gyro Knife awarded EU certification. New York NY: Thomson Reuters; April 15, 2008. Available at <http://www.reuters.com/article/pressRelease/idUS130278+15-Apr-2008+PRN20080415>. Accessed November 25, 2008.

Introduction

According to the American Cancer Society, 1,383,490 new body cancer cases are expected to be diagnosed in the United States in 2009 (This estimate does not include carcinoma in situ of any site except urinary bladder and basal and squamous cell cancers).¹² Approximately 533,990 of these newly diagnosed patients are expected to die from their cancer.¹² Treatments available for cancer include surgery, various forms of radiation therapy, and chemotherapy.

Stereotactic Body Radiation Therapy

In 1951, Dr. Lars Leskell and Borje Larsson introduced the concept of radiosurgery for use in intracranial conditions considered inoperable. Stereotactic radiosurgery (SRS) has been used to treat functional disorders of the brain such as trigeminal neuralgia or arteriovenous malformations, vascular malformations, and intracranial and spinal benign and malignant tumors. The development of stereotactic body radiation therapy (SBRT) began in the early 1990s at the Karolinska Institute (Stockholm, Sweden) and was derived from the techniques and procedures of SRS. Researchers Ingmar Lax and Henric Blomgren at the Karolinska Institute created a body frame to aide in targeting extracranial treatment sites. During this time in Japan, Minoru Uematsu began work on juxtaposing closely a computed tomography (CT) scanner and linear accelerator (linac) into a synthesized “FOCAL” (Fusion Of CT And Linac) unit in lung applications,¹³ leading to the development of performing SBRT without a body frame. By the late 1990s, researchers Robert Timmerman, Lech Papiez, and colleagues initiated a phase I trial of SBRT for medically inoperable lung cancer at Indiana University in North America.¹³

The American College of Radiology (ACR) and American Society for Radiation Oncology (ASTRO) define SBRT as “an external beam radiation therapy method used to very precisely deliver a high dose of radiation to an extracranial target within the body, using either a single dose or a small number of fractions.”¹ The similarity between SBRT and SRS is the combining of multiple finely collimated radiation beams and stereotaxy (3D target localization). The multiple radiation beams intersect to deliver an accurate, high dose of radiation to a carefully defined location. The differences between the two radiation treatments include the treatment sites (e.g., SRS involves the head and spine) and the number of fractions utilized (i.e., SBRT one or a small number of fractions, SRS is typically one fraction). SBRT has been used as a treatment for tumors of the abdomen, liver, lung, neck, pancreas, kidney, and prostate. This Technical Brief will focus on SBRT.

Stereotactic Body Radiation Therapy Terms

There are several terms that have been used to describe SBRT. These terms include “stereotactic radiotherapy,” “fractionated stereotactic radiosurgery,” “hypofractionated stereotactic radiosurgery,” and “staged radiosurgery.” Within actual practice the differentiation between these various terms is blurred, with terms commonly used interchangeably. Consensus does not exist for the definition of SBRT with respect to the minimum radiation dose per fraction, or the maximum number and diameter of lesions to be treated.² However, most define SBRT as the treatment of an extracranial lesion with a single or very few (≤ 5) high-dose fractions.¹⁴ Based on the current working definitions of ACR, the American Society for Radiation Oncology (ASTRO), and American Medical Association (AMA) common procedural

terminology (CPT) codes, this Technical Brief will use the term stereotactic body radiation therapy (SBRT).

SBRT Treatment Delivery and Treatment Planning

SBRT is characterized by patient immobilization, target localization and tracking software, limiting normal tissue exposure to high-dose radiation, preventing or accounting for organ motion (e.g., respiratory motion), the use of stereotaxy, and the subcentimeter accuracy of the delivered dose.^{3,4} Factors used to determine if SBRT is an appropriate procedure include tumor shape and stage, volume (1–35 cm³),¹⁵ location, histology, invasiveness, and the performance status of the patient. The key components of a SBRT procedure are target delineation,⁵ a simulation study, treatment planning, and treatment delivery. The treatment team includes a radiation oncologist, medical physicist, radiation therapist, and, depending on the body site and indication, a diagnostic radiologist, nurse, anesthetist, and dosimetrist as needed.⁶ The treatment team may also include specialists such as surgeons.

A simulation study is performed with computed tomography (CT) prior to the treatment planning. The CT table matches the treatment table and the dataset is then imported into the treatment-planning system. Treatment planning includes patient marking (e.g., tattoos, fiducials), preplanning imaging, plan development, and patient positioning. Along with CT simulation images, the treatment-planning system may also import and fuse diagnostic magnetic resonance imaging (MRI), positron emission tomography (PET), combined PET/CT, and/or angiography images with the CT simulation images to add functional data to optimize the treatment plan. The treatment team develops a plan for the procedure using software to select the shape, size, intensity, and entry point of the radiation beam to treat the targeted tumor.

SBRT is particularly challenging because of the added complexities introduced by target motion with natural physiologic processes (e.g., respiration).¹⁶ Techniques used to assist in decreasing organ or body motion include full body immobilization (e.g., vacuum pillows),⁵ abdominal compression devices, breath-hold techniques, gating, and tracking methods. The desire to treat lesions outside of the head using the highest precision dose delivery in the setting of fractionated stereotactic radiotherapy has led to the development of image-guided radiotherapy.¹⁰ SBRT devices can use image guidance (kV or MV⁵ x-ray imaging, CT, ultrasound) to intermittently monitor the position of the targeted tumor by tracking bony structures or implanted fiducials. Imaging can also visualize soft tissues (e.g., lung, prostate) without referencing bony structures or fiducials.⁵ Before treatment begins the patient is positioned on the treatment couch with or without an immobilization device and reoriented to the SBRT system.

In order to deliver treatment accurately in accordance with the treatment plan, it is imperative to accurately position the patient on the treatment system. On-board CT images or x-ray images are acquired with the patient positioned on the treatment couch and these images are compared with the treatment plan images to ensure a match between the planning geometry and the treatment geometry. If the geometries do not match, the treatment table is adjusted so that the treatment geometry then accurately aligns with the planned geometry. If the treatment team determines a change in the tumor morphology from imaging results (e.g., CT), the treatment plan needs the capability to be modified for the new tumor morphology.⁵ However, most tumors are not going to change that much between the treatment doses of a SBRT treatment course.⁵ The treatment can then begin.

At present, a medical linear accelerator (linac) is used for the delivery of SBRT. A linac emits x-ray photon radiation with typical energies ranging from 6 to 10 MV for SBRT. The angle of the radiation beam can be changed by either the rotation of the linac gantry or by the movement of a linac mounted to a robotic arm. The treatment table can also be adjusted to allow changes in the angle of the delivery beams.⁵

Statement of Work

The Agency for Healthcare Research and Quality requested a Technical Brief on Stereotactic Radiosurgery for Nonbrain Cancer. The following Guiding Questions were provided to the ECRI Institute Evidence-based Practice Center (EPC):

Guiding Question 1

1a. For which cancers (other than brain) has stereotactic radiosurgery been used?

1b. What are the theoretical advantages and disadvantages of stereotactic radiosurgery compared to other radiation and surgical therapies that are currently used for cancer treatment?

1c. What are the potential safety issues and harms of the use of stereotactic radiosurgery?

Guiding Question 2

2a. What specialized instrumentation is needed for stereotactic radiosurgery at sites other than in the brain and what is the FDA status of this instrumentation?

2b. What is an estimate of the number of hospitals that currently have the capability for stereotactic radiosurgery at sites other than the brain in the United States?

2c. What instrumentation technologies are in development?

Guiding Question 3. Systematic literature scans on studies on the use and safety of these therapies in cancers other than in the brain, with a synthesis of the following variables:

3a. Type of cancer/patient inclusion criteria

3b. Type of radiation/instrumentation and algorithms used

3c. Study design/size

3d. Comparator used in comparative studies

3e. Concurrent/prior treatments

3f. Length of followup

3g. Outcomes measured

3h. Adverse events/harms/safety issues reported

The first draft of this Technical Brief included a review of stereotactic radiosurgery (SRS) and SBRT treatment for all sites within the body (including spine and head) excluding the brain. However, based on the feedback of external reviewers and more recent working definitions of SRS and SBRT, the scope of this Technical Brief has been adjusted to focus on SBRT. The definition of SRS developed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the American Society for Radiation Oncology is as follows:⁷

Stereotactic radiosurgery is a distinct discipline that utilizes externally generated ionizing radiation in certain cases to inactivate or eradicate (a) defined target (s) in the head or spine without the need to make an incision. The target is defined by high-resolution stereotactic imaging. To assure quality of patient care the procedure involves a multidisciplinary team consisting of a neurosurgeon, radiation oncologist, and medical physicist.

Stereotactic radiosurgery is typically performed in a single session, using a rigidly attached stereotactic guiding device, other immobilization technology and/or a stereotactic image-guidance system, but can be performed in a limited number of sessions, up to a maximum of five.

Technologies that are used to perform SRS include linear accelerators, particle beam accelerators and multisource Cobalt 60 units. In order to enhance precision, various devices may incorporate robotics and real time imaging.

The American Medical Association (AMA) has common procedural terminology (CPT) codes for SRS and SBRT that are recognized by the Centers for Medicare and Medicaid Services (CMS). According to the CPT codes, SRS treatment is delivered to a cranial lesion or spinal lesion consisting of one session (CPT codes: 77371, 77372, 77432, 63620); while SBRT has two applicable codes (77373 and 77435) with treatment delivery not to exceed five fractions within the body.⁸

This Brief describes the current technologies available to deliver SBRT; the types and locations of tumors that have been treated with SBRT; the possible advantages and disadvantages of the technology; the extent of diffusion of the technology; and provides information about advances in the technology that are currently in development. This Technical Brief does not assess the quality of the retrieved studies, provide analysis of study outcomes, or come to any conclusions about the reported results and adverse events.

Methods

Literature Searches

Narrative review articles and gray literature searches were used to address Guiding Questions 1 and 2. We searched the Internet for gray literature applicable to the Background section, Guiding Question 1 and Guiding Question 2. We performed the Internet searches in the Google search engine, and visited relevant links within the first 10 pages of search results. Gray literature was also searched within *Windhover*, *Current HC News*, *Gray Sheet*, *The Wall Street Journal*, and *Clinica*. We also visited association and organization Web sites (e.g., International RadioSurgery Association), and Web sites posted within the organization's site. Information regarding instrumentation was captured by a search of the manufacturers' Web sites and a search of the Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) (<http://www.fda.gov/cdrh/>). Instrumentation information can be found in Appendix F, Currently Marketed Devices for SBRT. Additional information on device specifications and compatible accessories was obtained through interviews with manufacturers (Appendix N).

A systematic scan of the published medical literature was performed to address Guiding Question 3. Our search strategy involved Ovid, MEDLINE, EMBASE, the Cochrane Database, and the Health Technology Assessment Database. ECRI Institute's biomedical engineers and medical physicists suggested confining our searches to the past five to eight years given the technology changes. (There are reports in the literature as far back as 1993 for the use of SRS for ocular melanoma.) Given that this is a Technical Brief, our search range was limited to January 2000 through December 2010. The full search strategy can be found in Appendix A, Literature Search Methods.

Study Eligibility

The titles of the citations identified through the literature searches were screened for relevance to the topic. Articles with titles that seemed potentially relevant were then passed to the abstract- screening level. Abstracts were initially screened in duplicate (first 50 abstracts) by two reviewers to determine relevance for SBRT. Duplicate review was used as a quality control measure to determine inter-rater agreement in regard to the questions asked about the retrieved abstracts. After screening the first 50 abstracts in duplicate, both reviewers understood the questions and proceeded to screen subsequent abstracts individually. All relevant abstracts were ordered as full-text articles for further review. Again, the first 50 full-text articles were screened in duplicate to determine eligibility for data extraction, and subsequent articles were screened individually. Eligible studies were clinical studies of any design, studies in English, patient population of at least three patients, the use of SBRT, and with treatments delivered in 10 or fewer fractions. Studies not eligible for data extraction included treatment planning (e.g., dosing), treatment delivery (e.g., accuracy), nonmalignant tumors, the use of more than 10 treatment fractions, and fewer than three patients.

Data Extraction

SRS 4.0 (Mobius Analytics, Ottawa, Canada) was used for the data extraction process. If reported, the information extracted included: country of study, year of study, authors, study design, type of cancer, patient inclusion/exclusion criteria, comparators, size of patient

population, sex and age of patients, prior or concurrent treatment, instrumentation and type of radiation used (x-ray photons), algorithms, quality assurance and/or training procedures, tumor quantity and tumor size, total radiation dosage, number of fractions and dose of each fraction, length of followup, outcomes measured and how they were measured, and adverse events/harms.

Summary of Items of Interest

For Guiding Question 3, we organized the relevant literature by study design into two tables. Each table is arranged by year of publication (most recent year first) and then alphabetically by author. These tables include the following information: author, year, cancer type, instrumentation/algorithms, study design/study size, prior/concurrent treatment, length of followup, outcomes measured, and adverse events. The tables can be found in Appendix L, Results for Guiding Question 3. The cancer types found within the literature include lung/thorax, colon, liver, pancreas, kidney, pelvic, sacrum, uterus, thyroid, and prostate.

Software

To calculate overall means and medians for patient ages and lengths of followup, we used Microsoft Office Excel 2007 (Microsoft Corporation, Redmond, WA).¹⁷

Results

Guiding Question 1

1a. For which cancers has stereotactic body radiation therapy been used?

SBRT can be used as a primary therapy for early stage cancer or as a targeted treatment for metastatic disease. In the latter setting, SBRT is intended to be an adjuvant cytoreductive treatment in concert with ongoing systemic therapy.¹⁸ Based on our literature search, SBRT has been used for tumors located in the lung/ thorax, pancreas, liver, colon, uterus, pelvis, sacrum, kidney, prostate, and thyroid. The bulk of the studies identified in our searches were for tumors of the lung/thorax (k = 68).¹⁹⁻⁸⁶ Details for these studies can be found in Appendix L, Results for Guiding Question 3.

1b. What are the theoretical advantages and disadvantages of stereotactic body radiation therapy compared to other radiation therapies that are currently used for cancer treatment?

Standard Fractionated Radiotherapy

The goal of external beam radiation therapy (EBRT) is to deliver the prescribed amount of radiation to the targeted tumor and minimize the amount of radiation received by surrounding normal tissues. EBRT can be used as a therapeutic or palliative treatment and is delivered using linacs and various conformal techniques. Technology for the delivery of external radiation therapy includes two-dimensional (2D) conformal radiation therapy (RT), three-dimensional (3D) conformal RT, intensity modulated RT (IMRT), SBRT, proton therapy, carbon ion therapy, and electron therapy⁸⁷ (proton, electron, and carbon ion therapy are outside the scope of this Technical Brief.) AHRQ has recently commissioned a Technical Brief on proton therapy.⁸⁸

Two-dimensional radiation therapy (2D-CRT), which uses images from plain x-rays and fluoroscopy for planning purposes, delivers radiation beams of uniform intensity from one to six directions or arcs to the tumor.⁸⁹ Anatomical landmarks or fiducials help determine the location of the tumor. Three-dimensional conformal radiation therapy (3D-CRT), on the other hand uses three dimensional images from computed tomography, positron emission tomography or magnetic resonance imaging for treatment planning. 3D-CRT uses computer software and 3D imaging techniques (from a CT simulator) to display the size, shape, and location of the tumor.⁹⁰ The treatment planning team can determine the size and shape of the radiation beam to fit the targeted tumor by using a multi-leaf collimator (MLC) or custom fabricated field-shaping blocks.⁹⁰ IMRT is a type of therapy in which the leaves of the MLC can be moved while the radiation beam is “on” variably blocking parts of the field to increase the intensity of some of the beamlets and decrease the intensity of others.⁹¹ IMRT involves advanced treatment planning algorithms which allow the physician to input the desired radiation treatment dose constraints for the targeted tumor and the surrounding normal tissue into a computer. The computer software is used to develop a detailed treatment plan of the radiation beams required to deliver the prescribed radiation dose. Multiple iterations may be necessary to optimize the treatment plan. IMRT systems can shape the photon (x-ray) beam through step and shoot and/or dynamic MLCs (computer controlled). As a result, the beam intensity more closely matches the thickness of the

tumor. The EBRT treatment plan is reviewed and agreed upon by members of the treatment team (radiation oncologist, medical physicist, etc.) before the procedure can begin.

Differences Between Standard Fractionated Radiotherapy and SBRT

EBRT is a noninvasive procedure for patients undergoing cancer treatment. Patients are allowed to return to daily activities after the completion of the procedure, and most patients do not require any type of sedation to aid in immobilization during treatment. Patients are advised to complete scheduled follow-up procedures, as results of the treatment may not be visible during first follow-up visits. The importance of imaging techniques, accurate planning techniques, and accurate dose distribution are relevant for all forms of EBRT delivery. Minimizing the exposure of surrounding normal tissues from the radiation dose is also important for all forms of EBRT delivery. However, the ability to shape the radiation beam to the targeted tumor varies among EBRT delivery technologies.

With advances in technology and dose planning, the prescribed dose can be more closely tailored to the tumor volume with greater sparing of surrounding anatomy. The complexity of the treatment plan will depend on the tumor characteristics, surrounding tissue and goal of the treatment (palliative or therapeutic). 2D-CRT and 3D-CRT tend to include larger margins of surrounding normal tissue because of treatment- planning limitations. This may limit the total radiation dose that can be delivered to the target and may decrease the ability to treat the targeted tumor. Treatment planning for IMRT takes into account the dose constraints of the targeted tumor and the surrounding normal tissues with the goal of varying intensities across the treatment field. SBRT uses orthogonal x-ray beams to locate the targeted tumor, and several radiation beams that are finely collimated and that intersect to deliver a conformal, single, high dose of radiation.

When the treatment team determines that a patient is not a candidate for a single high dose treatment based on tumor location and size, tumor motion, and radiosensitivity, fractionated treatment is an option. The number of treatment fractions and overall length of treatment depends on the ability to conform the radiation beam to the shape of the tumor and to protect surrounding normal tissue and organs at risk from the radiation dose. As the number of fractions increase, the dose per fraction decreases. 2D-CRT, 3D-CRT, and IMRT are typically delivered in many more fractions than SBRT. Typical treatment fractions for 2D-CRT, 3D-CRT, and IMRT are 25–50 fractions delivered five days per week for approximately 5–10 weeks. A typical daily dose is approximately 2Gy per fraction. When these small doses are given repeatedly, the cumulative dose may not be as potent as an equivalent single fraction dose, so a higher overall dose is delivered. IMRT can also be used to deliver SBRT (1–5 fractions of a high dose). The two IMRT delivery methods are differentiated by the terms “conventional fraction IMRT” versus “SBRT-based IMRT.” Because SBRT delivers a high dose of radiation (20–60Gy), treatment can be completed in 1–5 fractions delivered in a few days (e.g., 1–5 days).

SBRT’s most important features and theoretical advantages compared to other forms of EBRT are the high degree of dose conformality, the use of high-dose radiation, the delivery of a single or very few fractions (thus decreasing the overall length of treatment), and an improved treatment response.⁵ However, SBRT can also be difficult to administer because of the high level of accuracy required, interfraction or intrafraction movements within the body (e.g., respiratory movements) and movements of the body.⁵ Similar to other forms of EBRT, SBRT can be used in combination with chemotherapy, and sometimes after other radiation therapy (RT)

interventions.⁹² As with other radiation treatments, geographic misses of the targeted tumor causes damage to surrounding healthy tissues. However, because each SBRT radiation fraction is a higher dose compared to other forms of EBRT, there is greater potential for radiation injury.⁹

Table 1. Radiation delivery techniques

	Description
2D-CRT	<ul style="list-style-type: none"> • Has a routine planning and treatment process • Useful in palliative treatment of metastatic tumors • Treatment can be initiated rapidly⁵ • Does not require multi-leaf collimator (MLC)⁵ • Typically only 2–4 delivery angles • Treatment is delivered in approximately 25–40 fractions over 5–10 weeks • Tumor is defined in only 2 dimensions • Higher radiation doses delivered to surrounding normal tissue⁵ • Does not have the capability to modify treatment if changes in tumor morphology⁵
3D-CRT	<ul style="list-style-type: none"> • Uses MLCs • Less radiation delivered to adjacent normal tissues than 2D-CRT • Improved target delineation than 2D-CRT⁵ • Uses CT planning⁵ • Better blocking than 2D-CRT⁵ • Typically five to seven treatment angles. As delivery angles increase, treatment times increase.⁵ • Treatment delivered in approximately 25–40 fractions over 5–10 weeks • Non-optimal dose distribution in complex cases
IMRT	<ul style="list-style-type: none"> • Minimum of 5 delivery angles. As delivery angles increase, treatment time increases.⁵ • Treatment delivered in approximately 25–40 fractions over 5–10 weeks
SBRT	<ul style="list-style-type: none"> • High dose delivered in a few fractions (typically 1–5) • Shorter overall treatment time as a result of fewer treatment fractions • Can treat tumors considered inoperable • Tumor size range approx. 1–35 cm³¹⁵ • Multiple delivery angles • Improved beam shaping • Some systems require stereotactic frames for immobilization • Near or real-time image guidance is necessary to maintain geographic accuracy of treatment

2D-CRT: Conventional radiation therapy

3D-CRT: Three-dimensional conformal radiation therapy

IMRT: Intensity modulated radiation therapy

MLC: Multi-leaf collimator

SBRT: Stereotactic body radiation therapy

1c. What are the potential safety issues and harms of the use of stereotactic body radiation therapy?

Quality Assurance and Quality Control of SBRT Treatment

SBRT is a high-dose radiation treatment. For high-dose radiation treatments, errors in radiation dose and spatial positioning must be minimized.¹⁰ SBRT treatments can be difficult to plan because tumors located within the body may move periodically (e.g., respiratory movement), irregularly (e.g., peristalsis), or with shrinkage of the tumor between fractionated treatments.

The quality assurance (QA) for SBRT must go beyond physical measurements and include a proper review of individual patient data (e.g., results of treatment).⁹³ An essential part of SBRT is the strict quality control of the tumor images and the regular verification of the image sets to maintain the accurate delivery of the prescribed dose. SBRT requires tight conformity of the prescription dose to the tumor volume, with rapid dose fall off.¹⁶ During treatment the targeted

tumor can be tracked by methods such as respiratory gating or target tracking (monitoring the motion of the tumor). Before a patient is treated, phantoms can be used as part of the QA process to make sure these tracking techniques are measuring the tumor location and movement correctly.⁹³

ACR/American Society for Radiation Oncology SBRT Guideline

In 2004, the American College of Radiology (ACR) and the American Society for Radiation Oncology (ASTRO) developed a practice guideline for the performance of SBRT. This guideline was revised in 2009. The purpose of the guideline is to provide guidance to practitioners considering using SBRT and to define quality criteria for the delivery of SBRT.¹ The advanced training of personnel and the careful management of patients are the key aspects for performing SBRT safely. Appendix D lists the qualifications and responsibilities of the personnel, and Appendix E provides a snapshot of the suggestions within the guideline for procedure specifications, quality control of accessories, quality control of images, quality control for the treatment-planning system, simulation and treatment, and followup. This guideline does not specify physician specialties (e.g., surgeons) for SBRT applications. However, specialists (e.g., surgeons) may play an integral role in the treatment process.

Guiding Question 2

2a. What specialized instrumentation is needed for stereotactic body radiation therapy and what is the FDA status of this instrumentation?

Linacs

SBRT can be delivered by dedicated and nondedicated linacs. These systems may require patient immobilization and/or a method to account for any organ motion during treatment. Nondedicated systems are capable of performing conventional radiation therapy, IMRT, along with SBRT, while dedicated systems are for SBRT treatments alone. Advanced patient positioning, patient immobilization, x-ray tracking (stereotactic), advanced control systems, and treatment-planning software are other requirements for linac modification when performing an SBRT treatment. SBRT can be delivered via a step and shoot method or by dynamic delivery.⁵ Step and shoot delivery turns the radiation beam off when the gantry rotates to the next planned delivery angle. The use of dynamic delivery enables continuous delivery of the radiation beam by adjusting the MLC as the gantry rotates. Advantages of dynamic delivery include a decrease in treatment time, less organ movement during the treatment session, and an increase in patient throughput.^{5,10}

A listing of 12 commercially available systems with identifiable features can be found in Appendix F, Currently Marketed Devices for SBRT. Accessories sold with or incorporated into linacs (nondedicated) include multi-leaf collimators (MLC) and micro-MLCs. MLCs consist of individual leaves usually made of tungsten alloy, which may be mounted to or integrated into the linac. MLC leaf widths typically range from 5 mm to 10 mm. Micro-MLCs have leaf widths ranging in size from 1 mm to 4 mm⁹⁴ and generally use smaller treatment fields than MLCs (see listing of available linac-based SBRT accessories including MLC sizes in Appendix G, Linac-based SBRT Accessories. In Appendix M, we provide the details on the energy source, beam angles, collimation techniques, body immobilization systems, imaging used for treatment

planning, treatment planning systems, tumor tracking, respiratory tracking and image guidance during treatment as reported in the studies included for Guiding Question 3. Various manufacturers were contacted to provide further detail on the devices that are capable of performing an SBRT treatment and accessories used with those devices. The information provided included treatment-planning and treatment-delivery techniques and necessary equipment and software. For more information, see Appendix N, Responses from Device Manufacturers on Device Specifications and Compatible Accessories (January 2010).

FDA Status of SBRT Equipment

SBRT devices are regulated by the FDA under the 510(k) process. Most of these devices are generally cleared for marketing for treatment of lesions, tumors, and conditions anywhere in the body. Indications currently approved by the FDA's Center for Devices and Radiological Health (CDRH) as well as marketing clearance information including 510(k) applicant/number, product code, and approval dates are provided in Appendix H, Applicant's FDA 510(k) Information. Devices and accessories used for the administration of SBRT can be accessed by searching the following CDRH codes: IXI, IYE, and MUJ. Information was captured by a search of the manufacturers Web sites (Appendix I, Manufacturer Web sites) and a search of the FDA's CDRH (<http://www.fda.gov/cdrh/>).

2b. What is an estimate of the number of hospitals that currently have the capability for stereotactic body radiation therapy in the United States?

According to the 2009 Edition of the American Hospital Association (AHA) Guide,⁹⁵ approximately 700 facilities claim to administer SRS in the United States. Of these 700, we identified 384 facilities describing capability to perform SBRT. This information was accessed by visiting the Web sites provided in the AHA guide and through manufacturer Web sites (see Appendix I, Manufacturer Web sites). An overall listing of these 384 facilities, including specific body sites treated and devices employed can be found in Appendix J, Facilities Performing SBRT for Solid Tumors. Information from Web sites was updated in September 2009.

2c. What instrumentation technologies are in development?

The Gyro Knife, manufactured by GammaStar Medical Group Ltd., is commercially available in the European Union having recently received the CE certification for European Union, medical devices.¹¹ The device, featuring a Cobalt 60 radioactive source and two vertical rotating gyros, currently awaits clearance by FDA.

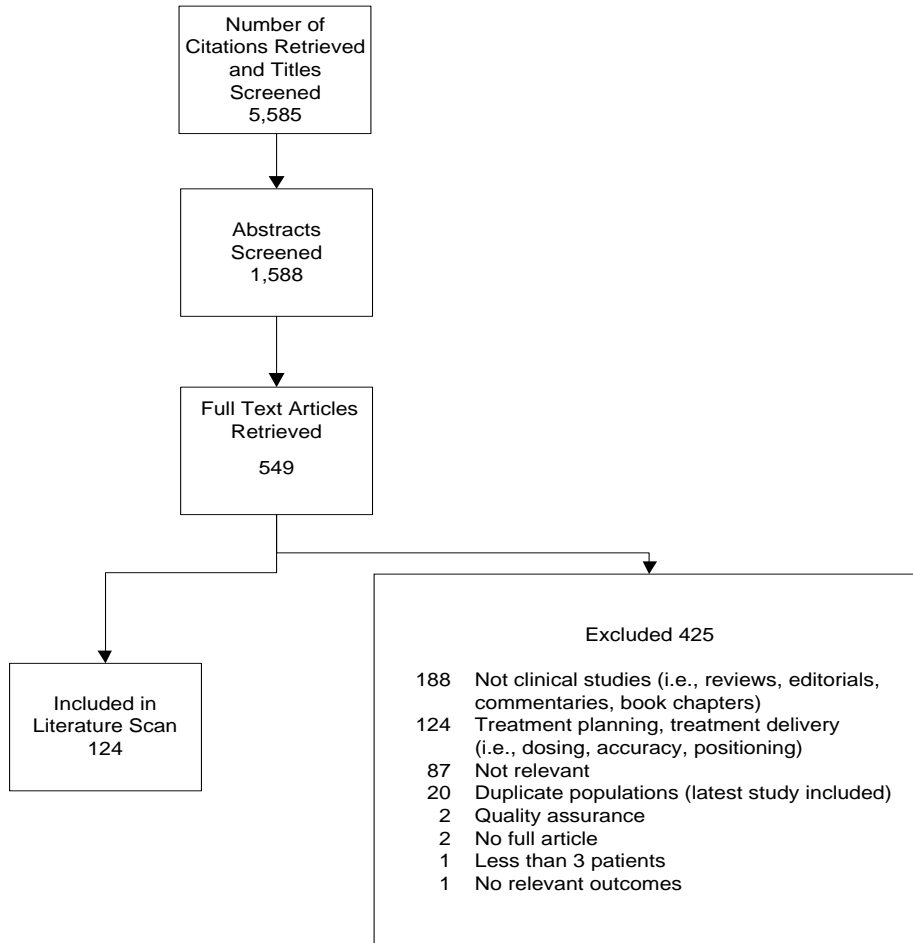
Guiding Question 3

Evidence Base

The goal of this systematic literature scan was to provide an overview of the studies of SBRT, not to evaluate the quality of the studies or to perform analysis of the data reported by the studies. We have screened the titles of 5,585 citations to determine if the abstract should be reviewed. A total of 1,588 abstracts were screened, and 550 full-text articles were ordered for further review. In total, 124 studies were relevant to the topic and data extraction was performed (see Figure 1). The included studies can be found in Appendix B. The excluded studies, along with reason for exclusion, can be found in Appendix C.

The included studies have been organized into two tables by whether they were prospective or retrospective (see Appendix L, Results for Guiding Question 3). These tables are organized by year of publication (most recent year first), and then alphabetically by author. The study details covered within the tables include author; year; cancer type; instrumentation; algorithms; study design; study size; prior and/or concurrent treatment; length of followup in months; outcomes measured; and adverse events. Patient inclusion criteria have not been included in these tables, but are presented in Table 2 in section 3.a.

Figure 1. Study selection process



3a. Type of cancer and patient inclusion criteria

Our search results identified studies of the use of SBRT for tumors located in the lung/thorax, pancreas, liver, colon, uterus, pelvis, sacrum, kidney, prostate, and thyroid. The bulk of the studies were for tumors of the lung/thorax ($k = 68$).¹⁹⁻⁸⁶ We found 27 studies for tumors located in the pancreas, liver, colon,⁹⁶⁻¹²² and fewer than 10 studies each for sites within uterus, pelvis, sacrum,¹²³⁻¹²⁷ kidney,¹²⁸⁻¹³³ prostate,¹³⁴⁻¹⁴⁰ and thyroid.¹⁴¹ There were 10 studies that included multiple treatment sites within the study.¹⁴²⁻¹⁵¹

Patient inclusion criteria for SBRT treatment varied based on cancer types and individual studies. Criteria commonly used regardless of cancer type include inoperable tumors or patients refusing surgery; biopsy-proven disease; minimum life expectancy; no prior RT or prior RT received at a minimum length of time before SBRT; and a minimum level of performance on the Karnofsky or World Health Organization (WHO)/Eastern Cooperative Oncology Group (ECOG) scales. The Karnofsky Performance Status (KPS) scoring system measures the cancer patient's abilities to perform ordinary tasks. The scoring system ranges from 0 to 100, with a higher score indicating a better ability to perform tasks.¹⁵² The retrieved studies often reported KPS scores of at least 40. The WHO/ECOG performance status assesses a patient's functional and/or physical performance. There are six codes used to evaluate a patient, and the codes seen within the retrieved studies were between 0 (fully active) and 2 (ambulatory, capable of self-care but unable to carry out work activities).¹⁵³ Since the level of detail of patient inclusion criteria varied with each study, we have provided an overview of the criteria frequently reported within the studies for each cancer type. Table 2 below also lists the number of studies retrieved and total number of patients.

Table 2. Patient inclusion criteria summary

Cancer Type	Number of Studies	Total Number of Patients (n)	Summary of Patient Inclusion Criteria
Gastrointestinal (Colon, Liver, and Pancreas)	27	1,281	Histologically proven disease, inoperable, unsuitable for resection, tumor size, no prior radiation therapy, minimum life expectancy, WHO/ECOG performance <2, Karnofsky performance >60
Kidney	6	88	Recurrent disease, inoperable, tumor size, minimum life expectancy, Karnofsky performance >60
Lung/Thorax	68	4,418	Histologically proven disease, inoperable, surgery refusal, tumor size (3–7 cm), lung function, no prior RT or RT received in an adequate time before SBRT, minimum life expectancy, involvement of surrounding tissue or structures, WHO/ECOG performance 0–2, Karnofsky performance <60
Multiple sites (e.g., lung, thyroid, renal, colon, etc. all in one study)	10	610	Inoperable, ≤5 metastases confined to one organ, WHO/ECOG performance <2, Karnofsky ≥70
Pelvis, Sacrum, and Uterus	5	89	Inoperable, tumor size, WHO/ECOG performance 1 or 2
Prostate	7	217	Low risk, favorable prognosis, intermediate prognosis
Thyroid	1	9	Inoperable recurrent lymph node(s), KPS ≥70

RT: Radiation therapy

SBRT: Stereotactic body radiation therapy

WHO/ECOG: World Health Organization/Eastern Cooperative Oncology Group

Based on our search results, the majority of studies (k = 49) performed since 2000 were in the United States for tumors located in the lung/thorax. Germany and Japan have also performed several lung studies in the past 10 years (see Table 3).

Table 3. Country and number of cancer types

Country	Number of Cancer Types	Total Number of Studies
Belgium	1 GI	1 ¹¹⁷
Canada	4 GI	4 ^{99,104,109,154}
Canada & USA	1 GI	1 ⁹⁶
China	1 GI	1 ¹¹⁵
Denmark	3 GI, 2 Lung,	5 ^{27,61,106,107,112}
Denmark, Norway, & Sweden	1 Lung	1 ²⁰
Germany	3 GI, 6 Lung, 2 Multiple Sites, 1 Pelvis, Sacrum, and Uterus	12 ^{46,50,51,58,69,77,110,118,119,126,144,149}
Germany & Switzerland	1 Lung	1 ²³
Italy	5 Lung, 1 Multiple Sites, 1 GI, 1 Prostate	8 ^{34,44,62,63,86,111,139,145}
Italy & Sweden	1 Kidney	1 ¹²⁸
Japan	14 Lung, 1 Multiple Sites	15 ^{26,31,32,39,41,48,53,55,60,66,70,79,81,82,147}
South Korea	1 Pelvis, Sacrum, and Uterus, 4 Lung, 6 GI, 2 Multiple Sites, 1 Thyroid	13 ^{19,57,71,72,97,98,103,114,116,120,124,141,142,151}
Spain	1 Pelvis, Sacrum, and Uterus	1 ¹⁵⁵
Sweden	1 GI, 1 Kidney, 1 Lung	3 ^{42,105,132}
Switzerland	1 Lung, 1 Pelvis, Sacrum, and Uterus	2 ^{47,127}
The Netherlands	1 GI, 4 Lung, 1 Multiple Sites, 1 Prostate	7 ^{24,28,40,59,108,138,146}
USA	6 GI, 2 Pelvis, Sacrum, and Uterus, 4 Kidney, 28 Lung, 3 Multiple Sites, 6 Prostate	49 ^{21,22,25,29,30,33,35-38,43,45,49,52,54,56,64,65,67,73-76,78,80,83-85,100-102,113,121-123,125,129-131,133-137,140,143,148,150,156}
USA & China	1 Lung	1 ⁶⁸

GI: Gastrointestinal

3b. Type of radiation and instrumentation and algorithms used

Photon radiation was used in all included studies for SBRT treatment. The instrumentation reported in all studies included modified linacs (k = 47), CyberKnife (k = 39), Novalis Shaped Beam or Clinac (k = 16), Body GammaKnife (k = 1), Tomotherapy Hi-Art (k = 2), FOCAL unit (k = 1), and Synergy systems (k = 6). Algorithms are used to plan and deliver treatment. The studies reported inverse treatment planning algorithms, pencil beam algorithms for dose calculation, and tissue maximum ratio calculation algorithms. Most of the studies described the device and photon energy, radiation beam angles, collimation technique, body immobilization technique, treatment planning imaging, treatment planning system/algorithm, tumor tracking, respiratory tracking/control, and image guidance during treatment (Appendix M, Literature Results Device Specifications). The number and type of radiation beams delivered during treatments included 1–12 conformal and/or nonconformal beams. The studies reported various body immobilization techniques including Smithers Medical Alpha Cradle (k = 16) and Elekta's stereotactic body frame (k = 26). CT, MRI, and PET imaging scans were often used to plan treatment. Treatment planning was conducted on software systems typically specific to the device used during treatment. Elekta's Render 3D, Varian's CadPlan and Eclipse, BrainLABs BrainScan systems, CyberKnife planning system, Philips Medical Systems Pinnacle Treatment Planning System (TPS), CMS Focus or Xio, and MDS Nordion Helax were the treatment planning systems most often reported. Studies reported breath-holding, respiratory gating (radiation beam turns on/off during respiratory cycle), and abdominal compression techniques to control respiratory movement. Lastly, the type of image guidance (MV or kV) utilized during treatment (e.g., just before treatment begins) included CT, cone-beam CT, and orthogonal x-rays. For more information, see Appendix M, Literature Results Device Specifications.

SBRT doses and fractions varied based on factors such as the type of cancer and location of tumor. According to ACR/ASTRO's SBRT definition¹ and the AMA CPT codes,⁸ SBRT is categorized as a treatment delivered in 1–5 fractions. Typically, doses were delivered in one to five fractions. Fourteen studies delivered treatment in more than five fractions, and also considered this to be SBRT. Table 4 lists the 14 studies delivering hypofractionated (more than five fractions) SBRT (also located in Appendix L, Results for Guiding Question 3) alphabetically by author, and details the cancer type, study design, study size (n), instrumentation/algorithms, and total dose (Gy)/number of fractions.

Table 4. Hypofractionated stereotactic body radiation therapy

Study	Country	Cancer Type	Study Design	Study Size (n)	Instrumentation/ Algorithms	Total Dose (Gy)	Number of Fractions
Chawla et al. (2009) ¹³³	USA	Adrenal metastases	Retrospective single group	n = 30	Novalis/NR	Median: 40 (Range: 16–50)	Median: 10 (Range: 4–16)
Guckenberger et al. (2009) ²³	Germany and Switzerland	Early stage NSCLC and pulmonary metastases	Retrospective single group	n = 40	Linac/Collapsed cone dose calculation algorithm	6–26	1–8
Haasbeek et al. (2009) ²⁴	The Netherlands	Second lung tumor in the contralateral lung	Prospective single group	n = 15	Linac/NR	60	3–8
Lee et al. (2009) ⁹⁹	Canada	Liver metastases	Prospective single group	n = 68	Linac/NR	Median: 41.4 (Range: 27.7–60)	6
Milano et al. (2009) ¹⁵⁰	USA	Oligometastases	Retrospective single group	n = 77: 42 liver, 21 lung, 5 thoracic lymph nodes, 9 bone n = 13 lung parenchymal and thoracic lymph nodes	Novalis/NR	Lung and liver: 50	Lung and liver: 10
Stephans et al. (2009) ³⁸	USA	Stage 1 lung cancer	Retrospective single group	n = 92	Novalis machine/NR	50–60	3–10
Lagerwaard et al. (2008) ²⁸	The Netherlands	Stage 1 NSCLC	Retrospective single group	n = 206	Linac/NR	60	3–8
Aoki et al. (2007) ⁴¹	Japan	Primary lung and metastases	Prospective single group	n = 19	Mitsubishi EXL-20TP 10-MV standard linac/NR	54	9
Dawson et al. (2006) ¹⁰⁴	Canada	HCC, IHC, liver metastases	Prospective single group	n = 79	Elekta Synergy/NR	24–57 (Median: 36.6)	6
Guckenberger et al. (2007) ⁴⁷	Switzerland	NSCLC and pulmonary metastatic lesions	Nonrandomized comparative study (Hypofractionated SBRT (3–8 fractions) vs. 1 fraction SRS)	n = 70	NR/NR	26–56	1–8

Table 4. Hypofractionated stereotactic body radiation therapy (continued)

Study	Country	Cancer Type	Study Design	Study Size (n)	Instrumentation/ Algorithms	Total Dose (Gy)	Number of Fractions
Katoh et al. (2008) ¹³⁰	USA	Adrenal tumors	Prospective single group	n = 9	Linac/NR	48 or 30	8
Tse et al. (2008) ¹⁰⁹	Canada	Unresectable HCC and IHC	Prospective single group	n = 41	NR/NR	24–54 (Median: 36)	6
Uematsu et al. (2001) ⁶⁶	Japan	Stage 1 NSCLC	Prospective single group	n = 50	FOCAL unit (combination of linac, CT scanner, X-ray simulator, carbon table)/NR	30–60	5–10
Xia et al. (2006) ⁶⁸	USA & China	Stage 1 and 2 NSCLC	Prospective single group	n = 43	Gamma-knife (30 rotary conical surface Cobalt 60)/ NR	50–70	10

Gy: Gray

HCC: Hepatocellular carcinoma

IHC: Intrahepatic cholangiocarcinoma

NR: Not reported

NSCLC: Non-small cell lung cancer

SBRT: Stereotactic body radiation therapy

SRS: Stereotactic radiosurgery

3c. Study design and study size

Study designs for SBRT include prospective, single-group studies and retrospective studies. Patient populations were heterogeneous across the cancer types. Study populations included as few as three patients for a prospective, single-group study and as many as 398 for a retrospective study. Table 5, below, lists the smallest and largest patient populations for the studies within each cancer type, and the type of studies conducted for each cancer type. We have also calculated an overall mean and median age for patients in the studies within each cancer type (see Table 6).

Table 5. Study designs and sizes

Cancer Type	Smallest (n)	Largest (n)	Prospective	Retrospective
GI (Colon, Liver, Pancreas)	n = 4	n = 398	18	9
Kidney	n = 3	n = 30	3	3
Lung/Thorax	n = 9	n = 379	35	33
Multiple Sites	n = 14	n = 141	4	6
Pelvis, Sacrum, and Uterus	n = 3	n = 23	1	4
Prostate	n = 10	n = 48	6	1
Thyroid	9	9	0	1
Total Number of Studies			67	57

GI: Gastrointestinal

Table 6. Overall Mean and Median (Range) for Age

Cancer Type	Mean Age (Years)	Median Age (Years)	Age Range (Years)
GI (Colon, Liver, Pancreas)	62.2	62.8	15–92
Kidney	62.8	64	39–79
Lung/Thorax	71.1	72	9–93
Multiple Sites	60.0	59.5	2–92
Pelvis, Sacrum, and Uterus	63.7	57	27–92
Prostate	69.1	68.5	46–83
Thyroid	46	46	34–81

GI: Gastrointestinal

3d. Comparator used in comparative studies

There were no included studies that compared SBRT to another form of radiation treatment. To date, the largest literature base for SBRT is treatment in the lung/thorax, but these were all single-group studies. We searched www.clinicaltrials.gov and identified 50 ongoing SBRT trials (see Appendix K, Ongoing Clinical Trials). The trials include metastatic breast cancer, biliary tract cancer, kidney cancer, liver cancer, lung cancers (principally non-small cell lung cancer), pancreatic cancer, prostate cancer, and unspecified treatment sites.

Only one of these ongoing trials involves a direct comparison of SBRT to a different form of radiation therapy. This trial commenced in April 2009 in France (NCT00870116), and is a nonrandomized comparison of SBRT delivered by CyberKnife vs. SBRT delivered by linac vs. conformational RT for treatment of NSCLC. The primary outcome measure is local control, and

planned enrollment is 120 patients. There are three other comparative trials which plan to use historical controls, one for metastatic breast cancer (NCT00167414), one in NSCLC (NCT00727350) and one in pancreatic cancer (NCT00350142). One of the lung cancer trials based in the Netherlands (NCT00687986) is a randomized study comparing SBRT to primary resection. The primary outcomes include local control, regional control, quality of life (QoL), and treatment costs. The estimated enrollment is 960 patients and is set for completion in December 2013. Another trial being conducted in China (NCT00840749) will compare SBRT to surgical resection in NSCLC. The enrollment target is 1030 patients, with planned completion in 2013. Another trial (NCT00843726) being conducted in Roswell, NY, will randomize 98 patients to either one or three fractions of SBRT for treatment of NSCLC.

3e. Concurrent and/or prior treatments used

The prior and concurrent treatments used varied with each study based on the population evaluated, and on inclusion and exclusion criteria (see the tables in Appendix L, Results for Guiding Question 3). Some studies included patients with prior and/or concurrent treatment, while other studies excluded patients with prior or concurrent treatment. Prior treatments reported include surgery, radiation therapy (e.g., IMRT, brachytherapy), pharmaceuticals (e.g., tamoxifen), and/or chemotherapy. Some studies specified that prior radiation therapy or chemotherapy had to be completed within a certain timeframe before SBRT (e.g., at least 12 weeks prior to SBRT). Chemotherapy was the concurrent treatment most often reported within the studies.

3f. Length of followup

The individual study length of followup was reported as a mean, median, and/or range. We have calculated an overall mean and median for the length of followup for each cancer type. The shortest mean and median followup was within the multiple site category (12.9 and 8.2 months [1-95 months] respectively). Studies of the tumors involving the pelvis, sacrum, and uterus had the longest mean/median followup (31 and 33 months [range 2-77 months]). Table 7 lists the cancer types and the calculated overall mean, median, and range of followup across studies within each cancer type.

Table 7. Overall mean and median followup

Cancer Type	Mean Followup (months)	Median Followup (months)	Follow-up Range (months)
GI (Colon, Liver, Pancreas)	20.0	16	1–103.2
Kidney	23.5	16	3–70
Lung/Thorax	19.7	17	1–107
Multiple Sites	12.9	8.2	1–95
Pelvis, Sacrum, Uterus	33.3	31	2–77
Prostate	20.1	9.3	2 weeks–74.4 months
Thyroid	23	23	4–63

GI: Gastrointestinal

3g. Outcomes measured

The outcomes measured typically included tumor control or tumor response, toxicity, and overall survival. Overall cause-specific survival rates (chances of death due to cancer at a

defined time point), overall survival rates (chances of death due to cancer and/or other complications at a defined time point), and disease-free survival rates were typically calculated using the Kaplan-Meier method. Most studies used the following four criteria to measure tumor control or tumor response: complete response (disappearance of tumor), partial response (percentage of decrease in tumor size), stable disease (smaller percentage change than with partial response), and progression of disease (increase in tumor size). The percentages of tumor response varied with each study. Table 8 provides a summary of the types of outcomes measured within each cancer type.

Table 8. Summary of outcomes measured

Cancer Type	Summary of Outcomes Measured
GI (Colon, Liver, Pancreas)	Toxicity, tumor response, overall survival, progression-free survival, regional failure, change in liver volume, maximum tolerated study dose, carbohydrate antigen levels (CA 19-9), QoL, late toxicities, deterioration of hepatic function
Kidney	Survival, pain assessment, tumor response, toxicity, kidney function, creatine levels
Lung/Thorax	Tumor response, overall survival, cause-specific survival, toxicity, local control, pulmonary status, disease progression, maximum standardized uptake value, normal tissue changes
Multiple Sites	Morbidity, tumor response, quality of treatment, survival, local failure, local progression, disease-free survival, toxicity, pain relief
Pelvis, Sacrum, Uterus	Pain relief, tumor response, toxicity, local failure
Prostate	PSA response, QoL, acute gastrointestinal toxicities, acute genitourinary toxicities
Thyroid	Tumor response, regional failure

GI: Gastrointestinal
 PSA: Prostate specific antigen
 QoL: Quality of Life

Evaluating the extent of cell destruction caused by SBRT can be a difficult task, as older calculation methods (e.g., linear quadratic model [LQ]) were developed for use with conventional radiation therapy. The LQ model assumes there are two components of radiation-induced cell destruction—one component proportional to dose and one component proportional to the square of the dose.¹⁶ The application of the LQ model for low dose conventional fractions may not have the same consequences as the use of the model with SBRT. The LQ model possibly overestimates cell destruction, and it may not describe the cell survival curve for the high doses of SBRT properly.¹⁶ Making comparisons between studies for SBRT can also be challenging. Studies may report equivalent prescription doses; however, differences in fractionation schedules can result in a substantial difference in the biologically effective dose (BED).¹⁶ The BED is an index that can serve as a useful parameter for comparing the potency of two different fractionation schedules.¹⁸

3h. Adverse events, harms, safety issues reported

Radiation Therapy Oncology Group criteria and Common Toxicity Criteria version 2.0 (RTOG/CTC) were typically used to grade acute and late toxicity at each followup. In general, Grade 1 toxicities require no treatment, Grade 2 toxicities require medication or a simple intervention, Grade 3 toxicities have more severe symptoms and require more complex interventions, and Grade 4 toxicities can be life threatening.¹³⁵ Some studies reported acute

versus late complications; however, they did not always specify complications related to individual patients. Some of the most frequently reported adverse events include pain, fatigue, nausea, bleeding, and diarrhea. Some of the patients in these studies had prior cancer treatment and received SBRT for recurring cancers, and some patients had comorbid conditions. Toxicities for large radiation doses are predominantly late occurrences which take more time to observe. Therefore, longer followup will be required for wider acceptance of SBRT.⁹

A total of 11 studies did not report any adverse events for tumors located at the following sites: one kidney,¹³¹ six lung,^{29,35,52,61,77,157} two multiple sites,^{148,150} and two GI (colon, liver, pancreas).^{100,103} Also, some studies did not report adverse events using the RTOG/CTC scale, or stated that investigators and/or patients observed or reported no adverse events. One study of SBRT for renal cell cancer stated that there were no adverse effects of treatment.¹³¹ Table 9 summarizes the reported adverse events for the studies within each cancer type.

Table 9. Summary of adverse events

Cancer Type	Summary of Adverse Events
GI (Colon, Liver, Pancreas)	Severe mucositis, epigastric pain, fatigue, deterioration of hepatic function, abdominal pain, bleeding esophageal varices, gastrointestinal bleeding
Kidney	Fatigue, cough, nausea, vomiting, local pain
Lung/Thorax	Grade 1–4 toxicities, rash, pneumonitis, cough, rib fracture, pneumothorax (fiducial placements), chest wall pain, fatigue, nausea, interstitial lung tissue changes, shortness of breath, dermatitis, pleural effusion, fibrosis
Multiple Sites	Grade 1–4 toxicities, pain, nausea, diarrhea, rectal bleeding
Pelvis, Sacrum, Uterus	Abdominal pain, rectal bleeding, nausea
Prostate	Mild rectal toxicity, urinary toxicity, rectal discomfort, diarrhea, occasional blood, constipation, frequency/nocturia
Thyroid	No grade 3 or higher adverse events

GI: Gastrointestinal

Discussion

This Technical Brief provides a broad overview of the current state of SBRT. Aspects of the brief include current technologies available to deliver SBRT; types and locations of tumors that have been treated with SBRT; the possible advantages and disadvantages of the technology; the extent of diffusion of the technology; and information about advances in the technology that are currently in development. We searched the Internet for gray literature to identify information for cancer sites, theoretical advantages and disadvantages of SBRT, and potential safety issues and harms. Specialized instrumentation for SBRT, the FDA status, technologies in development, and an estimate of the number of hospitals performing SBRT in the United States were also explored using the Internet. The information collected for Guiding Questions 1 and 2 may not be inclusive of all resources. For Guiding Question 3, we performed a systematic search of bibliographic databases, including MEDLINE, EMBASE, and Cochrane. If the literature searches for Guiding Question 3 returned relevant information, we also included it in the first two Guiding Questions. We also searched ClinicalTrials.gov to determine if any trials are currently in progress for SBRT. Appendix K lists the condition being studied, the intervention, study design, primary and secondary outcomes to be measured, estimated enrollment, planned duration, and location of ongoing trials.

The available literature addressing SBRT is considerably large. The bulk of the studies were for tumors located in the lung/thorax ($k = 68$). We found fewer than 10 studies each for tumors of the pancreas, liver, colon, uterus, pelvis, sacrum, kidney, prostate, and thyroid. This literature base also includes many theoretical treatment-planning studies and treatment technique studies. The study designs identified in our literature search for SBRT treatment included prospective and retrospective single-group studies. There were several studies that included duplicate populations.

Our literature search did not identify any published comparison (whether randomized or nonrandomized) studies. Currently (as of September 2010), there is one ongoing nonrandomized trial comparing two methods of delivering SBRT to conformal radiation for management of NSCLC with a planned enrollment of 120 patients. There are also two ongoing randomized clinical trials comparing SBRT vs. primary resection for lung cancer (see Appendix K, Ongoing Clinical Trials). A third randomized trial is comparing SBRT delivered in one vs. three fractions for NSCLC.

External beam radiation treatment has long been a mainstay of cancer treatment. Advances in this technology have allowed smaller and hard-to-target tumors to be treated; reducing the amount of radiation received by adjacent healthy tissue. SBRT requires accuracy in delivery of the high dose of radiation, patient immobilization, target localization, maneuvers to either limit or compensate for target movement (tracking software), and the use of stereotaxy. It can be completed in one to five fractions and may be a treatment option for patients who refuse surgery, for tumors considered inoperable, or when traditional RT is not an option.

One of the most critical aspects of SBRT is ensuring accurate delivery of the intended dose to the intended target, particularly given the higher dose of radiation typically used. This requires rigorous quality control and quality assurance measures for treatment planning and treatment delivery. Tumor sites within the body tend to move (e.g., respiratory movement) between fractionated treatments, causing difficulties immobilizing the targeted tumor. Therefore, tumor tracking techniques will continue to play an integral role in the procedure. Considerations for selection of appropriate treatment candidates include prior radiation history of the treatment

tissues, treatment volume, organ function, capacity for recovery, number of sites of disease, and many other individual cancer-related factors.⁹

Groups such as the American Association of Physicists in Medicine (AAPM) have urged participation in trials sponsored by the National Cancer Institute (NCI), or in trials run by the NCI-sponsored Radiation Therapy Oncology Group, a multi-institutional research cooperative. In a recent guidance document, AAPM pointed out that protocol-driven treatment in the context of such studies would reflect the guidelines produced by experts in the field (Also available: http://www.aapm.org/pubs/reports/RPT_101.pdf).¹⁵⁸ Future studies may help to determine the optimal number of radiation fractions, the minimum and maximum dose per fraction, the maximum number and diameter of lesions for various locations, and the radiobiological explanations for the efficacy of SBRT treatment.

Conclusion

In brief, there are many publications on SBRT for the treatment of cancer, principally cancer involving the lung. None of the currently available studies include comparison groups. Comparative studies (preferably randomized trials, but at the least, trials with concurrent controls) are needed to provide convincing evidence that the theoretical advantages of SBRT over other radiotherapies actually occur in the clinical setting. At present, there is only one small ongoing trial making such a comparison. Consequently, a full systematic review of the current literature cannot answer questions on the effectiveness and safety of SBRT compared to other radiotherapy interventions. Two large ongoing trials scheduled for completion in 2013 have the potential to answer questions about the effectiveness and safety of SBRT as compared to surgical resection in resectable early-stage lung cancer.

References

1. American College of Radiology (ACR). Practice guideline for the performance of stereotactic body radiation therapy. Reston VA: American College of Radiology (ACR); 2009:8.
2. Fuss M, Thomas CR, Jr. Stereotactic body radiation therapy: an ablative treatment option for primary and secondary liver tumors. *Ann Surg Oncol* 2004 Feb;11(2):130-8. PMID: 14761915.
3. Smink KA, Schneider SM. Overview of stereotactic body radiotherapy and the nursing role. *Clin J Oncol Nurs* 2008 Dec;12(6):889-93. PMID: 19064382.
4. Read PW. Stereotactic body radiation therapy: 2007 Update. *Community Oncol* 2007 Oct;4(10):616-20.
5. Miyamoto C. (Chairperson & Professor, Department of Radiation Oncology, Temple University School of Medicine). Personal Communication; 2010 Feb 23: 51.
6. American College of Radiology (ACR). Practice guideline for the performance of stereotactic body radiation therapy. Reston VA: American College of Radiology (ACR); 2004:8.
7. Barnett GH, Linskey ME, Adler JR, et al. Stereotactic radiosurgery—an organized neurosurgery-sanctioned definition. *J Neurosurg* 2007 Jan;106(1):1-5. PMID: 17240553.
8. Stereotactic radiotherapy (SRS)/stereotactic radiation therapy (SBRT) for Medicare plans. Policy #: SURGERY 058.1 T3. [Internet]. Trumbull CT: Oxford Health Plans, LLC; 2009 Jan [accessed 2009; Sep 3]: 5. Available at <https://www.oxhp.com>.
9. Meyer JL, Verhey L, Xia P, et al. New technologies in the radiotherapy clinic. *Front Radiat Ther Oncol* 2007;40:1-17. PMID: 17641499.
10. Chen JC, Rahimian J, Girvigian MR, et al. Contemporary methods of radiosurgery treatment with the Novalis linear accelerator system. *Neurosurg Focus* 2007;23(6):E4. PMID: 18081481.
11. GammaStar's Gyro Knife awarded EU certification. [Internet]. New York NY: Thomson Reuters; 2008 Apr 15 [accessed 2008; Nov 25]. Available at <http://www.reuters.com/article/pressRelease/idUS130278+15-Apr-2008+PRN20080415>.
12. American Cancer Society (ACS). Cancer facts & figures 2009. Atlanta GA: American Cancer Society (ACS); 2009: 72.. Also available at <http://www.cancer.org/downloads/STT/500809web.pdf>.
13. Kavanagh BD, Kelly K, Kane M. The promise of stereotactic body radiation therapy in a new era of oncology. *Front Radiat Ther Oncol* 2007;40:340-51. PMID: 17641518.
14. Dilling TJ, Hoffe SE. Stereotactic body radiation therapy: transcending the conventional to improve outcomes. *Cancer Control* 2008 Apr;15(2):104-11. PMID: 18376377.
15. Committee on Radiation Source Use and Replacement, National Research Council. Radiation source use and replacement: abbreviated version. Washington DC: National Academies Press Radiotherapy 2008:117-33. Also available at http://www.nap.edu/catalog.php?record_id=11976.
16. Chang BK, Timmerman RD. Stereotactic body radiation therapy: a comprehensive review. *Am J Clin Oncol* 2007 Dec;30(6):637-44. PMID: 18091059.
17. Microsoft Office Excel 2007, part of Microsoft Office Professional Plus 2007 [software program]. Redmond WA: Microsoft; 2006.
18. Kavanagh BD, Timmerman RD. Stereotactic radiosurgery and stereotactic body radiation therapy: an overview of technical considerations and clinical applications. *Hematol Oncol Clin North Am* 2006 Feb;20(1):87-95. PMID: 16580558.

19. Ahn SH, Han MS, Yoon JH, et al. Treatment of stage I non-small cell lung cancer with CyberKnife, image-guided robotic stereotactic radiosurgery. *Oncol Rep* 2009 Mar;21(3):693-6. PMID: 19212628.
20. Baumann P, Nyman J, Hoyer M, et al. Stereotactic body radiotherapy for medically inoperable patients with stage I non-small cell lung cancer—a first report of toxicity related to COPD/CVD in a non-randomized prospective phase II study. *Radiother Oncol* 2008 Sep;88(3):359-67. PMID: 18768228.
21. Chang JY, Balter PA, Dong L, et al. Stereotactic body radiation therapy in centrally and superiorly located stage I or isolated recurrent non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Nov 15;72(4):967-71. PMID: 18954709.
22. Collins BT, Vahdat S, Erickson K, et al. Radical cyberknife radiosurgery with tumor tracking: an effective treatment for inoperable small peripheral stage I non-small cell lung cancer. *J Hematol Oncol* 2009;2:1. PMID: 19149899.
23. Guckenberger M, Wulf J, Mueller G, et al. Dose-response relationship for image-guided stereotactic body radiotherapy of pulmonary tumors: relevance of 4D dose calculation. *Int J Radiat Oncol Biol Phys* 2009 May 1;74(1):47-54. PMID: 18977095.
24. Haasbeek CJ, Lagerwaard FJ, de Jaeger K., et al. Outcomes of stereotactic radiotherapy for a new clinical stage I lung cancer arising postpneumonectomy. *Cancer* 2009 Feb 1;115(3):587-94. PMID: 19130457.
25. Henderson M, McGarry R, Yiannoutsos C, et al. Baseline pulmonary function as a predictor for survival and decline in pulmonary function over time in patients undergoing stereotactic body radiotherapy for the treatment of stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Oct 1;72(2):404-9. PMID: 18394819.
26. Kawase T, Takeda A, Kunieda E, et al. Extrapulmonary soft-tissue fibrosis resulting from hypofractionated stereotactic body radiotherapy for pulmonary nodular lesions. *Int J Radiat Oncol Biol Phys* 2009 Jun 1;74(2):349-54. PMID: 19427551.
27. Kopek N, Paludan M, Petersen J, et al. Comorbidity index predicts for mortality after stereotactic body radiotherapy for medically inoperable early-stage non-small cell lung cancer. *Radiother Oncol* 2009 Dec;93(1):122-4. E-pub 2009 Jun 22. PMID: 19559492.
28. Lagerwaard FJ, Haasbeek CJ, Smit EF, et al. Outcomes of risk-adapted fractionated stereotactic radiotherapy for stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Mar 1;70(3):685-92. PMID: 18164849.
29. Milano MT, Philip A, Okunieff P. Analysis of patients with oligometastases undergoing two or more curative-intent stereotactic radiotherapy courses. *Int J Radiat Oncol Biol Phys* 2009 Mar 1;73(3):832-7. PMID: 18760543.
30. Milano MT, Chen Y, Katz AW, et al. Central thoracic lesions treated with hypofractionated stereotactic body radiotherapy. *Radiother Oncol* 2009 Jun;91(3):301-6. PMID: 19329210.
31. Norihisa Y, Nagata Y, Takayama K, et al. Stereotactic body radiotherapy for oligometastatic lung tumors. *Int J Radiat Oncol Biol Phys* 2008 Oct 1;72(2):398-403. PMID: 18374506.
32. Onishi H, Kuriyama K, Komiyama T, et al. Clinical outcomes of stereotactic radiotherapy for stage I non-small cell lung cancer using a novel irradiation technique: patient self-controlled breath-hold and beam switching using a combination of linear accelerator and CT scanner. *Lung Cancer* 2004 Jul;45(1):45-55. PMID: 15196734.
33. Pennathur A, Luketich JD, Heron DE, et al. Stereotactic radiosurgery for the treatment of stage I non-small cell lung cancer in high-risk patients. *J Thorac Cardiovasc Surg* 2009 Mar;137(3):597-604. PMID: 19258073.
34. Ricardi U, Filippi AR, Guarneri A, et al. Dosimetric predictors of radiation-induced lung injury in stereotactic body radiation therapy. *Acta Oncol* 2009;48(4):571-7. PMID: 19031164.

35. Rusthoven KE, Hammerman SF, Kavanagh BD, et al. 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* 2009;48(4):578-83. PMID: 19373699.
36. Rusthoven KE, Kavanagh BD, Burri SH, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for lung metastases. *J Clin Oncol* 2009 Apr 1;27(10):1579-84. PMID: 19255320.
37. Salazar OM, Sandhu TS, Lattin PB, et al. Once-weekly, high-dose stereotactic body radiotherapy for lung cancer: 6-year analysis of 60 early-stage, 42 locally advanced, and 7 metastatic lung cancers. *Int J Radiat Oncol Biol Phys* 2008 Nov 1;72(3):707-15. PMID: 18455322.
38. Stephans KL, Djemil T, Reddy CA, et al. Comprehensive analysis of pulmonary function test (PFT) changes after stereotactic body radiotherapy (SBRT) for stage I lung cancer in medically inoperable patients. *J Thorac Oncol* 2009 Jul;4(7):838-44. PMID: 19487961.
39. Takeda A, Sanuki N, Kunieda E, et al. Stereotactic body radiotherapy for primary lung cancer at a dose of 50 Gy total in five fractions to the periphery of the planning target volume calculated using a superposition algorithm. *Int J Radiat Oncol Biol Phys* 2009 Feb 1;73(2):442-8. PMID: 18990507.
40. van der Voort van Zyp NC, Prevost J-B, Hoogeman MS, et al. Stereotactic radiotherapy with real-time tumor tracking for non-small cell lung cancer: Clinical outcome. *Radiother Oncol* 2009 Jun;91(3):296-300. PMID: 19297048.
41. Aoki M, Abe Y, Kondo H, et al. Clinical outcome of stereotactic body radiotherapy of 54 Gy in nine fractions for patients with localized lung tumor using a custom-made immobilization system. *Radiat Med* 2007 Jul;25(6):289-94. PMID: 17634882.
42. Baumann P, Nyman J, Lax I, et al. Factors important for efficacy of stereotactic body radiotherapy of medically inoperable stage I lung cancer. A retrospective analysis of patients treated in the Nordic countries. *Acta Oncol* 2006;45(7):787-95. PMID: 16982541.
43. Brown WT, Wu X, Wen BC, et al. Early results of CyberKnife image-guided robotic stereotactic radiosurgery for treatment of lung tumors. *Comput Aided Surg* 2007 Sep;12(5):253-61. PMID: 17957532.
44. Casamassima F, Masi L, Bonucci I, et al. Relevance of biologically equivalent dose values in outcome evaluation of stereotactic radiotherapy for lung nodules. *Int J Radiat Oncol Biol Phys* 2008 May 1;71(1):145-51. PMID: 18164855.
45. Coon D, Gokhale AS, Burton SA, et al. Fractionated stereotactic body radiation therapy in the treatment of primary, recurrent, and metastatic lung tumors: the role of positron emission tomography/computed tomography-based treatment planning. *Clin Lung Cancer* 2008 Jul;9(4):217-21. PMID: 18650169.
46. Fritz P, Kraus HJ, Blaschke T, et al. Stereotactic, high single-dose irradiation of stage I non-small cell lung cancer (NSCLC) using four-dimensional CT scans for treatment planning. *Lung Cancer* 2008 May;60(2):193-9. PMID: 18045732.
47. Guckenberger M, Heilman K, Wulf J, et al. Pulmonary injury and tumor response after stereotactic body radiotherapy (SBRT): results of a serial follow-up CT study. *Radiother Oncol* 2007 Dec;85(3):435-42. PMID: 18053602.
48. Harada T, Shirato H, Ogura S, et al. Real-time tumor-tracking radiation therapy for lung carcinoma by the aid of insertion of a gold marker using bronchofiberscopy. *Cancer* 2002 Oct 15;95(8):1720-7. PMID: 12365020.
49. Hodge W, Tome WA, Jaradat HA, et al. Feasibility report of image guided stereotactic body radiotherapy (IG-SBRT) with tomotherapy for early stage medically inoperable lung cancer using extreme hypofractionation. *Acta Oncol* 2006;45(7):890-6. PMID: 16982555.

50. Hof H, Hoess A, Oetzel D, et al. Stereotactic single-dose radiotherapy of lung metastases. *Strahlenther Onkol* 2007 Dec;183(12):673-8. PMID: 18040611.
51. Hof H, Muentner M, Oetzel D, et al. Stereotactic single-dose radiotherapy (radiosurgery) of early stage nonsmall-cell lung cancer (NSCLC). *Cancer* 2007 Jul 1;110(1):148-55. PMID: 17516437.
52. Hoopes DJ, Tann M, Fletcher JW, et al. FDG-PET and stereotactic body radiotherapy (SBRT) for stage I non-small-cell lung cancer. *Lung Cancer* 2007 May;56(2):229-34. PMID: 17353064.
53. Ishimori T, Saga T, Nagata Y, et al. 18F-FDG and 11C-methionine PET for evaluation of treatment response of lung cancer after stereotactic radiotherapy. *Ann Nucl Med* 2004 Dec;18(8):669-74. PMID: 15682847.
54. Joyner M, Salter BJ, Papanikolaou N, et al. Stereotactic body radiation therapy for centrally located lung lesions. *Acta Oncol* 2006;45(7):802-7. PMID: 16982543.
55. Koto M, Takai Y, Ogawa Y, et al. A phase II study on stereotactic body radiotherapy for stage I non-small cell lung cancer. *Radiother Oncol* 2007 Dec;85(3):429-34. PMID: 18022720.
56. Le QT, Loo BW, Ho A, et al. Results of a phase I dose-escalation study using single-fraction stereotactic radiotherapy for lung tumors. *J Thorac Oncol* 2006 Oct;1(8):802-9. PMID: 17409963.
57. Lee SW, Choi EK, Park HJ, et al. Stereotactic body frame based fractionated radiosurgery on consecutive days for primary or metastatic tumors in the lung. *Lung Cancer* 2003 Jun;40(3):309-15. PMID: 12781430.
58. Muacevic A, Drexler C, Wowra B, et al. 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* 2007 Aug;6(4):321-8. PMID: 17668940.
59. Nuyttens JJ, Prevost JB, Praag J, et al. Lung tumor tracking during stereotactic radiotherapy treatment with the CyberKnife: marker placement and early results. *Acta Oncol* 2006;45(7):961-5. PMID: 16982564.
60. Onimaru R, Fujino M, Yamazaki K, et al. 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* 2008 Feb 1;70(2):374-81. PMID: 18029106.
61. Paludan M, Traberg HA, Petersen J, et al. Aggravation of dyspnea in stage I non-small cell lung cancer patients following stereotactic body radiotherapy: Is there a dose-volume dependency? *Acta Oncol* 2006;45(7):818-22. PMID: 16982545.
62. Ricardi U, Guarneri A, Mantovani C, et al. Stereotactic body radiation therapy for early non-small cell lung cancer: experience at the University of Turin. *J Thorac Oncol* 2007 May;2(5 Suppl):S47. PMID: 17457235.
63. Scorsetti M, Navarria P, Facoetti A, et al. Effectiveness of stereotactic body radiotherapy in the treatment of inoperable early-stage lung cancer. *Anticancer Res* 2007 Sep;27(5B):3615-9. PMID: 17972525.
64. Sinha B, McGarry RC. Stereotactic body radiotherapy for bilateral primary lung cancers: the Indiana University experience. *Int J Radiat Oncol Biol Phys* 2006 Nov 15;66(4):1120-4. PMID: 17145532.
65. Song DY, Benedict SH, Cardinale RM, et al. Stereotactic body radiation therapy of lung tumors: preliminary experience using normal tissue complication probability-based dose limits. *Am J Clin Oncol* 2005 Dec;28(6):591-6. PMID: 16317270.
66. Uematsu M, Shioda A, Suda A, et al. Computed tomography-guided frameless stereotactic radiotherapy for stage I non-small cell lung cancer: a 5-year experience. *Int J Radiat Oncol Biol Phys* 2001 Nov 1;51(3):666-70. PMID: 11597807.
67. Whyte RI, Crownover R, Murphy MJ, et al. Stereotactic radiosurgery for lung tumors: preliminary report of a phase I trial. *Ann Thorac Surg* 2003 Apr;75(4):1097-101. PMID: 12683544.

68. Xia T, Li H, Sun Q, et al. Promising clinical outcome of stereotactic body radiation therapy for patients with inoperable Stage I/II non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2006 Sep 1;66(1):117-25. PMID: 16765528.
69. Zimmermann FB, Geinitz H, Schill S, et al. Stereotactic hypofractionated radiotherapy in stage I (T1-2 N0 M0) non-small-cell lung cancer (NSCLC). *Acta Oncol* 2006;45(7):796-801. PMID: 16982542.
70. Nakagawa K, Aoki Y, Tago M, et al. Megavoltage CT-assisted stereotactic radiosurgery for thoracic tumors: original research in the treatment of thoracic neoplasms. *Int J Radiat Oncol Biol Phys* 2000 Sep 1;48(2):449-57. PMID: 10974461.
71. Yoon SM, Choi EK, Lee SW, et al. Clinical results of stereotactic body frame based fractionated radiation therapy for primary or metastatic thoracic tumors. *Acta Oncol* 2006;45(8):1108-14. PMID: 17118847.
72. Song SY, Choi W, Shin SS, et al. Fractionated stereotactic body radiation therapy for medically inoperable stage I lung cancer adjacent to central large bronchus. *Lung Cancer* 2009 Oct;66(1):89-93. PMID: 19168260.
73. Timmerman R, McGarry R, Yiannoutsos C, et al. 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* 2006 Oct 20;24(30):4833-9. PMID: 17050868.
74. Stephans KL, Djemil T, Reddy CA, et al. A comparison of two stereotactic body radiation fractionation schedules for medically inoperable stage I non-small cell lung cancer: the Cleveland Clinic experience. *J Thorac Oncol* 2009 Aug;4(8):976-82. PMID: 19633473.
75. Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA* 2010 Mar 17;303(11):1070-6. PMID: 20233825.
76. Vahdat S, Oermann EK, Collins SP, et al. CyberKnife radiosurgery for inoperable stage IA non-small cell lung cancer: 18F-fluorodeoxyglucose positron emission tomography/computed tomography serial tumor response assessment. *J Hematol Oncol* 2010;3:6. PMID: 20132557.
77. Hof H, Zgoda J, Nill S, et al. Time- and dose-dependency of radiographic normal tissue changes of the lung after stereotactic radiotherapy. *Int J Radiat Oncol Biol Phys* 2010 Aug 1;77(5):1369-74. E-pub 2009 Nov 24. PMID: 19932943.
78. Unger K, Ju A, Oermann E, et al. CyberKnife for hilar lung tumors: report of clinical response and toxicity. *J Hematol Oncol* 2010;3:39. PMID: 20969774.
79. Yamashita H, Kobayashi-Shibata S, Terahara A, et al. Prescreening based on the presence of CT-scan abnormalities and biomarkers (KL-6 and SP-D) may reduce severe radiation pneumonitis after stereotactic radiotherapy. *Radiat Oncol* 2010;5:32. PMID: 20459699.
80. Trovo M, Linda A, El N, I, et al. Early and late lung radiographic injury following stereotactic body radiation therapy (SBRT). *Lung Cancer* 2010 Jul;69(1):77-85. PMID: 19910075.
81. Takeda A, Ohashi T, Kunieda E, et al. Early graphical appearance of radiation pneumonitis correlates with the severity of radiation pneumonitis after stereotactic body radiotherapy (SBRT) in patients with lung tumors. *Int J Radiat Oncol Biol Phys* 2010 Jul 1;77(3):685-90. PMID: 20510193.
82. Hamamoto Y, Kataoka M, Yamashita M, et al. Local control of metastatic lung tumors treated with SBRT of 48 Gy in four fractions: in comparison with primary lung cancer. *Jpn J Clin Oncol* 2010 Feb;40(2):125-9. PMID: 19825814.
83. Grills IS, Mangona VS, Welsh R, et al. Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer. *J Clin Oncol* 2010 Feb 20;28(6):928-35. PMID: 20065181.

84. Dunlap NE, Cai J, Biedermann GB, et al. 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* 2010 Mar 1;76(3):796-801. E-pub 2009 May 8. PMID: 19427740.
85. Crabtree TD, Denlinger CE, Meyers BF, et al. Stereotactic body radiation therapy versus surgical resection for stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2010 Aug;140(2):377-86. PMID: 20400121.
86. Bradley JD, El Naqa I, Drzymala RE, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung cancer: the pattern of failure is distant. *Int J Radiat Oncol Biol Phys* 2010 Jul 15;77(4):1146-50. PMID: 19800181.
87. Gasent Blesa JM, Dawson LA. Options for radiotherapy in the treatment of liver metastases. *Clin Transl Oncol* 2008 Oct;10(10):638-45. PMID: 18940744.
88. New England Medical Center Evidence-based Practice Center. Particle beam radiation therapies for cancer. Rockville, MD: New England Medical Center Evidence-based Practice Center; 2008: 49.
89. Bucci MK, Bevan A, Roach M, III. Advances in radiation therapy: conventional to 3D, to IMRT, to 4D, and beyond. *CA Cancer J Clin* 2005 Mar;55(2):117-34.
90. RT answers - external beam radiation therapy treatments. [Internet]. Fairfax (VA): American Society for Therapeutic Radiology and Oncology; [accessed 2008 Aug 15]: 3. Available at http://www.ranswers.org/treatment/external_beam.htm.
91. Connell PP, Hellman S. Advances in radiotherapy and implications for the next century: a historical perspective. *Cancer Res* 2009 Jan 15;69(2):383-92. PMID: 19147546.
92. NeuroSource. Stereotactic radiosurgery: emerging trends & technology report. Chicago (IL): NeuroSource Inc.; 2004. 27 p. Also available at http://www.neurosource.com/white_papers.html.
93. Galvin JM, Bednarz G. Quality assurance procedures for stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys* 2008 May 1;71(1 Suppl):S122-S125. PMID: 18406909.
94. García-Garduño OA, Celis MA, Lárraga-Gutiérrez JM, et al. Radiation transmission, leakage and beam penumbra measurements of a micro-multileaf collimator using GafChromic EBT film. *J Appl Clin Med Phys* 2008;9(3):90-8.
95. AHA guide to the health care field. 2009 ed. Chicago IL: American Hospital Association; 2008:A15-A622.
96. Chang DT, Schellenberg D, Shen J, et al. Stereotactic radiotherapy for unresectable adenocarcinoma of the pancreas. *Cancer* 2009 Feb 1;115(3):665-72. PMID: 19117351.
97. Choi BO, Choi IB, Jang HS, et al. Stereotactic body radiation therapy with or without transarterial chemoembolization for patients with primary hepatocellular carcinoma: preliminary analysis. *BMC Cancer* 2008 Nov 27;8:351. PMID: 19038025
98. Kim MS, Yoo SY, Cho CK, et al. Stereotactic body radiation therapy using three fractions for isolated lung recurrence from colorectal cancer. *Oncology* 2009;76(3):212-9. PMID: 19218825.
99. Lee MT, Kim JJ, Dinniwell R, et al. Phase I study of individualized stereotactic body radiotherapy of liver metastases. *J Clin Oncol* 2009 Apr 1;27(10):1585-91. PMID: 19255313.
100. Olsen CC, Welsh J, Kavanagh BD, et al. Microscopic and macroscopic tumor and parenchymal effects of liver stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys* 2009 Apr 1;73(5):1414-24. PMID: 18990508.
101. Rusthoven KE, Kavanagh BD, Cardenes H, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for liver metastases. *J Clin Oncol* 2009 Apr 1;27(10):1572-8. PMID: 19255321.

102. Schellenberg D, Goodman KA, Lee F, et al. Gemcitabine chemotherapy and single-fraction stereotactic body radiotherapy for locally advanced pancreatic cancer. *Int J Radiat Oncol Biol Phys* 2008 Nov 1;72(3):678-86. PMID: 18395362.
103. Seong J, Lee IJ, Shim SJ, et al. A multicenter retrospective cohort study of practice patterns and clinical outcome on radiotherapy for hepatocellular carcinoma in Korea. *Liver Int* 2009;29(2):147-152. PMID: 18795897.
104. Dawson LA, Eccles C, Craig T. Individualized image guided iso-NTCP based liver cancer SBRT. *Acta Oncol* 2006;45(7):856-64. PMID: 16982550.
105. Gunven P, Blomgren H, Lax I. Radiosurgery for recurring liver metastases after hepatectomy. *Hepatogastroenterology* 2003 Sep;50(53):1201-4. PMID: 14571698.
106. Hoyer M, Roed H, Sengelov L, et al. Phase-II study on stereotactic radiotherapy of locally advanced pancreatic carcinoma. *Radiother Oncol* 2005 Jul;76(1):48-53. PMID: 15990186.
107. Hoyer M, Roed H, Traberg HA, et al. Phase II study on stereotactic body radiotherapy of colorectal metastases. *Acta Oncol* 2006;45(7):823-30. PMID: 16982546.
108. Mendez RA, Wunderink W, Hussain SM, et al. Stereotactic body radiation therapy for primary and metastatic liver tumors: A single institution phase i-ii study. *Acta Oncol* 2006;45(7):831-7. PMID: 16982547.
109. Tse RV, Hawkins M, Lockwood G, et al. Phase I study of individualized stereotactic body radiotherapy for hepatocellular carcinoma and intrahepatic cholangiocarcinoma. *J Clin Oncol* 2008 Feb 1;26(4):657-64. PMID: 18172187.
110. Wulf J, Guckenberger M, Haedinger U, et al. Stereotactic radiotherapy of primary liver cancer and hepatic metastases. *Acta Oncol* 2006;45(7):838-47. PMID: 16982548.
111. Polistina F, Costantin G, Casamassima F, et al. Unresectable locally advanced pancreatic cancer: a multimodal treatment using neoadjuvant chemoradiotherapy (gemcitabine plus stereotactic radiosurgery) and subsequent surgical exploration. *Ann Surg Oncol* 2010 Aug;17(8):2092-101. E-pub 2010 Mar 12. PMID: 20224860.
112. Kopek N, Holt MI, Hansen AT, et al. Stereotactic body radiotherapy for unresectable cholangiocarcinoma. *Radiother Oncol* 2010 Jan;94(1):47-52. PMID: 19963295.
113. Mahadevan A, Jain S, Goldstein M, et al. Stereotactic body radiotherapy and gemcitabine for locally advanced pancreatic cancer. *Int J Radiat Oncol Biol Phys* 2010 Nov 1;78(3):735-42. E-pub 2010 Feb 18. PMID: 20171803.
114. Son SH, Choi BO, Ryu MR, et al. Stereotactic body radiotherapy for patients with unresectable primary hepatocellular carcinoma: dose-volumetric parameters predicting the hepatic complication. *Int J Radiat Oncol Biol Phys* 2010 Nov 15;78(4):1073-80. E-pub 2010 Mar 6. PMID: 20207492.
115. Yang ZX, Wang D, Wang G, et al. Clinical study of recombinant adenovirus-p53 combined with fractionated stereotactic radiotherapy for hepatocellular carcinoma. *J Cancer Res Clin Oncol* 2010 Apr;136(4):625-630. PMID: 19882171.
116. Seo YS, Kim MS, Yoo SY, et al. Preliminary result of stereotactic body radiotherapy as a local salvage treatment for inoperable hepatocellular carcinoma. *J Surg Oncol* 2010 Sep 1;102(3):209-214. PMID: 20740576.
117. Louis C, Dewas S, Mirabel X, et al. Stereotactic radiotherapy of hepatocellular carcinoma: preliminary results. *Technol Cancer Res Treat* 2010 Oct;9(5):479-487. PMID: 20815419.
118. Stintzing S, Hoffmann RT, Heinemann V, et al. Radiosurgery of liver tumors: value of robotic radiosurgical device to treat liver tumors. *Ann Surg Oncol* 2010 Nov;17(11):2877-2883. PMID: 20574773.

119. Stintzing S, Hoffmann RT, Heinemann V, et al. Frameless single-session robotic radiosurgery of liver metastases in colorectal cancer patients. *Eur J Cancer* 2010 Apr;46(6):1026-1032. PMID: 20153959.
120. Shin YJ, Kim MS, Yoo SY, et al. Pilot study of stereotactic body radiotherapy for huge hepatocellular carcinoma unsuitable for other therapies. *Tumori* 2010 Jan;96(1):65-70. PMID: 20437860.
121. Goodman KA, Wiegner EA, Maturen KE, et al. Dose-escalation study of single-fraction stereotactic body radiotherapy for liver malignancies. *Int J Radiat Oncol Biol Phys* 2010 Oct 1;78(2):486-493. PMID: 20350791.
122. Cardenes HR, Price TR, Perkins SM, et al. Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma. *Clin Transl Oncol* 2010 Mar;12(3):218-225. PMID: 20231127.
123. Gerszten PC, Ozhasoglu C, Burton SA, et al. CyberKnife frameless single-fraction stereotactic radiosurgery for tumors of the sacrum. *Neurosurg Focus* 2003 Aug 15;15(2):E7. PMID: 15350038.
124. Kim MS, Choi C, Yoo S, et al. Stereotactic body radiation therapy in patients with pelvic recurrence from rectal carcinoma. *Jpn J Clin Oncol* 2008 Oct;38(10):695-700. PMID: 18723850.
125. Kunos C, von Gruenigen V, Waggoner S, et al. Cyberknife radiosurgery for squamous cell carcinoma of vulva after prior pelvic radiation therapy. *Technol Cancer Res Treat* 2008 Oct;7(5):375-80. PMID: 18783287.
126. Guckenberger M, Bachmann J, Wulf J, et al. Stereotactic body radiotherapy for local boost irradiation in unfavourable locally recurrent gynaecological cancer. *Radiother Oncol* 2010 Jan;94(1):53-9. PMID: 20079550.
127. Jorcano S, Molla M, Escude L, et al. Hypofractionated extracranial stereotactic radiotherapy boost for gynecologic tumors: a promising alternative to high-dose rate brachytherapy. *Technol Cancer Res Treat* 2010 Oct;9(5):509-14. PMID: 20815422.
128. Svedman C, Karlsson K, Rutkowska E, et al. Stereotactic body radiotherapy of primary and metastatic renal lesions for patients with only one functioning kidney. *Acta Oncol* 2008;47(8):1578-83. PMID: 18607859.
129. Beitler JJ, Makara D, Silverman P, et al. Definitive, high-dose-per-fraction, conformal, stereotactic external radiation for renal cell carcinoma. *Am J Clin Oncol* 2004 Dec;27(6):646-8. PMID: 15577450.
130. Katoh N, Onimaru R, Sakuhara Y, et al. Real-time tumor-tracking radiotherapy for adrenal tumors. *Radiother Oncol* 2008 Jun;87(3):418-24. PMID: 18439693.
131. Ponsky LE, Mahadevan A, Gill IS, et al. Renal radiosurgery: initial clinical experience with histological evaluation. *Surg Innov* 2007 Dec;14(4):265-9. PMID: 18178914.
132. Svedman C, Sandstrom P, Pisa P, et al. A prospective Phase II trial of using extracranial stereotactic radiotherapy in primary and metastatic renal cell carcinoma. *Acta Oncol* 2006;45(7):870-5. PMID: 16982552
133. Chawla S, Chen Y, Katz AW, et al. Stereotactic body radiotherapy for treatment of adrenal metastases. *Int J Radiat Oncol Biol Phys* 2009 Sep 1;75(1):71-75. PMID: 19250766.
134. Fuller DB, Naitoh J, Lee C, et al. Virtual HDR CyberKnife treatment for localized prostatic carcinoma: dosimetry comparison with HDR brachytherapy and preliminary clinical observations. *Int J Radiat Oncol Biol Phys* 2008 Apr 1;70(5):1588-1597. PMID: 18374232.
135. Madsen BL, Hsi RA, Pham HT, et al. Stereotactic hypofractionated accurate radiotherapy of the prostate (SHARP), 33.5 Gy in five fractions for localized disease: first clinical trial results. *Int J Radiat Oncol Biol Phys* 2007 Mar 15;67(4):1099-1105. PMID: 17336216.
136. Townsend NC, Huth BJ, Ding W, et al. Acute toxicity after CyberKnife-delivered hypofractionated radiotherapy for treatment of prostate cancer. *Am J Clin Oncol* 2011 Feb;34(1):6-10. E-pub 2010 Jan 8. PMID: 20065849.

137. Freeman DE, King CR. Stereotactic body radiotherapy for low-risk prostate cancer: five-year outcomes. *Radiat Oncol* 2011 Jan 10;6(1):3. PMID: 21219625.
138. Aluwini S, van RP, Hoogeman M, et al. CyberKnife stereotactic radiotherapy as monotherapy for low- to intermediate-stage prostate cancer: early experience, feasibility, and tolerance. *J Endourol* 2010 May;24(5):865-869. PMID: 20433370.
139. Bolzicco G, Favretto MS, Scremin E, et al. Image-guided stereotactic body radiation therapy for clinically localized prostate cancer: preliminary clinical results. *Technol Cancer Res Treat* 2010 Oct;9(5):473-477. PMID: 20815418.
140. Oermann EK, Slack RS, Hanscom HN, et al. A pilot study of intensity modulated radiation therapy with hypofractionated stereotactic body radiation therapy (SBRT) boost in the treatment of intermediate- to high-risk prostate cancer. *Technol Cancer Res Treat* 2010 Oct;9(5):453-462. PMID: 20815416.
141. Kim JH, Kim MS, Yoo SY, et al. Stereotactic body radiotherapy for refractory cervical lymph node recurrence of nonanaplastic thyroid cancer. *Otolaryngol Head Neck Surg* 2010 Mar;142(3):338-43. PMID: 20172377.
142. Choi CW, Cho CK, Yoo SY, et al. Image-guided stereotactic body radiation therapy in patients with isolated para-aortic lymph node metastases from uterine cervical and corpus cancer. *Int J Radiat Oncol Biol Phys* 2009 May 1;74(1):147-53. PMID: 18990511.
143. McCammon R, Schefter TE, Gaspar LE, et al. Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys* 2009 Jan 1;73(1):112-8. PMID: 18786780.
144. Ernst-Stecken A, Lambrecht U, Mueller R, et al. Hypofractionated stereotactic radiotherapy for primary and secondary intrapulmonary tumors: first results of a phase I/II study. *Strahlenther Onkol* 2006 Dec;182(12):696-702. PMID: 17149575.
145. Jereczek-Fossa BA, Kowalczyk A, D'Onofrio A, et al. Three-dimensional conformal or stereotactic reirradiation of recurrent, metastatic or new primary tumors. Analysis of 108 patients. *Strahlenther Onkol* 2008 Jan;184(1):36-40. PMID: 18188521.
146. Nuyttens JJ, Prevost JB, Van der Voort van Zijp NC, et al. Curative stereotactic robotic radiotherapy treatment for extracranial, extrapulmonary, extrahepatic, and extraspinal tumors: technique, early results, and toxicity. *Technol Cancer Res Treat* 2007 Dec;6(6):605-10. PMID: 17994790.
147. Shioyama Y, Nakamura K, Anai S, et al. Stereotactic radiotherapy for lung and liver tumors using a body cast system: setup accuracy and preliminary clinical outcome. *Radiat Med* 2005 Sep;23(6):407-13. PMID: 16389982.
148. Teh BS, Paulino AC, Lu HH, et al. Versatility of the Novalis system to deliver image-guided stereotactic body radiation therapy (SBRT) for various anatomical sites. *Technol Cancer Res Treat* 2007 Aug;6(4):347-354. PMID: 17668943.
149. Wulf J, Hadinger U, Oppitz U, et al. Stereotactic radiotherapy of targets in the lung and liver. *Strahlenther Onkol* 2001 Dec;177(12):645-655. PMID: 11789403.
150. Milano MT, Katz AW, Okunieff P. Patterns of recurrence after curative-intent radiation for oligometastases confined to one organ. *Am J Clin Oncol* 2010 Apr;33(2):157-163. E-pub 2009 Sep 18. PMID: 19770627.
151. Kang JK, Kim MS, Kim JH, et al. Oligometastases confined one organ from colorectal cancer treated by SBRT. *Clin Exp Metastasis* 2010 Apr;27(4):273-278. PMID: 20373133
152. Dictionary of cancer terms: Karnofsky performance status. [Internet]. Bethesda MD: National Cancer Institute; [accessed 2008 Dec 2]: 1.. Available at http://www.nci.nih.gov/Templates/db_alpha.aspx?CdrID=44156.
153. ISD data dictionary: WHO/ECOG performance status. [Internet]. Edinburgh, Scotland: ISD Scotland; [accessed 2008 Dec 2] : 1. Available at <http://www.datadictionaryadmin.scot.nhs.uk/isddd/11888.html>.

154. Emara K, Weisbrod DJ, Sahgal A, et al. Stereotactic radiotherapy in the treatment of juxtapapillary choroidal melanoma: preliminary results. *Int J Radiat Oncol Biol Phys* 2004 May 1;59(1):94-100. PMID: 15093904.
155. Miralbell R, Caro M, Weber DC, et al. Stereotactic radiotherapy for ocular melanoma: initial experience using closed eyes for ocular target immobilization. *Technol Cancer Res Treat* 2007 Oct;6(5):413-417. PMID: 17877429.
156. Collins BT, Erickson K, Reichner CA, et al. Radical stereotactic radiosurgery with real-time tumor motion tracking in the treatment of small peripheral lung tumors. *Radiat Oncol* 2007;2:39. PMID: 17953752.
157. Gerszten PC, Burton SA, Belani CP, et al. Radiosurgery for the treatment of spinal lung metastases. *Cancer* 2006 Dec 1;107(11):2653-61. PMID: 17063501.
158. Benedict SH, Yenice KM, Followill D, et al. Stereotactic body radiation therapy: the report of the AAPM Task Group 101. *Med Phys* 2010 Aug;37(8):4078-101.

Glossary

Biologically Effective Dose (BED)

The dose deposited corrected for variation in biological response.

Collimator

Defines the dimensions and direction of a beam of x-ray radiation, usually by eliminating the peripheral, more divergent part of the x-ray beam.

Fiducial

Markers that help to precisely identify the targeted tumor location. They may be located on a headframe, or surgically implanted for tumor locations throughout the body.

Fractionation

Dividing a prescribed treatment dose into smaller amounts.

Gray (Gy)

A measure of the absorbed radiation dose and equal to the absorption of one joule of energy by one kilogram of matter.

Multi-leaf Collimator (MLC)

A device with individual tungsten leaves that are programmed to moved independently in order to shape the prescribed beam profile to the targeted tumor.

Abbreviations

Abbreviation	Description
2D-CRT	Conventional radiation therapy
3D-CRT	Three-dimensional conformal radiation therapy
AAA	Anisotropic analytical algorithm
AAPM	American Association of Physicists in Medicine
ABC	Active breathing control
ACR	The American College of Radiology
AHA	The American Hospital Association
AHRQ	The Agency for Healthcare Research and Quality
ASTRO	American Society for Radiation Oncology
AVM	Arteriovenous malformation
BED	Biologically effective dose
Bq	Becquerel
CDRH	Center for Devices and Radiological Health
cGY/min	Centigray per minute
cm	Centimeter
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CRR	Clinical response rate
CT	Computed tomography
CT/MR	Computer tomography/magnetic resonance
CTC	Common toxicity criteria
DF	Distant failure
DFS	Disease-free survival
DMMLC	Dynamic Micro Multileaf Collimator
DOF	Degrees of freedom
DPFS	Disease progression-free survival
DRR	Digitally reconstructed radiographs
DSS	Disease-specific survival
DVH	Dose volume histogram
EBRT	External beam radiation therapy
ECOG	Eastern Cooperative Oncology Group
FDA	United States Food and Drug Administration
Gy	Gray
HCC	Hepatocellular carcinoma
HD	High definition
hFSRT	Hypofractionated stereotactic radiotherapy
HRQoL	Health-related quality of life
HSBRT	Hypofractionated stereotactic body radiotherapy

Abbreviation	Description
IGRT	Image guided radiation therapy
IHC	Intrahepatic cholangiocarcinoma
IMRT	Intensity modulated radiation therapy
IMSRS	Intensity modulated stereotactic radiosurgery
KPS	Karnofsky Performance Status
kV	Kilovolt
kVp	Peak kilovoltage
LC	Local control
LCR	Local control rate
LED	Light emitting diode
LF	Local failure
linac	Linear accelerator
LP	Local progression
LQ	Linear quadratic model
M	Male
MD	Minimum dose
MEV	Million electron volt
MLC	Multi-leaf collimator
mm	Millimeter
mMLC	micro Multi-leaf collimator
MRI	Magnetic resonance imaging
MTD	Maximum tolerated dose
MU/min	Monitor units per minute
MV	Megavolt
MVCT	Megavoltage computed tomography
NCI-CTC	National Cancer Institute-Common Toxicity Criteria
NR	Not reported
NS	Not specified
NSCLC	Non-small cell lung cancer
NTC	Normal tissue changes
OS	Overall survival
PALN	Para-aortic lymph nodes
PET	Positron emission tomography
PFS	Progression-free survival
PSA	Prostate specific antigen
QA	Quality assurance
QALY	Quality-adjusted life years
QC	Quality control
QoL	Quality of Life
RC	Regional control
RECIST	Response evaluation criteria in solid tumors

Abbreviation	Description
RFA	Radiofrequency ablation
RS	Radiosurgery
RT	Radiation therapy
RTOG	Radiation Therapy Oncology Group
SBF	Stereotactic body frame
SBRT	Stereotactic body radiation therapy
SRS	Stereotactic radiosurgery
SRT	Stereotactic radiotherapy
TACE	Transcatheter arterial chemoembolization
TACI	Transarterial chemoinfusion
VMAT	Volumetric modulated arc therapy
WHO	World Health Organization

Appendix A. Literature Search Methods

A variety of approaches were used to identify relevant information for this report, including searches of peer-reviewed literature, gray literature, and federal regulations.

Part I. This portion of the search report includes searches of bibliographic resources. ECRI Institute’s search strategies employ combinations of freetext keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. The strategies presented below are in OVID syntax; the searches were simultaneously conducted across EMBASE, MEDLINE, and CINAHL. Parallel strategies based on MeSH headings and keywords were used to search the databases comprising the Cochrane Library.

Electronic Database Searches

The following databases have been searched for relevant information:

Name	Date Limits	Platform/Provider
The Cochrane Central Register of Controlled Trials (CENTRAL)	Through 2010, Issue 3	www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	Through 2010, Issue 3	www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	Through 2010, Issue 3	www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	Through 2010, Issue 3	www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through December 29, 2010	OVID
Health Technology Assessment Database (HTA)	Through 2010, Issue 3	www.thecochranelibrary.com
MEDLINE	1990 through December 29, 2010	OVID
PreMEDLINE	Searched March 18, 2010	National Library of Medicine
U.K. National Health Service Economic Evaluation Database (NHS EED)	Through 2010, Issue 3	www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched November 7, 2008	www.ngc.gov

Hand Searches of Journal and Nonjournal Literature

Journals and supplements maintained in ECRI Institute’s collections were routinely reviewed. Nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies were also screened. Other mechanisms used to retrieve additional relevant information included review of bibliographies/reference lists from peer-reviewed and gray literature. (Gray literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature.)

The search strategies employed combinations of freetext keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. The strategy below is presented in OVID syntax; the search was simultaneously conducted across EMBASE and MEDLINE. A parallel strategy was used to search the databases comprising the Cochrane Library.

Medical Subject Headings (MeSH), Emtree, PsycINFO and Keywords

Conventions

OVID

\$	=	truncation character (wildcard)
exp	=	“explodes” controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary’s hierarchy)
.de.	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

PubMed

[mh]	=	MeSH heading
[majr]	=	MeSH heading designated as major topic
[pt]	=	publication type
[sb]	=	subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
[sh]	=	MeSH subheading (qualifiers used in conjunction with MeSH headings)
[tiab]	=	keyword in title or abstract
[tw]	=	text word

Topic-Specific Search Terms

Many controlled vocabulary terms and keywords were considered for inclusion in the search strategies. The following table contains an alphabetical listing of terms and keywords grouped by broad concepts. These are the terms and keywords that were actually included in the final search strategies.

Concept	Controlled Vocabulary	Keywords
Cancer	exp neoplasm/ exp neoplasms/	acoustic neuroma\$ antibody therap\$ biops\$ brain\$ cranial nerve Da Vinci epileps\$ farnesyl transferase inhibitor\$ glioma\$ gliomastosis hemangiocyoma\$ hemangiopericytoma\$ herpceptin laparoscop\$ mdl medulloblastoma\$ meningioma\$ neurocytoma\$ oligodendroglioma\$ pinealoma\$ pituitary plesiomorphic robot-assisted tumo?r\$ xanthoastrocytoma\$
Device		American Radiosurgery Brainlab Cyber knife Cyberknife Cyber-knife Elekta Elekta Axesse ExacTrac Gamma ART 6000 Gamma knife Linac Novalis Perfexion Rotating Gamma System Vertex360 Synchrony Synergy Synergy Trilogy XKnife

Concept	Controlled Vocabulary	Keywords
Radiosurgery	Radiosurgery/ Robotics/ Stereotaxic surgery/ Surgery, computer-assisted/is	hypo fractionated hypofractionated radiosurg* radiosurgery radiotherapy real-time tumor tracking robotic single-dose single-fraction stereotactic stereotaxis

English Embase/Medline

English language, human, remove overlap

Set Number	Concept	Search Statement
1	Device	(Gamma knife or Cyber knife or Cyberknife or Cyber-knife or linac or Novalis or Trilogy or XKnife or Synchrony or Synergy or Elekta or Elekta Axesse or Perfexion or Gamma ART 6000 or American Radiosurgery or Rotating Gamma System Vertex360 or Synergy or ExacTrac or BrainLAB).mp.
2	Radiosurgery	Radiosurgery/ or Robotics/ or Surgery, computer-assisted/is or Stereotaxic surgery/ or real-time tumor tracking.mp. or (robotic and (radiotherapy or radiosurgery)).mp. or (radiosurg* and (stereotactic or stereotaxis or hypo fractionated or hypofractionated or single-fraction or single-dose)).mp.
3	Combine sets	1 or 2
4	Cancer	exp neoplasms/ or exp neoplasm/ or (neoplasm\$ or cancer\$ or carcinoma\$ or adenoma\$ or sarcoma\$ or tumor?r\$).mp.
5	Combine sets	3 and 4
6	Cancer of the brain	(Tumor?r\$ adj2 (brain\$ or pituitary or cranial nerve)).ti.
7		(Glioma\$ or gliomastosis or hemangiocyoma\$ or hemangiopericytoma\$ or medulloblastoma\$ or mdl or meningioma\$ or neurocytoma\$ or oligodendroglioma\$ or pinealoma\$ or plesiomorphic xanthoastrocytoma\$ or acoustic neuroma\$ or epileps\$ or herpceptin or robot-assisted or laparoscop\$ or antibody therap\$ ir farnesyl transferase inhibitor\$ or Da Vinci or biops\$).ti.
8	Combine sets	6 or 7
9		5 not 8
10	Remove overlap	Remove duplicates from 9

Part 2. The following databases have been searched for relevant information for Guiding Questions 1 and 2.

Name	Date Limits	Platform/Provider
ClinicalTrials.gov	Searched 11/13/08, 09/22/2009, and 03/23/10	www.clinicaltrials.gov
ECRI Institute cross-search	Searched 5/28/2009	www.ecri.org
Lexis-Nexis Major Newspapers	Searched 8/20/08	www.lexis.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched 11/7/08	www.ngc.gov

The following Web sites have been mined for information.

Name	Date Limits	URL
Centers for Medicare and Medicaid Services (CMS)	4/30/2009	www.cms.gov

Appendix B. Included Studies

Studies Included To Address Guiding Question 3

Reference
Chang et al. (2009) ¹
Ahn et al. (2009) ²
Aluwini et al. (2010) ³
Aoki et al. (2007) ⁴
Baumann et al. (2006) ⁵
Baumann et al. (2008) ⁶
Beitler et al. (2004) ⁷
Bolzicco et al. (2010) ⁸
Bradley et al. (2010) ⁹
Brown et al. (2007) ¹⁰
Cardenes et al. (2010) ¹¹
Casamassima et al. (2008) ¹²
Chang et al. (2008) ¹³
Chawla et al. (2009) ¹⁴
Choi et al. (2008) ¹⁵
Choi et al. (2009) ¹⁶
Collins et al. (2009) ¹⁷
Coon et al. (2008) ¹⁸
Crabtree et al. (2010) ¹⁹
Dawson et al. (2006) ²⁰
Dunlap et al. (2010) ²¹
Ernst-Stecken et al. (2006) ²²
Freeman et al. (2011) ²³
Fritz et al. (2008) ²⁴
Fuller et al. (2008) ²⁵
Gerszten et al. (2003) ²⁶
Goodman et al. (2010) ²⁷
Grills et al. (2010) ²⁸
Guckenberger et al. (2007) ²⁹
Guckenberger et al. (2009) ³⁰
Guckenberger et al. (2010) ³¹
Gunven et al. (2003) ³²

Reference
Haasbeek et al. (2009) ³³
Hamamoto et al. (2010) ³⁴
Harada et al. (2002) ³⁵
Henderson et al. (2008) ³⁶
Hodge et al. (2006) ³⁷
Hof et al. (2007) ³⁸
Hof et al. (2007) ³⁹
Hof et al. (2009) ⁴⁰
Hoopes et al. (2007) ⁴¹
Hoyer et al. (2005) ⁴²
Hoyer et al. (2006) ⁴³
Ishimori et al. (2004) ⁴⁴
Jereczek-Fossa et al. (2008) ⁴⁵
Jorcano et al. (2010) ⁴⁶
Joyner et al. (2006) ⁴⁷
Kang et al. (2010) ⁴⁸
Kato et al. (2008) ⁴⁹
Kawase et al. (2009) ⁵⁰
Kim et al. (2008) ⁵¹
Kim et al. (2009) ⁵²
Kim et al. (2010) ⁵³
Kopek et al. (2009) ⁵⁴
Kopek et al. (2010) ⁵⁵
Koto et al. (2007) ⁵⁶
Kunos et al. (2008) ⁵⁷
Lagerwaard et al. (2008) ⁵⁸
Le et al. (2006) ⁵⁹
Lee et al. (2003) ⁶⁰
Lee et al. (2009) ⁶¹
Louis et al. (2010) ⁶²
Madsen et al. (2007) ⁶³
Mahadevan et al. (2010) ⁶⁴
McCammon et al. (2009) ⁶⁵
Milano et al. (2009) ⁶⁶
Milano et al. (2009) ⁶⁷
Milano et al. (2009) ⁶⁸

Reference
Muacevic et al. (2007) ⁶⁹
Nakagawa et al. (2000) ⁷⁰
Norihisa et al. (2008) ⁷¹
Nuyttens et al. (2006) ⁷²
Nuyttens et al. (2007) ⁷³
Oermann et al. (2010) ⁷⁴
Olsen et al. (2009) ⁷⁵
Onimaru et al. (2008) ⁷⁶
Onishi et al. (2004) ⁷⁷
Paludan et al. (2006) ⁷⁸
Pennathur et al. (2009) ⁷⁹
Polistina et al. (2010) ⁸⁰
Ponsky et al. (2007) ⁸¹
Ricardi et al. (2007) ⁸²
Ricardi et al. (2009) ⁸³
Romero et al. (2006) ⁸⁴
Rusthoven et al. (2009) ⁸⁵
Rusthoven et al. (2009) ⁸⁶
Rusthoven et al. (2009) ⁸⁷
Salazar et al. (2008) ⁸⁸
Schellenberg et al. (2008) ⁸⁹
Scorsetti et al. (2007) ⁹⁰
Seo et al. (2010) ⁹¹
Seong et al. (2009) ⁹²
Shin et al. (2010) ⁹³
Shioyama et al. (2005) ⁹⁴
Sinha et al. (2006) ⁹⁵
Son et al. (2010) ⁹⁶
Song et al. (2005) ⁹⁷
Song et al. (2009) ⁹⁸
Stephans et al. (2009) ⁹⁹
Stephans et al. (2009) ¹⁰⁰
Stintzing et al. (2010) ¹⁰¹
Stintzing et al. (2010) ¹⁰²
Svedman et al. (2006) ¹⁰³
Svedman et al. (2008) ¹⁰⁴

Reference
Takeda et al. (2009) ¹⁰⁵
Takeda et al. (2010) ¹⁰⁶
Teh et al. (2007) ¹⁰⁷
Timmerman et al. (2006) ¹⁰⁸
Timmerman et al. (2010) ¹⁰⁹
Townsend et al. (2010) ¹¹⁰
Trovo et al. (2010) ¹¹¹
Tse et al. (2008) ¹¹²
Uematsu et al. (2001) ¹¹³
Unger et al. (2010) ¹¹⁴
Vahdat et al. (2010) ¹¹⁵
Van der Voort van Zyp et al. (2009) ¹¹⁶
Whyte et al. (2003) ¹¹⁷
Wulf et al. (2001) ¹¹⁸
Wulf et al. (2006) ¹¹⁹
Xia et al. (2006) ¹²⁰
Yamashita et al. (2010) ¹²¹
Yang et al. (2010) ¹²²
Yoon et al. (2006) ¹²³
Zimmermann et al. (2006) ¹²⁴

Appendix C. Excluded Studies

Full Article Excluded Studies

Reference	Exclusion Reason
(2001) ¹²⁵	Not relevant
(2002) ¹²⁶	Not a clinical study
(2002) ¹²⁷	Not relevant
(2003) ¹²⁸	Not a clinical study
Abbas et al. (2007) ¹²⁹	Not a clinical study
Aboulafia et al. (2007) ¹³⁰	Not relevant
Ahn et al. (2000) ¹³¹	Not relevant
Anantham et al. (2007) ¹³²	Not relevant
Andrews (2007) ¹³³	Not a clinical study
Andrews et al. (2006) ¹³⁴	Not a clinical study
Arimura et al. (2009) ¹³⁵	Treatment planning
Armstrong (2001) ¹³⁶	Not a clinical study
Asamura (2006) ¹³⁷	Not a clinical study
Astrahan (2008) ¹³⁸	Not a clinical study
Attia et al. (2005) ¹³⁹	Not a clinical study
Auberger et al. (2007) ¹⁴⁰	Not relevant
Baisden et al. (2006) ¹⁴¹	Treatment planning
Bale and Sweeney (2002) ¹⁴²	Not a clinical study
Ball and Withers (2007) ¹⁴³	Not a clinical study
Ball D (2008) ¹⁴⁴	Not a clinical study
Bance and Guha (2001) ¹⁴⁵	Not a clinical study
Banki et al. (2009) ¹⁴⁶	Not a clinical study
Barnett et al. (2000) ¹⁴⁷	Not a clinical study
Baser et al. (2000) ¹⁴⁸	Not relevant
Bauman et al. (2006) ¹⁴⁹	Not relevant
Bayouth et al. (2007) ¹⁵⁰	Not a clinical study
Benedict et al. (2008) ¹⁵¹	Not a clinical study
Bernier et al. (2006) ¹⁵²	Not relevant
Bese et al. (2006) ¹⁵³	Not a clinical study
Bhatnagar et al. (2002) ¹⁵⁴	Not relevant
Bhatnagar et al. (2009) ¹⁵⁵	Not relevant
Bissonnette et al. (2009) ¹⁵⁶	Treatment planning

Reference	Exclusion Reason
Blute ML (2009) ¹⁵⁷	Not a clinical study
Bogart (2004) ¹⁵⁸	Not a clinical study
Bogart (2006) ¹⁵⁹	Not a clinical study
Bogart (2007) ¹⁶⁰	Not a clinical study
Bourland and Shaw (2003) ¹⁶¹	Not a clinical study
Bradley (2007) ¹⁶²	Not a clinical study
Brenner and Schwade (2007) ¹⁶³	Not a clinical study
Bridgewater and Spittle (2000) ¹⁶⁴	Not relevant
Brock (2007) ¹⁶⁵	Not a clinical study
Brock et al. (2008) ¹⁶⁶	Not a clinical study
Buatti et al. (2000) ¹⁶⁷	Not a clinical study
Buatti et al. (2000) ¹⁶⁸	Not relevant
Burton et al. (2002) ¹⁶⁹	Not relevant
Buyyounouski et al. (2010) ¹⁷⁰	Not a clinical study
Cadman (2007) ¹⁷¹	Treatment planning
Calcerrada Diaz-Santos et al. (2008) ¹⁷²	Not a clinical study
Casamassima et al. (2006) ¹⁷³	Treatment delivery
Cesaretti et al. (2008) ¹⁷⁴	Not a clinical study
Chang and Adler (2001) ¹⁷⁵	Not a clinical study
Chang and Adler (2001) ¹⁷⁶	Not a clinical study
Chang and Lo (2003) ¹⁷⁷	Not relevant
Chang and Roth (2007) ¹⁷⁸	Not a clinical study
Chang and Saif (2008) ¹⁷⁹	Editorial
Chang and Timmerman (2007) ¹⁸⁰	Not a clinical study
Chang et al. (2007) ¹⁸¹	Not a clinical study
Chang et al. (2007) ¹⁸²	Not a clinical study
Chang et al. (2008) ¹⁸³	Not a clinical study
Chang et al. (2009) ¹⁸⁴	Treatment planning
Chen et al. (2007) ¹⁸⁵	Not a clinical study
Cheung et al. (2007) ¹⁸⁶	Treatment planning
Chi et al. (2009) ¹⁸⁷	Not a clinical study
Chin et al. (2001) ¹⁸⁸	Not relevant
Cho et al. (2008) ¹⁸⁹	Not relevant
Chou et al. (2001) ¹⁹⁰	Not a clinical study
Christie et al. (2008) ¹⁹¹	Not a clinical study
Classen et al. (2003) ¹⁹²	Not relevant

Reference	Exclusion Reason
Clifford et al. (2009) ¹⁹³	Not relevant
Coker (2003) ¹⁹⁴	Not a clinical study
Collins et al. (2007) ¹⁹⁵	Duplicate population
Colombo et al. (2006) ¹⁹⁶	Not a clinical study
Crane and Willett (2009) ¹⁹⁷	Editorial
Curtis and Teh (2006) ¹⁹⁸	Not relevant
Dahele et al. (2008) ¹⁹⁹	Treatment planning
Dawood (2008) ²⁰⁰	Not a clinical study
Day (2002) ²⁰¹	Not a clinical study
De Mey et al. (2005) ²⁰²	Treatment delivery
De Pooter et al. (2007) ²⁰³	Treatment planning
Decker et al. (2006) ²⁰⁴	Not a clinical study
Demarco et al. (2002) ²⁰⁵	Not relevant
Derweesh and Novick (2003) ²⁰⁶	Not a clinical study
Dilling and Hoffe (2008) ²⁰⁷	Not a clinical study
Ding et al. (2005) ²⁰⁸	Not a clinical study
Dinka et al. (2005) ²⁰⁹	Not a clinical study
Dunlap et al. (2009) ²¹	No full article
Dunlap et al. (2010) ²¹⁰	Duplicate population
Dvorak et al. (2005) ²¹¹	Not a clinical study
Ebert et al. (2001) ²¹²	Treatment planning
Edler (2007) ²¹³	Not relevant
El Hamri et al. (2005) ²¹⁴	Not a clinical study
El-Sherif et al. (2005) ²¹⁵	Not a clinical study
Ewing et al. (2010) ²¹⁶	Treatment planning
Fatigante et al. (2005) ²¹⁷	Not relevant
Fenwick et al. (2006) ²¹⁸	Not a clinical study
FitzGerald et al. (2006) ²¹⁹	Not relevant
Flickinger et al. (2003) ²²⁰	Not a clinical study
Flickinger et al. (2007) ²²¹	Not a clinical study
Foote et al. (2004) ²²²	Not relevant
Fowler JF (2009) ²²³	Treatment planning
Friedman and Foote (2000) ²²⁴	Not a clinical study
Fritz et al. (2006) ²²⁵	Treatment delivery
Fuller DB (2009) ²²⁶	Editorial
Fuller et al. (2006) ²²⁷	Treatment delivery

Reference	Exclusion Reason
Fuss (2001) ²²⁸	Not a clinical study
Fuss and Thomas (2004) ²²⁹	Not a clinical study
Fuss et al. (2006) ²³⁰	Treatment planning
Fuss et al. (2007) ²³¹	Not a clinical study
Galvin and Bednarz (2008) ²³²	Quality Assurance
Ganslandt et al. (2003) ²³³	Not relevant
Ganz (2002) ²³⁴	Not a clinical study
Ganz (2007) ²³⁵	Not a clinical study
Gasent Blesa and Dawson (2008) ²³⁶	Not a clinical study
Gaspar (2007) ²³⁷	Not a clinical study
Gerber and Chan (2008) ²³⁸	Not a clinical study
Gerrard and Franks (2004) ²³⁹	Not relevant
Gerszten et al. (2006) ²⁴⁰	Not relevant
Gibbons et al. (2003) ²⁴¹	Not relevant
Gibbs (2006) ²⁴²	Not a clinical study
Gibbs and Chang (2003) ²⁴³	Not a clinical study
Gottlieb (2001) ²⁴⁴	Not relevant
Gottlieb (2001) ²⁴⁵	Not a clinical study
Grills et al. (2007) ²⁴⁶	Treatment planning
Gross and Engenhardt-Cabillic (2002) ²⁴⁷	Not a clinical study
Gross et al. (2003) ²⁴⁸	Treatment delivery
Grutters et al. (2010) ²⁴⁹	Not a clinical study
Guckenberger et al. (2006) ²⁵⁰	Treatment planning
Guckenberger et al. (2007) ²⁵¹	Treatment delivery
Guckenberger et al. (2009) ²⁵²	Treatment planning
Guckenberger et al. (2009) ²⁵³	Treatment planning
Guckenberger et al. (2010) ²⁵⁴	Treatment planning
Guerrero and Li (2004) ²⁵⁵	Treatment planning
Hadinger et al. (2002) ²⁵⁶	Treatment planning
Haedinger et al. (2005) ²⁵⁷	Treatment planning
Hansen et al. (2006) ²⁵⁸	Treatment delivery
Hara et al. (2007) ²⁵⁹	Not a clinical study
Heinzerling et al. (2008) ²⁶⁰	Treatment delivery
Herbert et al. (2003) ²⁶¹	Treatment delivery
Hermann et al. (2004) ²⁶²	Not a clinical study
Heron et al. (2003) ²⁶³	Not a clinical study

Reference	Exclusion Reason
Heron et al. (2009) ²⁶⁴	Not relevant
Heros (2005) ²⁶⁵	Not a clinical study
Hevezi (2003) ²⁶⁶	Not a clinical study
Hevezi et al. (2010) ²⁶⁷	Not a clinical study
Hinson et al. (2007) ²⁶⁸	Treatment delivery
Hiraoka et al. (2007) ²⁶⁹	Not a clinical study
Hocht et al. (2005) ²⁷⁰	Treatment planning
Hogle (2006) ²⁷¹	Not a clinical study
Hoh et al. (2007) ²⁷²	Not a clinical study
Holland (2001) ²⁷³	Not a clinical study
Holmes et al. (2008) ²⁷⁴	Not a clinical study
Hoogeman et al. (2008) ²⁷⁵	Treatment delivery
Hoogeman et al. (2009) ²⁷⁶	Treatment delivery
Horstmann et al. (2000) ²⁷⁷	Not relevant
Hui et al. (2004) ²⁷⁸	Not relevant
Huntzinger et al. (2007) ²⁷⁹	Not a clinical study
Imura et al. (2005) ²⁸⁰	Treatment delivery
Imura et al. (2008) ²⁸¹	Treatment delivery
Inoue et al. (2010) ²⁸²	Not relevant
Isaksson et al. (2005) ²⁸³	Not relevant
Jaffray et al. (2007) ²⁸⁴	Not a clinical study
Jamal et al. (2008) ²⁸⁵	Not a clinical study
Jawahar et al. (2004) ²⁸⁶	Not relevant
Jeremic et al. (2000) ²⁸⁷	Not relevant
Jin et al. (2005) ²⁸⁸	Treatment planning
Jin et al. (2009) ²⁸⁹	Treatment planning
Joensuu et al. (2000) ²⁹⁰	Not a clinical study
Jozsef et al. (2000) ²⁹¹	Treatment planning
Kassaee et al. (2003) ²⁹²	Treatment delivery
Katz et al. (2007) ²⁹³	Duplicate population
Kavanagh and Timmerman (2006) ²⁹⁴	Not a clinical study
Kavanagh et al. (2003) ²⁹⁵	Not a clinical study
Kavanagh et al. (2006) ²⁹⁶	Duplicate population
Kavanagh et al. (2007) ²⁹⁷	Not a clinical study
Kavanagh et al. (2007) ²⁹⁸	Not a clinical study
Kavanagh et al. (2008) ²⁹⁹	Not a clinical study

Reference	Exclusion Reason
Kawaguchi et al. (2004) ³⁰⁰	Less than 3 patients
Kelly (2000) ³⁰¹	Not a clinical study
Kenai et al. (2005) ³⁰²	Treatment planning
King et al. (2003) ³⁰³	Treatment delivery
King et al. (2008) ³⁰⁴	Duplicate population
King et al. (2009) ³⁰⁵	Duplicate population
King et al. (2009) ³⁰⁶	Editorial
Kitamura et al. (2002) ³⁰⁷	Not relevant
Kitamura et al. (2002) ³⁰⁸	Not relevant
Kitamura et al. (2003) ³⁰⁹	Treatment delivery
Koga et al. (2009) ³¹⁰	Not relevant
Kommu et al. (2006) ³¹¹	Not relevant
Kondziolka et al. (2000) ³¹²	Not a clinical study
Kondziolka et al. (2004) ³¹³	Not a clinical study
Kondziolka et al. (2005) ³¹⁴	Not a clinical study
Kondziolka et al. (2007) ³¹⁵	Not a clinical study
Kontrisoova et al. (2006) ³¹⁶	Treatment planning
Koong et al. (2004) ³¹⁷	Duplicate population
Koong et al. (2005) ³¹⁸	Duplicate population
Kopek et al. (2010) ³¹⁹	Duplicate population
Korreman et al. (2006) ³²⁰	Treatment planning
Kresl (2006) ³²¹	Not a clinical study
Kunieda et al. (2004) ³²²	Treatment planning
Kunieda et al. (2008) ³²³	Treatment delivery
Kunzler et al. (2007) ³²⁴	Treatment delivery
Kupferman and Hanna (2008) ³²⁵	Not a clinical study
Laigle-Donadey et al. (2005) ³²⁶	Not relevant
Langner et al. (2009) ³²⁷	Treatment delivery
Larre et al. (2007) ³²⁸	Not relevant
Lartigau et al. (2009) ³²⁹	Not a clinical study
Lawson et al. (2009) ³³⁰	Treatment planning
Lax et al. (2006) ³³¹	Treatment planning
Leavitt et al. (2001) ³³²	Treatment delivery
Lee et al. (2000) ³³³	Treatment planning
Lee WR (2009) ³³⁴	Not a clinical study
Leskell (2007) ³³⁵	Not a clinical study

Reference	Exclusion Reason
Li and Ma (2005) ³³⁶	Treatment planning
Liao et al. (2000) ³³⁷	Treatment planning
Lillard (2008) ³³⁸	Not a clinical study
Lind et al. (2001) ³³⁹	Not relevant
Lindquist and Paddick (2007) ³⁴⁰	Not relevant
Lindvall et al. (2008) ³⁴¹	Not relevant
Linskey and Johnstone (2003) ³⁴²	Not a clinical study
Linthout et al. (2009) ³⁴³	Treatment delivery
Liu et al. (2004) ³⁴⁴	Treatment planning
Livi et al. (2005) ³⁴⁵	Not relevant
Lo et al. (2008) ³⁴⁶	Not a clinical study
Lo et al. (2009) ³⁴⁷	Not a clinical study
Lomax et al. (2003) ³⁴⁸	Treatment planning
Lu et al. (2008) ³⁴⁹	Treatment planning
Ma et al. (2003) ³⁵⁰	Not relevant
Maarouf et al. (2005) ³⁵¹	Not relevant
Macdermed et al. (2008) ³⁵²	Not a clinical study
Martin and Gaya (2010) ³⁵³	Not a clinical study
Matsumoto et al. (2007) ³⁵⁴	Not relevant
McDermott et al. (2006) ³⁵⁵	Not relevant
McGarry et al. (2005) ³⁵⁶	Duplicate population
Meeks et al. (2003) ³⁵⁷	Treatment delivery
Mell and Mundt (2005) ³⁵⁸	Not relevant
Meretoja et al. (2008) ³⁵⁹	Not relevant
Mery et al. (2007) ³⁶⁰	Not a clinical study
Meyer et al. (2007) ³⁶¹	Not a clinical study
Meyer et al. (2007) ³⁶²	Treatment planning
Mignano et al. (2001) ³⁶³	Treatment planning
Minn et al. (2009) ³⁶⁴	Treatment planning
Molla et al. (2005) ³⁶⁵	Duplicate population
Morgia and De (2009) ³⁶⁶	Editorial
Muacevic et al. (2003) ³⁶⁷	Not relevant
Muacevic et al. (2004) ³⁶⁸	Not a clinical study
Muller et al. (2004) ³⁶⁹	Treatment delivery
Murphy (2004) ³⁷⁰	Not a clinical study
Murphy et al. (2002) ³⁷¹	Treatment delivery

Reference	Exclusion Reason
Murphy et al. (2003) ³⁷²	Treatment delivery
Murphy MJ (2009) ³⁷³	Treatment planning
Murray et al. (2007) ³⁷⁴	Treatment delivery
Naff (2007) ³⁷⁵	Not relevant
Nagata et al. (2007) ³⁷⁶	Not a clinical study
Nakagawa et al. (2003) ³⁷⁷	Treatment planning
Nakaji and Spetzler (2004) ³⁷⁸	Not relevant
Nakamura et al. (2001) ³⁷⁹	Treatment planning
Nedzi LA (2008) ³⁸⁰	Not a clinical study
Nguyen et al. (2008) ³⁸¹	Not a clinical study
Nieder et al. (2009) ³⁸²	Not a clinical study
Niranjan and Lunsford (2000) ³⁸³	Not a clinical study
Niranjan et al. (2003) ³⁸⁴	Not a clinical study
Niranjan et al. (2007) ³⁸⁵	Not a clinical study
Niranjan et al. (2007) ³⁸⁶	Not a clinical study
No Authors Listed (2003) ³⁸⁷	Not relevant
No authors listed (2006) ³⁸⁸	Not a clinical study
No Authors Listed (2007) ³⁸⁹	Not relevant
No Authors Listed (2007) ³⁹⁰	Not relevant
Noda et al. (2009) ³⁹¹	Not relevant
Okunieff et al. (2006) ³⁹²	Duplicate population
Onishi et al. (2003) ³⁹³	Treatment delivery
Orecchia (2007) ³⁹⁴	Not a clinical study
Pan et al. (2007) ³⁹⁵	Treatment delivery
Pang (2003) ³⁹⁶	Not a clinical study
Papiez and Timmerman (2008) ³⁹⁷	Not a clinical study
Papiez et al. (2003) ³⁹⁸	Not a clinical study
Park et al. (2008) ³⁹⁹	Treatment planning
Parman (2004) ⁴⁰⁰	Not a clinical study
Pass H (2008) ⁴⁰¹	Not a clinical study
Pawlicki et al. (2007) ⁴⁰²	Not a clinical study
Pennathur et al. (2007) ⁴⁰³	Duplicate population
Petersch et al. (2004) ⁴⁰⁴	Treatment delivery
Petrovich and Yu (2003) ⁴⁰⁵	Not relevant
Pishvaian et al. (2006) ⁴⁰⁶	Treatment delivery
Polina et al. (2010) ⁴⁰⁷	Not a clinical study

Reference	Exclusion Reason
Poll et al. (2008) ⁴⁰⁸	Not a clinical study
Pollock (2006) ⁴⁰⁹	Not a clinical study
Pott et al. (2005) ⁴¹⁰	Not relevant
Potters et al. (2005) ⁴¹¹	Not a clinical study
Prabhu and Demonte (2003) ⁴¹²	Not relevant
Prevost et al. (2008) ⁴¹³	Treatment delivery
Prevost et al. (2008) ⁴¹⁴	Treatment planning
Purdie et al. (2006) ⁴¹⁵	Treatment delivery
Quang et al. (2007) ⁴¹⁶	Not a clinical study
Quinn (2002) ⁴¹⁷	Not a clinical study
Rassiah-Szegedi et al. (2006) ⁴¹⁸	Treatment planning
Ratto et al. (2000) ⁴¹⁹	Not relevant
Regine (2003) ⁴²⁰	Not a clinical study
Regis et al. (2009) ⁴²¹	Not relevant
Riboldi et al. (2006) ⁴²²	Treatment planning
Rock et al. (2004) ⁴²³	Not a clinical study
Rockhill (2007) ⁴²⁴	Not a clinical study
Romanelli et al. (2003) ⁴²⁵	Not a clinical study
Romanelli et al. (2006) ⁴²⁶	Not a clinical study
Romanelli et al. (2006) ⁴²⁷	Not relevant
Rosahl et al. (2002) ⁴²⁸	Not a clinical study
Rosenzweig et al. (2003) ⁴²⁹	Not a clinical study
Rosenzweig et al. (2009) ⁴³⁰	Not a clinical study
Rousseau and Gibon (2000) ⁴³¹	Not a clinical study
Rutten and Deneufbourg (2000) ⁴³²	Not relevant
Ryken et al. (2001) ⁴³³	Treatment delivery
Samper et al. (2006) ⁴³⁴	Not relevant
Sankaranarayanan et al. (2003) ⁴³⁵	Treatment planning
Sarfaraz et al. (2007) ⁴³⁶	Not a clinical study
Sasai et al. (2000) ⁴³⁷	Treatment planning
Saunders (2007) ⁴³⁸	Not a clinical study
Savides (2006) ⁴³⁹	Not a clinical study
Saw et al. (2008) ⁴⁴⁰	Not a clinical study
Sawrie et al. (2010) ⁴⁴¹	Not a clinical study
Schefter et al. (2005) ⁴⁴²	Duplicate population
Scheib et al. (2004) ⁴⁴³	Not relevant

Reference	Exclusion Reason
Schellenberg et al. (2010) ⁴⁴⁴	Duplicate population
Schlaefer et al. (2005) ⁴⁴⁵	Treatment planning
Schweikard et al. (2000) ⁴⁴⁶	Treatment delivery
Schweikard et al. (2004) ⁴⁴⁷	Treatment delivery
Scorsetti and Bignardi (2008) ⁴⁴⁸	Not a clinical study
Seki et al. (2007) ⁴⁴⁹	Treatment planning
Senan et al. (2007) ⁴⁵⁰	Not a clinical study
Seppenwoolde et al. (2002) ⁴⁵¹	Treatment delivery
Sharma et al. (2010) ⁴⁵²	Not relevant
Shepard et al. (2000) ⁴⁵³	Treatment planning
Sherwood and Brock (2007) ⁴⁵⁴	Not a clinical study
Shibuya and Tsujii (2005) ⁴⁵⁵	Not relevant
Shirato et al. (2003) ⁴⁵⁶	Not relevant
Shirato et al. (2006) ⁴⁵⁷	Not a clinical study
Shirato et al. (2007) ⁴⁵⁸	Not a clinical study
Shiu et al. (2003) ⁴⁵⁹	Treatment delivery
Shoshan et al. (2005) ⁴⁶⁰	Not a clinical study
Shrieve et al. (2004) ⁴⁶¹	Not a clinical study
Siddiqui et al. (2009) ⁴⁶²	Not relevant
Silvano (2006) ⁴⁶³	Not a clinical study
Singletary (2001) ⁴⁶⁴	Not relevant
Siva et al. (2010) ⁴⁶⁵	Not a clinical study
Slotman et al. (2005) ⁴⁶⁶	Not relevant
Slotman et al. (2006) ⁴⁶⁷	Not a clinical study
Smink and Schneider et al. (2008) ⁴⁶⁸	Not a clinical study
Smit (2000) ⁴⁶⁹	Not a clinical study
Smith and Chuang (2007) ⁴⁷⁰	Not a clinical study
Snell et al. (2006) ⁴⁷¹	Treatment planning
Soete et al. (2006) ⁴⁷²	Treatment planning
Solberg et al. (2001) ⁴⁷³	Treatment planning
Solberg et al. (2004) ⁴⁷⁴	Not relevant
Solberg et al. (2008) ⁴⁷⁵	Quality Assurance
Solberg et al. (2008) ⁴⁷⁶	Not a clinical study
Song et al.(no year) ⁴⁷⁷	Not a clinical study
Sonke et al. (2009) ⁴⁷⁸	Treatment delivery
Sotiropoulou et al. (2009) ⁴⁷⁹	Not relevant

Reference	Exclusion Reason
Spadea et al. (2008) ⁴⁸⁰	Treatment delivery
St. George et al. (2002) ⁴⁸¹	Not relevant
Stancanello et al. (2005) ⁴⁸²	Treatment planning
Steinke (2006) ⁴⁸³	Not relevant
Sterzing et al. (2007) ⁴⁸⁴	Not relevant
Sterzing et al. (2008) ⁴⁸⁵	Not relevant
Storme et al. (2006) ⁴⁸⁶	Not a clinical study
Strassmann et al. (2004) ⁴⁸⁷	Treatment planning
Strassmann et al. (2006) ⁴⁸⁸	Treatment delivery
Suzuki et al. (2007) ⁴⁸⁹	Treatment delivery
Taguchi et al. (2007) ⁴⁹⁰	Treatment delivery
Takayama et al. (2005) ⁴⁹¹	Treatment planning
Takeda et al. (2005) ⁴⁹²	Treatment planning
Takeda et al. (2008) ⁴⁹³	Duplicate population
Takeda et al. (2009) ⁴⁹⁴	Treatment planning
Takeuchi et al. (2003) ⁴⁹⁵	Treatment delivery
Teh et al. (2007) ⁴⁹⁶	Not a clinical study
Theil and Winfield (2008) ⁴⁹⁷	Not a clinical study
Theodorou et al. (2000) ⁴⁹⁸	Treatment planning
Theodorou et al. (no year) ⁴⁹⁹	Not a clinical study
Thieke et al. (2006) ⁵⁰⁰	Treatment planning
Timmerman et al. (2003) ⁵⁰¹	Duplicate population
Timmerman et al. (2003) ⁵⁰²	Not a clinical study
Timmerman et al. (2006) ⁵⁰³	Not a clinical study
Timmerman et al. (2007) ⁵⁰⁴	Not a clinical study
Timmerman et al. (2007) ⁵⁰⁵	Treatment planning
Timmerman et al. (2007) ⁵⁰⁶	Not a clinical study
Timmerman et al. (2007) ⁵⁰⁷	Not a clinical study
Timmerman et al. (2009) ⁵⁰⁸	Not a clinical study
Tobler et al. (2004) ⁵⁰⁹	Treatment planning
Tonn (2004) ⁵¹⁰	Not a clinical study
Tsai et al. (2001) ⁵¹¹	Treatment planning
Uematsu et al. (2000) ⁵¹²	No relevant outcomes
Underberg et al. (2005) ⁵¹³	Treatment delivery
Underberg et al. (2006) ⁵¹⁴	Treatment delivery
Vaidya et al. (2002) ⁵¹⁵	Not relevant

Reference	Exclusion Reason
Van Houtte (2003) ⁵¹⁶	Not a clinical study
Van Der Voort Van Zyp et al. (2010) ⁵¹⁷	Duplicate population
Varga et al. (2009) ⁵¹⁸	Not a clinical study
Vassiliev et al. (2009) ⁵¹⁹	Treatment planning
Verbakel et al. (2009) ⁵²⁰	Treatment delivery
Verellen et al. (2006) ⁵²¹	Treatment planning
Videtic et al. (2010) ⁵²²	Duplicate population
Voynov et al. (2006) ⁵²³	Not relevant
Vricella et al. (2009) ⁵²⁴	Not a clinical study
Wagner et al. (2003) ⁵²⁵	Treatment planning
Wagner et al. (2007) ⁵²⁶	Not a clinical study
Wakelee et al. (2008) ⁵²⁷	Not a clinical study
Wakisaka et al. (2000) ⁵²⁸	Treatment planning
Wallen (2006) ⁵²⁹	Not a clinical study
Wiegner and King (2010) ⁵³⁰	No full article
Willoughby et al. (2006) ⁵³¹	Not relevant
Wilt et al. (2008) ⁵³²	Not relevant
Wu et al. (2003) ⁵³³	Treatment planning
Wu et al. (2008) ⁵³⁴	Treatment delivery
Wu et al. (2009) ⁵³⁵	Treatment planning
Wulf et al. (2004) ⁵³⁶	Duplicate population
Wunderink et al. (2007) ⁵³⁷	Treatment planning
Wurm et al. (2006) ⁵³⁸	Not relevant
Xiao et al. (2009) ⁵³⁹	Treatment delivery
Yaeger T.E. (2009) ⁵⁴⁰	Editorial
Yin et al. (2004) ⁵⁴¹	Treatment delivery
Yin et al. (2008) ⁵⁴²	Treatment delivery
Yousefi et al. (2007) ⁵⁴³	Treatment delivery
Yu and Shepard (2003) ⁵⁴⁴	Not a clinical study
Zamzuri et al. (2006) ⁵⁴⁵	Not relevant
Zimmermann et al. (2010) ⁵⁴⁶	Not a clinical study

Appendix D. Personnel Qualifications

Personnel Qualifications for Stereotactic Body Radiation Therapy

	Radiation Oncologist	Medical Physicists	Radiation Therapist
Qualifications	<ul style="list-style-type: none"> ✓ Certified in radiology, radiation oncology, or therapeutic radiology OR ✓ Satisfactory completion in an approved residency program ✓ Specific training on extracranial SRS 	<ul style="list-style-type: none"> ✓ Certified in therapeutic radiological physics or radiological physics ✓ Should be in accordance with the ACR Practice Guideline for Continuing Medical Education ✓ Specific training in SRS should be obtained prior to performing any SBRT procedures 	<ul style="list-style-type: none"> ✓ Fulfill state licensing requirements ✓ Certified in radiation therapy
Responsibilities	<ul style="list-style-type: none"> ✓ Manage overall disease-specific treatment regimen ✓ Recommend most ideal patient-positioning method ✓ Recommend procedure to account for inherent organ motion ✓ Supervise patient simulation; contour the outline of the gross tumor volume (GTV) on the treatment planning computer ✓ Coordinate design for proper planning target volume (PTV) ✓ Convey case-specific expectations for prescribing radiation dose and setting limits on dose to adjacent normal tissues ✓ Attend and direct actual treatment process ✓ Follow patient with attention to disease control ✓ Monitoring and treating potential complications 	<ul style="list-style-type: none"> ✓ Acceptance testing and commissioning of SBRT system ✓ Implementing and managing a QC program ✓ Establishing a comprehensive QC checklist ✓ Directly supervising or checking the 3D and/or intensity-modulated treatment planning process ✓ Consulting with radiation oncologist to discuss optimal patient plan ✓ Determine and check appropriate beam-delivery parameters (calculation of radiation beam parameters consistent with beam geometry) ✓ Double-checking beam delivery process to assure accurate fulfillment of prescription 	<ul style="list-style-type: none"> ✓ Preparing treatment room ✓ Assisting the treatment team with positioning/immobilization ✓ Operating treatment unit after radiation oncologist & medical physicists approved clinical technical aspects for beam delivery

Information derived from the American College of Radiology Practice Guideline 2006⁵⁴⁷

SBRT: Stereotactic body radiotherapy

SRS: Stereotactic radiosurgery

QC: Quality control

Appendix E. Recommendations

Recommendations for Stereotactic Body Radiation Therapy Procedures

Procedure Specifications	Accessory QC	Images QC	Treatment Planning QC	Simulation and Treatment	Followup
<ul style="list-style-type: none"> ✓ Treatment-delivery unit requires implementation of/adherence to QA program ✓ Mechanical tolerance must assure actual isocenter is within +/- 2 mm of planned isocenter ✓ Precision should be validated each treatment session by QA process ✓ QA: test beam alignment, calculate dose per unit time, measure MLC movement, measure gantry radiation fluence map for intensity modulated) 	<ul style="list-style-type: none"> ✓ Routinely monitor to assure proper function 	<ul style="list-style-type: none"> ✓ Digital images thoroughly investigated and corrected for significant spatial distortions ✓ Combining MRI with CT image fusion used to minimize geometrical distortions in MR images 	<ul style="list-style-type: none"> ✓ Various testing methods used with equal validity ✓ Maintain system log ✓ Check functionality and accuracy of input devices ✓ Assure functionality and accuracy of output devices ✓ Assure integrity of planning system files ✓ Verify transfer of MLC data and other parameters ✓ Assure system integrity of anatomical modeling ✓ Operational test before treating patients 	<ul style="list-style-type: none"> ✓ Comfortable position for the patient to "hold still" during treatment ✓ Respiratory motion accounting program ✓ Minimize the volume of surrounding normal tissues exposed to high dose levels ✓ Validate precision QC process with each treatment session and throughout the treatment process 	<ul style="list-style-type: none"> ✓ Maintenance of appropriate records ✓ Determine local control, survival, and normal tissue injury

Information derived from the American College of Radiology Practice Guideline 2006⁵⁴⁷

- CT: Computed tomography
- MLC: Multi-leaf collimator
- MR: Magnetic resonance
- MRI: Magnetic resonance imaging
- QA: Quality assurance
- QC: Quality control

Appendix F. Currently Marketed Devices for SBRT

Devices Currently Marketed for Stereotactic Body Radiation Therapy

Device Name	Manufacturer/ Distributor	Features	Dedicated to SRS	FDA Indication	Extracranial Indications Presented on Company Web site
Axesse™	Elekta	<ul style="list-style-type: none"> ✓ Beam delivery – wide range of noncoplanar angles ✓ Beam energy – multiple energy (photon) ✓ Collimation – MLC ✓ Design – image-guided robotic linac that combines high-conformance beam shaping with 4D Adaptive™ IGRT technology ✓ Dose delivery – multiple energy choices ✓ Imaging – CT/MR imaging with patient in immobilization (no fiducials necessary) ✓ Patient Positioning/Localization – BodyFIX dual vacuum-activated immobilization and fixation system; automatic reposition in up to 6 degrees of freedom ✓ Treatment Sessions – single and fractionated 	No	No response from FDA or manufacturer	Spinal metastases, lung, liver, prostate, head, neck

Device Name	Manufacturer/ Distributor	Features	Dedicated to SRS	FDA Indication	Extracranial Indications Presented on Company Web site
CyberKnife® robotic radiosurgery system	Accuray Incorporated	<ul style="list-style-type: none"> ✓ Beam delivery – noncoplanar and nonisocentric; anterior beam delivery ✓ Beam energy – 6 MV nominal (photon) ✓ Collimation – 12 fixed apertures; Xchange™ Robotic Collimator Changer automatically exchanges collimators ✓ Design – a treatment radiation generator, linear accelerator, manipulator (robot) with six degrees of freedom, and a target locating subsystem ✓ Dose delivery – A 6 MV X-band linac ✓ Field size – determined by the use of interchangeable secondary circular cones with diameters ranging from 5.0 to 60.0 mm ✓ Imaging – continuously delivers imaging to ensure target accuracy throughout the entire treatment; InTempo™ Adaptive Imaging System tracks and corrects for intra-fraction prostate motion ✓ Output – available at 800 MU/min at 80 cm, 600 MU/min, and 400 Mu/min ✓ Patient Positioning/Localization – only radiosurgery system to move to and with the patient; room-based stereo x-ray with 2D kV-kV match ✓ Tracking – Fiducial tracking, Xsight™ Spine Tracking, Xsight™ Lung Tracking, and Synchrony™ Respiratory Tracking for dynamic positioning and pointing of the linac ✓ Treatment Sessions – single and fractionated 	Yes	Treatment planning and image-guided SRS and precision RT for lesions, tumors and conditions anywhere in the body	Spine, lung, liver, prostate, pancreas, kidney, head, neck

Device Name	Manufacturer/ Distributor	Features	Dedicated to SRS	FDA Indication	Extracranial Indications Presented on Company Web site
Leksell Gamma Knife® Perfixion™	Elekta Inc.	<ul style="list-style-type: none"> ✓ Beam delivery – 192 cobalt-60 sources housed in the central body of the unit produce 192 collimated beams directed to a single focal point (isocenter) ✓ Collimation – 4,8, 16 mm diameter ✓ Design – a radiation unit with patient-positioning system and an operator console ✓ Dose delivery – multiple converging fixed beams of ionizing radiation ✓ Imaging – MRI/CT prior to treatment ✓ Output – >3 Gy/min ✓ Patient Fixation – head fixated in the Leksell® Stereotactic Frame. Awaiting approval on re-locatable frame. ✓ Total cobalt-60 activity at loading (approximate) – <6,300 Curie (2.33 x 10¹⁴ Bq) ✓ Treatment Sessions – single with availability of fractionated upon approval of Extend™ program 	No	Metastatic tumors, and head structure targets (a few millimeters to several centimeters)	Cervical spine, head, neck, larynx tumors
MHI-TM2000 Linear Accelerator System	Mitsubishi Heavy Industries (MHI)	<ul style="list-style-type: none"> ✓ Beam delivery – Gimballed x-ray irradiation offers tilt and pan-rotation functions enabling fine adjustments in any direction ✓ Collimation – MLC ✓ Design – O-ring-shaped mechanical structure provides a high level of rigidity; X-ray generator incorporates a compact accelerator tube ✓ Image Processing System – ExacTrac 3rd Party by BrainLAB (K072046 approved by FDA on 8/07) ✓ Treatment Sessions – single and fractionated 	No	Radiation therapy of lesions, tumors and conditions anywhere in the body	NR

Device Name	Manufacturer/ Distributor	Features	Dedicated to SRS	FDA Indication	Extracranial Indications Presented on Company Web site
Novalis TX™	BrainLAB/Varian Medical Systems	<ul style="list-style-type: none"> ✓ Accuracy - millimeter precision utilizing BrainLAB's iPlan and ExacTrac technologies ✓ Beam delivery – fixed beam positions and continuous arc delivery with RapidArc; anterior beam delivery and full 180 degree posterior beams ✓ Beam energy – 6-20 MV/6-20MEV ✓ Collimation –Varian's HD120 MLC 120 interleaved ultra thin collimators provides 2.5 mm collimation at isocenter and 5.0 mm collimations at the periphery. ✓ Design – includes Adaptive Gating and On-Board Imager devices ✓ Field size – 22 x 40 cm maximum ✓ Imaging – ExacTrac and x-ray 6D and Snap Verification ✓ Output – 1,000 MU at 100 cm ✓ Patient positioning/localization – 6D Robotic couch top, Varian Exact® couch ✓ Treatment Sessions – single and fractionated 	Yes	The Varian High Energy linear accelerator is intended to provide SRS and precision RT for lesions, tumors and conditions anywhere in the body	Spine, lung, liver, prostate, head, neck

Device Name	Manufacturer/ Distributor	Features	Dedicated to SRS	FDA Indication	Extracranial Indications Presented on Company Web site
Oncor ARTISTE, Impression, Avant-Garde, Expression	Siemens	<p>Artiste</p> <ul style="list-style-type: none"> ✓ Beam energy – 6 MV (photon) ✓ Collimation – 160 leaf MLC ✓ Design – includes an Electronic Portal Imaging Device (EPID), a 160 leaf MLC, and the syngo™ RT Therapist Express Workspace with MVision™ ✓ Imaging – OPTIVUE 1000ART amorphous silicon (a-Si) portal imaging system ✓ Patient-positioning verification – use of the OPTIVUE imaging system, including MVision™ Megavoltage Cone Beam (MVCB) Imaging and/or CTVision ✓ Respiratory Gating – ANZAI breathing belt system <p>Impression/Avant-Garde/Expression</p> <ul style="list-style-type: none"> ✓ Beam energy – 6/10 MV photon/ 6-21 MeV ✓ Collimation – OPTIFOCUS 82 leaf MLC (static and dynamic modes) ✓ Field size – 40 cm x 40 cm fully-conformal ✓ Imaging OPTIVUE 1000/ST electronic portal imaging device (EPID) and MVision™ megavoltage cone beam on-board imaging ✓ Output – 200-500 MU/min, special configuration-1,000 MU/min for maximum 5 x 5 cm field (Avant-Garde); 200-300 MU/min, special configuration-500 MU/min for maximum 5 x 5 field ✓ Patient position localization and setup – Adaptive Targeting™ supports alignment of 3D planning data with newly acquired 3D Cone Beam data ✓ Respiratory Gating – standard on Avant-Garde/ optional on Impression 	No	The delivery of x-ray radiation for therapeutic treatment of cancer.	Head, neck, extracranial areas

Device Name	Manufacturer/ Distributor	Features	Dedicated to SRS	FDA Indication	Extracranial Indications Presented on Company Web site
Synergy®S	Elekta Inc.	<ul style="list-style-type: none"> ✓ Beam delivery – a 62 cm treatment head in combination with industry best isocenter clearance allows for a wide variety of treatment approaches including noncoplanar ✓ Beam energy – 4, 6, 10, 15, 18, and 25 MV photon; 6, 9, 12, 15, 18, and 25 MeV ✓ Collimation – Beam Modulator, an integrated high-resolution, multi-leaf collimator designed for extracranial SRS ✓ Dose delivery system – includes an integrated multi-leaf collimator ✓ Field size – 16 cm x 21 cm ✓ Imaging – 4D Adaptive™ IGRT technology ✓ Patient positioning/localization – BodyFix® and HeadFix® immobilization accessories ✓ Treatment Sessions – single and fractionated 	No	Radiation therapy treatment of malignant neoplastic diseases	Spine, lung, liver, prostate, pancreas, head, neck
TomoTherapy® Hi-Art®	TomoTherapy Inc.	<ul style="list-style-type: none"> ✓ Accuracy – beam modulating technology that divides a single beam into “beamlets” to better conform to tumors ✓ Beam delivery – 360 degree ✓ Beam energy – 6 MV (photon) ✓ Collimation – 64 leaf MLC ✓ Design – linac mounted to a CT scanner-like ring gantry ✓ Field size – 40 cm x 1.6 meters maximum ✓ Imaging – integrated, 3D daily CTrue™ imaging ✓ Output – 850 cGy/min (photon)* ✓ Patient positioning/localization – AlignRT® (consisting of 2 ceiling-mounted 3D camera units) registers real-time image data and subsequently updates couch coordinates. Complements CTrue™ imaging when tumor is deep-seated or can move internally w/o external evidence ✓ Treatment Sessions – single and fractionated 	No	To tumors or other targeted tissues	Lung, liver, prostate, head, neck

Device Name	Manufacturer/ Distributor	Features	Dedicated to SRS	FDA Indication	Extracranial Indications Presented on Company Web site
Trilogy™	Varian Medical Systems	<ul style="list-style-type: none"> ✓ Accuracy – beam modulating technology that divides a single beam into “beamlets” to better conform to tumors ✓ Beam delivery – choice of Intensity modulated radiosurgery (IM-RS) with multi-leaf collimation – for lesions >2.5 cm, irregular shaped and >3 lesions OR Cone-based SRS for lesions <2.5 cm, not irregular and 1-3 lesions ✓ Beam energy – 6 MV (photon)/4-22 MeV (6 energies) ✓ Collimation – 120 leaf MLC and conical collimator ✓ Design – external system gating interface, remote couch motion ✓ Field size – 15 cm x 15 cm ✓ Imaging – PortalVision MV imager, On-Board kV Imager (amorphous silicon detector-based radiographic, fluoro and cone-beam CT). ✓ Output – 1,000 MU/min (photon and electron) ✓ Patient position/localization – optional optical imaging-based patient positioning (FrameArray, BodyArray, and SonArray) ✓ Respiratory Gating – Real-time Position Management™ (RPM) System ✓ Treatment Sessions – single and fractionated 	No	Lesions, tumors and conditions anywhere in the body	Whole body

*Data derived from⁵⁴⁸

AVM: Arteriovenous malformation

Bq: Becquerel

cGY/min: Centigray per minute

cm: Centimeter

CT/MR: Computed tomography/magnetic resonance

FDA: United States Food and Drug Administration

IGRT: Image guided radiation therapy

kV: Kilovolt

Linac: Linear accelerator

MEV: Million electron volt

MLC: Multi-leaf collimator

mm: Millimeter

MU/min: Monitor units per minute

MV: Megavolt

NR: Not reported

RS: Radiosurgery

RT: Radiotherapy

SRS: Stereotactic radiosurgery

SRT: Stereotactic radiotherapy

Appendix G. Linac-Based SBRT Accessories

Linac Accessories

Device Name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA Indications	Indications Presented on Company Web site	Compatibility
AccuChanger	Direx Systems Corporated	A linac-mounted, computer-controlled, fully automated collimator changer for multi arc or step-and-shoot cone based SRS. A unique fixed arrangement of multi-sized taped tungsten cones provides for fast and precise changing and positioning of the collimators. The available 16 circular fields, with diameters in the range of 4 mm to 34 mm in 2 mm steps, enable sharp radiosurgical delivery.	Yes	Collimation of megavoltage photon beams in conjunction with SRS and SRT treatments.	NR	Various linacs
AccuLeaf	Direx Systems Corporated	A computer controlled, video-guided micro multi-leaf collimator (MMLC). A unique two-level perpendicular leaf configuration, with a field size of approximately 100 mm x 110 mm, reduces effective leaf thickness and achieves a higher resolution, low leakage collimator for both conformal shaping and IMRT/IMSRS delivery.	No	Enables irregular field's treatments to be performed with finely shaped patterns; performs the same function as customized beam shaping blocks, and circular or cut blocks collimators.	NR	Various linacs

Device Name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA Indications	Indications Presented on Company Web site	Compatibility
Beam Modulator™	Elekta Inc.	Integrated multi-leaf collimator with a generous 16 x 21 cm field size. The field comprises 80 individually controlled leaves, each with a travel range of more than 21 cm. Because opposing leaves can pass each other (interdigitate), clinicians can create a range of finely shaped, high-resolution fields simultaneously within one field. This contributes to improved conformal avoidance of critical structures. The integrated design means no compromise in clearance for conventional and noncoplanar beams.	No	X-ray collimator, used with the Elekta range of medical linacs; intended to assist a licensed practitioner in the delivery of radiation in single or multiple fractions to defined target volumes anywhere in the body (e.g., lesions, AVMs, malignant and benign tumors) sparing surrounding normal tissue and critical organs from excess radiation.	NR	Elekta linacs
Dynamic Micro Multileaf Collimator (DMMLC)	Elekta Inc.	3 dynamic micro multileaf add-on collimators: a 3 mm, 5 mm and 7 mm leaf width (at isocenter) and 7x7, 10x12, and 10x17 field size (at isocenter) respectively. All options offer the facility for dynamic treatments and the improved homogeneity in target shaping, including minimizing dose to critical organs. The 3 mm and 5 mm DMMLCs are certified for use up to 18 MV making it an extremely versatile tool for SRT and SRS. To optimize beam shaping provided by the Elekta add on DMMLC, the leaves have been designed to be dual focused, minimizing and homogenizing the penumbra. Leakage and unwanted dose outside the target area is limited by the unique design of the leaves and the 8 cm leaf height.	No	Indicated for use when additional flexibility is required in conforming the radiation beam to the anatomy to be exposed.	NR	Elekta and a range of linacs from other vendors

Device Name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA Indications	Indications Presented on Company Web site	Compatibility
HD 120 MLC	Varian Medical Systems	HD120 provides 120 interleaved leaves: 64 – 2.5 mm centrally located 56 – 5 mm peripherally with a fixed treatment field of 22 cm x 40 cm and a modulated field of 22 cm x 32 cm., Output – 1,000 MU/min at 100 cm. Options: Gating – Real Time Position Management; Aria.	No	Target volumes during RS and RT		Varian's Trilogy
m³® (micro-Multileaf Collimator)	BrainLAB AG	The m ³ is a therapeutic collimator. It comprises multiple motorized tungsten leaves, which are suited to shaping specific therapeutic X-ray fields, both in a static fashion as well as dynamically via leaf-movement during treatment.	No	In conjunction with Elekta and GE Linacs, the m ³ performs with same function as customized shadow blocks or stereotactic collimators. This standard configuration is suitable for static conformal treatments and “step and shoot IMRT”. The advanced m ³ Siemens integration feature available for Siemens Linacs allows additionally to perform “dynamic arc” and automated “step and shoot IMRT” treatments with the m ³ . The advanced Varian integration feature available for Varian Linacs allows to perform “dynamic arc” and “dynamic IMRT” treatments with the m ³ .	To accommodate a higher-resolution dose delivery, new multileaf collimator designs with 5 mm thick leaves allow the delivery of fractionated SRS, but are not generally acceptable for single-fraction radiosurgery. For radiosurgery, the recommended limit for dose gradient in the beam penumbra (from 80% to 20%) is greater than or equal to 60%/3 mm. The m ³ with its 3 mm-thin leaves has an effective penumbra of less than 3 mm for all SRS field sizes and meets all SRS requirements.	Elekta, GE, Siemens, Varian

Device Name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA Indications	Indications Presented on Company Web site	Compatibility
micro MLC	Siemens Medical Solutions USA Inc.	The microMLC is a conformal RT and RS device that is mounted to a standard RT linac. The microMLC receives input from planning-system software that determines the collimator aperture shapes at different gantry positions along the arc around the target area. Radiation is delivered at a constant rate.	No	The microMLC is a conformal RT and RS device that delivers a shaped x-ray beam from a RT source. The microMLC is attached to a linac and consists of a series of pairs of tungsten leaves that collimate the radiation delivery to a target based on a treatment plan generated by planning software. The device is used to assist the clinician in the delivery of well-defined target volumes of radiation while sparing the surrounding tissues and organs.		
ModuLeaf™ Mini Multileaf Collimator	Siemens Medical Solutions	Features of the ModuLeaf™ include: 2.5 mm width at the isocenter, 80 leaves, 10 cm x 12 cm maximum field size at isocenter	No	A conformal RT and RS device that delivers a shaped X-ray beam from a RT source. The ModuLeaf is attached to a linac and consists of pairs of tungsten leaves that collimate the radiation delivery to a target based on a treatment plan generated by planning software. The device is used to help the clinician deliver well-defined target volumes of radiation while sparing the surrounding tissues and organs.	Extracranial target volumes where highest precision is required	Major linac systems

Device Name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA Indications	Indications Presented on Company Web site	Compatibility
XKnife™MMLC™	Radionics	A complete system consisting of an independent device that attaches to a Siemens linac for small field conformal radiosurgery or radiotherapy.		The delivery of radiation to well-defined target volumes while sparing surrounding normal tissue and critical organs from excess radiation. With Radionics' XPlan Conformal Treatment Planning Software or any treatment-planning system, the MMLC enables static conformal treatments to be performed with finely shaped field patterns. In this application, the MMLC performs the same function as customized beam shaping blocks, and circular or cut block collimators.	Spine and other sites	Siemens and a variety of other linacs

AVM: Arteriovenous malformation
 cm: Centimeter
 DMMLC: Dynamic Micro Multileaf Collimator
 FDA: United States Food and Drug Administration
 HD: High definition
 IMRT: Intensity modulated radiation therapy
 IMSRS: Intensity modulated stereotactic radiosurgery
 mm: Millimeter

MMLC: Micro multi-leaf collimator
 MU/min: Monitor units per minute
 MV: Megavolts
 NR: Not reported
 RS: Radiosurgery
 RT: Radiotherapy
 SRS: Stereotactic radiosurgery
 SRT: Stereotactic radiotherapy

Appendix H. Applicants' FDA 510K Information

Regulatory Status of Devices

Device Name	Manufacturer/ Distributor	510(k) Applicant	Substantial Equivalence	Classification Name	Product Code(s)	510(k) Number	Approval Date
AccuChanger⁵⁴⁹	Direx Systems Corporated	Direx Systems Corp.	AccuLeaf; Cranial stereotactic equipment k010065 Arplay/BrainLAB; Radionics XKnife*	Accelerator, Linear, Medical	IXI	K043409	05/05
AccuLeaf⁵⁵⁰	Direx Systems Corporated	Direx Systems Corp.	BrainLAB MMLC*	Accelerator, Linear, Medical	IXI	K040553	04/04
AxesseTM	Elekta Inc.			Approval documentation requested from FDA and manufacturer			
Beam Modulator^{TM 551}	Elekta Inc.	Elekta Ltd.	Millenium MLC (now Varian's HD 120 MLC); Moduleaf MLC (Siemens)	Radiation therapy beam-shaping block	90 IYE and IXI	K042794	01/05
CyberKnife® Robotic Radiosurgery System⁵⁵²	Accuray Incorporated	Accuray Corporation	Predicate device	Medical charged particle radiotherapy device	IYE	K072504	09/07
Dynamic Micro Multileaf Collimator (DMMLC)⁵⁵³	Elekta Limited	Elekta Limited	Predicate device	Medical Linear Accessory, IYE	IYE	K082122	08/08
HD 120 MLC⁵⁵⁴	Varian Medical Systems	Varian Medical Systems	Predicate device	Medical Charged Particle Radiation Therapy System	90 IYE	K071992	08/07
Leksell Gamma Knife® Perfexion^{TM 555}	Elekta Inc.	Elekta Ltd.	Predicate device	Radionuclide radiation therapy system	IWB	K063512	03/07

Device Name	Manufacturer/ Distributor	510(k) Applicant	Substantial Equivalence	Classification Name	Product Code(s)	510(k) Number	Approval Date
m3® (micro-Multileaf Collimator) ⁵⁵⁶	BrainLAB AG	BrainLAB AG	Predicate device	Accelerator, Linear, Medical	90 IYE	K020860	06/02
MHI-TM2000 ⁵⁵⁷	MHI Medical Systems/Hiroshima Machinery Works	Mitsubishi Heavy Industries, Ltd.	Trilogy; Hi-Art System	Accelerator, Linear, Medical	IYE	K072047	08/07
Micro MLC ⁵⁵⁸	Siemens Medical Solutions USA, Inc.	Siemens Medical Solutions	Predicate device	Accelerator, Linear, Medical	IXI	K032790	10/03
Moduleaf™ mini Multileaf Collimator ⁵⁵⁹	Siemens Medical Solutions	MRC Systems GmbH	Predicate device	Block, Beam Shaping, Radiation Therapy	90 IXI	K030609	03/03
Novalis TX™ ^{554,560-562}	BrainLAB AG/ Varian Medical Systems	BrainLAB AG/ Varian Medical Systems			Trilogy – 90 IYE HD120-90 IYE ETX™ (Exac- Trac) – IYE OBI – 90 IYE	Trilogy – K081188 HD120-K071992 ETX – K072046 OBI – K042720	07/08 08/07 10/07 10/04
Oncor Artiste, Impression, Avant-Garde, and Expression ⁵⁶³⁻⁵⁶⁵	Siemens Healthcare	Siemens Medical Solutions USA, Inc.	ONCOR linac family	Accelerator, Linear, Medical	IYE	Artiste – K072485 Avant-Garde – K031764 Expression – K060226	12/07 03/06 09/03
Synergy®S ⁵⁶⁶	Elekta	Elekta Limited	Predicate device	Medical Linear Accelerator Accessory 90 IYE	90 IYE	K051932	08/05
TomoTherapy® Hi-Art® ⁵⁶⁷⁻⁵⁷⁰	TomoTherapy, Inc.	TomoTherapy, Inc.	Varian Clinac 600*	Medical charged- particle radiation therapy system	MUJ	K082005 K060912 K042739 K013673	08/08 04/06 11/04 01/02

Device Name	Manufacturer/ Distributor	510(k) Applicant	Substantial Equivalence	Classification Name	Product Code(s)	510(k) Number	Approval Date
Trilogy™⁵⁶⁰	Varian Medical Systems	Varian Medical Systems	BrainLAB Novalis® Shaped Beam Surgery System; Varian Medical Systems' Clinac 2300 C/D	Medical charged- particle radiation therapy system	90 IYE	K081188	07/08
XKnife™ MMLC™⁵⁷¹ (Miniature multi-leaf collimator)	Radionics	Radionics		Radiotherapy beam shaping block	90 IYE	K993594 Asked Radionics to confirm	12/99

* Purged from CDRH database

CDRH: Center for Devices and Radiological Health

HD: High definition

MLC: Multi-leaf collimator

MMLC: Micro multi-leaf collimator

NR: Not reported

Appendix I. Manufacturer Web Sites

Manufacturers

Company	Web site
Accuray Incorporated ⁵⁷²	http://www.accuray.com
BrainLAB AG ⁵⁷³	http://www.brainlab.com http://www.poweringhope.com
Direx Systems Corp. ⁵⁷⁴	http://www.direxusa.com
Elekta Inc. ⁵⁷⁵	http://www.elekta.com
MHI Medical Systems Inc. ⁵⁷⁶	http://www.mhi.co.jp/en/index.html
Radionics ⁵⁷⁷	http://www.radionics.com
Siemens USA ⁵⁷⁸	http://www.medical.siemens.com
TomoTherapy Incorporated ⁵⁷⁹	http://www.tomotherapy.com
Varian Medical Systems ⁵⁸⁰	http://www.varian.com

Appendix J. Facilities Performing SBRT for Solid Tumors

Facilities (Information updated September 2009)

Hospital Name	State	City	Device(s)	Treatment Site(s)
St. Vincent's Medical Center	AK	Little Rock	Novalis TX	NS
CyberKnife of Birmingham	AL	Birmingham	CyberKnife	Colon, Kidney, Lung, Ovaries, Pancreas, Prostate, Uterus
Gulf Coast Cancer Centers	AL	Foley	Novalis	Liver mets, Lung
University of Alabama Hospital	AL	Birmingham	Tomotherapy	Prostate
University of Southern Alabama	AL	Mobile	CyberKnife	NS
Banner Good Samaritan Med Center	AZ	Phoenix	Tomotherapy, Novalis TX	NS
Mayo Clinic Hospital	AZ	Phoenix	NR	NS
Scottsdale Healthcare-Osborn	AZ	Scottsdale	Novalis	Breast, Liver, Lung, Pancreas, Prostate, Rectal
Scottsdale Healthcare-Shea	AZ	Scottsdale	Novalis	Breast, Liver, Lung, Pancreas, Prostate, Rectum
St. Joseph's/Carondolette	AZ	Tucson	Novalis TX	NS
St. Joseph's Hospital and Med Center	AZ	Phoenix	CyberKnife	Abdomen, Chest
University Medical Center	AZ	Tucson	Novalis	Liver and other extracranial locations
Cedars-Sinai Medical Center	CA	Los Angeles	NR	Lung
City of Hope National Medical Center	CA	Duarte	Tomotherapy	Lung, Prostate
Community Reg MC/CA Cancer Center	CA	Fresno	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate
Comprehensive Blood and Cancer Center	CA	Bakersfield	CyberKnife	NS
CyberKnife Centers of San Diego, Inc. Ruffin	CA	San Diego	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
CyberKnife Centers of San Diego, Inc., Encinitas	CA	Encinitas	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
CyberKnife of Southern California at Vista	CA	Vista	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Eisenhower Medical Center	CA	Rancho Mirage	Novalis TX	Prostate
El Camino Hospital	CA	Mountain View	Novalis	NS
Hoag Memorial Hospital Presbyterian	CA	Newport Beach	Tomotherapy	Liver Mets, Lung Mets
John Muir Medical Center, Walnut Creek	CA	Walnut Creek	Novalis	Breast, Colon, Liver, Liver Mets, Lung Mets, Prostate

Hospital Name	State	City	Device(s)	Treatment Site(s)
Kaiser Permanente	CA	San Francisco	CyberKnife	NS
Kaiser – Roseville	CA	Roseville	Novalis TX	NS
Long Beach Memorial Medical Center	CA	Long Beach	Tomotherapy	Pelvis, Prostate
Miller Children’s Hospital	CA	Long Beach	Tomotherapy	NS
Newport Diagnostic Center	CA	Newport Beach	CyberKnife	Prostate (pending)
Palo Alto Medical Center	CA	Palo Alto	Novalis TX	NS
Palomar Hospital	CA	Escondido	Novalis TX	NS
Pomona Valley Hospital Medical Center	CA	Pomona	Trilogy	Prostate and other extracranial sites
Saint Agnes Medical Center	CA	Fresno	Novalis	NS
Santa Barbara Hospital	CA	Santa Barbara	Novalis TX	NS
Select Healthcare (Orange County Memorial)	CA	Fountain Valley	CyberKnife	Liver, Lung
Sharp Grossmont Hospital	CA	La Mesa	Tomotherapy, Novalis	Prostate and other extracranial sites
Sharp Memorial Hospital	CA	San Diego	Novalis	Prostate and other extracranial sites
St. Bernardine Medical Center	CA	San Bernardino	Tomotherapy	Prostate and other extracranial sites
St. Joseph Hospital	CA	Orange	Trilogy	NS
Stanford Hospital and Clinics	CA	Palo Alto	CyberKnife (2)	Liver, Lung, Pancreas, Prostate
UCLA	CA	Los Angeles	Novalis TX	NS
UCSF Medical Center	CA	San Francisco	CyberKnife	Lung, Pancreas, Prostate
Univ of CA San Diego Medical Center	CA	San Diego	Trilogy	NS
Univ of CA, Davis Medical Center	CA	Sacramento	Novalis	NS
Univ of CA, Irvine Medical Center	CA	Orange	Trilogy	NS
Boulder Community Hospital	CO	Boulder	CyberKnife	NS
Denver CyberKnife Center	CO	Lone Tree	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Penrose Hospital	CO	Colorado Springs	CyberKnife	Liver, Lung, Pancreas, Prostate
Poudre Valley Hospital	CO	Fort Collins	NR	NS
Rocky Mountain Cancer Center	CO	Aurora	Novalis TX	NS
Rocky Mountain CyberKnife	CO	Boulder	CyberKnife	Liver, Lung, Musculoskeletal, Pancreas, Prostate
University of CO Hospital/Anschutz Cancer Pavilion	CO	Aurora	Novalis	NS

Hospital Name	State	City	Device(s)	Treatment Site(s)
St. Anthony's Hospital	CO	Denver	Novalis TX	NS
Cyberknife Center at St. Francis	CT	Hartford	CyberKnife	Liver, Lung, Pancreas, Prostate
CyberKnife Center at Stamford Hospital	CT	Stamford	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Hartford Hospital	CT	Hartford	Trilogy	NS
Hospital of Central CT	CT	New Britain	Novalis	Lung, Prostate
Yale University	CT	New Haven	Novalis TX	NS
Hospital of Saint Raphael	CT	New Haven	CyberKnife	Liver, Lung, Pancreas, Prostate
Georgetown University Hospital –MedStar Health	DC	Washington	CyberKnife	Kidney, Liver, Lung
Washington Hospital Center	DC	Washington	Trilogy	NS
Christiana Hospital	DE	Newark	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate
Baptist Hospital of Miami	FL	Miami	Tomotherapy	Bone, Breast, Lung, Prostate
Baptist Hospital/University of Northern FL	FL	Jacksonville	Novalis TX	NS
Bethesda Memorial Hospital	FL	Boynton Beach	Trilogy	Kidney, Liver, Lung, Pancreas
Blake Medical Center	FL	Bradenton	CyberKnife	Spine
Boca Raton Community Hospital	FL	Boca Raton	Novalis TX	NS
Brandon Regional Hospital HCA	FL	Brandon	CyberKnife	Bile Duct, Bone, Colon/rectum, Kidney, Liver, Lung, Lymph node, Pancreas, Prostate
Broward General Medical Center	FL	Fort Lauderdale	CyberKnife, Trilogy	Liver, Lung, Pancreas
Cancer Care Centers of Brevard	FL	Melbourne	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvic Organs, Prostate, Skin
Capital Regional Medical Center	FL	Tallahassee	Tomotherapy	Prostate
Coastal CyberKnife and Radiation Oncology	FL	Fort Pierce	CyberKnife	NS
CyberKnife Cancer Center	FL	Jacksonville	CyberKnife	Liver (primary and mets), Pancreas, Prostate
CyberKnife Center of Miami	FL	Miami	CyberKnife	Bladder, Breast, Gynecologic, Liver, Lung, Pancreas, Prostate
CyberKnife Center of Palm Beach	FL	Palm Beach Gardens	CyberKnife	Liver, Lung, Pancreas, Prostate
CyberKnife Center of Tampa Bay	FL	Tampa	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Doctors Hospital	FL	Coral Gables	Tomotherapy	Bone, Breast, Lung, Prostate
Florida Hospital	FL	Orlando	Trilogy	NS

Hospital Name	State	City	Device(s)	Treatment Site(s)
H. Lee Moffitt Cancer Center	FL	Tampa	Tomotherapy, Novalis	NS
HCA Central Florida	FL	Sanford	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis, Prostate
Jackson Health System	FL	Miami	CyberKnife	Breast
Jupiter Medical Center	FL	Jupiter	CyberKnife, Trilogy	NS
Martin Memorial Hospital	FL	Stuart	Novalis TX	NS
Mayo Clinic Jacksonville	FL	Jacksonville	NR	NS
M.D. Anderson Cancer Center/Orlando	FL	Orlando	Novalis	Lung
Melbourne Internal Medicine Associates	FL	Melbourne	Novalis TX	NS
Memorial Hospital of Jacksonville	FL	Jacksonville	CyberKnife	Liver, Lung, Pancreas, Prostate
Mount Sinai Medical Center	FL	Miami Beach	Trilogy	NS
New Millenium CyberKnife	FL	Brandon	CyberKnife	NS
North Broward Medical Center	FL	Deerfield Beach	CyberKnife, Trilogy	Liver, Lung, Pancreas
North Florida Regional Medical Center	FL	Gainesville	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate
Orlando Regional Medical Center	FL	Orlando	Tomotherapy, Novalis	Liver, Lung
Sacred Heart Hospital of Pensacola	FL	Pensacola	Trilogy	NS
Shands at the University of Florida	FL	Gainesville	Trilogy	NS
South Miami Hospital	FL	Miami	Tomotherapy	NS
University of Florida	FL	Gainesville	Trilogy TX	NS
Wellington Regional Medical Center	FL	Wellington	Novalis	NS
Emory Crawford Long Hospital	GA	Atlanta	Trilogy	NS
Emory University	GA	Atlanta	Trilogy TX	NS
Fannin Regional Hospital	GA	Blue Ridge	NR	NS
Medical College of Georgia Health	GA	Augusta	Trilogy	NS
Memorial Health	GA	Savannah	Trilogy	NS
Piedmont Hospital	GA	Atlanta	Trilogy	NS
South Georgia Medical Center	GA	Valdosta	Synergy	NS
Wellstar Kennestone Hospital	GA	Marietta	CyberKnife	NS
Clarinda Regional Health Center	IA	Clarinda	Novalis	NS
CyberKnife Radiosurgery Center of Iowa	IA	Des Moines	CyberKnife	Liver, Lung

Hospital Name	State	City	Device(s)	Treatment Site(s)
Mercy Medical Center	IA	Cedar Rapids	Tomotherapy	Prostate
Mercy Medical Center-Des Moines	IA	Des Moines	NR	Spine
Saint Alphonsus Regional Medical Center	ID	Boise	Novalis	Liver, Lung, Prostate
Advocate Christ Medical Center	IL	Oak Lawn	CyberKnife	Lung, Pancreas, Prostate
Advocate Good Samaritan Hospital	IL	Downers Grove	CyberKnife	Liver, Lung, Pancreas, Prostate
Advocate Lutheran General Hospital	IL	Park Ridge	Tomotherapy	Bone Mets, Gynecologic, Pancreas, Prostate
CyberKnife Service at Community Cancer Center	IL	Normal	CyberKnife	NS
Edward Hospital	IL	Naperville	Trilogy	Lung, Prostate
Elmhurst Memorial Hospital	IL	Elmhurst	CyberKnife	Liver, Lung, Pancreas, Prostate
Evanston Hospital	IL	Evanston	Novalis	Breast, Liver, Lung, Prostate
Loyola University Medical Center	IL	Maywood	Novalis	NS
Northwest Community Hospital	IL	Arlington Heights	CyberKnife	Liver, Lung, Pancreas, Prostate
OSF Saint Francis Medical Center	IL	Peoria	Trilogy	NS
Provena Saint Joseph Hospital	IL	Elgin	Trilogy	NS
Provena Saint Joseph Medical Center	IL	Joliet	Trilogy	NS
Rush University Medical Center	IL	Chicago	Tomotherapy	Prostate
Saint Joseph Hospital	IL	Chicago	Tomotherapy	NS
Univ of IL Medical Center at Chicago	IL	Chicago	Trilogy	Metastatic treatment
University of Chicago Medical Center	IL	Chicago	Trilogy	Metastatic treatment
Clarian Health Partners	IN	Indianapolis	Novalis	NS
Community Hospital	IN	Munster	CyberKnife, Trilogy	Liver, Lung, Pancreas
CyberKnife Center St. Catherine Hospital	IN	East Chicago	CyberKnife	Liver Mets, Lung, Pancreas
CyberKnife of Indianapolis	IN	Indianapolis	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate
Goshen General Hospital	IN	Goshen	Tomotherapy, Trilogy	Breast, Colon, Liver, Lung, Prostate
Memorial Hospital of South Bend	IN	South Bend	Trilogy	NS
Methodist Hospitals	IN	Gary	NR	Lung Mets
Parkview Health	IN	Fort Wayne	CyberKnife	Liver, Lung, Pancreas, Pelvis
St. Mary's Medical Center of Evansville	IN	Evansville	Novalis, Tomotherapy	NS
St. Vincent Indianapolis Hospital	IN	Indianapolis	Novalis	Liver, Lung, and Prostate

Hospital Name	State	City	Device(s)	Treatment Site(s)
St. Vincent Jennings Hospital	IN	North Vernon	Novalis	Liver, Lung, and Prostate
St. Vincent Randolph Hospital	IN	Winchester	Novalis	Liver, Lung, and Prostate
Menorah Medical Center	KS	Overland Park	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Providence Medical Center	KS	Kansas City	Trilogy	Liver, Lung, Pancreas
University of Kansas Hospital	KS	Kansas City	Novalis	NS
Via Christi Regional Medical Center	KS	Wichita	CyberKnife	NS
Baptist Hospital East	KY	Louisville	Novalis	Liver, Lung, Prostate
Central Baptist Hospital	KY	Lexington	CyberKnife	NS
CyberKnife Ctr W. Jefferson Med Center	LA	Marrero	CyberKnife	Liver, Lung, Pancreas
CyberKnife of Louisiana	LA	Lafayette	CyberKnife	Liver, Lung, Pancreas, Prostate, Skeletal
East Jefferson Hospital	LA	Metairie	Novalis TX	NS
Mary Bird Perkins Cancer Center	LA	Baton Rouge	Tomotherapy, Novalis	Prostate, Liver
Rapides Regional Medical Center	LA	Alexandria	Trilogy	NS
Slidell Memorial Hospital	LA	Slidell	Trilogy	NS
Baystate Medical center	MA	Springfield	NR	NS
Beth Israel Deaconess Medical Center	MA	Boston	CyberKnife	Liver, Lung, Pancreas, Prostate
Boston Medical Center	MA	Boston	CyberKnife	Liver, Lung, Pancreas, Prostate
Brigham and Women's Hospital	MA	Boston	NR	Lung, Prostate
Brigham and Women's/Harvard	MA	Boston	Novalis TX	NS
Dana Farber Cancer Institute	MA	Boston	Novalis	NS
Children's Hospital Boston	MA	Boston	Novalis	NS
Lahey Clinic Hospital	MA	Burlington	Trilogy	Liver, Lung, Pancreas
Lowell General Hospital	MA	Lowell	Synergy	Prostate
Massachusetts General Hospital	MA	Boston	NR	NS
Mercy Medical Center	MA	Springfield	Synergy	NS
Milford Regional Medical Center	MA	Milford	NR	NS
New England Medical Center	MA	Boston	Axesse	Liver Mets, Lung, Prostate
Northshore Medical Center	MA	Peabody	Novalis TX	NS
St. Ann's Hospital	MA	Fall River	Novalis TX	NS

Hospital Name	State	City	Device(s)	Treatment Site(s)
UMass Memorial Medical Center	MA	Worcester	NR	NS
Anne Arundel Medical Center	MD	Annapolis	Novalis	Liver, Lung, Prostate
Baltimore Washington Medical Center	MD	Glen Burnie	NR	Lung, Nasal, Skeletal Mets
Franklin Square Hospital Center	MD	Baltimore	CyberKnife	Lung
Frederick Memorial Hospital	MD	Frederick	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate, Skeletal Mets
Johns Hopkins Hospital	MD	Baltimore	Tomotherapy	Prostate
Maryland Regional Cancer Care	MD	Rockville	Novalis	Liver, Lung, Prostate
Peninsula Regional Health System	MD	Salisbury	Trilogy	NS
Sinai Hospital of Baltimore	MD	Baltimore	CyberKnife (2)	Liver, Lung, Pancreas, Prostate
St. Agnes HealthCare	MD	Baltimore	Tomotherapy	NS
University of Maryland Medical Center	MD	Baltimore	Trilogy	NS
York Hospital	ME	York	Trilogy	NS
Bay Regional Medical Center	MI	Bay City	Tomotherapy	NS
Beaumont Hospital - Royal Oak	MI	Royal Oak	Synergy	Breast, Lung, Pancreas, Prostate
Henry Ford – Downriver	MI	Trenton	Trilogy TX	NS
Henry Ford Hospital	MI	Detroit	Trilogy TX, Novalis	Adrenal, Liver, Lung, Pancreas
Henry Ford Hospital – WBC	MI	West Bloomfield Campus	Novalis TX	NS
Karmanos Cancer Center	MI	Detroit	Tomotherapy	Lung, Prostate
Lemme Holton Cancer Center	MI	Grand Rapids	Novalis TX	
McLaren Regional Medical Center	MI	Flint	Tomotherapy	NS
MidMichigan Medical Center-Midland	MI	Midland	NR	Kidney, Liver, Lung Mets, Prostate
North Oakland Medical Centers	MI	Pontiac	Tomotherapy	NS
Oakwood Hospital/Med Center	MI	Dearborn	NR	Adrenal, Kidney, Liver, Lung, Pelvis
Saint Mary's Health Care	MI	Grand Rapids	Tomotherapy	NS
Sparrow Health System	MI	Lansing	Tomotherapy	NS
Spectrum Health	MI	Grand Rapids	Novalis	NS
St. Joseph Mercy	MI	Ann Arbor	CyberKnife	Liver, Lung, Pancreas, Prostate
St. Mary's of Michigan	MI	Saginaw	CyberKnife, Tomotherapy	Liver, Lung, Pancreas, Prostate
Abbott Northwestern Hospital	MN	Minneapolis	Trilogy	Pancreas

Hospital Name	State	City	Device(s)	Treatment Site(s)
Park Nicollet Health – Frauenshuh Cancer Ctr	MN	St. Louis Park	Novalis	Liver, Lung, Pancreas
St. Cloud Hospital	MN	Saint Cloud	Synergy	NS
St. Joseph’s Hospital	MN	Saint Paul	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis, Prostate
St. Luke’s Hospital	MN	Duluth	NR	NS
Barnes-Jewish Hospital	MO	Saint Louis	NR	Gynecologic, Lung Mets
Ellis Fischel Cancer Center	MO	Columbia	Trilogy	NS
Lake Saint Louis Oncology/SLU Hospital	MO	Saint Louis	CyberKnife	Liver, Lung, Pancreas, Prostate
Mercy Saint John’s Cancer Center	MO	Springfield	CyberKnife	Liver, Lung, Pancreas
Research Medical Center	MO	Kansas City	NR	Liver, Pancreas
Saint Francis Medical Center	MO	Cape Girardeau	NR	NS
Saint Louis University Hospital	MO	Saint Louis	CyberKnife	Liver, Lung, Pancreas, Prostate
Saint Luke’s Hospital of Kansas City	MO	Kansas City	Novalis	NS
Southeast Missouri Hospital	MO	Cape Girardeau	Novalis	NS
SSM DePaul Health Center	MO	Bridgeton	Tomotherapy	NS
St. Anthony’s Medical Center	MO	Saint Louis	Trilogy	Lung and other extracranial sites
St. Luke’s Hospital	MO	Chesterfield	Trilogy	NS
University of Missouri/Ellis Fischel	MO	Columbia	Trilogy TX	NS
Baptist Medical Center	MS	Jackson	CyberKnife	Liver, Lung, Pancreas
Mississippi Baptist Medical Center	MS	Jackson	CyberKnife	Liver, Lung, Pancreas
Benefis Healthcare System	MT	Great Falls	CyberKnife	Lung, Pancreas, Prostate
Kalispell Regional Medical Center	MT	Kalispell	Trilogy	NS
Carloinas Medical Center	NC	Charlotte	Novalis TX	NS
Columbus Reg Healthcare System	NC	Whiteville	NR	NS
Duke University Hospital	NC	Durham	Novalis TX	Liver
East Carolina University CyberKnife Center	NC	Greenville	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Grace Hospital	NC	Morganton	Novalis	NS
Mission Hospitals	NC	Asheville	CyberKnife	Kidney, Liver, Lung, Pancreas

Hospital Name	State	City	Device(s)	Treatment Site(s)
North Carolina Baptist Hospital (Wake Forest University Baptist Medical Center)	NC	Winston-Salem	NR	Lung
University of North Carolina Hospitals	NC	Chapel Hill	CyberKnife	Adrenals, Kidney, Liver, Lung, Pancreas, Prostate
Alegent Health Bergan Mercy M Center	NE	Omaha	Tomotherapy	Breast, Lung, Prostate
Alegent Health Lakeside Hospital	NE	Omaha	Tomotherapy	Breast, Lung, Prostate
Columbus Community Hospital	NE	Columbus	NR	NS
Nebraska Medical Center	NE	Omaha	Novalis	Liver, Lung, Prostate
St. Elizabeth CyberKnife Center	NE	Lincoln	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Dartmouth-Hitchcock Medical Center	NH	Lebanon	Trilogy	Lung
Elliot Hospital	NH	Manchester	Novalis	Prostate
Huggins Hospital	NH	Wolfeboro	NR	NS
Wentworth-Douglas Medical Center	NH	Dover	Novalis TX, Trilogy TX	NS
Capital Health System at Mercer	NJ	Trenton	CyberKnife	Liver, Lung, Pancreas
CentraState Healthcare System	NJ	Freehold	NR	Liver, Lung
Christ Hospital	NJ	Jersey City	NR	NS
Community Medical Center	NJ	Toms River	Tomotherapy	NS
Cooper CyberKnife Center	NJ	Mount Laurel	CyberKnife	Liver, Lung, Pancreas, Prostate
Cooper Health System	NJ	Camden	CyberKnife	Bone (primary/mets), Liver, Lung, Pancreas, Prostate
Monmouth Medical Center	NJ	Long Branch	Tomotherapy	Lung, Prostate
Morristown Memorial Hospital	NJ	Morristown	CyberKnife	Liver/ Lung/Spine (primary/mets), Pancreas, and Prostate
Newark Beth Israel Medical Center	NJ	Newark	Tomotherapy	NS
Overlook Hospital	NJ	Summit	CyberKnife	Liver, Lung, Pancreas, Prostate
Riverview Medical Center	NJ	Red Bank	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate
Robert Wood Johnson Univ Hosp	NJ	Hamilton	NR	NS
Robert Wood Johnson Univ Hospital	NJ	New Brunswick	NR	NS
Saint Barnabas Medical Center	NJ	Livingston	Tomotherapy, CyberKnife	Prostate and other extracranial sites
Somerset Medical Center	NJ	Somerset	Novalis TX	NS

Hospital Name	State	City	Device(s)	Treatment Site(s)
University of Medicine -University Hospital	NJ	Newark	Tomotherapy	NS
Valley Hospital	NJ	Ridgewood	Tomotherapy	NS
Presbyterian Hospital	NM	Albuquerque	NR	Lung
Banner Churchill Community Hospital	NV	Fallon	Tomotherapy	NS
CyberKnife of Reno	NV	Reno	CyberKnife	Liver, Lung, Musculoskeletal, Pancreas, Prostate
Renown Regional Medical Center	NV	Reno	Tomotherapy	Bone, Breast, Colon, Gynecolog., Lymph Nodes, Rectum, Pancreas, Stomach
Columbia University	NY	New York	Trilogy TX	NS
CyberKnife Center of New York	NY	Johnson City	CyberKnife	Liver, Lung, Pancreas, Prostate
Highland Hospital of Rochester	NY	Rochester	Tomotherapy, Trilogy, Novalis	Liver and other extracranial sites
Long Island Jewish Medical Center	NY	New Rochelle	NR	NS
Memorial Sloan-Kettering Cancer Center	NY	New York	Trilogy	Bone Mets, Lung, Pelvis, Prostate, Skin
Mount Sinai Hospital	NY	New York	Novalis	Liver, Lung
New York-Presbyterian Hospital	NY	New York	CyberKnife	NS
North Shore University Hospital	NY	Manhasset	Novalis	Liver, Lung, Prostate
Northern Westchester Hospital	NY	Mount Kisco	Trilogy	NS
Roswell Park Cancer Institute	NY	Buffalo	Trilogy	Breast, Liver, Lung, Pancreas, Prostate
St. Peter's Hospital	NY	Albany	Novalis	Liver, Lung
Stony Brook University Hospital	NY	Stony Brook	NR	NS
Strong Memorial Hospital	NY	Rochester	Novalis, Trilogy	NS
United Health Services Hosp	NY	Binghamton	CyberKnife	Liver, Lung, Pancreas, Prostate
Westchester County Medical Center	NY	Valhalla	Novalis	NS
Winthrop University Hospital	NY	Mineola	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Cleveland Clinic Foundation	OH	Cleveland	Novalis	Kidney, Liver, Lung
Doctors Hospital	OH	Columbus	Trilogy	Lung
Flower Hospital	OH	Sylvania	Tomotherapy, Trilogy	NS
Grady Memorial Hospital	OH	Delaware	Trilogy	Lung
Grant Medical Center	OH	Columbus	Trilogy	Lung
James Cancer Hospital	OH	Columbus	NR	NS

Hospital Name	State	City	Device(s)	Treatment Site(s)
Jewish Hospital	OH	Cincinnati	Trilogy	NS
Mercy Medical Center	OH	Canton	Trilogy	NS
Precision Radiotherapy	OH	West Chester	Novalis, Tomotherapy	Breast, Gynecol., Liver, Lung, Pancreas, Prostate, Rectum
Riverside Methodist Hospital	OH	Columbus	Trilogy	Lung
Southern Ohio Medical Center	OH	Portsmouth	Synergy	NS
Southwest General Health Center	OH	Middleburg Heights	CyberKnife, Tomotherapy	Breast, Gynecologic, Kidney, Liver, Lung, Pancreas, Prostate
Summa Health System	OH	Akron	Novalis	NS
Univ Hosp Geauga Regional Hospital	OH	Chardon	CyberKnife, Novalis	Liver, Lung, Pancreas, Prostate
University Hospital	OH	Cincinnati	Lexar	NS
University Hospitals Case Medical Center	OH	Cleveland	CyberKnife, Novalis	Breast, Gynecological, Kidney, Liver, Lung, Pancreas, Prostate
Baptist Medical Center	OK	Oklahoma City	Novalis TX	NS
Deaconess Hospital	OK	Oklahoma City	Tomotherapy	Prostate
Hillcrest Medical Center	OK	Tulsa	CyberKnife	NS
Mercy Health Center	OK	Oklahoma City	CyberKnife	NS
Oklahoma CyberKnife	OK	Tulsa	CyberKnife	Liver, Lung, Pancreas, Prostate
OU Medical Center	OK	Oklahoma City	Trilogy	NS
Saint Anthony Hospital	OK	Oklahoma City	CyberKnife	NS
St. John Medical Center	OK	Tulsa	CyberKnife	Liver, Lung, Pancreas, Prostate
Legacy Emanuel Hospital and Health center	OR	Portland	Novalis	Breast, Liver, Lung, Prostate
OHSU Hospital	OR	Portland	Trilogy, Novalis TX	NS
Providence Portland Medical Center	OR	Portland	CyberKnife	Lung
Abington Memorial Hospital	PA	Abington	NR	NS
Allegheny General Hospital	PA	Pittsburgh	Xknife	Lung
Easton Hospital	PA	Easton	Tomotherapy, Trilogy	NS
Fox Chase Cancer Center	PA	Philadelphia	Trilogy, CyberKnife	Lung mets (Trilogy), NS (CyberKnife)
Frankford Hospital	PA	Philadelphia	Trilogy	Prostate
Geisinger Medical Center	PA	Danville	Trilogy	Lung

Hospital Name	State	City	Device(s)	Treatment Site(s)
Hamot Medical Center	PA	Erie	Trilogy	NS
Hospital of the Univ of PA	PA	Philadelphia	Trilogy, Oncor, Synergy	NS
Lankenau Hospital	PA	Wynnewood	NR	NS
Meadville Medical Center	PA	Meadville	Trilogy	NS
Penn State Milton S. Hershey Medical Center	PA	Hershey	Trilogy	NS
Pennsylvania Hospital	PA	Philadelphia	Trilogy, Oncor	NS
Philadelphia CyberKnife Center	PA	Havertown	CyberKnife	Liver, Lung, Musculoskeletal, Pancreas, Pelvis, Prostate
Pocono Medical Center	PA	East Stroudsburg	NR	NS
Reading Hospital and Medical Center	PA	West Reading	Trilogy	Kidney, Liver, Lung, Pancreas
St. Luke's Hospital - Bethlehem Campus	PA	Bethlehem	Trilogy	Lung
St. Luke's Miner's Memorial Hospital	PA	Coaldale	Trilogy	Lung
Temple University Hospital	PA	Philadelphia	Synergy	NS
Thomas Jefferson University Hospital	PA	Philadelphia	Novalis	NS
UPMC Bedford Memorial	PA	Everett	Trilogy	NS
UPMC Mercy	PA	Pittsburgh	Trilogy, Cyberknife	NS
UPMC Presbyterian	PA	Pittsburgh	Trilogy	NS
UPMC Shadyside Hospital	PA	Pittsburgh	Trilogy, Cyberknife	Abdomen, Lung, Pelvis
Western Pennsylvania Hospital	PA	Pittsburgh	XKnife	Lung
HIMA San Pablo	PR	Caguas	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Rhode Island Hospital	RI	Providence	Trilogy, CyberKnife	Breast, Kidney, Liver, Lung, Pancreas, Pelvis, Prostate, Skin
Cancer Centers of the Carolinas and Greenville Hospital System	SC	Greenville	Novalis	Liver, Lung, Prostate
MUSC Medical Center	SC	Charleston	Tomotherapy	Abdomen, Prostate
Roper Hospital	SC	Charleston	CyberKnife	Liver, Lung, Pancreas, Prostate
Sanford Univ of SD Medical Center	SD	Sioux Falls	Novalis	NS
Centennial Medical Center	TN	Nashville	CyberKnife	Liver, Lung, Pancreas, Prostate
University of Tennessee Medical Center	TN	Knoxville	CyberKnife	Liver, Lung, Pancreas, Prostate
Vanderbilt University	TN	Nashville	Novalis TX	NS

Hospital Name	State	City	Device(s)	Treatment Site(s)
Wellmont Bristol Regional Med Center	TN	Bristol	CyberKnife	NS
Baylor Medical Center at Garland	TX	Garland	CyberKnife	NS
Baylor/Sammons Cancer Center	TX	Dallas	Novalis TX	NS
Baylor University Medical Center	TX	Dallas	CyberKnife	NS
Brain and Spine Center/Brackenridge Hospital	TX	Austin	CyberKnife	Liver, Lung, Pancreas, Prostate
East Texas Medical Center Tyler	TX	Tyler	CyberKnife	Lung, Pancreas, Prostate
Harris Methodist Hospital	TX	Fort Worth	Novalis TX	NS
Memorial Herman Hospital SW	TX	Houston	Trilogy TX	NS
Methodist Hospital	TX	San Antonio	CyberKnife, Novalis, Tomotherapy	Liver, Lung, Prostate
North Cypress Medical Center	TX	Cypress	NR	Kidney, Liver/Lung Mets, Lung, Pancreas, Pelvis, Prostate
Richardson Regional Medical Center	TX	Richardson	Novalis	Liver, Lung, Prostate
South Texas Oncology and Hematology at the START Center	TX	San Antonio	CyberKnife, Tomotherapy	NS
Spring Branch Medical Center	TX	Houston	NR	Adrenals, Liver, Lung, Pancreas, Pelvis, Prostate
St. Luke's Episcopal Health System Corp.	TX	Houston	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate
Tyler Cancer Center	TX	Tyler	Novalis TX	NS
Texas Health Harris Methodist Fort Worth	TX	Fort Worth	CyberKnife	NS
Texas Health Presbyterian Hosp	TX	Dallas	CyberKnife	NS
The Methodist Hospital	TX	Houston	NR	Liver, Lung
Univ of TX (CTRC)	TX	San Antonio	Novalis TX	NS
Univ of TX M. D. Anderson Cancer Center	TX	Houston	NR	Lung
Univ of TX Medical Branch	TX	Galveston	Novalis	Abdomen, Liver, Lung
Univ of TX Southwestern Medical Center	TX	Dallas	CyberKnife	Prostate and other extracranial sites
Walls Regional Hospital	TX	Cleburne	CyberKnife	Liver, Lung, Pancreas, Prostate
Primary Children's Medical Center	UT	Salt Lake City	Trilogy	NS
Salt Lake CyberKnife	UT	Salt Lake City	CyberKnife	Liver, Lung, Musculoskeletal, Pancreas, Prostate
University of Utah	UT	Salt Lake City	Novalis	NS

Hospital Name	State	City	Device(s)	Treatment Site(s)
Carilion Health	VA	Roanoke	CyberKnife	Kidney, Lung, Pancreas, Prostate
Carilion New river Valley Medical Center	VA	Christiansburg	CyberKnife	NS
Centra Health	VA	Lynchburg	Trilogy	NS
CJW Medical Center	VA	Richmond	Trilogy	NS
Inova Fairfax Hospital	VA	Falls Church	NR	Skeletal
Riverside Regional Medical Center	VA	Newport News	Synergy	NS
Sentara Advanced Radiosurgery Center	VA	Norfolk	CyberKnife	Liver, Lung, Pancreas
University of Virginia Medical Center	VA	Charlottesville	Tomotherapy	Liver, Lung
VCU Health System	VA	Richmond	Tomotherapy	NS
Virginia Hospital Center	VA	Arlington	CyberKnife	Lung, Prostate
Harborview Medical Center	WA	Seattle	NR	NS
Multicare Health System	WA	Tacoma	Trilogy	NS
Southwest Washington Medical Center	WA	Vancouver	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis
St. Joseph Hospital	WA	Bellingham	Tomotherapy	Gastrointestinal, Gynecologic, Prostate
Swedish Health Services	WA	Seattle	CyberKnife, Synergy	NS
Swedish Medical Center	WA	Seattle	CyberKnife, Synergy	Prostate
University of Washington Med Center	WA	Seattle	Tomotherapy	NS
Virginia Mason Medical Center	WA	Seattle	NR	Prostate
Appleton Medical Center	WI	Appleton	CyberKnife, Tomotherapy, Trilogy	NS
Aurora Medical Center	WI	Kenosha	CyberKnife	Lung, Pancreas
Aurora Memorial Hospital of Burlington	WI	Burlington	CyberKnife	Lung, Pancreas
Aurora St. Luke's Medical Center	WI	Milwaukee	CyberKnife	Lung, Pancreas
Columbia St. Mary's - Columbia Campus	WI	Milwaukee	Trilogy	Breast, Kidney, Liver, Lung, Pancreas, Pelvis, Prostate, Skin
Saint Joseph's Hospital	WI	Marshfield	Trilogy	NS
St. Vincent Hospital	WI	Green Bay	Trilogy	NS
Theda Clark Medical Center	WI	Neenah	CyberKnife, Tomotherapy	NS
University of Wisconsin Hosp	WI	Madison	Tomotherapy	NS
Waukesha Memorial Hospital	WI	Waukesha	CyberKnife	Liver, Lung, Pancreas, Prostate

Hospital Name	State	City	Device(s)	Treatment Site(s)
Wheaton Franciscan Cancer Care – St. Joseph	WI	Glendale	Novalis	NS
St. Mary's CyberKnife Center	WV	Huntington	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis

NR: Not reported
NS: Not specified

Appendix K. Ongoing Clinical Trials

Ongoing Clinical Trials

Condition	ClinicalTrials.gov Identifier	Study Design	Intervention	Primary Outcome Measures	Secondary Outcome Measures	Estimated Enrollment	Planned Duration	Location
Breast Cancer, Metastatic	NCT00167414	Nonrandomized; historical control	HSBRT	OS, DFS	CRR, chemical and radiobiological response, QoL	80	December 2000–Ongoing	Rochester, NY
Cholangiocarcinoma Klatskin Tumor Biliary Tract Cancer	NCT00630890	Single group	External beam radiation and CyberKnife radiosurgery boost and capecitabine	Acute toxicities, MTD	LC, radiographic response, delayed and long-term toxicities, DSS, OS	11	October 2007–October 2011	San Francisco, CA
Cholangiocarcinoma	NCT00983541	Single group	SBRT, brachytherapy, fluorouracil (5-FU), gemcitabine	Toxicity	OS, PFS, tumor response, LC, rate of distant mets	12	September 2009–September 2011	Salt Lake City, UT
Colorectal Cancer (fewer than 5 metastases)	NCT00807313	Single group	SBRT	Metabolic complete remission rate	Toxicity, PFS, LC, OS	81	December 2008–Ongoing	Brussels, Belgium
Hepatocellular Carcinoma	NCT00746655	Single group	SBRT with TACE	Feasibility and toxicity	LC, RC, HRQoL	12	July 2009–Ongoing	University of Pittsburgh, Pittsburgh, PA
Hepatocellular Carcinoma	NCT00914355	Single group	SBRT	Local PFS	PFS, OS, QoL, toxicity, cytokine response	47	August 2007–August 2010	Toronto, Canada
Hepatocellular Carcinoma	NCT00243841	Nonrandomized	SBRT	6 month LC	Not specified	60	May 2004–December 2015	Indianapolis, IN
Hepatocellular Carcinoma	NCT01020812	Single group	SBRT with TACE	Efficacy, toxicity	PFS, OS, correlate tumor marker alpha-fetoprotein (AFP) with tumor response and survival	24	September 2009–September 2013	Stanford, CA

Condition	ClinicalTrials.gov Identifier	Study Design	Intervention	Primary Outcome Measures	Secondary Outcome Measures	Estimated Enrollment	Planned Duration	Location
Kidney Cancer	NCT00445757	Single group	Conventional surgery; neoadjuvant therapy; SRS	MTD, toxicity	DFS, LP, DF, DSS	20	January 2007–January 2012	Cleveland, OH
Kidney Cancer	NCT00458484	Single group	SRS	MTD	OS, DFS, LP, DF	32	February 2007–February 2012	Cleveland, OH
Liver Cancer	NCT01030757	Single group	SBRT with Tomotherapy	Tumor response	Toxicity, PFS, OS	43	June 2009–January 2014	Albuquerque, NM
Liver Cancer	NCT00607828	Single group	SBRT	Toxicity, MTD	Not specified	28	November 2007–October 2009	Omaha, NE
Liver Cancer	NCT00777894	Single group	SBRT; Three-dimensional RT; IMRT	Dose limiting toxicity; objective response	Adverse events, tumor response, PFS, OS, Child-Pugh Score	73	November 2008–March 2012	Haifa, Israel; Jerusalem, Israel; Masstricht, Netherlands; Aarau, Switzerland; Zurich, Switzerland; Bellinzona, Switzerland; Bern, Switzerland; St. Gallen, Switzerland; Basel, Switzerland
Liver Cancer	NCT00607828 ¹	Single group	SBRT	Toxicity, MTD	NS	28	November 2007–October 2009	Omaha, NE
Liver Metastases	NCT00914615	Single group	SBRT	Local PFS	PFS, OS, QoL, toxicity, cytokine response	17	August 2007–August 2010	Toronto, Canada
Liver Metastases	NCT00938457	Single group	SBRT	MTD, minimum effective dose	Adverse events, toxicity, tumor response, LC, time to progression, blood chemistry and hepatic function	60	July 2009–November 2017	Rochester, MN
Primary and Metastatic Liver Tumors	NCT00691691	Single group	SBRT	CRR	Toxicity	71	November 2007–November 2008	Calgary, Alberta, Canada

Condition	ClinicalTrials.gov Identifier	Study Design	Intervention	Primary Outcome Measures	Secondary Outcome Measures	Estimated Enrollment	Planned Duration	Location
Liver Metastases	NCT00567970 ¹	Single group	SBRT	MTD	Toxicity; adverse events; QoL; Response; physical exam results	18	April 2007–October 2008	Jacksonville, FL
Liver Metastases	NCT00547677	Single group	SBRT	Toxicity	Tumor response	27	July 2004–December 2007	Dallas, TX; Minneapolis, MN
Lung and Liver Tumors	NCT00178477 ¹	Single group	SBRT	NS	NS	48	January 2002–January 2006	Rochester, NY
Lung Tumors	NCT00632281	Single group	SBRT	Disease status	Toxicity	750	January 2006–Ongoing	University of Florida, Gainesville, FL
Lung Tumors	NCT00832780	Single group	SBRT using Tomotherapy	CRR (complete and partial)		45	January 2008–October 2011	University of New Mexico, Albuquerque, NM
Lung Cancer	NCT00238602	Single group	SRS (CyberKnife)	MTD, symptoms and radiographic responses	NR	60	March 2000–Ongoing	Stanford, CA
Lung Cancer	NCT00687986	Randomized	SRT vs. Primary Resection	LC, RC, QoL; treatment costs	OS; QALY; total costs	960	August 2008–December 2013	Amsterdam, Netherlands
Lung Cancer	NCT01051037	Single group	SBRT and radiofrequency ablation	Toxicity	One year LC, PFS, OS	35	January 2010–January 2013	Los Angeles, CA
Non-small Cell Lung Cancer	NCT00643318	Single group	CyberKnife SRS	CRR, LCR, PFS, OS	QoL, procedures related outcomes	156	April 2006–July 2013	Pittsburgh, PA
Non-small Cell Lung Cancer	NCT00870116	3-group comparison (nonrandomized)	SBRT (CyberKnife) vs. SBRT (linac) vs. Conformational RT	LC	Economic, QoL, PFS, OS	120	April 2009–March 2013	Multiple centers, France
Non-small Cell Lung Cancer	NCT00551369	Single group	SBRT followed by surgical resection in patients with progression	LC	Toxicity, LC, RC, DFS, OS	33	December 2007–June 2012	Multicenter, U.S. and Canada
Non-small Cell Lung Cancer	NCT00843726	Randomized	SBRT—one vs. three fractions	Toxicity, OS	NS	98	September 2008–April 2013	Roswell Park Cancer Institute, New York, NY

Condition	ClinicalTrials.gov Identifier	Study Design	Intervention	Primary Outcome Measures	Secondary Outcome Measures	Estimated Enrollment	Planned Duration	Location
Non-small Cell Lung Cancer	NCT00087438 ²	Single group	SBRT	LC	RC, DFS, OS	52	May 2004– March 2009	University of Rochester, Rochester, NY
Non-small Cell Lung Cancer	NCT00547105	Single group	Erlotinib hydrochloride and SBRT	PFS	Disease progression, Toxicity, OS	24	June 2007– June 2010	University of Texas, Dallas, TX
Non-small Cell Lung Cancer	NCT00238875	Single group	SBRT	OS at 3 years	RFS, Toxicity, PFS, OS	167	July 2004– November 2011	Multiple sites, Japan
Non-small Cell Lung Cancer	NCT00591838	Single group	SBRT	Toxicity	LC, RC, DFS, OS	45	August 2006– August 2016	Washington University Hospital, St. Louis, MO
Non-small Cell Lung Cancer	NCT00727350	Single group, historical control	SBRT	Toxicity	LC, OS, DFS, PFS, QoL	44	March 2007– December 2012	Brussels, Belgium
Non-small Cell Lung Cancer (Stage I, Stage II, or peripheral lung recurrence)	NCT00489008	Three uncontrolled groups	SBRT	DFS, OS	Not reported	138	November 2005– September 2012	M.D. Anderson Cancer Center, Houston, TX
Non-small Cell Lung Cancer	NCT00750269	Single group	SBRT	Toxicity	LC, PFS, OS	94	February 2009– May 2012	Multiple sites, U.S. and Canada
Non-small Cell Lung Cancer	NCT00840749	Randomized, open label	SBRT vs. surgical resection	OS	DSS, PFS, Toxicity	1,030	December 2008– December 2013	Multiple sites, U.S. and China
Non-small Cell Lung Cancer	NCT00246181 ¹	Single group	SBRT	Dosage	Efficacy	117	December 1999– December 2009	Indianapolis, IN
Pancreatic Neoplasms	NCT00833859	Single group	SBRT and Gemcitabine, Docetaxel and Capecitabine	Rate of surgical resection with negative margins	Toxicity, OS	24	March 2009– March 2012	Tampa, FL
Pancreatic Cancer	NCT00350142 ¹	Single group, historical control	SBRT	OS, QoL	NS	40	December 2004– October 2008 (completed)	Stanford University, Stanford, CA

Condition	ClinicalTrials.gov Identifier	Study Design	Intervention	Primary Outcome Measures	Secondary Outcome Measures	Estimated Enrollment	Planned Duration	Location
Pancreatic Cancer	NCT00425841	Single group	Gemcitabine hydrochloride, oxaliplatin, adjuvant therapy, hypofractionated radiation therapy, neoadjuvant therapy, SRS	CRR	Toxicity, time to progression, time to death, tumor response	29	May 2006–NS ¹	Munich, Germany
Pancreatic Cancer	NCT01068327	Single group	SBRT, gemcitabine hydrochloride, leucovorin calcium, fluorouracil, nelfinavir mesylate; conventional surgery	Dose limiting toxicity, MTD	Tumor response;	24	November 2007–December 2012	Omaha, NE
Pancreatic Cancer	NCT01025882	Single group	SBRT, gemcitabine hydrochloride, pancreato-duodenectomy	Toxicity, morbidity, tumor response, length of hospital stay	NS	30	October 2009–October 2014	Dallas, TX
Prostate Cancer	NCT00643617	Single group	CyberKnife SRS	Biochemical DFS, rates of acute and late gastrointestinal and genitourinary toxicities	LF, DF, DFS, DSS, OS, QoL	253	November 2007–January 2014	San Diego, CA; Fresno, CA; Great Falls, MT; Oklahoma City, OK; Tyler, TX
Prostate Cancer	NCT00619515	Single group	SRS	Rate of acute toxicities	Rate of late grade 3–5 toxicities, DFS, OS, LF, DF, QoL	102	December 2007–December 2009	Cleveland, OH; Chardon, OH; Mentor, OH; Canton, OH; South Euclid, OH; Orange Village, OH; Westlake, OH; Middleburgh Heights; OH

Condition	ClinicalTrials.gov Identifier	Study Design	Intervention	Primary Outcome Measures	Secondary Outcome Measures	Estimated Enrollment	Planned Duration	Location
Prostate Cancer	NCT00643994	Single group	CyberKnife SRS	Rates of acute and late grade 3–5 gastrointestinal and genitourinary toxicities, rate of biochemical DFS	LF, DF, DFS, DSS, OS, QoL	298	December 2007–January 2014	Jupiter, FL; Arlington Heights, IL; Lexington, KY; Boston, MA; Ann Arbor, MI; Trenton, NJ; Seattle, WA
Prostate Cancer	NCT00941915	Single group	SBRT with continuous real-time evaluation of prostate motion and IMRT for plan reoptimization based on “anatomy of the day”	Toxicity	DFS, QoL	60	September 2009–December 2012	Duke University, Durham, NC
Prostate Cancer	NCT00547339	Single group	SBRT	Toxicity	OS, LC, RC, DSS	97	July 2006–October 2010	University of Texas, Dallas, TX
Prostate Cancer	NCT01059513	Single group	SBRT	Long term toxicities; tumor control	Not specified	60	January 2010–January 2017	Los Angeles, CA
Unspecified Adult Solid Tumor	NCT00311597	Single group	SRS	MTD, MD	Radiographic response rate, median time to progression, toxicity, cause of death	48	June 2002–Ongoing	Winston-Salem, NC
Extracranial Recurrent, Metastatic Cancer or Primary Tumors	NCT00006456 ¹	Single group	SRS	NR	NR	10–25 within 2–3 years	February 1999–Ongoing	Richmond, VA

¹ Although the estimated completion date has expired, the trial is still ongoing and “active” according to ClinicalTrials.gov at the time of this report.

² This study has been completed and results have been published. See Appendix L. Literature Results.¹⁰⁹

CRR: Clinical response rate

DF: Distant failure

DFS: Disease-free survival

DSS: Disease-specific survival

HRQoL: Health-related quality of life

HSBRT: Hypofractionated stereotactic body radiotherapy

IMRT: Intensity modulated radiation therapy

LC: Local control

LCR: Local control rate

LF: Local failure

LP: Local progression

M: Male

MD: Minimum dose

MTD: Maximum tolerated dose

NS: Not specified
OS: Overall survival
PFS: Progression-free survival
QALY: Quality-adjusted life years
QoL: Quality of life

RC: Regional control
RT: Radiation therapy
SBRT: Stereotactic body radiation therapy
SRS: Stereotactic radiosurgery
TACE: Transcatheter arterial chemoembolization

Appendix L. Results for Guiding Question 3

Prospective Single Group Studies

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Freeman et al. (2011) ²³	USA	Low-risk prostate cancer	Cyberknife/NR	n = 41	None	Median: 60 (Range: 50.4–74.4)	PSA levels; toxicity; QoL	Acute: dysuria, urinary urgency, frequency, nocturia, tenesmus Late: grade 1N3 urinary, grade 1N2 rectal
Aluwini et al. (2010) ³	The Netherlands	Low to intermediate risk prostate cancer	Cyberknife/NR	n = 10	NR	Median: 5.1 (Range: 2–13)	Early and intermediate toxicity scores; early PSA response	Acute grade 1N2: rectal bleeding; urinary toxicity
Bolzicco et al. (2010) ⁸	Italy	Prostate cancer	Cyberknife/NR	n = 22 low risk n = 23 intermediate risk	Prior: hormone therapy; transurethral resection n = 17 concurrent androgen deprivation	Median: 20 (Range: 6–42)	Toxicity; PSA response	Grade 1-3: urgency, urinary frequency, rectal urgency or stool frequency Late: occasional rectal bleeding
Bradley et al. (2010) ⁹	Italy	Stage I NSCLC	NR/NR	n = 91	None	Median: 18 (Range: 6–42)	Local control; nodal failures; distant failures	Skin reaction; grade 2 radiation pneumonitis; painful subcutaneous inflammatory reaction adjacent to treated chest wall; rib fracture; chest wall pain at site of treatment; brachial plexopathy
Cardenes et al. (2010) ¹¹	USA	Primary HCC	Linac/NR	n = 17 with 25 lesions	None	Median: 24 (Range: 10–42) n = 10 patients alive without progression	Toxicity; tumor response; maximum tolerated dose; survival	Grade 3 and higher: elevation of bilirubin, hypokalaemia, hyperbilirubinaemia, radiation induced liver disease

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Goodman et al. (2010) ²⁷	USA	Primary and metastatic liver tumors	Cyberknife/NR	n = 19 hepatic mets n = 5 IHCC n = 2 recurrent HCC	None	Median: 17.3 (Range: 2–55)	Local control; survival; overall survival,	Grade 1: nausea, abdominal pain, fever, fatigue Grade 2: duodenal ulcer, gastrointestinal bleeding, musculoskeletal toxicity
Kopek et al. (2010) ⁵⁵	Denmark	Cholangiocarcinoma	Siemens Primus/NR	n = 27	None	Median: 64.8 (Range: 27.6–103.2 entire cohort)	Local control; progression-free survival; overall survival; acute and late radiation induced toxicities	Grade ≥3 nausea, vomiting, pain, analgesia, ulceration, duodenal stenosis, hepatic failure
Oermann et al. (2010) ⁷⁴	USA	Prostate cancer	Cyberknife/Inverse treatment plan	N = 13 intermediate risk N = 11 high risk	Concurrent: IMRT given immediately after SBRT	Median: 9.3 (Range: 6.6–16.9)	Toxicity; QoL; PSA response	Grade 2: urinary symptoms requiring alpha blockers; bowel frequency/spasms requiring antidiarrheals
Polistina et al. (2010) ⁸⁰	Italy	Locally advanced pancreatic adenocarcinoma	CyberKnife/NR	n = 23	None	Mean: 11 +3.95 Median: 9	Gastrointestinal toxicity; tumor response; local control; pain; QoL; overall survival time	n = 5 grade 1 vomiting/nausea; n = 3 enteric bleedings diagnosed endoscopically as bleeding from duodenal wall cancer invasion
Shin et al. (2010) ⁹³	Korea	HCC	Cyberknife/Pencil beam	n = 6	n = 6 prior TACE	Three alive patients: Median: 25.9 (Range: 8.1–56)	Tumor response; local failure; acute and late toxicities; radiation induced liver disease; dose limiting toxicity; survival	Alkaline phosphatase and liver enzymes increased due to disease progression During treatment: mild nausea, transient asymptomatic, right-sided pleural effusion

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Stintzing et al. (2010) ¹⁰¹	Germany	Metastatic liver tumors of colorectal cancer	Cyberknife/NR	n = 14	n = 6 prior chemo; n = 9 prior surgery; n = 1 prior chemo-embolization	Median: 16.8	Local control; toxicity; progression-free survival; overall survival	No patients reported side-effects of RT; bleeding, ulcers, or strictures have not been detected
Stintzing et al. (2010) ¹⁰²	Germany	Liver tumors	Cyberknife/NR	n = 36 with 54 mets	Prior: chemo; surgery; RFA; chemoembolization; selective internal radiotherapy; laser-induced thermal therapy	Median: 21.3 (Range: 2.8–44)	Local tumor control; survival; toxicity	Grade 1 fatigue and nausea
Timmerman et al. (2010) ¹⁰⁹	USA	Early stage inoperable NSCLC	Linac/NR	n = 55	None	Median: 34.4 (Range: 4.8–49.9 all evaluable) Median: 38.7 (Range: 30.2–49.9 still living)	Tumor response; 3 year primary tumor control rate; local and regional failures; 3 year rates disseminated recurrence; disease-free survival; overall survival	Grade 1–5 toxicities; n = 6 events related to SBRT (n = 3 complications of skin or ribs)
Vahdat et al. (2010) ¹¹⁵	USA	Inoperable stage IA NSCLC	CyberKnife/NR	n = 20	None	Median: 43	Disease spread; survival; serial change in maximum standardized uptake value (SUV[max]); local control	Radiation induced pneumonitis and infiltrating lung fibrosis
Collins et al. (2009) ¹⁷	USA	Stage 1 NSCLC	CyberKnife/ Inverse-planning algorithm	n = 20	n = 1 concurrent gefitinib treatment	Median: 25 (Range: 6–36 for survivors)	Pulmonary status; tumor response; disease progression; survival	Pneumothorax requiring tube thoracotomy (after fiducial placement); mild transient fatigue; chest wall discomfort; acute grade III radiation pneumonitis and infiltrate; hypoxia

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Haasbeek et al. (2009) ³³	The Netherlands	Second lung tumor in the contralateral lung	Linac/NR	n = 15	Prior pneumonectomy for an earlier lung tumor; radiation therapy	Median: 16.5 (Range: 4–55)	Overall survival; distant metastasis free survival; local control; regional failure free survival; disease-free survival; toxicity	Mild fatigue, grade 3 late toxicity; grade 3 radiation pneumonitis; grade 3 complication
Kim et al. (2009) ⁵²	Korea	Pulmonary metastatic colorectal cancer	CyberKnife/NR	n = 13	Prior chemo; surgery	Median: 28 (Range: 15–57)	Overall survival; local control; progression-free survival	Grade 1–2 toxicities: musculoskeletal discomfort and asymptomatic radiation pneumonitis
Kopek et al. (2009) ⁵⁴	Denmark	Early stage NSCLC	Linac/NR	n = 88	None	Median: 44 (Range: 1.6–96.5)	Tumor response; actuarial local control; freedom from failure; median cancer-specific survival; overall survival	Deterioration in performance status by >3 grade points, >3 grade point worsening in analgesia use, 3 grade point deterioration in dyspnea; rib fracture
Lee et al. (2009) ⁶¹	Canada	Liver metastases	Linac/NR	n = 68	n = 7 prior surgery; n = 8 prior RFA; prior lines of chemo: n = 9 (0), n = 15 (1), n = 29 (2), n = 15 (>3); n = 1 prior Whipple operation and prior radiotherapy to celiac axis lymph nodes	Median: 10.8	Maximum tolerated study dose (MSD); tumor response; local control; progression-free survival; overall survival	Grade 3 or higher acute toxicity; thrombocytopenia; grade 3 liver enzymes; subacute liver pain; transient gastritis/esophagitis; grade 2 colitis Late: grade 4 duodenal bleed; grade 5 malignant small bowel obstruction; grade 4 small bowel obstruction through an abdominal hernia; grade 2 nontraumatic rib fractures; transient grade 2 chest wall pain; grade 2 dyspepsia

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Milano et al. (2009) ⁶⁷	USA	Oligometastases	Novalis linac/NR	n = 32	n = 10 prior curative intent local therapy; n = 9 prior resection; n = 1 prior radio-frequency ablation (RFA); n = 1 prior radiation therapy (RT)	Median (deceased): 8 (Range: 3–20); Median (survivors): 7 (Range: 2–32)	Overall survival; progression-free survival; local failure	NR
Olsen et al. (2009) ⁷⁵	USA	Liver metastases	Linac/NR	n = 15	None	NR	Change in normal liver volume	NR
Rusthoven et al. (2009) ⁸⁶	USA	Liver metastases	Linac/NR	n = 47	Mean 1.7 (Range: 0–7) prior systemic treatment regimens; n = 7 prior local therapy for liver metastases	Median: 16 (Range: 6–54)	Local control, toxicity; progression-free survival; distant progression-free survival; overall survival	Grade 3 soft tissue toxicity: skin erythema, pain
Rusthoven et al. (2009) ⁸⁷	USA	Lung metastases	Linac/NR	n = 38	Mean 1.2 (Range: 0–5) prior systemic therapy regimens for metastatic disease	Median: 15.4 (Range: 6–48)	In-field local control; overall survival; toxicity; distant progression; local progression; distant progression-free survival	Grade 3 toxicity rib fracture; grade 2 radiation dermatitis; grade 1 pneumonitis; symptomatic radiation pneumonitis

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
van der Voort van Zyp et al. (2009) ¹¹⁶	The Netherlands	NSCLC	CyberKnife/NR	n = 70	None	Median: 15	Local control; overall survival; cause-specific survival	Fiducial placement: grade 3 toxicity (pneumothorax requiring a chest drain and cardiac arrhythmia required a pacemaker); grade 2 toxicity pneumothorax but required no chest drain; grade 1 toxicity: minor dyspnea, pneumothorax without clinical symptoms, and self-limiting pulmonary hemorrhage After treatment: acute grades 1–2 toxicity (fatigue, dyspnea, cough); acute grade 3 toxicity requiring morphine, late grade 3 toxicity, radiation pneumonitis, thoracic pain, rib fracture
Chang et al. (2008) ¹³	USA	Centrally and superiorly located stage 1 NSCLC or isolated lung parenchymal recurrent NSCLC	Linac/NR	n = 27	None	Median: 17 (Range: 6–40)	Local control; tumor response	Grade 2 pneumonitis; grade 2–3 dermatitis and chest wall pain; brachial plexus neuropathy; partial arm paralysis
Fuller et al. (2008) ²⁵	USA	Prostate cancer	CyberKnife/NR	n = 10	Concurrent distribution of high dose rate brachytherapy	2 week, 4 week, 8 week, and 4 month follow-up done	Early PSA response	No urinary obstruction observed to date, mild and transient rectal toxicity; no acute rectal bleeding observed
Henderson et al. (2008) ³⁶	USA	Inoperable stage 1 NSCLC	Linac/NR	n = 70	None	Median: 2.17 years (Range: 0.12–3.62 years)	Survival; pulmonary function	Grade 2 or higher pulmonary toxicity: pneumonitis, pneumonia, and other pulmonary toxicity
Katoh et al. (2008) ⁴⁹	USA	Adrenal tumors	Linac/NR	n = 9	None	Median: 16 (Range: 5–21)	Disease progression; local failure	No decline in hormone level, tumor-related flank pain

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Salazar et al. (2008) ⁸⁸	USA	Primary and metastatic lung cancer	Linac/NR	n = 104	n = 29 concurrent external beam radiation therapy (EBRT)	Median: 38 (Range: 2–84)	Local tumor response; local tumor control; failure analysis	<u>Grade 1 and 2 acute toxicity:</u> shortness of breath, fatigue, cough, esophagitis, nausea and vomiting, nonmalignant symptomatic pleural effusion, skin reaction; <u>Grade 2 symptomatic subacute or chronic toxicities:</u> symptomatic RT-induced pneumonitis, severe symptomatic fibrosis with sustained shortness of breath; asymptomatic fibrosis of varying degrees
Schellenberg et al. (2008) ⁸⁹	USA	Adenocarcinoma of the pancreas	CyberKnife/NR	n = 16	Gemcitabine infusion chemo dose of 1,000 mg/m ² weekly	Median: 9.1 for all patients; Median: 22.3 for living patients	Local control, toxicities, time to progression, overall survival, carbohydrate antigen (CA 19–9) levels	Pain and gastritis (n = 3); 1 patient required J-tube placement 6 weeks after treatment which was attributed to the SBRT <u>Late toxicities:</u> n = 5 treated medically for ulcer formation (grade 2), 1 required duodenal stent for a non-neoplastic stricture (grade 3), and 1 required surgery after duodenal perforation (grade 4)
Tse et al. (2008) ¹¹²	Canada	Unresectable hepatocellular carcinoma (HCC) and intrahepatic cholangio-carcinoma (IHC)	NR/NR	n = 41	NR	Median: 17.6 (Range: 10.8–39.2)	Survival; local control rate; overall RECIST response rate (complete response, partial response, stable disease)	Transient biliary obstruction; death result of a pulmonary embolus; grade 3 liver enzymes; grade 3 thrombocytopenia; transient asymptomatic right-sided pleural effusion; progression from Child-Pugh A classification to B; late toxicity

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Aoki et al. (2007) ⁴	Japan	Primary lung or metastases	Mitsubishi EXL-20TP 10-MV standard linac/NR	n = 19	n = 10 repeat SRT; n = 1 prior RT	Median: 17.7 (Range: 9.4–39.5)	Tumor response; crude local tumor control rate; overall survival rate (Kaplan-Meier)	Grade 1 radiation pneumonia; grade 1 radiation fibrosis
Hof et al. (2007) ³⁸	Germany	Pulmonary metastases	NR/Pencil beam algorithm for dose calculation	n = 61	None	Median: 14 (Range: 1.5–82)	Local control	Grade 1, 2, 3 toxicities
Hof et al. (2007) ³⁹	Germany	Early stage lung cancer	Siemens Mevatron Linac/ Pencil beam algorithm for dose calculation	n = 42	None	Median: 15 (Range: 1.5–72)	Actuarial overall survival rates & local tumor control rates (Kaplan-Meier)	Minor cough; slightly increased dyspnea
Hoopes et al. (2007) ⁴¹	USA	NSCLC	NR/NR	n = 58	None	Median: 42.5 (Range: 27–61)	Local failure; regional progression; metastatic dissemination	NR
Koto et al. (2007) ⁵⁶	Japan	Stage 1 NSCLC	Varian Clinac 23EX/NR	n = 31	None	Median: 32 (Range: 4–87)	3-year overall survival rate; cause specific survival after 3 years	Grade 1 acute pneumonitis; grade 2 acute pneumonitis; grade 3 acute pneumonitis
Madsen et al. (2007) ⁶³	USA	Localized prostate cancer	NR/NR	n = 40	None	Median: 41 (Range: 12–60)	PSA levels	<u>Acute:</u> rectal discomfort, constipation, diarrhea, tenesmus <u>Late:</u> proctitis, occasional blood, rectal discomfort, frequent stools, constipation, diarrhea
Muacevic et al. (2007) ⁶⁹	Germany	Lung tumors	CyberKnife/ Nonisocentric inverse planning algorithm	n = 15	None	2 month intervals	NR	Pneumothorax; nausea; pneumonitis

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Nuyttens et al. (2007) ⁷³	The Netherlands	Metastases (para-aortic or pelvic lymph nodes, abdominal wall, muscle tissue, rib, retroperitoneal fat, local recurrences in pelvis, neck)	CyberKnife/NR	n = 14	n = 3 prior chemo; n = 3 prior surgery; n = 4 prior irradiation	Median: 18 (Range: 6–26)	Local failure; local regional progression; tumor progression at a distance or new metastasis; local control and disease-free survival calculated Kaplan-Meier method; toxicity	<u>Acute:</u> transient grade 1 lymphedema in leg, grade 1 abdominal pain, nausea, and diarrhea; grade 1 dermatitis; <u>Late:</u> grade 1 rectal bleeding, chronically painful grade 2 subcutaneous fibrosis, grade 1 diarrhea, grade 2 pain in surgical scar on belly
Ponsky et al. (2007) ⁸¹	USA	Renal	NR/NR	n = 3	Partial or radical nephrectomy 8 weeks after RS	Mean: 12.8 (Range: 12–14)	Tumor response	None reported
Ricardi et al. (2007) ⁸²	Italy	NSCLC	NR/NR	n = 43	None	Median: 14.7 (Range: 3–44)	Tumor control, complications	Temporary erythema; radiation pneumonitis (grade 1); acute pneumonitis; rib fracture; thoracic pain
Scorsetti et al. (2007) ⁹⁰	Italy	NSCLC	Linac/NR	n = 43	NR	Median: 14 (Range: 6–36)	Actuarial survival; morbidity	Acute and late grade I or grade II
Dawson et al. (2006) ²⁰	Canada	Hepatocellular carcinoma, intrahepatic cholangio-carcinoma, liver metastases	Elekta Synergy/ NR	n = 79	NR	Maximum: 34	Primary end point: rate of radiation-induced liver toxicity or severe toxicity occurring within three months of treatment	None observed
Ernst-Stecken et al. (2006) ²²	Germany	Lung cancer, thyroid cancer	Novalis/Dose calculation done by pencil beam algorithm	n = 21	None	Median: 6.3 (Range: 1-21)	Quality of hFSRT; local tumor control; survival	Grade 1 and 3 toxicity

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Hodge et al. (2006) ³⁷	USA	NSCLC	Tomotherapy Hi-Art/NR	n = 9	n = 2 single IMRT	Median: 2.1 (Range: 1.8–13.3)	Tumor response	No reports of grade 2 or higher acute toxicity
Hoyer et al. (2006) ⁴³	Denmark	Colorectal metastases	Siemens Primus or Varian Clinac 2100/2300/NR	n = 65	n = 16 surgery; n = 4 RFA or other treatment; n = 33 neoadjuvant chemo	Median: 51.6 (Range: 2.4–75.6)	Survival (Kaplan-Meier); tumor response (local control, local or distant progression); survival; toxicity	Death related to hepatic failure; perforation of colonic ulceration; duodenal ulceration; abdominal pain, increased consumption of analgesics; grade 2 or higher pain score; WHO performance status deterioration; moderate nausea; moderate diarrhea; skin toxicity
Le et al. (2006) ⁵⁹	USA	NSCLC or metastases	CyberKnife/NR	n = 32	n = 10 prior lung resection; n = 6 prior thoracic RT; n = 10 prior systemic therapy	Median: 18 (Range: 9–32)	Treatment response - partial response; minor response; stable disease	Pneumothorax; mild COPD; grade 2 to 3 pneumonitis
Nuyttens et al. (2006) ⁷²	The Netherlands	Early stage lung cancer	CyberKnife/NR	n = 20	None	Median: 4 (Range: 2–11)	Tumor response	Intrathoracic pain
Romero et al. (2006) ⁸⁴	The Netherlands	Primary liver tumors and metastases	Siemens Primus linac/NR	n = 25	None	Median: 12.9 (Range: 0.5–31)	Local control and survival (Kaplan-Meier)	Decompensated portal hypertension; bleeding from esophageal varices; ascites grade 2; elevation of gamma glutamyl transferase (GGT) grade 3; asthenia grade 3
Svedman et al. (2006) ¹⁰³	Sweden	Primary and metastatic renal cell carcinoma	Linac 6MV/NR	n = 30	n = 26 nephrectomy; n = 2 interferon alpha; n = 2 tamoxifen	Median: 52 (Range: 11–66)	Local tumor response (primary); toxicity, pain, and survival (secondary endpoint)	Cough, fatigue, skin rash, focal pain, one patient died—cannot be ruled out may have been treatment-related

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Timmerman et al. (2006) ¹⁰⁸	USA	Early stage NSCLC	Linac/NR	n = 70	None	Median: 17.5 (Range: 0.6–44.2)	Tumor response, disease control, survival	Grade 5 toxicities resulting in 6 deaths due to lung cancer treatment: 4 associated with bacterial pneumonia, 1 as a result of complications from pericardial effusion, 1 associated with massive hemoptysis; grade 3-4: decline in pulmonary function tests, pneumonitis, pleural effusions, apnea, skin reaction; grade 1-2: fatigue, musculoskeletal discomfort, radiation pneumonitis
Wulf et al. (2006) ¹¹⁹	Germany	Primary liver cancer and hepatic metastases	NR/Dose distribution calculated based on a pencil beam algorithm	n = 56	None	Median: 15 (Range: 2–48)	Local tumor control; local failure; Secondary: treatment-related acute and late toxicity; freedom from systemic progression; overall survival	Pain; fever; chills; liver fibrosis; portal hypertension; ascites; bleeding from esophageal varices
Yoon et al. (2006) ¹²³	South Korea	Thoracic (38 primary or 53 metastatic)	NR/NR	n = 91	NR	Median: 14 (Range: 4–56)	Overall response	None greater than RTOG toxicity criteria grade 2 were observed
Xia et al. (2006) ¹²⁰	USA & China	Stage 1 or Stage 2 NSCLC	Gamma-knife (30 rotary conical surface Cobalt 60); NR	n = 43	None	Median: 27 (Range: 24–54)	Local tumor control – complete response; partial response; progressive disease	Acute radiation induced esophagitis; acute radiation induced pneumonitis; mild radiation induced acute whole body reactions (anorexia, nausea, and vomiting); grade 1 neutropenia; late radiation induced local fibrosis

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Zimmermann et al. (2006) ¹²⁴	Germany	Stage 1 NSCLC	NR/NR	n = 68	None	Median and Mean: 17 (Range: 3–44)	Tumor response—complete remission; partial remission; local progression; distant progression; overall and cancer-specific survival; acute and late toxicity	Pneumonitis; late lung fibrosis; fatigue; shivering; nausea; dermatitis; benign pleural effusion; rib fracture; fibrosis of soft tissue
Hoyer et al. (2005) ⁴²	Denmark	Pancreatic cancer	Siemens Primus or Varian Clinac/NR	n = 22	None	2–34	Toxicity; tumor response; overall survival; progression-free survival	Severe mucositis or ulceration of stomach or duodenum; perforation of stomach due to ulcer
Shiroyama et al. (2005) ⁹⁴	Japan	Lung and liver tumors	Varian Clinac 21 Ex/NR	n = 20	None	1–15	Accuracy of fixation; local tumor response; survival and local rates calculated by Kaplan-Meier method; toxicities	NCI-CTC grade 2 complications
Song et al. (2005) ⁹⁷	USA	Lung tumors	NR/Tissue maximum ratio calculation algorithm	n = 17	None	Median: 14	Tumor response; toxicity	Fatigue; mild rib pain & tenderness; rib fracture; nonproductive cough; dyspnea; bronchial stenosis; collapse
Ishimori et al. (2004) ⁴⁴	Japan	Solitary lung cancer	Varian Clinac 2300 C/D/NR	n = 9	None	Range: 2–17	Local response – complete response; partial response; no change; progressive disease	Radiation induced pneumonitis

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Onishi et al. (2004) ⁷⁷	Japan	Stage 1 NSCLC	Linac/NR	n = 35	None	Range: 6–27	Locally progression; tumor response	Acute interstitial pneumonitis
Gerszten et al. (2003) ²⁶	USA	Sacrum	CyberKnife/NR	n = 18	n = 15 prior EBRT	NR	Pain improvement	No acute radiation toxicity or new neurological deficits occurred
Lee et al. (2003) ⁶⁰	South Korea	Primary and metastatic lung tumors	NR/NR	n = 28	NR	Median: 18 (Range: 7–35)	Survival time (Kaplan-Meier method); acute toxicity; late complications; response to radiation; patterns of treatment failure	All patients developed grade 1 radiation pneumonitis within 3 months; none had symptomatic complications after SRS treatment.
Whyte et al. (2003) ¹¹⁷	USA	Primary lung cancer and metastases	CyberKnife/ Nonisocentric inverse-planning algorithm	n = 23	n = 1 right lower lobectomy	Mean: 7 (Range: 1–26)	Complete tumor response; Partial tumor response; Stable; Progressive; Death of nontreatment related causes	Pneumothoraces; exacerbation of underlying chronic obstructive pulmonary disease
Harada et al. (2002) ³⁵	Japan	Lung tumors	NR/NR	n = 18	n = 1 prior RT	Median: 9 (Range: 5–15)	Overall response rate	Pneumonitis
Uematsu et al. (2001) ¹¹³	Japan	Stage 1 NSCLC	FOCAL unit (combination of linac, CT scanner, X-ray simulator, carbon table)/NR	n = 50	n = 18 prior conventional treatment (40-60 Gy in 20-33 fractions, 4-6 weeks)	Median: 36 (Range: 22–66)	Overall cause specific survival rates (Kaplan-Meier Method); local control	Rib fracture; vertebral compression fracture; mild and temporary pleural pain; lung fibroses and/or atelectasis

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Wulf et al. (2001) ¹¹⁸	Germany	Lung and liver	NR/NR	n = 51	n = 18 chemo	Median lung: 8 (Range: 2–33); Median liver: 9 (Range: 2–28)	Crude local control; actuarial local control; actuarial overall patient survival	Grade 1/2; grade 3; grade 4; grade 5
Nakagawa et al. (2000) ⁷⁰	Japan	Thoracic neoplasms	Megavoltage computed tomography assisted SRS/NR	n = 15	n = 1 prior Gamma Knife SRS to a solitary brain metastasis; n = 8 conventional fractionated RT following SRS	Median: 10 (Range: 2–82)	Tumor response; survival	No patient reported adverse acute symptoms; all patients who survived for over 3 months showed some interstitial change in the local lung tissue.

COPD: Chronic obstructive pulmonary disease
 CT: Computed tomography
 EBRT: External beam radiation therapy
 HCC: Hepatocellular carcinoma
 hFSRT: Hypofractionated stereotactic radiotherapy
 IHCC: Intrahepatic cholangiocarcinoma
 IMRT: Intensity modulated radiation therapy
 NCI-CTC: National Cancer Institute-Common Toxicity Criteria
 NSCLC: Non-small cell lung cancer
 NR: Not reported
 PSA: Prostate specific antigen

QoL: Quality of life
 RECIST: Response evaluation criteria in solid tumors
 RFA: Radiofrequency ablation
 RS: Radiosurgery
 RT: Radiation therapy
 RTOG: Radiation Therapy Oncology Group
 SBRT: Stereotactic body radiation therapy
 SRS: Stereotactic radiosurgery
 TACE: Transcatheter arterial embolization
 WHO: World Health Organization

Retrospective Studies

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Crabtree et al. (2010) ¹⁹ *	USA	Stage I NSCLC	Trilogy/NR	n = 76 treated with SBRT n = 462 treated with surgical resection	None	SBRT Median: 19 Surgical Median: 31	Local recurrence; disease-specific survival; overall survival	SBRT: grade 1–2 pneumonitis; grade 3 pneumonia; rib fractures; pleural effusions; lung collapse; hemoptysis; bacterial pneumonia Surgery: arrhythmias; pneumonia / respiratory

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Dunlap et al. (2010) ²¹	USA	Primary NSCLC	Hi-Art Helical TomoTherapy/Inverse planning software	n = 60	None	Median: 12.5 (Range: 2–35) Median: 11.1 (Range: 3–35)	Tumor response; local recurrence; regional nodal recurrence, distant systemic metastases; survival; local control	Chest wall pain; rib fracture; symptomatic pulmonary complications (>grade 1); grade 3-4 pneumonitis
Grills et al. (2010) ^{28 †}	USA	Stage I NSCLC	NR/NR	n = 55 treated with SBRT n = 69 treated with wedge resection	None	Median: 30	Regional recurrence; locoregional recurrence; distant metastasis; freedom from any failure; overall survival; cause-specific survival	Grade 2–3 radiation pneumonitis; rib fractures; grade 1 skin toxicities; acute or chronic myositis
Guckenberger et al. (2010) ³¹	Germany	Locally recurrent gynecological cancer	Linac/NR	n = 12 cervical cancer n = 7 endometrial cancer	n = 12 prior surgery n = 6 prior surgery and adjuvant RT n = 1 prior RT n = 6 concurrent EBRT followed by SBRT boost	Median: 22	Survival; systemic control; local control	Acute: grade 2 diarrhea, nausea, proctitis, dysuria, dermatitis; grade 3 pollakisuria Late: grade 2 proctitis, nausea, stenosis of yerefer, neuralgic pain; grade 4 small bowel ileus, intestine vaginal fistula
Hamamoto et al. (2009) ³⁴	Japan	Primary lung cancer and metastatic lung tumors	Linac/Pencil beam	n = 52 primary lung cancer n = 10 metastatic lung tumors	n = 2 prior intravenous systemic chemo	All tumors Median: 14 (Range: 3–34) Primary Median: 14 (Range: 3–34) Metastatic Median: 19 (Range: 9–31)	Overall survival; local control	None reported

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Jorcano et al. (2010) ⁴⁶	Switzerland	Gynecologic tumors	Novalis/NR	n = 9 cervical cancer n = 17 endometrial cancer	Prior: hysterectomy, pelvic lymphadenectomy, chemo, para-aortic irradiation, WPRT Concurrent: traditional RT followed by SBRT boost	Median: 47 (Range: 4–77)	Toxicity; local disease control; distant failures; overall survival; failure-free survival rate	Acute: grade 0–2 sexual, grade 0–3 urinary, grade 0–3 rectal Late: grade 0–3 sexual, grade 0–2 urinary, grade 0–3 rectum
Kang et al. (2010) ⁴⁸	Korea	Oligometastases confined to one organ from colorectal cancer	Cyberknife/NR	n = 55 with 78 lesions (lung, liver, pelvic aortic lymph nodes, mediastinal lymph nodes, bone)	n = 21 prior curative intent local therapy (resection, RFA) n = 49 prior chemo	Median: 32 (Range: 9–80)	Tumor response; toxicity; local control; overall survival	Acute: grade 1–2 - nausea, vomiting, musculoskeletal discomfort; grade 4 intestinal perforation, obstruction
Kim et al. (2010) ⁵³	Korea	Nonanaplastic thyroid cancer	Cyberknife/NR	n = 9	n = 3 prior neck RT, neck surgery, radioisotope	Median: 23 (Range: 4–63)	Tumor response; regional failure	No grade 3 or higher Adverse events
Louis et al. (2010) ⁶²	Belgium	HCC	Cyberknife/NR	n = 25	n = 3 prior chemoembolization n = 1 prior sorafenib n=3 prior surgery n = 2 prior radiofrequency ablation	Median: 12.7 (Range: 1–24)	Local control; tumor response; toxicity; survival; overall survival; disease free survival	Acute: grade 3 liver pain; grade 3 hepatic toxicity; grade 2 digestive in nature Late: grade 2-3 duodenal ulcers
Mahadevan et al. (2010) ⁶⁴	USA	Nonmetastatic locally advanced unresectable pancreatic cancer	CyberKnife/NR	n = 36	None	Median: 24 (Range: 12–33)	Local control; acute toxicity; local and distant progression; overall survival	Fatigue; nausea; persistent nausea; cramping, vomiting, dehydration; worsening inferior vena cava thrombosis that developed at exploratory laparotomy; gastrointestinal bleeding requiring transfusion (late toxicity)

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Seok Seo et al. (2010) ⁹¹	Korea	Inoperable HCC	Cyberknife /NR	n = 38	n = 38 prior TACE	Median: 15 (Range: 3–47) at this time 17 patients had died	Local progression-free survival; disease progression-free survival; overall survival	Grade 1–2: decline in liver function; acute radiation dermatitis with wet desquamation Grade 3: soft tissue toxicity
Son et al. (2010) ⁹⁶	South Korea	Small unresectable primary hepatocellular carcinoma	CyberKnife	n = 36	None	NS	Radiation induced hepatic toxicity; deterioration of hepatic function	Grade 2–4 toxicities
Takeda et al. (2010) ¹⁰⁶	Japan	Primary lung cancer and metastatic lung tumors	NR/superposition algorithm	n = 111 primary lung cancer n = 22 lung metastasis	None	Median: 12 (Range: 5–45)	Toxicity	Grade 0–3 radiation pneumonitis
Townsend et al. (2010) ¹¹⁰	USA	Prostate cancer	CyberKnife/NR	n = 48	n = 11 IMRT, Tomotherapy followed by SBRT boost	Mean: 2.76 Median: 2.64	Acute gastrointestinal and genitourinary toxicities	Mild increase in frequency/nocturia; acute grade 1–3 gastrointestinal and genitourinary
Trovo et al. (2010) ¹¹¹	USA	Lung cancer	Trilogy/superposition convolution algorithm	n = 68 with 70 tumors	None	Four follow-up periods: 6 weeks; 2–6 months; 7–12 months; 13–18 months after SBRT	Radiographical changes; toxicity; local control	Pleural thickening; pleural effusion; bronchiectasis; radiation fibrosis Late radiographical injuries; grade 2 lung toxicity; grade 2 pulmonary toxicity; grade 2–4 emphysema
Unger et al. (2010) ¹¹⁴	USA	Primary hilar lung cancer or hilar lung metastases	Cyberknife/Non-isocentric, inverse-planning algorithm	n = 20	None	Median: 10	Local tumor recurrence; toxicity; overall survival	Acute grade 2 esophagitis; dyspnea and infiltrate; mainstem bronchus fistula; mild fatigue

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Yamashita et al. (2010) ¹²¹	Japan	Primary lung cancer and metastatic or recurrent lung cancer	Synergy/Collapsed cone convolution	n = 74 primary lung cancer n = 43 metastatic or recurrent lung tumors	None	Median: 14.7 (Range: 0.3–76.2)	Toxicity	Grade 0–5 radiation pneumonitis
Yang et al. (2010) ¹²²	China	HCC	Body Gamma Knife treatment system/NR	n = 40	Prior and Concurrent: n = 17 prior and concurrent rAd-p53 (recombinant adenovirus-mediated wild-type p53 gene – rAd-p53)	Median: 35 (Range: 11–44)	Response; toxicity; survival	Grade 1–2: Fever; gastrointestinal toxicity; abnormal liver function; thrombocytopenia; leukopenia
Hof et al. (2009) ⁴⁰	Germany	Lung tumors	Linac/NR	n = 49	None	Median: 19.3 (Range: 6.44–51.1 with NTC) Median: 12.9 (Range: 4.6–31.3 without NTC)	Normal tissue changes (NTC)	None reported
Ahn et al. (2009) ²	Korea	Stage 1 NSCLC	CyberKnife/NR	n = 8	None	Range: 5–49	Tumor response; local control	Mild malaise; mild asymptomatic radiation pneumonitis
Chang et al. (2009) ¹	Canada and USA	Unresected pancreatic adenocarcinoma	CyberKnife/NR	n = 77	Prior: n = 9 RT, n = 15 chemo Concurrent: n = 16 IMRT, n = 59 chemo	Median: 6 (Range: 3–31) Median (Survivors): 12 (Range: 3–31)	Local progression; progression-free survival; overall survival; local control	Grade 2–4 toxicities

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Chawla et al. (2009) ¹⁴	USA	Adrenal metastases	Novalis/NR	n = 30 3 of 30 also had metastases in the lungs and/or thoracic lymph nodes, liver, or abdominal and/or pelvic lymph nodes	n = 17 prior chemo; n = 9 SBRT	Median: 9.8 (Range: 3.2–28.3)	Overall survival, survival, distant control, local control, tumor response, pain	Grade 1 nausea, mild fatigue
Choi et al. (2009) ¹⁶	Korea	Para-aortic lymph node (PALN) metastases from uterine cervical and corpus cancer	CyberKnife/SBRT planning algorithm	n = 30	n = 2 prior chemo; n = 9 concurrent chemo	Median: 15 months, Range: 2–65	Tumor response; overall survival; disease progression-free survival (DPFS); local control; toxicity	Grade 3 or higher toxicity Acute hematologic toxicities of grade 3 or higher during chemo Late toxicity: ureteral stricture
Guckenberger et al. (2009) ³⁰	Germany and Switzerland	Early stage NSCLC and pulmonary metastases	Linac/Collapsed cone dose calculation algorithm	n = 40	None	Mean: 21, Median: 14, Maximum: 91 - early stage NSCLC Mean: 17, Median: 14, Maximum: 80 - pulmonary metastases	Local control; regional and systemic control for early-stage NSCLC; survival	Pneumonitis grade 2; pneumonitis grade 3; pneumothorax grade 2; pleural effusion grade 2; dyspnea grade 2; esophageal ulceration grade 3

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Kawase et al. (2009) ⁵⁰	Japan	Isolated T1-T2N0M0 primary or metastatic lung tumors	Linac/Collapsed-cone algorithm of Pinnacle3 or the multigrid superposition algorithm of XiO with a density heterogeneity correction	n = 379	None	Median 29 (Range: 1–72)	Development of extra-pulmonary soft-tissue mass	Co-existing swelling; chest pain; thumb numbness; arm edema
McCammon et al. (2009) ⁶⁵	USA	Lung and liver tumors	Linac/Pencil-beam algorithm for tissue inhomogeneity correction	n = 141	None	Median (All): 8.2 (Range: 1.4–44.4) Median (Survivors): 18.3 Median (Deceased): 5.9	Tumor response; local control	Grade 2, 3, and 4 events: grade 2, 3, 4 pneumonitis, grade 2 or 3 dermatitis, grade 2 or higher soft tissue/muscle inflammation, fibrosis, vertebral fractures
Milano et al. (2009) ⁶⁶	USA	Central thoracic lesions	Linac/NR	n = 53	n = 6 concurrent SBRT boost; n = 9 multiple courses of SBRT (2–3 courses)	Median 10 (Range: <1–78)	Survival; distant progression; local control	Acute grade 1, 2 esophageal toxicity; grade 2 radiation pneumonitis; grades 1–2 hemoptysis; grade 2 pneumonia; grade 3 pneumonia; grade 2 pneumothorax; fatal hemoptysis; grade 3 pericarditis
Milano et al. (2009) ⁶⁸	USA	Oligometastases	Novalis/NR	n = 77: 42 liver, 21 lung, 5 thoracic lymph nodes, 9 bone n = 13 lung parenchymal and thoracic lymph nodes	62 of 77: systemic therapy for metastatic disease prior to SBRT 11 of 13 systemic therapy before SBRT	n = 77 Overall Median (n = 77): 23 (Range: 5–85) Living Median (n = 77): 45 (Range: 14–95) Overall Median (n = 13): 21 (Range: 6–66) Living Median (n = 13): 54 (Range: 42–66)	Patterns of recurrence after curative-intent SBRT	NR

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Pennathur et al. (2009) ⁷⁹	USA	Stage NSCLC	Linac/NR	n = 21	None	Mean: 24	Tumor response; survival; local progression	Pneumothorax (after fiducial placement)
Ricardi et al. (2009) ⁸³	Italy	Stage 1 NSCLC	Elekta Precise linac/NR	n = 60	None	Median: 30.9 (Range: 6.7–56.7)	Radiation-induced lung injury scoring; mean lung dose; normal tissue complication probability	Grade 0–3 pulmonary toxicity
Rusthoven et al. (2009) ⁸⁵	USA	Metastatic lung cancer	Linac/NR	n = 64	Prior first-line systemic therapy (cytotoxic chemo and/or molecular targeted therapies)	NR	Progression	NR
Seong et al. (2009) ⁹²	Korea	Hepatocellular carcinoma	CyberKnife/NR	n = 398	Prior: n = 312 TACE, n = 54 transarterial chemoinfusion (TACI), n = 10 systemic chemotherapy, n = 35 RFA, n = 34 iA-chemotherapy, n = 25 surgery, n = 8 percutaneous ethanol injection, n = 7 holmium	Median: 12 (Range: 0.4–42)	Survival	NR
Stephans et al. (2009) ⁹⁹	USA	Stage 1 lung cancer	Novalis/NR	n = 92	None	Median: 18.4 (Range: 1.7–48)	Pulmonary function test; overall survival, local control	Grade 2 radiation pneumonitis

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Stephans et al. (2009) ¹⁰⁰	USA	Stage 1 NSCLC	Novalis/NR	n = 86 receiving 50 Gy or 60 Gy	None	Overall median: 15.3 (Range: 1.9– 47.6) 50 Gy Median: 19.8 (Range: 1.9– 47.6) 60 Gy Median: 9.5 (Range: 2.1– 19.5)	Local control, nodal failure, distant metast asis, overall survival	Grade 2 radiation pneumonitis; grade 1 or 2 chest wall toxicity
Song et al. (2009) ⁹⁸	Korea	Stage 1 NSCLC	Linac/NR	n = 32	None	Median: 26.5 (Range: 5.2–92)	Local tumor control, survival, patterns of failure	Grade 3 severe pulmonary toxicities; 1 death due to bleeding aspiration and pneumonia from SBRT-induced complete bronchial stricture; stricture of lobar bronchus and secondary lung collapse
Takeda et al. (2009) ¹⁰⁵	Japan	Primary lung cancer Stage 1A and 1B	Linac/MG- superposition algorithm with heterogeneity correction	n = 63	None	Median of inoperable patients (n = 49) 31 months (Range: 1–72 months)	Local control; disease-free survival; overall survival; regional recurrence- free; distant metast asis-free; cause-specific survival	Grade 2 or higher radiation pneumonitis; fatal bacterial pneumonia (authors considered SBRT to have possibly contributed to the events leading to death)

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Baumann et al. (2008) ⁶	Sweden, Denmark, Norway	Stage 1 NSCLC	Linac/Pencil beam algorithms with heterogeneity correction	n = 57	None	Median: 23 (Range: 3–42)	Tumor control; toxicity; lung function and performance status	Overall: grade 1, 2, and 3 toxicity <u>Lung-related toxicity:</u> grade 1–2 cough, grade 3 cough, grade 1–2 dyspnea, grade 3 dyspnea, grade 1–2 pneumonia, grade 3 pneumonia, grade 1–2 pneumonitis, grade 1–2 fibrosis, grade 3 fibrosis, grade 1–2 atelectasis, grade 3 atelectasis, grade 1–2 pleural effusion, grade 3 pleural effusion, grade 1–2 heart disorder, grade 3 heart disorder, grade 1–2 esophagitis <u>General toxicity:</u> grade 1–2 skin, grade 1–2 pain, grade 3 pain, grade 1–2 rib fracture, grade 3 rib fracture, grade 1–2 upper airway infection, grade 1–2 fever, grade 1–2 nausea, grade 1–2 emesis, grade 1–2 fatigue, grade 3 fatigue
Casamassima et al. (2008) ¹²	Italy	NSCLC or metastases	Elekta Synergy/ Pencil beam algorithm for dose calculation	n = 104	Metastases prior chemo	Median: 13.88 (Range: 1.37–49.4)	Overall survival (Kaplan-Meier method); tumor response	Acute lung toxicity; dysphagia

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Choi et al. (2008) ¹⁵	South Korea	Hepatocellular carcinoma	CyberKnife/NR	n = 31	Prior: n = 17 (TACE, n = 3) percutaneous ethanol injection (PEI, n = 6 RFA)	Median 10.5 (Range: 2–18.5)	Tumor response; survival	Treatment-related toxicity: liver enzymes grade 0, 1, 3; bilirubin grade 0–1; albumin grade 0–1; leukocytes grade 0–2; platelets grade 0, 1, 3; nausea grade 0–1; progression of Child-Pugh classification from A to B
Coon et al. (2008) ¹⁸	USA	NSCLC, recurrent disease, or solitary lung metastases	CyberKnife/NR	n = 51	NR	Median primary and recurrent cancer: 11 (Range: 2–24); Median metastases: 12 (Range: 2–24)	Complete response; partial response; stable disease; disease progression	Grade 2 radiation pneumonitis; exacerbation of preexisting COPD
Fritz et al. (2008) ²⁴	Germany	Stage 1 NSCLC	Elekta Precise Sli/NR	n = 40	NR	Median: 20 (Range: 6–61.5)	Tumor response as categorized by WHO	Grade 1 radiation dermatitis; grade 1 subcutaneous fibrosis; grade 4 rib fracture
Jereczek-Fossa et al. (2008) ⁴⁵	Italy	Breast, lung, head and neck, urologic, gynecologic, gastrointestinal, CNS, other primaries	Linac (6–18 MV, used for 3D-CRT and SRT)/NR	n = 108	Prior radiation doses ranged from 8 to 74.4 Gy (Mean: 37 Gy); n = 95 conventional or 3D-CRT; n = 13 SRT; n = 55 chemo; n = 3 concurrent brachytherapy	Median: 7 (Range: 1–50)	Overall survival; tumor response	No severe toxicity was reported
Kim et al. (2008) ⁵¹	South Korea	Pelvic recurrence from rectal carcinoma	CyberKnife/NR	n = 23	Prior lower anterior resection, abdominoperineal resection; adjuvant chemo; concurrent chemoradiotherapy; all salvage chemo before SBRT	Median: 31 (Range: 7–65)	Tumor response; local failure	Nausea, vomiting, pain (Grade 1 & 2; grade 3 & 4 reported); rectal perforation

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Kunos et al. (2008) ⁵⁷	USA	Squamous cell carcinoma of the vulva	CyberKnife/NR	n = 3	n = 3 prior pelvic radiation for vulvar cancer	At least 2	Tumor response	No skin, urinary, or gastrointestinal toxicities were observed during course
Lagerwaard et al. (2008) ⁵⁸	The Netherlands	Stage 1 NSCLC	Linac/NR	n = 206	Prior: n = 7 pneumonectomy, n = 2 bilobectomy, n = 17 lobectomy, n = 2 wedge resection, n = 3 chemoradiotherapy, n = 5 radiotherapy, n = 1 endobronchial therapy	Median 12 (Range: 3–44)	Overall survival; disease-free progression; local failure; regional failure; distance progression-free survival	Fatal cerebrovascular accident during treatment; fatigue, local chest wall pain; nausea; dyspnea; cough; grade 3 or greater pneumonitis; rib fractures; chronic thoracic pain syndromes
Norihisa et al. (2008) ⁷¹	Japan	Oligometastatic lung tumors	Linac/NR	n = 34	Most prior surgical resection and chemo for primary cancer	Median 27 (Range: 10–80)	Overall survival rate; local relapse free rate; progression-free rate; disease free interval; local response	Pulmonary toxicity (grade 1 and 2): cough, hemoptysis, dyspnea, pleural effusion, radiographic changes, bacterial pneumonia, grade 3 pulmonary toxicity, grade 1 skin toxicity with faint erythema or pigmentation, skin ulcer Musculoskeletal: bone fracture of the rib, chest wall pain, mild pain, grade pericardial effusion, temporal liver dysfunction
Onimaru et al. (2008) ⁷⁶	Japan	NSCLC	NR/treatment planning made with Focus or Xio calculation algorithm: 31 Clarkson, 10 Superposition	n = 41	None	Median: 27 (Range: 9–62)	Overall actuarial survival and cause-specific survival (Kaplan-Meier); deaths from causes other than lung cancer; local control rate	Radiation pneumonitis; pleural effusion; chest wall pain from radiation pleuritis

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Svedman et al. (2008) ¹⁰⁴	Sweden and Italy	Primary or metastatic renal disease	Linac/Pencil beam algorithm (dose planning)	n = 7	n = 1 prior metastatic surgery; n = 1 prior interferon-alpha	Maximum 70	Creatinine levels; local control; kidney function	Grade 1–2: nausea, fatigue, local pain
Brown et al. (2007) ¹⁰	USA	Stage 1 NSCLC and lung metastases	CyberKnife/NR	n = 88	n = 7 prior conventional fractionated external radiotherapy	Range: 1-36	Complete response; partial response; stable disease; progression of disease	Lung and esophagus toxicity, radiation pneumonitis; esophagitis; mild fatigue
Guckenberger et al. (2007) ²⁹	Switzerland	NSCLC or pulmonary metastatic lesions	NR/NR	n = 70	NR	Median: 16 (Range: 1.5–85)	Actuarial local tumor control; complete response	Symptomatic pneumonitis; mild cough or dyspnea not requiring steroids; grade 2 pneumonitis; pleural effusion
Teh et al. (2007) ¹⁰⁷	USA	Spine, bone, soft tissue/organ, and lymph node	Novalis/NR	n = 80	Prior RT; n = 1 prior surgery for sacral nerve neuroma	NR	Pain relief; symptom control; tumor response	NR
Baumann et al. (2006) ⁵	Sweden	Stage 1 NSCLC	Linac/NR	n = 141	None	Median: 33 (Range: 1–107)	Tumor response - complete response; partial response; stable disease; local failure	Mild toxicity; skin rash; costal fracture; cough; radiological pneumonitis/ fibrosis; atelectasis; grade 3-4 toxicity
Joyner et al. (2006) ⁴⁷	USA	Metastases or Recurrence NSCLC	Linac/NR	n = 9	None	Median: 10.6 (Range: 2.5–42.5)	Overall survival; local tumor control; normal tissue imaging changes	Transient pneumonitis; fibrotic reactions; some degree of wall thickening; lobe atelectasis; narrowing of lobe bronchus
Paludan et al. (2006) ⁷⁸	Denmark	Stage 1 NSCLC	NR/DVH parameters calculated by use of a pencil beam algorithm	n = 28	None	Median: 6.7 (Range: 2.1–7.5)	Dyspnea development	NR

Study	Country	Cancer Type	Instrumentation/ Algorithms	Study Size	Prior or Concurrent Treatment	Length of Followup (Months)	Outcomes Measured	Adverse Events
Sinha et al. (2006) ⁹⁵	USA	Bilateral primary lung cancer	NR/NR	n = 10	n = 1 prior resection of lesion	Mean: 20.7, Median: 18.5 (Range: 7–42)	Tumor response	Grade 1 and 2 complications
Beitler et al. (2004) ⁷	USA	Renal cell carcinoma	NR/NR	n = 9	n = 1 prior nephrectomy	Median: 26.7	Survival calculated by Kaplan-Meier method	Nausea, vomiting, glandular atypia in the stomach
Gunven et al. (2003) ³²	Sweden	Recurring liver metastases of colorectal cancer	Linac/NR	n = 4	Prior surgical resection	10–101	Tumor sizes and evolution; tumor regression	Epigastric pain; slight diffuse mucosal redness

* Author's retrospectively reviewed two case series: patients treated with SBRT (February 2004 – May 2007) and patients treated with surgery (January 2000 – December 2006)

† Author's retrospectively reviewed two case series: patients treated with SBRT or wedge resection (February 2003 – February 2009)

3D-CRT: Three-dimensional conformal radiation therapy

CNS: Central nervous system

COPD: Chronic obstructive pulmonary disease

DPFS: Disease progression-free survival

DVH: Dose volume histogram

Gy: Gray

IMRT: Intensity modulated radiation therapy

NSCLC: Non-small cell lung cancer

NR: Not reported

NTC: Normal tissue changes

PALN: Para-aortic lymph nodes

PSA: Prostate specific antigen

RFA: Radiofrequency ablation

RT: Radiation therapy

SBRT: Stereotactic body radiation therapy

SRT: Stereotactic radiotherapy

TACE: Transcatheter arterial chemoembolization

TACI: Transarterial chemoinfusion

WHO: World Health Organization

WPRT: Whole pelvic radiation therapy

Appendix M. Literature Results Device Specifications

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Freeman et al. (2011) ²³	Cyberknife 6 MV	150-200 noncoplanar beams	NS	NS	CT, MRI	NS	Fiducial markers (3-4)	NS	Orthogonal x-ray images
Aluwini et al. (2010) ³	Cyberknife	NS	NS	NS	CT, MRI	NS	NS	NS	NS
Bolzicco et al. (2010) ⁹	Cyberknife 6 MV	Noncoplanar	NS	NS	CT	Non-isocentric inverse treatment planning	4 Fiducials	NS	Orthogonal x-ray images
Bradley et al. (2010) ⁹	NS	8-11 beams	NS	SBF, BodyFix, Alpha Cradle	4D CT	Tissue heterogeneity corrections	NS	NS	NS
Cardenes et al. (2010) ¹¹	Linac 6MV	7-12 non-opposing, noncoplanar fields	NS	SBF	CT	NS	NS	NS	Cone-beam computed tomography
Crabtree et al. (2010) ¹⁹	Trilogy	10-12 noncoplanar beams	NS	NS	NS	NS	Fiducials	NS	NS
Dunlap et al. (2010) ²¹	Hi-Art Tomotherapy	NS	NS	Stereotactic frame	CT	Inverse planning software (Tomotherapy) and BrainScan planning software (BrainLab)	Fiducial markers	NS	NS
Goodman et al. (2010) ²⁷	Cyberknife	NS	NS	Alpha Cradle	CT, PET	Multiplan (Accuray)	Fiducials (3-5) 5mm x 1mm	Synchrony	NS
Grills et al. (2010) ²⁸	NS	6-9 coplanar and noncoplanar beams	NS	SBF or Alpha cradle	4D CT, PET	Pinnacle	NS	NS	Cone-beam computed tomography
Guckenberger et al. (2010) ³¹	NS	NS	NS	SBF or BodyFix system	CT, cone-beam CT	NS	NS	NS	Verification imaging
Hamamoto et al. (2010) ³⁴	Linac 4 MV	8-11 noncoplanar static beams	mMLC	BodyFix	CT	3D treatment planning (BrainSCAN)/pencil beam algorithm	NS	NS	NS
Jorcano et al. (2010) ⁴⁶	Novalis 6 MV	NS	mMLC	Customized vacuum body cast	CT, MRI	NS	Infrared (IR) reflecting metallic markers	NS	Infrared cameras

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Kang et al. (2010) ⁴⁸	Cyberknife	NS	NS	Alpha cradle	CT, MRI, PET	NS	NS	4 belts to compress abdomen	NS
Kim et al. (2010) ⁵³	Cyberknife	NS	NS	Customized thermoplastic mask and vacuum cushion	Contrast-enhanced CT	On-target Planning System	NS	NS	Orthogonal x-ray images
Kopek et al. (2010) ⁵⁵	Seimens Primus	5–8 static coplanar or noncoplanar beams	MLC with leaf width 5 or 10 mm at isocenter	Customized vacuum pillow fixed in SBF (Elekta)	CT	Helax-TMS (MDS-Nordion, Freiburg, Germany) treatment planning system	NS	Abdominal compression	CT scan first treatment day; portal imaging with matching to vertebral column
Louis et al. (2010) ⁶²	Cyberknife	NS	NS	Vacuum mattress or self-expanding foam mattress	CT	Multiplan (Accuray)	Fiducials (2–6) 0.88 mm x 5 mm	Synchrony	NS
Mahadevan et al. (2010) ⁶⁴	CyberKnife 6MV	NS	NS	Memory foam placed over customized Vac-Lok (CIVCO Medical Solutions) immobilization cradle	CT	MultiPlan workstation (Accuray)	Fiducials (3–5) 5 mm x 0.8 mm	Synchrony	NS
Oermann et al. (2010) ⁷⁴	Cyberknife	NS	NS	NS	CT, MRI	Multiplan (Accuray)	At least 4 gold fiducials	NS	NS
Polistina et al. (2010) ⁸⁰	CyberKnife 6MV	Noncoplanar	NS	Alpha cradle immobilization device; vacuum preformed bed	CT	NS	Fiducial markers 3 or more	Synchrony	NS
Seo et al. (2010) ⁹¹	Cyberknife	NS	NS	Alpha Cradle	CT, MRI, PET	NS	Fiducials (6) 4 mm x 0.8 mm	4 belts to compress abdomen	Orthogonal x-ray images
Shin et al. (2010) ⁹³	Cyberknife	NS	20, 25, 30, 35, 40 mm diameter circular collimator	Alpha cradle	CT, MRI, PET	Pencil beams	Fiducials (6) 4 mm x 0.8 mm	4 belts to compress abdomen	NS

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Son et al. (2010) ⁹⁶	CyberKnife 6MV	NS	NS	NS	NS	NS	Skin markers	Abdominal compression, breath hold	NS
Stintzing et al. (2010) ¹⁰²	Cyberknife 6 MV	NS	NS	NS	CT, MRI	NS	Gold fiducials 5 mm x 0.5 mm	NS	Orthogonal x-ray images
Stintzing et al. (2010) ¹⁰¹	Cyberknife 6 MV	NS	NS	NS	CT, MRI	NS	Fiducials (1–2) 5 mm x 0.5 mm	NS	Orthogonal x-ray images
Takeda et al. (2010) ¹⁰⁶	NS	NS	NS	NS	CT	Superposition algorithm	NS	NS	NS
Timmerman et al. (2010) ¹⁰⁹	Linac	NS	NS	NS	CT	No tissue density heterogeneity correction was allowed	NS	Abdominal compression, gating, breath hold	4D CT scans, fluoroscopy
Townsend et al. (2010) ¹¹⁰	CyberKnife 6MV	NS	NS	Custom-fit body mold	CT	Inverse planning technique	Fiducial markers	NS	NS
Trovo et al. (2010) ¹¹¹	Trilogy 6 MV	Multiple coplanar and noncoplanar beams	NS	SBF or BodyFix	CT	Superposition/convolution algorithm	NS	NS	NS
Unger et al. (2010) ¹¹⁴	Cyberknife	NS	NS	NS	CT	Nonisocentric, inverse-planning algorithm with tissue density heterogeneity	Fiducials (3–5) 0.8–1 mm x 3–7 mm	Form fitting vest with 3 red light emitting surface markers	Orthogonal x-ray images
Vahdat et al. (2010) ¹¹⁵	CyberKnife 6MV	Hundreds of beams	Single collimator 20-30 mm in diameter	NS	CT	Nonisocentric inverse planning algorithm with tissue heterogeneity corrections	Fiducials; 3 LEDs placed on patients anterior torso	NS	Orthogonal x-ray images; live camera array signal and correlation model
Yamashita et al. (2010) ¹²¹	Synergy	At least 8 beams	NS	Body frame	CT	3D treatment planning machine (Pinnacle3)	NS	Abdominal pressure board	NS
Yang et al. (2010) ¹²²	Body GammaKnife	NS	NS	Vacuum cushion	CT	3D treatment planning system	NS	NS	NS

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Hof et al. (2009) ⁴⁰	Linac 6 MeV	6–7 isocentric portals	NS	Vacuum pillow inside stereotactic frame	CT	3D treatment planning VIR-TUOS software (German Cancer research center)/pencil beam algorithm dose calculation	NS	NS	NS
Ahn et al. (2009) ²	CyberKnife 6MV	NS	NS	NS	NS	NS	NS	NS	NS
Chawla et al. (2009) ¹⁴	Novalis	Conformal arcs	NS	NS	CT, PET	BrainLAB 3D Brain SCAN system	NS	Breath hold technique	ExacTrac
Choi et al. (2009) ¹⁶	CyberKnife 6MV	NS	NS	Alpha Cradle and four belts to restrict respiratory motion (Smithers Medical)	CT	CyberKnife planning system	Six 4 mm length x 0.8 mm diameter fiducials	NS	NS
Collins et al. (2009) ¹⁷	CyberKnife 6MV	NS	NS	NS	CT	Nonisocentric inverse plan	3–5 gold fiducials 0.8–1 mm (diameter) x 3–7 mm (length)	NS	Light emitting diodes (LEDs) on patients anterior torso; Orthogonal x-ray imagers
Guckenberger et al. (2009) ³⁰	Linac	NS	NS	SBF (Elekta); BodyFix system (Medical Intelligence)	CT	NS	NS	Abdominal compression	Out of room CT scanner, in-room single slice CT scanner; integrated cone-beam CT (Elekta)
Haasbeek et al. (2009) ³³	Linac	8–11 radiation beams	NS	NS	4D CT	BrainLAB BrainScan version 5.31 treatment planning software and Philips medical Systems Pinnacle Treatment Planning System	NS	NS	Orthogonal x-ray images or conebeam CT

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Kopek et al. (2009) ⁵⁴	Siemens Primus or Varian Clinac 2100/2300 6 or 8MV	5–8 static coplanar or noncoplanar beams	MLC leaf width 5–1 mm at isocenter	SBF (Elekta)	CT	MDS Nordion Helax TMS or Varian CadPlan Plus/Eclipse treatment-planning systems / pencil beam algorithm dose calculation with heterogeneity correction	NS	Diaphragmatic compression	Portal field imaging and CT scan
Kawase et al. (2009) ⁵⁰	Linac	NS	NS	NS	CT	Koninklijke Philips Electronics Pinnacle ³ planning system or CMS Xio	NS	NS	NS
Kim et al. (2009) ⁵²	CyberKnife 6 MV	NS	Single 20, 25, or 30 mm diameter collimator	Alpha Cradle (Smithers Medical)	CT	CyberKnife planning system/pencil beam	6 gold fiducials 4 mm (long) x 0.8 mm (diameter)	4 belts to compress the abdomen	NS
King et al. (2009) ³⁰⁵	CyberKnife 6 MV	NS	NS	Alpha cradle	CT	NS	3 gold fiducials	NS	Image guidance
Milano et al. (2009) ⁶⁸	Novalis	NS	NS	NS	NS	BrainScan system	NS	Breath hold technique or shallow breathing	ExacTrac
Milano et al. (2009) ⁶⁶	Linac	Conformal arcs	NS		CT, PET	BrainLAB BrainScan treatment planning system	NS	NS	ExacTrac
Milano et al. (2009) ⁶⁷	Novalis	Conformal arcs or multiple fixed coplanar beams	NS	Vacuum bag	CT	BrainLAB BrainScan treatment planning system	NS	NS	ExacTrac
Lee et al. (2009) ⁶¹	Linac	NS	NS	Customized body mold	CT, MRI	NS	NS	Elekta ABC or abdominal compression	2D orthogonal MV image guidance; 3D kV cone beam CT combined with 2D kV fluoroscopy

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Olsen et al. (2009) ⁷⁵	Linac	NS	NS	NS	NS	NS	NS	Assisted breathing device or abdominal compression plate	NS
Pennathur et al. (2009) ⁷⁹	Linac	NS	NS	Alpha Cradle (Smithers Medical)	CT	NS	1–4 fiducials implanted	Breath hold, Synchrony	Rea- time image guidance
Ricardi et al. (2009) ⁸³	Elekta Precise linac 6 and 10 MV	6–8 static nonopposing, noncoplanar	NS	Vacuum pillow and SBF (Elekta)	CT	OTP version 1.5 software for treatment planning Nucletron/collapsed cone algorithm dose calculation	NS	Abdominal compression devices	Orthogonal electronic portal images, DRRs
Seong et al. (2009) ⁹²	CyberKnife 6 MV	NS	NS	NS	NS	NS	NS	NS	NS
Rusthoven et al. (2009) ⁸⁵	Linac	NS	NS	NS	NS	NS	NS	NS	NS
Rusthoven et al. (2009) ⁸⁶	Linac 6-15 MV	Dynamic conformal arcs or multiple noncoplanar static beams >7 noncoplanar fields	NS	External vacuum type or synthetic body mold	CT	NS	Fiducial markers on body immobilization or infrared markers on patients surface	ABC or abdominal compression	Orthogonal x-rays or onboard CT imaging
Rusthoven et al. (2009) ⁸⁷	Linac 6-15 MV	Dynamic conformal arcs or multiple noncoplanar static beams	NS	External vacuum type; synthetic body mold; or abdominal compression	CT	NS	NS	Facilitated breath hold or abdominal compression	Orthogonal x-rays or onboard CT imaging
Song et al. (2009) ⁹⁸	Linac	Median: 6 (Range: 4–8) coplanar or noncoplanar beams	NS	SBF, vacuum fitted (Elekta)	CT	Elekta Render 3D planning system or Varian Eclipse planning system	NS	ABC, abdominal compression, or respiratory gated therapy (Varian and GE Lightspeed)	Cone-beam or CT simulation; on-board imager with cone beam CT

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Stephans et al. (2009) ¹⁰⁰	Novalis 6MV	7 field noncoplanar IMRT with heterogeneity corrections or 3 or more dynamic arcs without heterogeneity corrections	NS	BodyFix vacuum bag	CT	BrainScan 5.31 planning software	NS	Abdominal compression	Orthogonal films and Exactrac
Stephans et al. (2009) ⁹⁹	Novalis	NS	NS	BodyFix (Elekta)	CT	BrainLAB BrainScan 5.31 planning software	NS	Abdominal compression device	Exactrac, Orthogonal films
van der Voort van Zyp et al. (2009) ¹¹⁶	CyberKnife 6MV	130 noncoplanar beams	1 or 2 circular collimator cone sizes 20–60 mm	NS	CT	Accuray version 3.4.1 on target treatment-planning system	Minimum of 3 implanted markers	Synchrony	Orthogonal X-ray images
Baumann et al. (2008) ⁶	Linac 6MV	5-9 noncoplanar or coplanar beams	MLC	SBF (Elekta)	CT	Helax TMS or Eclipse systems/pencil beam algorithms with heterogeneity correction	NS	Abdominal compression	CT scan before treatment
Casamassima et al. (2008) ¹²	Elekta Synergy 6 MV	Dynamic arc technique; arc interval in the transverse plane minimum of 180 to 270, subarcs of 30; non coplanar arcs were used in some patients	MLC	SBF	CT	Treatment planning system ERGO 3D line/pencil beam algorithm dose calculation	NS	NS	Cone-beam CT for online setup corrections
Chang et al. (2008) ¹	CyberKnife 6MV	6 degrees of freedom	NS	Alpha Cradle (Smithers Medical)	CT, PET	NS	3–5 implanted fiducials	Synchrony	Orthogonal x-ray sources & amorphous silicon detectors
Chang et al. (2008) ¹³	Linac 6MV	6–9 noncoplanar beams	NS	NS	CT	NS	NS	NS	CT on-rail simulation during each treatment fraction; orthogonal films
Choi et al. (2008) ¹⁵	CyberKnife 6MV	NS	NS	NS	CT	NS	4 gold markers	Breath hold	NS

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Coon et al. (2008) ¹⁸	CyberKnife 6MV	6 axis robotic arm	NS	NS	PET, CT	Non isocentric inverse planning algorithm	1–4 gold fiducial markers	Synchrony	Orthogonal x-rays
Fritz et al. (2008) ²⁴	Elekta Precise Sli linac	5–8 coplanar fields planned	MLC leaf width 10 mm	SBF (Elekta)	4D CT	Eclipse 3D planning system version 7.3.10/ pencil beam algorithm dose planning with heterogeneity correction	NS	NS	CT immediately before treatment
Fuller et al. (2008) ²⁵	CyberKnife 6MV	NS	NS	NS	CT, MRI	NS	Implanted gold fiducial markers	NS	NS
Henderson et al. (2008) ³⁶	Linac 6 and 15MV	7–10 noncoplanar compensated beams	NS	SBF and vacuum pillow (Elekta)	CT	NS	Prepatellar and sterna positioning marks	Abdominal pressure device	NS
Jereczek-Fossa et al. (2008) ⁴⁵	Linac 6-18 MV	1–3 noncoplanar conformal dynamic arc	mMLC	Vacuum pillow fixed on a carbon fiber tray	CT, PET, MRI	BrainLAB BrainScan treatment planning v 5.31	NS	NS	ExacTrac
Katoh et al. (2008) ⁴⁹	Linac	NS	MLC	No immobilization	CT	NS	Implanted 2 mm gold marker	Synchrony	4 fluoroscopy image processor units
Kim et al. (2008) ⁵¹	CyberKnife 6MV	NS	NS	Alpha Cradle (Smithers Medical)	CT, PET	CyberKnife planning system	6 gold fiducials 4 mm (long) x 0.8 mm (diameter)	NS	NS
Kunos et al. (2008) ⁵⁷	CyberKnife 6MV	NS	NS	Vacuum bag pelvic	CT	Accuray inverse treatment planning system	6 single 1.6 x 3 mm gold soft tissue markers	NS	Cross plane radiographic imaging
Lagerwaard et al. (2008) ⁵⁸	Linac	8–12 noncoplanar static beams	mMLC	NS	4D CT	BrainLAB BrainScan v 5.2	NS	NS	Varian real-time position management system

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McCammon et al. (2008) ⁶⁵	Conventional linac and Novalis dedicated linac 6MV	Single or multiple dynamic conformal arcs or multiple noncoplanar static beams	MLC	Vac-Lok, MedTec OR Alpha Cradle (Smithers Medical)	CT, PET, MRI	BrainLAB BrainScan software/ pencil-beam algorithm for tissue inhomogeneity correction	Fiducial skin markers	Elekta ABC, abdominal compression	ExacTrac, CT scan, or stereoscopic image guidance
Onimaru et al. (2008) ⁷⁶	Linac 4, 6, and 10MV	NS	NS	NS	CT	CMS Focus or Xio planning systems	Gold markers	Breath hold	NS
Norihisa et al. (2008) ⁷¹	Linac 6MV	5–7 noncoplanar static beams	MLC	SBF (Elekta)	CT	Varian CADPLAN version 3.1 and Eclipse version 7.1	NS	NS	NS
Salazar et al. (2008) ⁸⁸	Linac	3–9 fields	MLC	SBF	CT, PET	NS	External fiducial markers on immobilization device	ABC mask	NS
Schellenberg et al. (2008) ⁸⁹	CyberKnife 6MV	NS	NS	Alpha cradle	CT, PET	CyberKnife planning system	Implanted gold fiducial seeds	Respiratory gating, Synchrony	NS
Svedman et al. (2008) ¹⁰⁴	Linac 6 MV	5–8 coplanar or noncoplanar static beams	MLC	SBF	CT	Helix TMS planning system/ pencil beam algorithm dose calculation	NS	Abdominal pressure device	NS
Takeda et al. (2008) ¹⁰⁵	Linac	10 dynamic conformal arcs with or without additional static conformal ports	NS	NS	CT	CMS XiO version 4.2 or 4.3 3D treatment-planning system/ MG-superposition algorithm dose calculation with heterogeneity correction	NS	Long scan time CT to account for breathing motion	NS
Tse et al. (2008) ¹¹²	Linac 6-18 MV	3–10 coplanar or noncoplanar beams	NS	Abdominal compression	CT, MRI	Conformal planning	NS	Elekta ABC or abdominal compression	Orthogonal MV image guidance or kV cone beam CT imaging and kV orthogonal fluoroscopy

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Aoki et al. (2007) ⁴	Linac EXL-20TP Mitsubishi 10 MV	4–6 fixed multiple noncoplanar conformal beams; 3 noncoplanar oblique anterior beams plus 2 coplanar oblique posterior beams plus 1 coplanar lateral beam	NS	Thermo-shell and custom made MoldCare head rest (Alcare)	CT	XiO version 4.1.1 CMS 3D radiotherapy treatment-planning machine/ dose calculation with Clarkson method by 3D-RTP corrected for inhomogeneity	NS	NS	Electronic portal imaging device for tumor localization before each treatment
Brown et al. (2007) ¹⁰	CyberKnife 6MV	Noncoplanar beams	NS	NS	CT	Inverse planning module	Xsight Lung, fiducial markers	Breath hold, Synchrony	NS
Guckenberger et al. (2007) ²⁹	NS	5–7 coplanar and noncoplanar beams	NS	SBF (Elekta)	CT	NS	NS	Abdominal compression	CT simulation prior to treatment fractions
Hof et al. (2007) ³⁸	Siemens linac 6MV	At least 6 different coplanar or noncoplanar isocentric beam directions	MLC leaf width at isocenter 1 cm	SBF with and vacuum pillow	CT	Voxelplan 3D treatment planning/ pencil beam algorithm dose calculation	NS	Abdominal compression	NS
Hof et al. (2007) ³⁹	Siemens Mevatron linac 6MV	6–8 different coplanar or noncoplanar isocentric beam directions	MLC leaf width at isocenter 1 cm	SBF with vacuum pillow	CT	Voxelplan software DKFZ 3D treatment planning with/pencil beam algorithm dose calculation	Bony landmarks	Abdominal compression device	Orthogonal portal images compared to DRR
Hoopes et al. (2007) ⁴¹	NS	7–10 noncoplanar compensated beams	NS	SBF (Elekta)	CT	3D treatment planning	Prepatellar and sterna positioning marks permanently applied	Abdominal clamping pressure	NS
Koto et al. (2007) ⁵⁶	Clinac 23Ex, Varian 6MV	Noncoplanar multi-dynamic arcs and/or multi-static beams	NS	Half body vacuum cast	CT	CadPlan and Eclipse 3D radiotherapy treatment-planning system/modified Batho power law tissue heterogeneity correction algorithm	Gold markers 3.0 x 0.8 mm	Respiratory gating and ABC	X-ray tubes mounted directly to gantry and 2 sets of amorphous silicon flat panel x-ray sensors

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Muacevic et al. (2007) ⁶⁹	CyberKnife 6MV	NS	NS	NS	NS	Inverse planning algorithm	Gold fiducials, Xsight	X-ray system	Orthogonally position x-ray cameras
Nuyttens et al. (2007) ⁷³	CyberKnife 6MV	NS	NS	NS	NS	NS	NS	Synchrony	NS
Ponsky et al. (2007) ⁸¹	NS	NS	NS	Plastic mold	CT	Treatment-planning software	Gold fiducials, Xsight	NS	NS
Ricardi et al. (2007) ⁸²	NS	6–8 noncoplanar static multiple fields	NS	SBF	CT, PET	NS	NS	Diaphragm control device	NS
Scorsetti et al. (2007) ⁹⁰	Linac	4 or more dynamic arcs	3D Line mMLC	Immobilization system with vacuum lock and/or thermoplastic mask	NS	3D Line Medical Systems Ergo treatment-planning system	NS	NS	NS
Teh et al. (2007) ¹⁰⁷	Novalis	NS	NS	Body cast	PET, CT, MRI	NS	Bony lesions or radio-opaque markers	Abdominal compression, gating, or ABC	Stereoscopic x-rays
Baumann et al. (2006) ⁵	Linac 6MV	5–9 noncoplanar or coplanar beams	MLC	SBF(Elekta)	CT	3D dose planning	NS	Diaphragm control device	CT scans for image guidance for verification
Dawson et al. (2006) ²⁰	Elekta Synergy	1–2 segments per beam when required to obtain optimal plans	NS	NS	4D CT	Forward planning	NS	Breath hold using ABC	MV images and orthogonal kV fluoroscopic images
Ernst-Stecken et al. (2006) ²²	Novalis	1–6 either dynamic conformal arc or static conformal beams	NS	Self-constructed abdominal press	CT	Novalis BrainScan version 5.31 - Brain Lab/ pencil beam algorithm dose calculation	NS	NS	ExacTrac
Hodge et al. (2006) ³⁷	Tomotherapy Hi-Art	NS	NS	Custom made double vacuum	CT	Tomotherapy treatment-planning system	NS	Abdominal pressure pillow	MVCT scan and fused with planning CT

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Hoyer et al. (2006) ⁴³	Siemens Primus or Varian Clinac 2100/2300 6-8 MV	5–8 static coplanar or noncoplanar beams	MLC leaf width 5–10 mm at isocenter	SBF (Elekta), vacuum pillow	CT	Helax-TMS or Varian CadPlan/Eclipse	Invasive skin marks	NS	Portal imaging
Joyner et al. (2006) ⁴⁷	Linac	NS	NS	BodyFix (Medical Intelligence)	CT, PET	Nomos Corp Corvus treatment planning station 5.0/6.0	NS	NS	CT imaging control
Le et al. (2006) ⁵⁹	CyberKnife 6 MV	NS	NS	Vac Bag, MedTech	CT	NS	Fiducial markers on body immobilization or infrared markers on patients surface	Synchrony, Breath hold technique	Orthogonal x-ray image pairs
Madsen et al. (2006) ⁶³	Linac	6 stationary noncoplanar fields	Custom blocking	NS	CT, MRI	NS	3 fiducial markers	NS	Isoloc Northwest Medical Physics Equipment for daily treatment position; orthogonal images
Nuyttens et al. (2006) ⁷²	CyberKnife 6 MV	NS	NS	NR	CT	NS	Fiducial markers	Synchrony	2 diagnostic x-ray sources with amorphous silicon detectors to acquire live digital radiographic images
Paludan et al. (2006) ⁷⁸	Siemens Primus or Varian Clinac 2100/2300	5–8 static coplanar or noncoplanar beams	MLC	SBF (Elekta), vacuum pillow	CT	Helax TMS treatment-planning system / pencil beam algorithm tissue density inhomogeneity correction	Laser guided skin marks	NS	CT scan verification image
Romero et al. (2006) ⁸⁴	Siemens Primus linac	4–10 coplanar and noncoplanar beams	NS	SBF (Elekta)	CT	Varian CadPlan treatment planning system	Implanted gold fiducials	Abdominal compression	CT scan, electronic portal images
Sinha et al. (2006) ⁹⁵	Linac 6 MV and 15 MV	7–10 noncoplanar, nonopposing beams	NS	SBF (Elekta)	CT	3D treatment planning	NS	Abdominal clamping pressure	NS

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Svedman et al. (2006) ¹⁰³	Linac 6MV	5–8 coplanar or noncoplanar static beams	MLC	SBF (Elekta), vacuum pillow	CT	Helax TMS/pencil beam algorithm dose calculation	NS	NS	CT scan
Timmerman et al. (2006) ¹⁰⁸	Linac	10–12 noncoplanar, nonopposing beams	NS	SBF (Elekta), vacuum pillow	CT	Elekta Render 3D planning system	NS	Abdominal compression	NS
Wulf et al. (2006) ¹¹⁹	Elekta Synergy S 6–18 MV	Noncoplanar beams	NS	SBF (Elekta)	CT	Helax TMS version 4.01A, 4.01B, 5.1 and 6.1A Theranostic B.V 3D treatment planning system/pencil beam algorithm dose calculation	Fiducial markers in frame	NS	CT verification
Xia et al. (2006) ¹²⁰	Body gammaknife 30 Co(60)	NS	3, 12, 18 aperture diameter collimators	Vacuum bag	CT	NS	NS	NS	NS
Yoon et al. (2006) ¹²³	NS	Coplanar and/or noncoplanar beams	NS	SBF (Elekta)	NS	Elekta 3D treatment-planning system Render plan	NS	ABC; diaphragm controller	NS
Zimmermann et al. (2006) ¹²⁴	NS	Multiple static beams and/or dynamic arcs	MLC leaf width at isocenter 1 cm	Vacuum couch (Medical Intelligence)	CT	Siemens Helax TMS system/pencil beam algorithms	NS	NS	CT scans superimposed with ExacTrac
Hoyer et al. (2005) ⁴²	Siemens Primus or Varian Clinac 2100/2300	5–8 static coplanar or noncoplanar beams	MLC leaf width 5–10 mm at isocenter	Vacuum pillow, SBF (Elekta)	CT	Helax-TMS or Varian CadPlan Plus/Eclipse	Skin marks	NS	Portal film or electronic portal imaging
Molla et al. (2005) ³⁶⁵	Novalis linac 6 MV	Dynamic arc treatments	mMLC	Customized vacuum body cast	CT	BrainLAB BrainScan TPS	NS	5–7 infrared metallic markers asymmetrically fixed to skin of abdomen before treatment planning	ExacTrac, Infrared cameras mounted to the ceiling

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Shioyama et al. (2005) ⁹⁴	Clinac 12 Ex Varian 6 or 10MV	5–8 noncoplanar static ports	MLC	Thermoplastic body cast with vacuum pillow and arm & leg holding devices (Ximatron Varian)	CT	Varian Eclipse version 6.5 3D RT treatment planning machine	X-ray simulator for tumor	Respiratory gating	CT verification
Song et al. (2005) ⁹⁷	NS	4–8 coplanar beams or single plane dynamic arcs	NS	Custom fitted immobilization	CT	BrainLAB version 5.2/tissue maximum ratio calculation algorithm; Philips Pinnacle ³ monitor units confirmed/inhomogeneity corrections	6–7 infrared reflective skin markers and lateral isocenter tattoos	NS	Infrared marker system, orthogonal films, CT verification
Beitler et al. (2004) ⁷	NS	Coplanar and noncoplanar arrangements	NS	SBF	CT	NS	Fiducial markers on the box	NS	NS
Ishimori et al. (2004) ⁴⁴	Clinac 2300 6MV Varian	6–10 field noncoplanar	NS	SBF (Elekta)	NS	Varian 3D treatment-planning system CadPlan R.6.0.8	NS	NS	NS
Onishi et al. (2004) ⁷⁷	EXL-15DP Mitsubishi	10 different noncoplanar dynamic arcs	NS	NS	CT	CMS 3D treatment-planning computer FOCUS version 3.2.1	Skin marker	Self breath hold	Electronic portal imaging
Gerszten et al. (2003) ²⁶	CyberKnife 6MV	NS	NS	NS	CT	Inverse treatment plan	Fiducial placement	NS	Two diagnostic x-ray cameras orthogonal to acquire real time images
Gunven et al. (2003) ³²	Linac 6MV	NS	NS	Stereotactic frame	CT	NS	NS	External abdominal pressure	NS
Lee, et al. (2003) ⁶⁰	NS	4–8 field coplanar and/or noncoplanar beams	MLC with 1 cm thick leaves	SBF with vacuum pillow	CT	Elekta 3D planning system Render Plan	NS	Diaphragm controller	CT scan and verification films before each treatment

Study	Device and Photon Energy	Beam Angles	Collimation Technique	Body Immobilization Technique	Treatment Planning Imaging	Treatment Planning System/Algorithm	Tumor Tracking	Respiratory Tracking/Control	Imaging Guidance During Treatment
Whyte et al. (2003) ¹¹⁷	CyberKnife 6MV	NS	NS	Alpha cradle (Smithers Medical)	CT	CyberKnife inverse planning system and nonisocentric radiation delivery	Implanted metal fiducial markers	Breath hold technique or tracking LEDs placed on the patient's skin	Real-time image processing
Harada et al. (2002) ³⁵	Linac	NS	NS	NS	NS	3D radiotherapy planning system	Gold marker	NS	X-ray system in floor and on ceiling
Uematsu (2001) ¹¹³	Fusion of CT and linac (FOCAL)	NS	NS	NR	NS	NS	NS	Abdominal pressure belt and/or shallow respirations with oxygen mask	NS
Wulf et al. (2001) ¹¹⁸	Linac 5-18 MV	Symmetric 5 beam arrangement individualized by addition of rotational beams or opposing beams	NS	SBF, vacuum pillow	CT	Helax TMS version 4.01A and 4.01B MDS Nordion 3D treatment planning system	NS	Diaphragm control device	CT verification
Nakagawa et al. (2000) ⁷⁰	NS	NS	Dynamic MLC	NS	CT	NS	NS	NS	MV CT-assisted verification

2D: Two-dimensional
 3D: Three-dimensional
 4D: Four-dimensional
 ABC: Active breathing control
 CT: Computed tomography
 DRR: Digitally reconstructed radiographs
 IMRT: Intensity modulated radiation therapy
 kV: Kilovolt
 LED: Light emitting diode
 MEV: Million electron volt
 mm: Millimeter
 MRI: Magnetic resonance imaging
 MV: Megavolt
 mMLC: micro-Multileaf collimator
 MLC: Multileaf collimator
 NS: Not specified
 PET: Positron emission tomography
 SBF: Stereotactic body frame

Appendix N. Responses From Device Manufacturers on Device Specifications and Compatible Accessories (January 2010)

	Elekta Axesse ⁵⁸¹	Elekta Synergy-S ⁵⁸¹	Elekta Synergy ⁵⁸¹	Elekta Infinity ⁵⁸¹	Tomo- Therapy- HiArt ⁵⁸²	Accuray CyberKnife® Robotic Radiosurgery System ⁵⁸³	Varian Clinac iX ⁵⁸⁴	Varian Trilogy ⁵⁸⁴	Varian/BrainLAB Novalis Tx ⁵⁸⁴
<i>Device Type (e.g., robot, ring gantry, standard linac)</i>	Standard linac and robotic table	Standard linac and robotic table	Standard linac and robotic table	Standard linac and optional robotic table	Ring gantry	Robotic mounted linac	C-Arm Linac	C-Arm Linac	C-Arm Linac
<i>Photon Energy, MV</i>	6, 10, 12, or 15 MV	6, 10, 12, or 15 MV	6, 10, 12, 15, or 18 MV	6, 10, 12, 15, or 18 MV	6 MV	6 MV	6 MV plus one of 10,15,18,20 HighX	6 MV plus one of 10,15,18,20 HighX	6 MV plus one of 10, 15, 18, 20 HighX
<i>Maximum Dose Rate (MU/min)</i>	600 MU/min	600 MU/min	600 MU/min	600 MU/min	850 cGy/min	1,000 MU/min	600 MU/min ¹	1,000 MU/min ¹	1,000 MU/min ¹
<i>Number of Independent Beam Angles</i>	Infinite ²	Infinite ²	Infinite ²	Infinite ²	51 per rotation, continuous delivery modeled by treatment (7 degree arcs)	>1,200 noncoplanar, independent beam angles	Continuously variable along gantry, collimator & couch rotational axes plus couch & collimator translational axes ³	Continuously variable along gantry, collimator & couch rotational axes plus couch & collimator translational axes ³	Continuously variable along gantry, collimator & couch rotational axes plus couch & collimator translational axes ³
<i>Collimation Technique (e.g., MLC, etc.)</i>	MLC or cones	MLC or cones	Add-on MLC or cones	Add-on MLC or cones	MLC	Variable aperture collimator and fixed circular collimator ⁴	MLC ⁵	MLC ⁵	MLC and SRS cones ⁶
<i>Smallest Collimation Resolution</i>	4 mm throughout or cones ⁷	4 mm throughout or cones ⁷	3 mm or 2.5 mm throughout or cones ⁷	3 mm or 2.5 mm throughout or cones ⁷	6.25 mm x 10 mm	Field sizes of 5 mm ⁸	5.0 mm	5.0 mm	2.5 mm
<i>Minimum Treatment Size</i>	MLC: 4 mm	MLC: 4 mm	MLC: 3 mm or 2.5 mm	MLC: 3 mm or 2.5 mm	Not limited by collimator	5 mm ⁸	MLC: 5 mm x 5 mm SRS cone: 4 mm	MLC: 5 mm x 5 mm SRS cone: 4 mm	MLC: 2.5 mm x 2.5 mm SRS cone: 4 mm

	Elekta Axesse⁵⁸¹	Elekta Synergy-S⁵⁸¹	Elekta Synergy⁵⁸¹	Elekta Infinity⁵⁸¹	Tomo-Therapy-HiArt⁵⁸²	Accuray CyberKnife® Robotic Radiosurgery System⁵⁸³	Varian Clinac iX⁵⁸⁴	Varian Trilogy⁵⁸⁴	Varian/BrainLAB Novalis Tx⁵⁸⁴
<i>Maximum Treatment Size</i>	MLC: 16 cm x 21 cm	MLC: 16 cm x 21 cm	MLC: 7 cm x 7 cm or 12 cm x 12 cm	MLC: 7 cm x 7 cm or 12 cm x 12 cm	NR	Conformal beam targeting allows treatment of tumors >maximum field size of 60 mm	Fixed field: 40 cm x 40 cm Modulated field: 40 cm x 32 cm	Fixed field: 40 cm x 40 cm Modulated field: 40 cm x 32 cm	Fixed field: 22 cm x 40 cm Modulated field: 22 cm x 32 cm
<i>Body Immobilization Technique (e.g., third party)</i>	BodyFIX or HeadFIX	BodyFIX or HeadFIX	BodyFIX or HeadFIX	BodyFIX or HeadFIX	BodyFIX ⁹	Not required, optional "vac-bags" ⁹	Medical Intelligence CIVCO; Q-Fix; Aktina ⁹	Medical Intelligence CIVCO; Q-Fix; Aktina ⁹	Medical Intelligence; CIVCO; Q-Fix; Aktina ⁹
<i>Treatment Planning Imaging (e.g., CT, PET-CT, MRI, etc.)</i>	CT and/or MRI and/or PET	CT and/or MRI and/or PET	CT and/or MRI and/or PET	CT and/or MRI and/or PET	CT on HiArt planning station, multi-modality on third party fusion/contouring station	CT, 4D CT, MR, PET, and XA (3DRA)	CT, MR, PET, CT/PET	CT, MR, PET, CT/PET	CT, MR, PET, CT/PET
<i>Treatment Planning Options (e.g., software)</i>	ERGO++ and/or Pinnacle3 ⁹	ERGO++ and/or Pinnacle3 ⁹	ERGO++ and/or Pinnacle3 ⁹	ERGO++ and/or Pinnacle3 ⁹	Tomo-Helical and Tomo-Direct delivery mode, each with IMRT and 3D options	The MultiPlan® Treatment Planning System	Varian Eclipse recommended	Varian Eclipse recommended	BrainLAB iPlan Standard; Varian Eclipse recommended in addition
<i>Treatment Planning Algorithm (e.g., Monte Carlo, forward, inverse)</i>	Inverse and/or Monte Carlo	Inverse and/or Monte Carlo	Inverse and/or Monte Carlo	Inverse and/or Monte Carlo	Convolution/superposition	Inverse planning with Monte Carlo or ray-tracing methods	Eclipse: AAA and Pencil Beam	Eclipse: AAA and Pencil Beam	Varian Eclipse: AAA and Pencil Beam, BrainLAB iPlan: Pencil Beam and Monte Carlo
<i>Patient Positioning Accuracy (mm)</i>	<1 mm	<1 mm	<1 mm	<1 mm	Approx 0.5 mm	During set-up: 1 mm	Follows AAPM and ASTRO recommendations ¹⁰	Follows AAPM and ASTRO recommendations ¹⁰	Follows AAPM and ASTRO recommendations ¹⁰

	Elekta Axesse⁵⁸¹	Elekta Synergy-S⁵⁸¹	Elekta Synergy⁵⁸¹	Elekta Infinity⁵⁸¹	Tomo- Therapy- HiArt⁵⁸²	Accuray CyberKnife® Robotic Radiosurgery System⁵⁸³	Varian Clinac iX⁵⁸⁴	Varian Trilogy⁵⁸⁴	Varian/BrainLAB Novalis Tx⁵⁸⁴
<i>Patient Position Correction (degrees of freedom)</i>	6D standard	3D standard, optional 6D	3D standard, optional 6D	3D standard, optional 6D	Translation plus roll	RoboCouch® System provides 6-DOF motion capabilities	4	4	6
<i>Image Guided Technology (during treatment)</i>	2D or 3D cone-beam CT	2D or 3D cone-beam CT	2D or 3D cone-beam CT	2D or 3D cone-beam CT	MVCT prior to delivery	Orthogonal X-ray (kV), registers to DRRs	Varian Cone-Beam CT; MV Portal Imaging; Fluoro kV, MV/kV	Varian Cone-Beam CT; MV Portal Imaging; Fluoro kV, MV/kV	Varian Cone-Beam CT; MV Portal Imaging; Fluoro kV, MV/kV, BrainLAB, ExacTrac Stereo X-Ray, ExacTrac Optical (IR), SNAP (kV image w/beam on)
<i>Tumor Tracking (e.g., fiducials, third party, manufacturer)</i>	Active Breathing Coordinator (ABC) and/or Elekta Symmetry 4D cone-beam CT	ABC and/or Elekta Symmetry 4D cone-beam CT	ABC and/or Elekta Symmetry 4D cone-beam CT	ABC and/or Elekta Symmetry 4D cone-beam CT	No tracking during treatment	Xsight Lung Tracking System and fiducial-based tracking	Varian Fluoro kV and via Calypso or VisionRT ⁹	Varian Fluoro kV and via Calypso or VisionRT ⁹	Varian Fluoro kV and via BrainLAB SNAP (kV image w/ beam on) and Calypso or VisionRT ⁹
<i>Respiratory Gating (Yes/No)</i>	Yes, ABC	Yes, ABC	Yes, ABC	Yes, ABC	No	No—Uses Synchrony® Respiratory Tracking System	Varian RPM: Respiratory Position Management	Varian RPM: Respiratory Position Management	Varian RPM: Respiratory Position Management BrainLAB: Adaptive Gating
<i>Standard Treatment Time Per Fraction¹¹</i>	2–45 mins (lower with VMAT, higher with SRS)	2–45 mins (lower with VMAT, higher with SRS)	2–45 mins (lower with VMAT, higher with SRS)	2–45 mins (lower with VMAT, higher with SRS)	Typically beam on 20 minutes and time in room 45 minutes	Avg. 30–60 min per fraction imaging interval and tracking method used	5–35 ¹²	3–20 ¹²	3–20 ¹²

¹ Varian states the dose rate is at 100 centimeters (cm).

² Based on rotation of linac and control of patient table.

³ Varian states: linacs rotate continuously + 185 degrees (370 degrees total) about the isocenter from vertical; the couch can yaw + 100 degrees; rotate the multileaf collimator + 165 (+ 0.5 degrees); the leaf positions are continuously variable with a + 0.01 mm leaf position resolution; Exact Couch has a lateral travel of + 25 cm and a longitudinal travel of 145.8 cm; BrainLAB's robotic couch top, standard on the Novalis Tx (and optional on the Trilogy and Clinac iX), can roll and pitch + 2.7 degrees and + 4 degrees respectively.

⁴ 5–60 mm diameter.

5 Millennium 120 MLC: 80 -5 mm leaves bounded by 40 (2 x 20) 10 mm leaves.
6 HD120 MLC: 64 2.5 mm leaves bounded by 56 (2 x 28) 5 mm leaves.
7 2.5 mm to 50 mm.
8 This represents the smallest collimator size; Accuray states collimator resolution is not applicable for the CyberKnife system.
9 Third party device or software.
10 Varian states they follow recommendations of AAPM and ASTRO⁵⁸⁵
11 Standard treatment time may vary with each patient depending on factors such as tumor size, etc.
12 Varian based the treatment time on a treatment dose range of 8-20 Gy and delivery using RapidArc or Fixed Gantry.

4D CT: Four-dimensional computed tomography
AAA: Anisotropic analytical algorithm
AAPM: American Association of Physicists in Medicine
ABC: Active Breathing Coordinator
ASTRO: American Society for Radiation Oncology
cGY/min: Centigray per minute
cm: Centimeter
CT: Computed tomography
DOF: Degrees of freedom
DRR: Digitally reconstructed radiograph
IMRT: Intensity modulated radiation therapy
kV: Kilovolt
MLC: Multi-leaf collimator
mm: Millimeter
MRI: Magnetic resonance imaging
MU/min: Monitor units per minute
MV: Megavolt
MVCT: Megavoltage computed tomography
PET: Positron emission tomography
SRS: Stereotactic radiosurgery
VMAT: Volumetric modulated arc therapy

Appendix O. References Cited in Appendixes

1. Chang DT, Schellenberg D, Shen J, et al. Stereotactic radiotherapy for unresectable adenocarcinoma of the pancreas. *Cancer* 2009 Feb 1;115(3):665-72. PMID: 19117351
2. Ahn SH, Han MS, Yoon JH, et al. Treatment of stage I non-small cell lung cancer with CyberKnife, image-guided robotic stereotactic radiosurgery. *Oncol Rep* 2009 Mar;21(3):693-6. PMID: 19212628
3. Aluwini S, van RP, Hoogeman M, et al. CyberKnife stereotactic radiotherapy as monotherapy for low- to intermediate-stage prostate cancer: early experience, feasibility, and tolerance. *J Endourol* 2010 May;24(5):865-9. PMID: 20433370
4. Aoki M, Abe Y, Kondo H, et al. Clinical outcome of stereotactic body radiotherapy of 54 Gy in nine fractions for patients with localized lung tumor using a custom-made immobilization system. *Radiat Med* 2007 Jul;25(6):289-94. PMID: 17634882
5. Baumann P, Nyman J, Lax I, et al. Factors important for efficacy of stereotactic body radiotherapy of medically inoperable stage I lung cancer. A retrospective analysis of patients treated in the Nordic countries. *Acta Oncol* 2006;45(7):787-95. PMID: 16982541
6. Baumann P, Nyman J, Hoyer M, et al. Stereotactic body radiotherapy for medically inoperable patients with stage I non-small cell lung cancer - a first report of toxicity related to COPD/CVD in a non-randomized prospective phase II study. *Radiother Oncol* 2008 Sep;88(3):359-67. PMID: 18768228
7. Beitler JJ, Makara D, Silverman P, et al. Definitive, high-dose-per-fraction, conformal, stereotactic external radiation for renal cell carcinoma. *Am J Clin Oncol* 2004 Dec;27(6):646-8. PMID: 15577450
8. Bolzicco G, Favretto MS, Scremin E, et al. Image-guided stereotactic body radiation therapy for clinically localized prostate cancer: preliminary clinical results. *Technol Cancer Res Treat* 2010 Oct;9(5):473-7. PMID: 20815418
9. Bradley JD, El Naqa I, Drzymala RE, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung cancer: the pattern of failure is distant. *Int J Radiat Oncol Biol Phys* 2010 Jul 15;77(4):1146-50. PMID: 19800181
10. Brown WT, Wu X, Wen BC, et al. Early results of CyberKnife image-guided robotic stereotactic radiosurgery for treatment of lung tumors. *Comput Aided Surg* 2007 Sep;12(5):253-61. PMID: 17957532
11. Cardenes HR, Price TR, Perkins SM, et al. Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma. *Clin Transl Oncol* 2010 Mar;12(3):218-25. PMID: 20231127
12. Casamassima F, Masi L, Bonucci I, et al. Relevance of biologically equivalent dose values in outcome evaluation of stereotactic radiotherapy for lung nodules. *Int J Radiat Oncol Biol Phys* 2008 May 1;71(1):145-51. PMID: 18164855
13. Chang JY, Balter PA, Dong L, et al. Stereotactic body radiation therapy in centrally and superiorly located stage I or isolated recurrent non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Nov 15;72(4):967-71. PMID: 18954709
14. Chawla S, Chen Y, Katz AW, et al. Stereotactic body radiotherapy for treatment of adrenal metastases. *Int J Radiat Oncol Biol Phys* 2009 Sep 1;75(1):71-5. PMID: 19250766
15. Choi BO, Choi IB, Jang HS, et al. Stereotactic body radiation therapy with or without transarterial chemoembolization for patients with primary hepatocellular carcinoma: preliminary analysis. *BMC Cancer* 2008 Nov 27;8:351. PMID: 19038025
16. Choi CW, Cho CK, Yoo SY, et al. Image-guided stereotactic body radiation therapy in patients with isolated para-aortic lymph node metastases from uterine cervical and corpus cancer. *Int J Radiat Oncol Biol Phys* 2009 May 1;74(1):147-53. PMID: 18990511

17. Collins BT, Vahdat S, Erickson K, et al. Radical cyberknife radiosurgery with tumor tracking: an effective treatment for inoperable small peripheral stage I non-small cell lung cancer. *J Hematol Oncol* 2009;2:1. PMID: 19149899
18. Coon D, Gokhale AS, Burton SA, et al. Fractionated stereotactic body radiation therapy in the treatment of primary, recurrent, and metastatic lung tumors: the role of positron emission tomography/computed tomography-based treatment planning. *Clin Lung Cancer* 2008 Jul;9(4):217-21. PMID: 18650169
19. Crabtree TD, Denlinger CE, Meyers BF, et al. Stereotactic body radiation therapy versus surgical resection for stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2010 Aug;140(2):377-86. PMID: 20400121
20. Dawson LA, Eccles C, Craig T. Individualized image guided iso-NTCP based liver cancer SBRT. *Acta Oncol* 2006;45(7):856-64. PMID: 16982550
21. Dunlap NE, Cai J, Biedermann GB, et al. 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* 2010 Mar 1;76(3):796-801. Epub 2009 May 8. PMID: 19427740
22. Ernst-Stecken A, Lambrecht U, Mueller R, et al. Hypofractionated stereotactic radiotherapy for primary and secondary intrapulmonary tumors: first results of a phase I/II study. *Strahlenther Onkol* 2006 Dec;182(12):696-702. PMID: 17149575
23. Freeman DE, King CR. Stereotactic body radiotherapy for low-risk prostate cancer: five-year outcomes. *Radiat Oncol* 2011 Jan 10;6(1):3. PMID: 21219625
24. Fritz P, Kraus HJ, Blaschke T, et al. Stereotactic, high single-dose irradiation of stage I non-small cell lung cancer (NSCLC) using four-dimensional CT scans for treatment planning. *Lung Cancer* 2008 May;60(2):193-9. PMID: 18045732
25. Fuller DB, Naitoh J, Lee C, et al. Virtual HDR CyberKnife treatment for localized prostatic carcinoma: dosimetry comparison with HDR brachytherapy and preliminary clinical observations. *Int J Radiat Oncol Biol Phys* 2008 Apr 1;70(5):1588-97. PMID: 18374232
26. Gerszten PC, Ozhasoglu C, Burton SA, et al. CyberKnife frameless single-fraction stereotactic radiosurgery for tumors of the sacrum. *Neurosurg Focus* 2003 Aug 15;15(2):E7. PMID: 15350038
27. Goodman KA, Wiegner EA, Maturen KE, et al. Dose-escalation study of single-fraction stereotactic body radiotherapy for liver malignancies. *Int J Radiat Oncol Biol Phys* 2010 Oct 1;78(2):486-93. PMID: 20350791
28. Grills IS, Mangona VS, Welsh R, et al. Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer. *J Clin Oncol* 2010 Feb 20;28(6):928-35. PMID: 20065181
29. Guckenberger M, Heilman K, Wulf J, et al. Pulmonary injury and tumor response after stereotactic body radiotherapy (SBRT): results of a serial follow-up CT study. *Radiother Oncol* 2007 Dec;85(3):435-42. PMID: 18053602
30. Guckenberger M, Wulf J, Mueller G, et al. Dose-response relationship for image-guided stereotactic body radiotherapy of pulmonary tumors: relevance of 4D dose calculation. *Int J Radiat Oncol Biol Phys* 2009 May 1;74(1):47-54. PMID: 18977095
31. Guckenberger M, Bachmann J, Wulf J, et al. Stereotactic body radiotherapy for local boost irradiation in unfavourable locally recurrent gynaecological cancer. *Radiother Oncol* 2010 Jan;94(1):53-9. PMID: 20079550
32. Gunven P, Blomgren H, Lax I. Radiosurgery for recurring liver metastases after hepatectomy. *Hepatogastroenterology* 2003 Sep;50(53):1201-4. PMID: 14571698
33. Haasbeek CJ, Lagerwaard FJ, de Jaeger K., et al. Outcomes of stereotactic radiotherapy for a new clinical stage I lung cancer arising postpneumonectomy. *Cancer* 2009 Feb 1;115(3):587-94. PMID: 19130457

34. Hamamoto Y, Kataoka M, Yamashita M, et al. Local control of metastatic lung tumors treated with SBRT of 48 Gy in four fractions: in comparison with primary lung cancer. *Jpn J Clin Oncol* 2010 Feb;40(2):125-9. PMID: 19825814
35. Harada T, Shirato H, Ogura S, et al. Real-time tumor-tracking radiation therapy for lung carcinoma by the aid of insertion of a gold marker using bronchofiberscopy. *Cancer* 2002 Oct 15;95(8):1720-7. PMID: 12365020
36. Henderson M, McGarry R, Yiannoutsos C, et al. Baseline pulmonary function as a predictor for survival and decline in pulmonary function over time in patients undergoing stereotactic body radiotherapy for the treatment of stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Oct 1;72(2):404-9. PMID: 18394819
37. Hodge W, Tome WA, Jaradat HA, et al. Feasibility report of image guided stereotactic body radiotherapy (IG-SBRT) with tomotherapy for early stage medically inoperable lung cancer using extreme hypofractionation. *Acta Oncol* 2006;45(7):890-6. PMID: 16982555
38. Hof H, Hoess A, Oetzel D, et al. Stereotactic single-dose radiotherapy of lung metastases. *Strahlenther Onkol* 2007 Dec;183(12):673-8. PMID: 18040611
39. Hof H, Muentner M, Oetzel D, et al. Stereotactic single-dose radiotherapy (radiosurgery) of early stage nonsmall-cell lung cancer (NSCLC). *Cancer* 2007 Jul 1;110(1):148-55. PMID: 17516437
40. Hof H, Zgoda J, Nill S, et al. Time- and dose-dependency of radiographic normal tissue changes of the lung after stereotactic radiotherapy. *Int J Radiat Oncol Biol Phys* 2010 Aug 1;77(5):1369-74. Epub 2009 Nov 24. PMID: 19932943
41. Hoopes DJ, Tann M, Fletcher JW, et al. FDG-PET and stereotactic body radiotherapy (SBRT) for stage I non-small-cell lung cancer. *Lung Cancer* 2007 May;56(2):229-34. PMID: 17353064
42. Hoyer M, Roed H, Sengelov L, et al. Phase-II study on stereotactic radiotherapy of locally advanced pancreatic carcinoma. *Radiother Oncol* 2005 Jul;76(1):48-53. PMID: 15990186
43. Hoyer M, Roed H, Traberg HA, et al. Phase II study on stereotactic body radiotherapy of colorectal metastases. *Acta Oncol* 2006;45(7):823-30. PMID: 16982546
44. Ishimori T, Saga T, Nagata Y, et al. 18F-FDG and 11C-methionine PET for evaluation of treatment response of lung cancer after stereotactic radiotherapy. *Ann Nucl Med* 2004 Dec;18(8):669-74. PMID: 15682847
45. Jereczek-Fossa BA, Kowalczyk A, D'Onofrio A, et al. Three-dimensional conformal or stereotactic reirradiation of recurrent, metastatic or new primary tumors. Analysis of 108 patients. *Strahlenther Onkol* 2008 Jan;184(1):36-40. PMID: 18188521
46. Jorcano S, Molla M, Escude L, et al. Hypofractionated extracranial stereotactic radiotherapy boost for gynecologic tumors: a promising alternative to high-dose rate brachytherapy. *Technol Cancer Res Treat* 2010 Oct;9(5):509-14. PMID: 20815422
47. Joyner M, Salter BJ, Papanikolaou N, et al. Stereotactic body radiation therapy for centrally located lung lesions. *Acta Oncol* 2006;45(7):802-7. PMID: 16982543
48. Kang JK, Kim MS, Kim JH, et al. Oligometastases confined one organ from colorectal cancer treated by SBRT. *Clin Exp Metastasis* 2010 Apr;27(4):273-8. PMID: 20373133
49. Katoh N, Onimaru R, Sakuhara Y, et al. Real-time tumor-tracking radiotherapy for adrenal tumors. *Radiother Oncol* 2008 Jun;87(3):418-24. PMID: 18439693
50. Kawase T, Takeda A, Kunieda E, et al. Extrapulmonary soft-tissue fibrosis resulting from hypofractionated stereotactic body radiotherapy for pulmonary nodular lesions. *Int J Radiat Oncol Biol Phys* 2009 Jun 1;74(2):349-54. PMID: 19427551
51. Kim MS, Choi C, Yoo S, et al. Stereotactic body radiation therapy in patients with pelvic recurrence from rectal carcinoma. *Jpn J Clin Oncol* 2008 Oct;38(10):695-700. PMID: 18723850
52. Kim MS, Yoo SY, Cho CK, et al. Stereotactic body radiation therapy using three fractions for isolated lung recurrence from colorectal cancer. *Oncology* 2009;76(3):212-9. PMID: 19218825

53. Kim JH, Kim MS, Yoo SY, et al. Stereotactic body radiotherapy for refractory cervical lymph node recurrence of nonanaplastic thyroid cancer. *Otolaryngol Head Neck Surg* 2010 Mar;142(3):338-43. PMID: 20172377
54. Kopeck N, Paludan M, Petersen J, et al. Co-morbidity index predicts for mortality after stereotactic body radiotherapy for medically inoperable early-stage non-small cell lung cancer. *Radiother Oncol* 2009 Dec;93(1):122-4. Epub 2009 Jun 22. PMID: 19559492
55. Kopeck N, Holt MI, Hansen AT, et al. Stereotactic body radiotherapy for unresectable cholangiocarcinoma. *Radiother Oncol* 2010 Jan;94(1):47-52. PMID: 19963295
56. Koto M, Takai Y, Ogawa Y, et al. A phase II study on stereotactic body radiotherapy for stage I non-small cell lung cancer. *Radiother Oncol* 2007 Dec;85(3):429-34. PMID: 18022720
57. Kunos C, von Gruenigen V, Waggoner S, et al. Cyberknife radiosurgery for squamous cell carcinoma of vulva after prior pelvic radiation therapy. *Technol Cancer Res Treat* 2008 Oct;7(5):375-80. PMID: 18783287
58. Lagerwaard FJ, Haasbeek CJ, Smit EF, et al. Outcomes of risk-adapted fractionated stereotactic radiotherapy for stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Mar 1;70(3):685-92. PMID: 18164849
59. Le QT, Loo BW, Ho A, et al. Results of a phase I dose-escalation study using single-fraction stereotactic radiotherapy for lung tumors. *J Thorac Oncol* 2006 Oct;1(8):802-9. PMID: 17409963
60. Lee SW, Choi EK, Park HJ, et al. Stereotactic body frame based fractionated radiosurgery on consecutive days for primary or metastatic tumors in the lung. *Lung Cancer* 2003 Jun;40(3):309-15. PMID: 12781430
61. Lee MT, Kim JJ, Dinniwell R, et al. Phase I study of individualized stereotactic body radiotherapy of liver metastases. *J Clin Oncol* 2009 Apr 1;27(10):1585-91. PMID: 19255313
62. Louis C, Dewas S, Mirabel X, et al. Stereotactic radiotherapy of hepatocellular carcinoma: preliminary results. *Technol Cancer Res Treat* 2010 Oct;9(5):479-87. PMID: 20815419
63. Madsen BL, Hsi RA, Pham HT, et al. Stereotactic hypofractionated accurate radiotherapy of the prostate (SHARP), 33.5 Gy in five fractions for localized disease: first clinical trial results. *Int J Radiat Oncol Biol Phys* 2007 Mar 15;67(4):1099-105. PMID: 17336216
64. Mahadevan A, Jain S, Goldstein M, et al. Stereotactic body radiotherapy and gemcitabine for locally advanced pancreatic cancer. *Int J Radiat Oncol Biol Phys* 2010 Nov 1;78(3):735-42. Epub 2010 Feb 18. PMID: 20171803
65. McCammon R, Schefter TE, Gaspar LE, et al. Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys* 2009 Jan 1;73(1):112-8. PMID: 18786780
66. Milano MT, Chen Y, Katz AW, et al. Central thoracic lesions treated with hypofractionated stereotactic body radiotherapy. *Radiother Oncol* 2009 Jun;91(3):301-6. PMID: 19329210
67. Milano MT, Philip A, Okunieff P. Analysis of patients with oligometastases undergoing two or more curative-intent stereotactic radiotherapy courses. *Int J Radiat Oncol Biol Phys* 2009 Mar 1;73(3):832-7. PMID: 18760543
68. Milano MT, Katz AW, Okunieff P. Patterns of recurrence after curative-intent radiation for oligometastases confined to one organ. *Am J Clin Oncol* 2010 Apr;33(2):157-63. Epub 2009 Sep 18. PMID: 19770627
69. Muacevic A, Drexler C, Wowra B, et al. 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* 2007 Aug;6(4):321-8. PMID: 17668940

70. Nakagawa K, Aoki Y, Tago M, et al. Megavoltage CT-assisted stereotactic radiosurgery for thoracic tumors: original research in the treatment of thoracic neoplasms. *Int J Radiat Oncol Biol Phys* 2000 Sep 1;48(2):449-57. PMID: 10974461
71. Norihisa Y, Nagata Y, Takayama K, et al. Stereotactic body radiotherapy for oligometastatic lung tumors. *Int J Radiat Oncol Biol Phys* 2008 Oct 1;72(2):398-403. PMID: 18374506
72. Nuyttens JJ, Prevost JB, Praag J, et al. Lung tumor tracking during stereotactic radiotherapy treatment with the CyberKnife: marker placement and early results. *Acta Oncol* 2006;45(7):961-5. PMID: 16982564
73. Nuyttens JJ, Prevost JB, Van der Voort van Zijp NC, et al. Curative stereotactic robotic radiotherapy treatment for extracranial, extrapulmonary, extrahepatic, and extraspinal tumors: technique, early results, and toxicity. *Technol Cancer Res Treat* 2007 Dec;6(6):605-10. PMID: 17994790
74. Oermann EK, Slack RS, Hanscom HN, et al. A pilot study of intensity modulated radiation therapy with hypofractionated stereotactic body radiation therapy (SBRT) boost in the treatment of intermediate- to high-risk prostate cancer. *Technol Cancer Res Treat* 2010 Oct;9(5):453-62. PMID: 20815416
75. Olsen CC, Welsh J, Kavanagh BD, et al. Microscopic and macroscopic tumor and parenchymal effects of liver stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys* 2009 Apr 1;73(5):1414-24. PMID: 18990508
76. Onimaru R, Fujino M, Yamazaki K, et al. 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* 2008 Feb 1;70(2):374-81. PMID: 18029106
77. Onishi H, Kuriyama K, Komiyama T, et al. Clinical outcomes of stereotactic radiotherapy for stage I non-small cell lung cancer using a novel irradiation technique: patient self-controlled breath-hold and beam switching using a combination of linear accelerator and CT scanner. *Lung Cancer* 2004 Jul;45(1):45-55. PMID: 15196734
78. Paludan M, Traberg HA, Petersen J, et al. Aggravation of dyspnea in stage I non-small cell lung cancer patients following stereotactic body radiotherapy: Is there a dose-volume dependency? *Acta Oncol* 2006;45(7):818-22. PMID: 16982545
79. Pennathur A, Luketich JD, Heron DE, et al. Stereotactic radiosurgery for the treatment of stage I non-small cell lung cancer in high-risk patients. *J Thorac Cardiovasc Surg* 2009 Mar;137(3):597-604. PMID: 19258073
80. Polistina F, Costantin G, Casamassima F, et al. Unresectable locally advanced pancreatic cancer: a multimodal treatment using neoadjuvant chemoradiotherapy (gemcitabine plus stereotactic radiosurgery) and subsequent surgical exploration. *Ann Surg Oncol* 2010 Aug;17(8):2092-101. Epub 2010 Mar 12. PMID: 20224860
81. Ponsky LE, Mahadevan A, Gill IS, et al. Renal radiosurgery: initial clinical experience with histological evaluation. *Surg Innov* 2007 Dec;14(4):265-9. PMID: 18178914
82. Ricardi U, Guarneri A, Mantovani C, et al. Stereotactic body radiation therapy for early non-small cell lung cancer: experience at the University of Turin. *J Thorac Oncol* 2007 May;2(5 Suppl):S47. PMID: 17457235
83. Ricardi U, Filippi AR, Guarneri A, et al. Dosimetric predictors of radiation-induced lung injury in stereotactic body radiation therapy. *Acta Oncol* 2009;48(4):571-7. PMID: 19031164
84. Mendez RA, Wunderink W, Hussain SM, et al. Stereotactic body radiation therapy for primary and metastatic liver tumors: A single institution phase I-II study. *Acta Oncol* 2006;45(7):831-7. PMID: 16982547
85. Rusthoven KE, Hammerman SF, Kavanagh BD, et al. 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* 2009;48(4):578-83. PMID: 19373699
86. Rusthoven KE, Kavanagh BD, Cardenes H, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for liver metastases. *J Clin Oncol* 2009 Apr 1;27(10):1572-8. PMID: 19255321

87. Rusthoven KE, Kavanagh BD, Burri SH, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for lung metastases. *J Clin Oncol* 2009 Apr 1;27(10):1579-84. PMID: 19255320
88. Salazar OM, Sandhu TS, Lattin PB, et al. Once-weekly, high-dose stereotactic body radiotherapy for lung cancer: 6-year analysis of 60 early-stage, 42 locally advanced, and 7 metastatic lung cancers. *Int J Radiat Oncol Biol Phys* 2008 Nov 1;72(3):707-15. PMID: 18455322
89. Schellenberg D, Goodman KA, Lee F, et al. Gemcitabine chemotherapy and single-fraction stereotactic body radiotherapy for locally advanced pancreatic cancer. *Int J Radiat Oncol Biol Phys* 2008 Nov 1;72(3):678-86. PMID: 18395362
90. Scorsetti M, Navarria P, Facoetti A, et al. Effectiveness of stereotactic body radiotherapy in the treatment of inoperable early-stage lung cancer. *Anticancer Res* 2007 Sep;27(5B):3615-9. PMID: 17972525
91. Seo YS, Kim MS, Yoo SY, et al. Preliminary result of stereotactic body radiotherapy as a local salvage treatment for inoperable hepatocellular carcinoma. *J Surg Oncol* 2010 Sep 1;102(3):209-14. PMID: 20740576
92. Seong J, Lee IJ, Shim SJ, et al. A multicenter retrospective cohort study of practice patterns and clinical outcome on radiotherapy for hepatocellular carcinoma in Korea. *Liver Int* 2009;29(2):147-52. PMID: 18795897
93. Shin YJ, Kim MS, Yoo SY, et al. Pilot study of stereotactic body radiotherapy for huge hepatocellular carcinoma unsuitable for other therapies. *Tumori* 2010 Jan;96(1):65-70. PMID: 20437860
94. Shioyama Y, Nakamura K, Anai S, et al. Stereotactic radiotherapy for lung and liver tumors using a body cast system: setup accuracy and preliminary clinical outcome. *Radiat Med* 2005 Sep;23(6):407-13. PMID: 16389982
95. Sinha B, McGarry RC. Stereotactic body radiotherapy for bilateral primary lung cancers: the Indiana University experience. *Int J Radiat Oncol Biol Phys* 2006 Nov 15;66(4):1120-4. PMID: 17145532
96. Son SH, Choi BO, Ryu MR, et al. Stereotactic body radiotherapy for patients with unresectable primary hepatocellular carcinoma: dose-volumetric parameters predicting the hepatic complication. *Int J Radiat Oncol Biol Phys* 2010 Nov 15;78(4):1073-80. Epub 2010 Mar 6. PMID: 20207492
97. Song DY, Benedict SH, Cardinale RM, et al. Stereotactic body radiation therapy of lung tumors: preliminary experience using normal tissue complication probability-based dose limits. *Am J Clin Oncol* 2005 Dec;28(6):591-6. PMID: 16317270
98. Song SY, Choi W, Shin SS, et al. Fractionated stereotactic body radiation therapy for medically inoperable stage I lung cancer adjacent to central large bronchus. *Lung Cancer* 2009 Oct;66(1):89-93. PMID: 19168260
99. Stephans KL, Djemil T, Reddy CA, et al. Comprehensive analysis of pulmonary function test (PFT) changes after stereotactic body radiotherapy (SBRT) for stage I lung cancer in medically inoperable patients. *J Thorac Oncol* 2009 Jul;4(7):838-44. PMID: 19487961
100. Stephans KL, Djemil T, Reddy CA, et al. A comparison of two stereotactic body radiation fractionation schedules for medically inoperable stage I non-small cell lung cancer: the Cleveland Clinic experience. *J Thorac Oncol* 2009 Aug;4(8):976-82. PMID: 19633473
101. Stintzing S, Hoffmann RT, Heinemann V, et al. Frameless single-session robotic radiosurgery of liver metastases in colorectal cancer patients. *Eur J Cancer* 2010 Apr;46(6):1026-32. PMID: 20153959
102. Stintzing S, Hoffmann RT, Heinemann V, et al. Radiosurgery of liver tumors: value of robotic radiosurgical device to treat liver tumors. *Ann Surg Oncol* 2010 Nov;17(11):2877-83. PMID: 20574773
103. Svedman C, Sandstrom P, Pisa P, et al. A prospective Phase II trial of using extracranial stereotactic radiotherapy in primary and metastatic renal cell carcinoma. *Acta Oncol* 2006;45(7):870-5. PMID: 16982552

104. Svedman C, Karlsson K, Rutkowska E, et al. Stereotactic body radiotherapy of primary and metastatic renal lesions for patients with only one functioning kidney. *Acta Oncol* 2008;47(8):1578-83. PMID: 18607859
105. Takeda A, Sanuki N, Kunieda E, et al. Stereotactic body radiotherapy for primary lung cancer at a dose of 50 Gy total in five fractions to the periphery of the planning target volume calculated using a superposition algorithm. *Int J Radiat Oncol Biol Phys* 2009 Feb 1;73(2):442-8. PMID: 18990507
106. Takeda A, Ohashi T, Kunieda E, et al. Early graphical appearance of radiation pneumonitis correlates with the severity of radiation pneumonitis after stereotactic body radiotherapy (SBRT) in patients with lung tumors. *Int J Radiat Oncol Biol Phys* 2010 Jul 1;77(3):685-90. PMID: 20510193
107. Teh BS, Paulino AC, Lu HH, et al. Versatility of the Novalis system to deliver image-guided stereotactic body radiation therapy (SBRT) for various anatomical sites. *Technol Cancer Res Treat* 2007 Aug;6(4):347-54. PMID: 17668943
108. Timmerman R, McGarry R, Yiannoutsos C, et al. 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* 2006 Oct 20;24(30):4833-9. PMID: 17050868
109. Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA* 2010 Mar 17;303(11):1070-6. PMID: 20233825
110. Townsend NC, Huth BJ, Ding W, et al. Acute toxicity after CyberKnife-delivered hypofractionated radiotherapy for treatment of prostate cancer. *Am J Clin Oncol* 2011 Feb;34(1):6-10. Epub 2010 Jan 8. PMID: 20065849
111. Trovo M, Linda A, El N, I, et al. Early and late lung radiographic injury following stereotactic body radiation therapy (SBRT). *Lung Cancer* 2010 Jul;69(1):77-85. PMID: 19910075
112. Tse RV, Hawkins M, Lockwood G, et al. Phase I study of individualized stereotactic body radiotherapy for hepatocellular carcinoma and intrahepatic cholangiocarcinoma. *J Clin Oncol* 2008 Feb 1;26(4):657-64. PMID: 18172187
113. Uematsu M, Shioda A, Suda A, et al. Computed tomography-guided frameless stereotactic radiotherapy for stage I non-small cell lung cancer: a 5-year experience. *Int J Radiat Oncol Biol Phys* 2001 Nov 1;51(3):666-70. PMID: 11597807
114. Unger K, Ju A, Oermann E, et al. CyberKnife for hilar lung tumors: report of clinical response and toxicity. *J Hematol Oncol* 2010;3:39. PMID: 20969774
115. Vahdat S, Oermann EK, Collins SP, et al. CyberKnife radiosurgery for inoperable stage IA non-small cell lung cancer: 18F-fluorodeoxyglucose positron emission tomography/computed tomography serial tumor response assessment. *J Hematol Oncol* 2010;3:6. PMID: 20132557
116. van der Voort van Zyp NC, Prevost JB, Hoogeman MS, et al. Stereotactic radiotherapy with real-time tumor tracking for non-small cell lung cancer: Clinical outcome. *Radiother Oncol* 2009 Jun;91(3):296-300. PMID: 19297048
117. Whyte RI, Crownover R, Murphy MJ, et al. Stereotactic radiosurgery for lung tumors: preliminary report of a phase I trial. *Ann Thorac Surg* 2003 Apr;75(4):1097-101. PMID: 12683544
118. Wulf J, Hadinger U, Oppitz U, et al. Stereotactic radiotherapy of targets in the lung and liver. *Strahlenther Onkol* 2001 Dec;177(12):645-55. PMID: 11789403
119. Wulf J, Guckenberger M, Hadinger U, et al. Stereotactic radiotherapy of primary liver cancer and hepatic metastases. *Acta Oncol* 2006;45(7):838-47. PMID: 16982548
120. Xia T, Li H, Sun Q, et al. Promising clinical outcome of stereotactic body radiation therapy for patients with inoperable Stage I/II non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2006 Sep 1;66(1):117-25. PMID: 16765528

121. Yamashita H, Kobayashi-Shibata S, Terahara A, et al. Prescreening based on the presence of CT-scan abnormalities and biomarkers (KL-6 and SP-D) may reduce severe radiation pneumonitis after stereotactic radiotherapy. *Radiat Oncol* 2010;5:32. PMID: 20459699
122. Yang ZX, Wang D, Wang G, et al. Clinical study of recombinant adenovirus-p53 combined with fractionated stereotactic radiotherapy for hepatocellular carcinoma. *J Cancer Res Clin Oncol* 2010 Apr;136(4):625-30. PMID: 19882171
123. Yoon SM, Choi EK, Lee SW, et al. Clinical results of stereotactic body frame based fractionated radiation therapy for primary or metastatic thoracic tumors. *Acta Oncol* 2006;45(8):1108-14. PMID: 17118847
124. Zimmermann FB, Geinitz H, Schill S, et al. Stereotactic hypofractionated radiotherapy in stage I (T1-2 N0 M0) non-small-cell lung cancer (NSCLC). *Acta Oncol* 2006;45(7):796-801. PMID: 16982542
125. Cyberknife image-guided radiosurgery system successful. *Expert Rev Anticancer Ther* 2001 Aug;1(2):166
126. Images from Headache. Tumor-related headache as a late complication of radiosurgery. *Headache* 2002 Sep;42(8):834
127. Minimally invasive procedure and robotic technology combined to treat prostate cancer. *Expert Rev Anticancer Ther* 2002 Oct;2(5):482
128. Radiation therapy. A valuable treatment tool. *Mayo Clin Health Lett* 2003 Jun;21(6):1-3
129. Abbas G, Schuchert MJ, Pennathur A, et al. Ablative treatments for lung tumors: radiofrequency ablation, stereotactic radiosurgery, and microwave ablation. *Thorac Surg Clin* 2007 May;17(2):261-71. PMID: 17626404
130. Aboulafia AJ, Levine AM, Schmidt D, et al. Surgical therapy of bone metastases. *Semin Oncol* 2007 Jun;34(3):206-14. PMID: 17560982
131. Ahn YC, Lee KC, Kim DY, et al. Fractionated stereotactic radiation therapy for extracranial head and neck tumors. *Int J Radiat Oncol Biol Phys* 2000 Sep 1;48(2):501-5. PMID: 10974468
132. Anantham D, Feller-Kopman D, Shanmugham LN, et al. Electromagnetic navigation bronchoscopy-guided fiducial placement for robotic stereotactic radiosurgery of lung tumors: a feasibility study. *Chest* 2007 Sep;132(3):930-5. PMID: 17646225
133. Andrews DW. Chained lightning: Part III - Emerging technology, novel therapeutic strategies, and new energy modalities for radiosurgery - Commentary. *Neurosurgery* 2007 Dec;61(6):1129.
134. Andrews DW, Bednarz G, Evans JJ, et al. A review of 3 current radiosurgery systems. *Surg Neurol* 2006 Dec;66(6):559-64. PMID: 17145309
135. Arimura H, Egashira Y, Shioyama Y, et al. Computerized method for estimation of the location of a lung tumor on EPID cine images without implanted markers in stereotactic body radiotherapy. *Phys Med Biol* 2009 Feb 7;54(3):665-77. PMID: 19131668
136. Armstrong J. Advances in radiation technology can improve survival and quality of life for cancer patients. *Ir J Med Sci* 2001 Jan;170(1):63-8. PMID: 11440417
137. Asamura H. Treatment of choice for stage I non-small cell lung cancer: surgery or radiotherapy? *J Thorac Oncol* 2006 Oct;1(8):766-7. PMID: 17409957
138. Astrahan M. BED calculations for fractions of very high dose: in regard to Park et al. (*Int J Radiat Oncol Biol Phys* 2007;69:S623-S624). *Int J Radiat Oncol Biol Phys* 2008 Jul 1;71(3):963. PMID: 18514798
139. Attia M, Menhel J, Alezra D, et al. Radiosurgery--LINAC or gamma knife: 20 years of controversy revisited. *Isr Med Assoc J* 2005 Sep;7(9):583-8. PMID: 16190483
140. Auberger T, Seydl K, Futschek T, et al. Photons or protons: precision radiotherapy of lung cancer. *Strahlenther Onkol* 2007 Dec;183(Spec No 2):3-6. PMID: 18166995

141. Baisden JM, Reish AG, Sheng K, et al. Dose as a function of liver volume and planning target volume in helical tomotherapy, intensity-modulated radiation therapy-based stereotactic body radiation therapy for hepatic metastasis. *Int J Radiat Oncol Biol Phys* 2006 Oct 1;66(2):620-5. PMID: 16904845
142. Bale RJ, Sweeney RA. In regard to Salter et al., *IJROBP* 2001;51:555-562. *Int J Radiat Oncol Biol Phys* 2002 May 1;53(1):253-4. PMID: 12007968
143. Ball D, Withers HR. Stereotactic radiotherapy for stage I non-small-cell lung cancer--the triumph of technology over biology? *Nat Clin Pract Oncol* 2007 Nov;4(11):614-5. PMID: 17848932
144. Ball D. Extracranial stereotactic body radiotherapy for stage I non-small cell lung cancer: still investigational or standard of care? *J Thorac Oncol* 2008 Nov;3(11):1209-10. PMID: 18978553
145. Bance M, Guha A. Radiation-induced malignant tumors after stereotactic radiosurgery. *Otol Neurotol* 2001 Jan;22(1):124-5. PMID: 11314707
146. Banki F, Luketich JD, Chen H, et al. Stereotactic radiosurgery for lung cancer. *Minerva Chir* 2009 Dec;64(6):589-98. PMID: 20029356
147. Barnett GH, Suh JH, Crownover RL. Recent advances in the treatment of skull base tumors using radiation. *Neurosurg Clin North Am* 2000 Oct;11(4):587-96. PMID: 11082169
148. Baser ME, Evans DG, Jackler RK, et al. Neurofibromatosis 2, radiosurgery and malignant nervous system tumours. *Br J Cancer* 2000 Feb;82(4):998. PMID: 10732777
149. Bauman G, Wong E, McDermott M. Fractionated radiotherapy techniques. *Neurosurg Clin North Am* 2006 Apr;17(2):99-110. PMID: 16793502
150. Bayouth JE, Kaiser HS, Smith MC, et al. Image-guided stereotactic radiosurgery using a specially designed high-dose-rate linac. *Med Dosim* 2007;32(2):134-41. PMID: 17472892
151. Benedict SH, Bova FJ, Clark B, et al. Anniversary Paper: the role of medical physicists in developing stereotactic radiosurgery. *Med Phys* 2008 Sep;35(9):4262-77. PMID: 18841876
152. Bernier J, Viale G, Orecchia R, et al. Partial irradiation of the breast: Old challenges, new solutions. *Breast* 2006 Aug;15(4):466-75. PMID: 16439129
153. Bese NS, Kiel K, El-Gueddari B, et al. Radiotherapy for breast cancer in countries with limited resources: program implementation and evidence-based recommendations. *Breast J* 2006 Jan;12 Suppl 1:S96-102. PMID: 16430403
154. Bhatnagar A, Heron DE, Kondziolka D, et al. Analysis of repeat stereotactic radiosurgery for progressive primary and metastatic CNS tumors. *Int J Radiat Oncol Biol Phys* 2002 Jul 1;53(3):527-32. PMID: 12062593
155. Bhatnagar JP, Novotny J, Niranjana A, et al. First year experience with newly developed Leksell Gamma Knife Perfexion. *J Med Phys* 2009 Jul;34(3):141-8. PMID: 20098561
156. Bissonnette JP, Purdie TG, Higgins JA, et al. Cone-beam computed tomographic image guidance for lung cancer radiation therapy. *Int J Radiat Oncol Biol Phys* 2009 Mar 1;73(3):927-34. PMID: 19095368
157. Blute ML. No proof of inferiority: open radical retropubic prostatectomy remains state-of-the-art surgical technique for localized prostate cancer. *J Urol* 2009 Jun;181(6):2421-3. PMID: 19371882
158. Bogart JA. Hypofractionated radiotherapy for advanced non-small-cell lung cancer: is the LINAC half full. *J Clin Oncol* 2004 Mar 1;22(5):765-8. PMID: 14990629
159. Bogart JA. Definitive radiotherapy for stage I non-small cell lung cancer: ain't nothing like the real thing. *J Thorac Oncol* 2006 Oct;1(8):763-5. PMID: 17409956
160. Bogart JA. Stereotactic body radiotherapy for poor-risk lung cancer: "more cyber, less knife?". *Cancer J* 2007 Mar;13(2):75-7. PMID: 17476132

161. Bourland JD, Shaw EG. The evolving role of biological imaging in stereotactic radiosurgery. *Technol Cancer Res Treat* 2003 Apr;2(2):135-9. PMID: 12680794
162. Bradley J. Radiographic response and clinical toxicity following SBRT for stage I lung cancer. *J Thorac Oncol* 2007 Jul;2(7 Suppl 3):S118-S124. PMID: 17603307
163. Brenner MJ, Schwade J. Response to letter: colonic apple-core lesion resulting from cyberknife treatment of unresectable pancreatic cancer. *Pancreas* 2007 Jan;34(1):167-8. PMID: 17198203
164. Bridgewater CH, Spittle MF. The future of radiotherapy and chemotherapy in head and neck cancer. *J Laryngol Otol* 2000 Jun;114(6):411-3. PMID: 10962670
165. Brock KK. Image registration in intensity-modulated, image-guided and stereotactic body radiation therapy. *Front Radiat Ther Oncol* 2007;40:94-115. PMID: 17641504
166. Brock J, Ashley S, Bedford J, et al. Review of hypofractionated small volume radiotherapy for early-stage non-small cell lung cancer. *Clin Oncol (R Coll Radiol)* 2008 Nov;20(9):666-76. PMID: 18676130
167. Buatti JM, Meeks SL, Friedman WA, et al. Stereotactic radiosurgery: techniques and clinical applications. *Surg Oncol Clin N Am* 2000 Jul;9(3):469-87. PMID: 10853137
168. Buatti JM, Friedman WA, Meeks SL, et al. RTOG 90-05: the real conclusion. *Int J Radiat Oncol Biol Phys* 2000 May 1;47(2):269-71. PMID: 10802348
169. Burton KE, Thomas SJ, Whitney D, et al. Accuracy of a relocatable stereotactic radiotherapy head frame evaluated by use of a depth helmet. *Clin Oncol (R Coll Radiol)* 2002 Feb;14(1):31-9. PMID: 11898783
170. Buyyounouski MK, Price RA, Jr., Harris EE, et al. Stereotactic body radiotherapy for primary management of early-stage, low- to intermediate-risk prostate cancer: report of the American Society for Therapeutic Radiology and Oncology Emerging Technology Committee. *Int J Radiat Oncol Biol Phys* 2010 Apr;76(5):1297-304. PMID: 20338473
171. Cadman P. An investigation of beam parameters for Co-60 tomotherapy. *Med Phys* 2007 Oct;34(10):3838-43. PMID: 17985629
172. Calcerrada Diaz-Santos N, Blasco Amaro JA, Cardiel GA, et al. The safety and efficacy of robotic image-guided radiosurgery system treatment for intra- and extracranial lesions: A systematic review of the literature. *Radiother Oncol* 2008 Dec;89(3):245-53. PMID: 18760852
173. Casamassima F, Cavedon C, Francescon P, et al. Use of motion tracking in stereotactic body radiotherapy: Evaluation of uncertainty in off-target dose distribution and optimization strategies. *Acta Oncol* 2006;45(7):943-7. PMID: 16982561
174. Cesaretti JA, Pennathur A, Rosenstein BS, et al. Stereotactic radiosurgery for thoracic malignancies. *Ann Thorac Surg* 2008 Feb;85(2):S785-S791. PMID: 18222218
175. Chang SD, Adler JR. Robotics and radiosurgery--the cyberknife. *Stereotact Funct Neurosurg* 2001;76(3-4):204-8. PMID: 12378098
176. Chang SD, Adler JR, Jr. Current status and optimal use of radiosurgery. *Oncology (Huntingt)* 2001 Feb;15(2):209-16. PMID: 11252934
177. Chang EL, Lo S. Diagnosis and management of central nervous system metastases from breast cancer. *Oncologist* 2003;8(5):398-410. PMID: 14530493
178. Chang JY, Roth JA. Stereotactic body radiation therapy for stage I non-small cell lung cancer. *Thorac Surg Clin* 2007 May;17(2):251-9. PMID: 17626403
179. Chang BW, Saif MW. Stereotactic body radiation therapy (SBRT) in pancreatic cancer: is it ready for prime time? *JOP* 2008;9(6):676-82. PMID: 18981547
180. Chang BK, Timmerman RD. Stereotactic body radiation therapy: a comprehensive review. *Am J Clin Oncol* 2007 Dec;30(6):637-44. PMID: 18091059
181. Chang CY, Tu CH, Chiang TS, et al. Acute gastric ulcer associated with gamma knife treatment (conformal stereotactic radiotherapy) of recurrent hepatocellular carcinoma. *Endoscopy* 2007 Feb;39 Suppl 1:E154. PMID: 16673314

182. Chang ST, Goodman KA, Yang GP, et al. Stereotactic body radiotherapy for unresectable pancreatic cancer. *Front Radiat Ther Oncol* 2007;40:386-94. PMID: 17641521
183. Chang JY, Dong L, Liu H, et al. Image-guided radiation therapy for non-small cell lung cancer. *J Thorac Oncol* 2008 Feb;3(2):177-86. PMID: 18303441
184. Chang J, Yenice KM, Jiang K, et al. Effect of MLC leaf width and PTV margin on the treatment planning of intensity-modulated stereotactic radiosurgery (IMSRS) or radiotherapy (IMSRT). *Med Dosim* 2009;34(2):110-6. PMID: 19410139
185. Chen JC, Rahimian J, Girvigian MR, et al. Contemporary methods of radiosurgery treatment with the Novalis linear accelerator system. *Neurosurg Focus* 2007;23(6):E4. PMID: 18081481
186. Cheung JY, Ng KP, Yu CP, et al. Comparative study of treatment dose plans after the refinement of Leksell Gamma Knife single-beam dose profiles. *Med Phys* 2007 Sep;34(9):3556-61. PMID: 17926958
187. Chi A, Liao Z, Nguyen NP, et al. Systemic review of the patterns of failure following stereotactic body radiation therapy in early-stage non-small-cell lung cancer: clinical implications. *Radiother Oncol* 2010 Jan;94(1):1-11. Epub 2010 Jan 13. PMID: 20074823
188. Chin LS, Ma L, DiBiase S. Radiation necrosis following gamma knife surgery: a case-controlled comparison of treatment parameters and long-term clinical follow up. *J Neurosurg* 2001 Jun;94(6):899-904. PMID: 11409517
189. Cho B, Suh Y, Dieterich S, et al. A monoscopic method for real-time tumour tracking using combined occasional x-ray imaging and continuous respiratory monitoring. *Phys Med Biol* 2008 Jun 7;53(11):2837-55. PMID: 18460750
190. Chou RH, Wilder RB, Wong MS, et al. Recent advances in radiotherapy for head and neck cancers. *Ear Nose Throat J* 2001 Oct;80(10):704-7, 711. PMID: 11605568
191. Christie NA, Pennathur A, Burton SA, et al. Stereotactic radiosurgery for early stage non-small cell lung cancer: rationale, patient selection, results, and complications. *Semin Thorac Cardiovasc Surg* 2008;20(4):290-7. PMID: 19251167
192. Classen J, Schmidberger H, Meisner C, et al. Radiotherapy for stages IIA/B testicular seminoma: final report of a prospective multicenter clinical trial. *J Clin Oncol* 2003 Mar 15;21(6):1101-6. PMID: 12637477
193. Clifford W, Sharpe H, Khu KJ, et al. Gamma Knife patients' experience: lessons learned from a qualitative study. *J Neurooncol* 2009 May;92(3):387-92. PMID: 19357964
194. Coker NJ. The radiosurgical option: too many unanswered questions. *Arch Otolaryngol Head Neck Surg* 2003 Aug;129(8):906-7. PMID: 12925355
195. Collins BT, Erickson K, Reichner CA, et al. Radical stereotactic radiosurgery with real-time tumor motion tracking in the treatment of small peripheral lung tumors. *Radiat Oncol* 2007;2:39. PMID: 17953752
196. Colombo F, Francescon P, Cavedon C. Head frames to image guidance, a brief history of stereotactic radiosurgery. *Nowotwory* 2006;56(3):235-41.
197. Crane CH, Willett CG. Stereotactic radiotherapy for pancreatic cancer. *Cancer* 2009 Feb 1;115(3):468-72. PMID: 19117338
198. Doh L, Curtis AE, Teh BS. Renal-cell carcinoma. *N Engl J Med* 2006 Mar 9;354(10):1095-6. PMID: 16525153
199. Dafele M, Pearson S, Purdie T, et al. Practical considerations arising from the implementation of lung stereotactic body radiation therapy (SBRT) at a comprehensive cancer center. *J Thorac Oncol* 2008 Nov;3(11):1332-41. PMID: 18978570
200. Dawood O. CyberKnife Treatment of Prostate Cancer: A Reply to Bentzen and Wasserman. *Int J Radiat Oncol Biol Phys* 2008 Sep 1;72(1):14-8.
201. Day JD. Malignant schwannoma. *J Neurosurg* 2002 Apr;96(4):805-6. PMID: 11990826

202. De Mey J., Van De Steene J., Vandembroucke F, et al. Percutaneous placement of marking coils before stereotactic radiation therapy of malignant lung lesions. *J Vasc Interv Radiol* 2005 Jan;16(1):51-6. PMID: 15640410
203. de Pooter JA, Wunderink W, Mendez RA, et al. PTV dose prescription strategies for SBRT of metastatic liver tumours. *Radiother Oncol* 2007 Nov;85(2):260-6. PMID: 17905455
204. Decker RH, Tanoue LT, Colasanto JM, et al. Evaluation and definitive management of medically inoperable early stage non-small-cell lung cancer. Part 2: newer treatment modalities. *Oncology (Huntingt)* 2006 Jul;20(8):899-905. PMID: 16922260
205. Demarco JJ, Chetty IJ, Solberg TD. A Monte Carlo tutorial and the application for radiotherapy treatment planning. *Med Dosim* 2002;27(1):43-50. PMID: 12019965
206. Derweesh IH, Novick AC. Small renal tumors: natural history, observation strategies and emerging modalities of energy based tumor ablation. *Can J Urol* 2003 Jun;10(3):1871-9. PMID: 12892573
207. Dilling TJ, Hoffe SE. Stereotactic body radiation therapy: transcending the conventional to improve outcomes. *Cancer Control* 2008 Apr;15(2):104-11. PMID: 18376377
208. Ding M, Newman F, Raben D. New radiation therapy techniques for the treatment of head and neck cancer. *Otolaryngol Clin North Am* 2005 Apr;38(2):371-95. PMID: 15823599
209. Dinka D, Nyce JM, Timpka T. GammaKnife surgery: safety and the identity of users. *Technol Health Care* 2005;13(6):485-95. PMID: 16340092
210. Dunlap NE, Larner JM, Read PW, et al. Size matters: a comparison of T1 and T2 peripheral non-small-cell lung cancers treated with stereotactic body radiation therapy (SBRT). *J Thorac Cardiovasc Surg* 2010 Sep;140(3):583-9. Epub 2010 May 15. PMID: 20478576
211. Dvorak P, Georg D, Bogner J, et al. Impact of IMRT and leaf width on stereotactic body radiotherapy of liver and lung lesions. *Int J Radiat Oncol Biol Phys* 2005 Apr 1;61(5):1572-81. PMID: 15817364
212. Ebert MA, Herbert CE, Spry NA, et al. System validation and work practice efficiency gains of a new localization method for stereotactic radiotherapy. *Australas Radiol* 2001;45(2):182-8. PMID: 11380361
213. Edler A. Special anesthetic considerations for stereotactic radiosurgery in children. *J Clin Anesth* 2007 Dec;19(8):616-8. PMID: 18083476
214. El Hamri AK, Monk J, Plowman PN. Stereotactic radiosurgery at St. Bartholomew's hospital: third quinquennial review. *Br J Radiol* 2005 May;78(929):384-93. PMID: 15845929
215. El-Sherif A, Luketich JD, Landreneau RJ, et al. New therapeutic approaches for early stage non-small cell lung cancer. *Surg Oncol* 2005 Jul;14(1):27-32. PMID: 15777887
216. Ewing MM, DesRosiers C, Fakiris AJ, et al. Conformality study for stereotactic radiosurgery of the lung. *Med Dosim* 36(1):14-20. Epub 2010 Jan 27. PMID: 20110162
217. Fatigante L, Ducci F, Campoccia S, et al. Long-term results in patients affected by testicular seminoma treated with radiotherapy: risk of second malignancies. *Tumori* 2005 Mar;91(2):144-50. PMID: 15948542
218. Fenwick JD, Tome WA, Soisson ET, et al. Tomotherapy and other innovative IMRT delivery systems. *Semin Radiat Oncol* 2006 Oct;16(4):199-208. PMID: 17010902
219. FitzGerald TJ, Aronowitz J, Giulia CM, et al. The effect of radiation therapy on normal tissue function. *Hematol Oncol Clin North Am* 2006 Feb;20(1):141-63. PMID: 16580561
220. Flickinger JC, Kondziolka D, Lunsford LD. Radiobiological analysis of tissue responses following radiosurgery. *Technol Cancer Res Treat* 2003 Apr;2(2):87-92. PMID: 12680788

221. Flickinger JC, Kondziolka D, Niranjan A, et al. Dose selection in stereotactic radiosurgery. 2007;28-42.
222. Foote RL, Pollock BE, Link MJ, et al. Leksell Gamma Knife coordinate setting slippage: how often, how much? *J Neurosurg* 2004 Oct;101(4):590-3. PMID: 15481711
223. Fowler JF. Sensitivity analysis of parameters in linear-quadratic radiobiologic modeling. *Int J Radiat Oncol Biol Phys* 2009 Apr 1;73(5):1532-7. PMID: 19306749
224. Friedman WA, Foote KD. Linear accelerator radiosurgery for skull base tumors. *Neurosurg Clin North Am* 2000 Oct;11(4):667-80. PMID: 11082177
225. Fritz P, Kraus HJ, Dolken W, et al. Technical note: gold marker implants and high-frequency jet ventilation for stereotactic, single-dose irradiation of liver tumors. *Technol Cancer Res Treat* 2006 Feb;5(1):9-14. PMID: 16417397
226. Fuller DB. Balancing on a knife's edge: evidence-based medicine and the marketing of health technology. In regard to Bentzen et al. (*Int J Radiat Oncol Biol Phys* 2008;72:12-14). *Int J Radiat Oncol Biol Phys* 2009 Feb 1;73(2):637-8. PMID: 19147029
227. Fuller CD, Thomas CR, Schwartz S, et al. Method comparison of ultrasound and kilovoltage x-ray fiducial marker imaging for prostate radiotherapy targeting. *Phys Med Biol* 2006 Oct 7;51(19):4981-93. PMID: 16985282
228. Fuss M. Analysis of dose distribution in multiple-target gamma knife radiosurgery. *Int J Radiat Oncol Biol Phys* 2001 Mar 1;49(3):901-2. PMID: 11265658
229. Fuss M, Thomas CR, Jr. Stereotactic body radiation therapy: an ablative treatment option for primary and secondary liver tumors. *Ann Surg Oncol* 2004 Feb;11(2):130-8. PMID: 14761915
230. Fuss M, Shi C, Papanikolaou N. Tomotherapeutic stereotactic body radiation therapy: Techniques and comparison between modalities. *Acta Oncol* 2006;45(7):953-60. PMID: 16982563
231. Fuss M, Boda-Heggemann J, Papanikolaou N, et al. Image-guidance for stereotactic body radiation therapy. *Med Dosim* 2007;32(2):102-10. PMID: 17472889
232. Galvin JM, Bednarz G. Quality assurance procedures for stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys* 2008 May 1;71(1 Suppl):S122-S125. PMID: 18406909
233. Ganslandt O, Mueller R, Mueller W, et al. Simple invasive fixation device for fractionated stereotactic LINAC based radiotherapy. *Acta Neurochir* 2003 Apr;145(4):289-94. PMID: 12748889
234. Ganz JC. Gamma knife radiosurgery and its possible relationship to malignancy: a review. *J Neurosurg* 2002 Dec;97(5 Suppl):644-52. PMID: 12507113
235. Ganz JC. Surgery or gamma knife. *J Neurosurg* 2007 May;106(5):937-8. PMID: 17542547
236. Gasent Blesa JM, Dawson LA. Options for radiotherapy in the treatment of liver metastases. *Clin Transl Oncol* 2008 Oct;10(10):638-45. PMID: 18940744
237. Gaspar LE. Stereotactic body radiation therapy for lung tumors: system-related issues and complications. *Clin Lung Cancer* 2007 Jan;8(4):233. PMID: 17311686
238. Gerber DE, Chan TA. Recent advances in radiation therapy.[summary for patients in *Am Fam Physician*. 2008 Dec 1;78(11):1263-4; PMID: 19069019]. *Am Fam Physician* 2008 Dec 1;78(11):1254-62. PMID: 19069018
239. Gerrard GE, Franks KN. Overview of the diagnosis and management of brain, spine, and meningeal metastases. *J Neurol Neurosurg Psychiatry* 2004 Jun;75 Suppl 2:ii37-ii42. PMID: 15146038
240. Gerszten PC, Burton SA, Belani CP, et al. Radiosurgery for the treatment of spinal lung metastases. *Cancer* 2006 Dec 1;107(11):2653-61. PMID: 17063501
241. Gibbons JP, Mihailidis D, Worthington C, et al. Technical note: the effect of the 4-mm-collimator output factor on gamma knife dose distributions. *J Appl Clin Med Phys* 2003;4(4):386-9. PMID: 14604431

242. Gibbs IC. Frameless image-guided intracranial and extracranial radiosurgery using the Cyberknife robotic system. *Cancer Radiother* 2006 Sep;10(5):283-7. PMID: 16859948
243. Gibbs IC, Chang SD. Radiosurgery and radiotherapy for sacral tumors. *Neurosurg Focus* 2003 Aug 15;15(2):E8. PMID: 15350039
244. Gottlieb N. Radiotherapy technique tackles challenge of moving target. *J Natl Cancer Inst* 2001 Mar 21;93(6):422. PMID: 11259463
245. Gottlieb N. Robotics and more: new technologies emerge for radiotherapy. *J Natl Cancer Inst* 2001 Mar 21;93(6):421-3. PMID: 11259462
246. Grills IS, Fitch DL, Goldstein NS, et al. Clinicopathologic analysis of microscopic extension in lung adenocarcinoma: defining clinical target volume for radiotherapy. *Int J Radiat Oncol Biol Phys* 2007 Oct 1;69(2):334-41. PMID: 17570609
247. Gross MW, Engenhart-Cabillic R. Normal tissue reactions after linac-based radiosurgery and stereotactic radiotherapy. *Front Radiat Ther Oncol* 2002;37:140-50. PMID: 11764656
248. Gross MW, Spahn U, Engenhart-Cabillic R. Assessment of the accuracy of a conventional simulation for radiotherapy of head and skull base tumors. *Technol Cancer Res Treat* 2003 Aug;2(4):345-51. PMID: 12892518
249. Grutters JP, Pijls-Johannesma M, Ruysscher DD, et al. The cost-effectiveness of particle therapy in non-small cell lung cancer: exploring decision uncertainty and areas for future research. *Cancer Treat Rev* 2010 Oct;36(6):468-76. PMID: 20303217
250. Guckenberger M, Meyer J, Wilbert J, et al. Cone-beam CT based image-guidance for extracranial stereotactic radiotherapy of intrapulmonary tumors. *Acta Oncol* 2006;45(7):897-906. PMID: 16982556
251. Guckenberger M, Meyer J, Wilbert J, et al. Intra-fractional uncertainties in cone-beam CT based image-guided radiotherapy (IGRT) of pulmonary tumors. *Radiother Oncol* 2007 Apr;83(1):57-64. PMID: 17306394
252. Guckenberger M, Wilbert J, Krieger T, et al. Mid-ventilation concept for mobile pulmonary tumors: internal tumor trajectory versus selective reconstruction of four-dimensional computed tomography frames based on external breathing motion. *Int J Radiat Oncol Biol Phys* 2009 Jun 1;74(2):602-9. PMID: 19427559
253. Guckenberger M, Krieger T, Richter A, et al. Potential of image-guidance, gating and real-time tracking to improve accuracy in pulmonary stereotactic body radiotherapy. *Radiother Oncol* 2009 Jun;91(3):288-95. PMID: 18835650
254. Guckenberger M, Baier K, Polat B, et al. Dose-response relationship for radiation-induced pneumonitis after pulmonary stereotactic body radiotherapy. *Radiother Oncol* 2010;97(1):65-70.
255. Guerrero M, Li XA. Extending the linear-quadratic model for large fraction doses pertinent to stereotactic radiotherapy. *Phys Med Biol* 2004 Oct 21;49(20):4825-35. PMID: 15566178
256. Hadinger U, Thiele W, Wulf J. Extracranial stereotactic radiotherapy: evaluation of PTV coverage and dose conformity. *Z Med Phys* 2002;12(4):221-9. PMID: 12575435
257. Haedinger U, Krieger T, Flentje M, et al. Influence of calculation model on dose distribution in stereotactic radiotherapy for pulmonary targets. *Int J Radiat Oncol Biol Phys* 2005 Jan 1;61(1):239-49. PMID: 15629617
258. Hansen AT, Petersen JB, Hoyer M. Internal movement, set-up accuracy and margins for stereotactic body radiotherapy using a stereotactic body frame. *Acta Oncol* 2006;45(7):948-52. PMID: 16982562
259. Hara W, Soltys SG, Gibbs IC. CyberKnife robotic radiosurgery system for tumor treatment. *Expert Rev Anticancer Ther* 2007 Nov;7(11):1507-15. PMID: 18020920
260. Heinzerling JH, Anderson JF, Papiez L, et al. Four-dimensional computed tomography scan analysis of tumor and organ motion at varying levels of abdominal compression during stereotactic treatment of lung and liver. *Int J Radiat Oncol Biol Phys* 2008 Apr 1;70(5):1571-8. PMID: 18374231

261. Herbert CE, Ebert MA, Barclay D, et al. Effect of bite tray impression technique on relocation accuracy in frameless stereotactic radiotherapy. *Med Dosim* 2003;28(1):27-30. PMID: 12747615
262. Hermann RM, Christiansen H, Schmidberger H, et al. Comment on 'Dieckmann K, Georg D, Zehetmayer M, Bogner J, Georgopoulos M, Potter R. LINAC based stereotactic radiotherapy of uveal melanoma: 4 years clinical experience.' [Radiother Oncol. 2003;67(2):199-206]. *Radiother Oncol* 2004 Feb;70(2):211. PMID: 15028413
263. Heron DE, Godette KD, Wynn RA, et al. Radiation medicine innovations for the new millenium. *J Natl Med Assoc* 2003 Jan;95(1):55-63. PMID: 12656450
264. Heron DE, Ferris RL, Karamouzis M, et al. Stereotactic body radiotherapy for recurrent squamous cell carcinoma of the head and neck: results of a phase I dose-escalation trial. *Int J Radiat Oncol Biol Phys* 2009 Dec 1;75(5):1493-500. Epub 2009 May 21. PMID: 19464819
265. Heros RC. Radiosurgery and neurosurgeons. *J Neurosurg* 2005 Aug;103(2):203-5. PMID: 16175846
266. Hevezi JM. Emerging technology in cancer treatment: radiotherapy modalities. *Oncology (Williston Park)* 2003 Oct;17(10):1445-56. PMID: 14606366
267. Hevezi JM. Current IGRT, SBRT, and SRS procedures and reimbursement. *J Am Coll Radiol* 2010 Sep;7(9):739-40.
268. Hinson WH, Kearns WT, Ellis TL, et al. Reducing set-up uncertainty in the Elekta Stereotactic Body Frame using Stealthstation software. *Technol Cancer Res Treat* 2007 Jun;6(3):181-6. PMID: 17535026
269. Hiraoka M, Matsuo Y, Nagata Y. Stereotactic body radiation therapy (SBRT) for early-stage lung cancer. *Cancer Radiother* 2007 Jan;11(1-2):32-5. PMID: 17158081
270. Hocht S, Stark R, Seiler F, et al. Proton or stereotactic photon irradiation for posterior uveal melanoma? A planning intercomparison. *Strahlenther Onkol* 2005 Dec;181(12):783-8. PMID: 16362788
271. Hogle WP. The state of the art in radiation therapy. *Semin Oncol Nurs* 2006 Nov;22(4):212-20. PMID: 17095397
272. Hoh DJ, Liu CY, Chen JC, et al. Chained lightning: part III--Emerging technology, novel therapeutic strategies, and new energy modalities for radiosurgery. *Neurosurgery* 2007 Dec;61(6):1111-29. PMID: 18162890
273. Holland J. New treatment modalities in radiation therapy. *J Intraven Nurs* 2001 Mar;24(2):95-101. PMID: 11836839
274. Holmes TW, Hudes R, Dziuba S, et al. Stereotactic image-guided intensity modulated radiotherapy using the HI-ART II helical tomotherapy system. *Med Dosim* 2008;33(2):135-48. PMID: 18456165
275. Hoogeman MS, Nuyttens JJ, Levendag PC, et al. Time dependence of intrafraction patient motion assessed by repeat stereoscopic imaging. *Int J Radiat Oncol Biol Phys* 2008 Feb 1;70(2):609-18. PMID: 17996389
276. Hoogeman M, Prevost JB, Nuyttens J, et al. Clinical accuracy of the respiratory tumor tracking system of the cyberknife: assessment by analysis of log files. *Int J Radiat Oncol Biol Phys* 2009 May 1;74(1):297-303. PMID: 19362249
277. Horstmann GA, Schopgens H, van Eck AT, et al. First clinical experience with the automatic positioning system and Leksell gamma knife Model C. Technical note. *J Neurosurg* 2000 Dec;93(Suppl 3):193-7. PMID: 11143247
278. Hui SK, Das RK, Kapatoes J, et al. Helical tomotherapy as a means of delivering accelerated partial breast irradiation. *Technol Cancer Res Treat* 2004 Dec;3(6):639-46. PMID: 15560722
279. Huntzinger C, Friedman W, Bova F, et al. Trilogy image-guided stereotactic radiosurgery. *Med Dosim* 2007;32(2):121-33. PMID: 17472891
280. Imura M, Yamazaki K, Shirato H, et al. Insertion and fixation of fiducial markers for setup and tracking of lung tumors in radiotherapy. *Int J Radiat Oncol Biol Phys* 2005 Dec 1;63(5):1442-7. PMID: 16109463

281. Imura M, Yamazaki K, Kubota KC, et al. Histopathologic consideration of fiducial gold markers inserted for real-time tumor-tracking radiotherapy against lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Feb 1;70(2):382-4. PMID: 17881147
282. Inoue T, Katoh N, Aoyama H, et al. Clinical outcomes of stereotactic brain and/or body radiotherapy for patients with oligometastatic lesions. *Jpn J Clin Oncol* 2010 Aug;40(8):788-94. Epub 2010 Apr 20. PMID: 20406944
283. Isaksson M, Jalden J, Murphy MJ. On using an adaptive neural network to predict lung tumor motion during respiration for radiotherapy applications. *Med Phys* 2005 Dec;32(12):3801-9. PMID: 16475780
284. Jaffray D, Kupelian P, Djemil T, et al. Review of image-guided radiation therapy. *Expert Rev Anticancer Ther* 2007;7(1):89-103. PMID: 17187523
285. Jamal K, Patel P, Sooriakumaran P. Minimally invasive surgical modalities in the management of localized prostate cancer. *Expert Rev Anticancer Ther* 2008 Jun;8(6):957-66. PMID: 18533805
286. Jawahar A, Jawahar LL, Nanda A, et al. Stereotactic radiosurgery using the Leksell Gamma Knife: current trends and future directives. *Front Biosci* 2004 Jan 1;9:932-8. PMID: 14766419
287. Jeremic B, Becker G, Plasswilm L, et al. Activity of extracranial metastases as a prognostic factor influencing survival after radiosurgery of brain metastases. *J Cancer Res Clin Oncol* 2000 Aug;126(8):475-80. PMID: 10961391
288. Jin JY, Yin FF, Ryu S, et al. Dosimetric study using different leaf-width MLCs for treatment planning of dynamic conformal arcs and intensity-modulated radiosurgery. *Med Phys* 2005 Feb;32(2):405-11. PMID: 15789586
289. Jin JY, Kong FM, Chetty IJ, et al. Impact of fraction size on lung radiation toxicity: hypofractionation may be beneficial in dose escalation of radiotherapy for lung cancers. *Int J Radiat Oncol Biol Phys* 2010 Mar 1;76(3):782-8. Epub 2009 Jul 4. PMID: 19577855
290. Joensuu H. Novel cancer therapies: more efficacy, less toxicity and improved organ preservation. *Ann Med* 2000 Feb;32(1):31-3. PMID: 10711575
291. Jozsef G, Luxton G, Formenti SC. Application of radiosurgery principles to a target in the breast: a dosimetric study. *Med Phys* 2000 May;27(5):1005-10. PMID: 10841403
292. Kassaei A, Das IJ, Tochner Z, et al. Modification of Gill-Thomas-Cosman frame for extracranial head-and-neck stereotactic radiotherapy. *Int J Radiat Oncol Biol Phys* 2003 Nov 15;57(4):1192-5. PMID: 14575852
293. Katz AW, Carey-Sampson M, Muhs AG, et al. Hypofractionated stereotactic body radiation therapy (SBRT) for limited hepatic metastases. *Int J Radiat Oncol Biol Phys* 2007 Mar 1;67(3):793-8. PMID: 17197128
294. Kavanagh BD, Timmerman RD. Stereotactic radiosurgery and stereotactic body radiation therapy: an overview of technical considerations and clinical applications. *Hematol Oncol Clin North Am* 2006 Feb;20(1):87-95. PMID: 16580558
295. Kavanagh BD, Timmerman RD, Benedict SH, et al. How should we describe the radiobiologic effect of extracranial stereotactic radiosurgery: equivalent uniform dose or tumor control probability? *Med Phys* 2003 Mar;30(3):321-4. PMID: 12674231
296. Kavanagh BD, Schefter TE, Cardenas HR, et al. Interim analysis of a prospective phase I/II trial of SBRT for liver metastases. *Acta Oncol* 2006;45(7):848-55. PMID: 16982549
297. Kavanagh BD, Schefter TE, Wersall PJ. Liver, renal, and retroperitoneal tumors: stereotactic radiotherapy. *Front Radiat Ther Oncol* 2007;40:415-26. PMID: 17641524
298. Kavanagh BD, Kelly K, Kane M. The promise of stereotactic body radiation therapy in a new era of oncology. *Front Radiat Ther Oncol* 2007;40:340-51. PMID: 17641518

299. Kavanagh B. Clinical experience shows that catastrophic late effects associated with ablative fractionation can be avoided by technological innovation. *Semin Radiat Oncol* 2008 Oct;18(4):223-8. PMID: 18725107
300. Kawaguchi O, Kunieda E, Fujii H, et al. Adenoid cystic carcinoma with hyperostosis after stereotactic radiosurgery. *Radiat Med* 2004 May;22(3):198-200. PMID: 15287538
301. Kelly PJ. Stereotactic surgery: what is past is prologue. *Neurosurgery* 2000 Jan;46(1):16-27. PMID: 10626931
302. Kenai H, Yamashita M, Nakamura T, et al. Tolerance dose in gamma knife surgery of lesions extending to the anterior visual pathway. *J Neurosurg* 2005 Jan;102 Suppl:230-3. PMID: 15662816
303. King CR, Lehmann J, Adler JR, et al. CyberKnife radiotherapy for localized prostate cancer: rationale and technical feasibility. *Technol Cancer Res Treat* 2003 Feb;2(1):25-30. PMID: 12625751
304. King CR, Brooks JD, Gill H, et al. Stereotactic body radiotherapy for localized prostate cancer: interim results of a prospective phase II clinical trial. *Int J Radiat Oncol Biol Phys* 2009 Mar 15;73(4):1043-8. PMID: 18755555
305. King CR, Brooks JD, Gill H, et al. Stereotactic body radiotherapy for localized prostate cancer: interim results of a prospective phase II clinical trial. *Int J Radiat Oncol Biol Phys* 2009 Mar 15;73(4):1043-8. PMID: 18755555
306. King CR, Lo A, Kapp DS. Testicular dose from prostate cyberknife: a cautionary note. *Int J Radiat Oncol Biol Phys* 2009 Feb 1;73(2):636-7. PMID: 19147028
307. Kitamura K, Shirato H, Shimizu S, et al. Registration accuracy and possible migration of internal fiducial gold marker implanted in prostate and liver treated with real-time tumor-tracking radiation therapy (RTRT). *Radiother Oncol* 2002 Mar;62(3):275-81. PMID: 12175558
308. Kitamura K, Shirato H, Seppenwoolde Y, et al. Three-dimensional intrafractional movement of prostate measured during real-time tumor-tracking radiotherapy in supine and prone treatment positions. *Int J Radiat Oncol Biol Phys* 2002 Aug 1;53(5):1117-23. PMID: 12128110
309. Kitamura K, Shirato H, Seppenwoolde Y, et al. Tumor location, cirrhosis, and surgical history contribute to tumor movement in the liver, as measured during stereotactic irradiation using a real-time tumor-tracking radiotherapy system. *Int J Radiat Oncol Biol Phys* 2003 May 1;56(1):221-8. PMID: 12694842
310. Koga T, Maruyama K, Igaki H, et al. The value of image coregistration during stereotactic radiosurgery. *Acta Neurochir (Wien)* 2009 May;151(5):465-71. PMID: 19319470
311. Kommu SS, Andrews RJ, Mah RW. Real-time multiple microsensor tissue recognition and its potential application in the management of prostate cancer. *BJU Int* 2006 Feb;97(2):222-3. PMID: 16430616
312. Kondziolka D, Lunsford LD, Witt TC, et al. The future of radiosurgery: radiobiology, technology, and applications. *Surg Neurol* 2000 Dec;54(6):406-14. PMID: 11240166
313. Kondziolka D, Lunsford LD, Loeffler JS, et al. Radiosurgery and radiotherapy: observations and clarifications. *J Neurosurg* 2004 Oct;101(4):585-9. PMID: 15481710
314. Kondziolka D, Lunsford LD, Flickinger JC, et al. Emerging indications in stereotactic radiosurgery. *Clin Neurosurg* 2005;52:229-33. PMID: 16626075
315. Kondziolka D, Niranjan A, Lunsford LD, et al. Radiobiology of radiosurgery. *Prog Neurol Surg* 2007;20:16-27. PMID: 17317973
316. Kontrisoa K, Stock M, Dieckmann K, et al. Dosimetric comparison of stereotactic body radiotherapy in different respiration conditions: a modeling study. *Radiother Oncol* 2006 Oct;81(1):97-104. PMID: 16962675

317. Koong AC, Le QT, Ho A, et al. Phase I study of stereotactic radiosurgery in patients with locally advanced pancreatic cancer. *Int J Radiat Oncol Biol Phys* 2004 Mar 15;58(4):1017-21. PMID: 15001240
318. Koong AC, Christofferson E, Le QT, et al. 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* 2005 Oct 1;63(2):320-3. PMID: 16168826
319. Kopek N, Holt MI, Hansen AT, et al. Stereotactic body radiotherapy for unresectable cholangiocarcinoma. *Radiother Oncol* 2010 Jan;94(1):47-52. PMID: 19963295
320. Korreman S, Mostafavi H, Le QT, et al. Comparison of respiratory surrogates for gated lung radiotherapy without internal fiducials. *Acta Oncol* 2006;45(7):935-42. PMID: 16982560
321. Kresl JJ. St. Joseph's Hospital and Barrow Neurological Institute stereotactic radiotherapy experience: Comparison of Gamma Knife and CyberKnife. *Nowotwory* 2006;56(2):125-30.
322. Kunieda E, Kawaguchi O, Saitoh H, et al. Measurement of beam-axis displacement from the isocenter during three-dimensional conformal radiosurgery with a micro-multileaf collimator. *Radiother Oncol* 2004 Jan;70(1):45-8. PMID: 15036851
323. Kunieda E, Deloar HM, Kishitani N, et al. Variation of dose distribution of stereotactic radiotherapy for small-volume lung tumors under different respiratory conditions. *Phys Med* 2008 Dec;24(4):204-11. PMID: 18396083
324. Kunzler T, Grezdo J, Bogner J, et al. Registration of DRRs and portal images for verification of stereotactic body radiotherapy: a feasibility study in lung cancer treatment. *Phys Med Biol* 2007 Apr 21;52(8):2157-70. PMID: 17404461
325. Kupferman ME, Hanna EY. Paragangliomas of the head and neck. *Curr Oncol Rep* 2008 Mar;10(2):156-61. PMID: 18377829
326. Laigle-Donadey F, Taillibert S, Martin-Duverneuil N, et al. Skull-base metastases. *J Neurooncol* 2005 Oct;75(1):63-9. PMID: 16215817
327. Langner UW, Keall PJ. Accuracy in the localization of thoracic and abdominal tumors using respiratory displacement, velocity, and phase. *Med Phys* 2009 Feb;36(2):386-93. PMID: 19291977
328. Larre S, Salomon L, Abbou CC. Choices for surgery. *Recent Results Cancer Res* 2007;175:163-78. PMID: 17432559
329. Lartigau E, Mirabel X, Prevost JB, et al. Extracranial stereotactic radiotherapy: preliminary results with the CyberKnife. *Onkologie* 2009 Apr;32(4):209-15. PMID: 19372719
330. Lawson JD, Fox T, Waller AF, et al. Multileaf collimator-based linear accelerator radiosurgery: five-year efficiency analysis. *J Am Coll Radiol* 2009 Mar;6(3):190-3. PMID: 19248995
331. Lax I, Panettieri V, Wennberg B, et al. Dose distributions in SBRT of lung tumors: Comparison between two different treatment planning algorithms and Monte-Carlo simulation including breathing motions. *Acta Oncol* 2006;45(7):978-88. PMID: 16982567
332. Leavitt DD, Watson G, Tobler M, et al. Intensity-modulated radiosurgery/radiotherapy using a micromultileaf collimator. *Med Dosim* 2001;26(2):143-50. PMID: 11444516
333. Lee EK, Fox T, Crocker I. Optimization of radiosurgery treatment planning via mixed integer programming. *Med Phys* 2000 May;27(5):995-1004. PMID: 10841402
334. Lee WR. Extreme hypofractionation for prostate cancer. *Expert Rev Anticancer Ther* 2009;9(1):61-5. PMID: 19105707
335. Leksell D. Epilogue: The future of radiosurgery. 2007;388-91.
336. Li K, Ma L. A constrained tracking algorithm to optimize plug patterns in multiple isocenter gamma knife radiosurgery planning. *Med Phys* 2005 Oct;32(10):3132-5. PMID: 16279066

337. Liao R, Williams JA, Myers L, et al. Optimization of multiple-isocenter treatment planning for linac-based stereotactic radiosurgery. *Comput Aided Surg* 2000;5(4):220-33. PMID: 11029156
338. Lillard A. SBRT - the new treatment of choice. *Imaging Technol News* 2008 Sep;28, 31.
339. Lind CR, Costello SA, Mathur S, et al. Stereotactic radiosurgery in New Zealand. *N Z Med J* 2001 Apr 27;114(1130):182-4. PMID: 11396666
340. Lindquist C, Paddick I. The Leksell Gamma Knife Perfexion and comparisons with its predecessors. *Neurosurgery* 2007 Sep;61(3 Suppl):130-40. PMID: 17876243
341. Lindvall P, Bergstrom P, Lofroth PO, et al. Reproducibility and geometric accuracy of the Fixster system during hypofractionated stereotactic radiotherapy. *Radiat Oncol* 2008;3:16. PMID: 18507861
342. Linskey ME, Johnstone PA. Radiation tolerance of normal temporal bone structures: implications for gamma knife stereotactic radiosurgery. *Int J Radiat Oncol Biol Phys* 2003 Sep 1;57(1):196-200. PMID: 12909233
343. Linthout N, Bral S, Van dV, I, et al. Treatment delivery time optimization of respiratory gated radiation therapy by application of audio-visual feedback. *Radiother Oncol* 2009 Jun;91(3):330-5. PMID: 19368987
344. Liu R, Wagner TH, Buatti JM, et al. Geometrically based optimization for extracranial radiosurgery. *Phys Med Biol* 2004 Mar 21;49(6):987-96. PMID: 15104321
345. Livi L, Paiar F, Buonamici FB, et al. Accelerated intensity-modulated external radiotherapy as a new technical approach to treat the index quadrant after conserving surgery in early breast cancer: a preliminary study. *Tumori* 2005 May;91(3):227-32. PMID: 16206645
346. Lo SS, Cardenes HR, Teh BS, et al. Stereotactic body radiation therapy for nonpulmonary primary tumors. *Expert Rev Anticancer Ther* 2008 Dec;8(12):1939-51. PMID: 19046114
347. Lo SS, Fakiris AJ, Teh BS, et al. Stereotactic body radiation therapy for oligometastases. *Expert Rev Anticancer Ther* 2009 May;9(5):621-35. PMID: 19445579
348. Lomax NJ, Scheib SG. Quantifying the degree of conformity in radiosurgery treatment planning. *Int J Radiat Oncol Biol Phys* 2003 Apr 1;55(5):1409-19. PMID: 12654454
349. Lu XQ, Shanmugham LN, Mahadevan A, et al. Organ deformation and dose coverage in robotic respiratory-tracking radiotherapy. *Int J Radiat Oncol Biol Phys* 2008 May 1;71(1):281-9. PMID: 18406892
350. Ma L, Chin LS, DiBiase SJ, et al. Concomitant boost of stratified target area with gamma knife radiosurgery: a treatment planning study. *Am J Clin Oncol* 2003 Aug;26(4):e100-e105. PMID: 12902906
351. Maarouf M, Treuer H, Kocher M, et al. Radiation exposure of extracranial organs at risk during stereotactic linac radiosurgery. *Strahlenther Onkol* 2005 Jul;181(7):463-7. PMID: 15995840
352. Macdermed DM, Weichselbaum RR, Salama JK. A rationale for the targeted treatment of oligometastases with radiotherapy. *J Surg Oncol* 2008 Sep 1;98(3):202-6. PMID: 18618604
353. Martin A, Gaya A. Stereotactic body radiotherapy: a review. *Clin Oncol (R Coll Radiol)* 2010 Apr;22(3):157-72. Epub 2010 Jan 25. PMID: 20092981
354. Matsumoto Y, Horiike S, Fujimoto Y, et al. Effectiveness and limitation of gamma knife radiosurgery for relapsed central nervous system lymphoma: a retrospective analysis in one institution. *Int J Hematol* 2007 May;85(4):333-7. PMID: 17483078
355. McDermott LN, Wendling M, Sonke JJ, et al. Anatomy changes in radiotherapy detected using portal imaging. *Radiother Oncol* 2006 May;79(2):211-7. PMID: 16698097
356. McGarry RC, Papiez L, Williams M, et al. Stereotactic body radiation therapy of early-stage non-small-cell lung carcinoma: phase I study. *Int J Radiat Oncol Biol Phys* 2005 Nov 15;63(4):1010-5. PMID: 16115740

357. Meeks SL, Buatti JM, Bouchet LG, et al. Ultrasound-guided extracranial radiosurgery: technique and application. *Int J Radiat Oncol Biol Phys* 2003 Mar 15;55(4):1092-101. PMID: 12605989
358. Mell LK, Mundt AJ. Radiation therapy in the elderly. *Cancer J* 2005 Nov;11(6):495-505. PMID: 16393484
359. Meretoja TJ, Von Smitten KA, Kuokkanen HO, et al. Complications of skin-sparing mastectomy followed by immediate breast reconstruction: A prospective randomized study comparing high-frequency radiosurgery with conventional diathermy. *Ann Plast Surg* 2008 Jan;60(1):24-8. PMID: 18281791
360. Mery CM, Cooke DT, Chandra V, et al. The road to innovation: emerging technologies in surgery. *Bull Am Coll Surg* 2007 Jul;92(7):19-33. PMID: 17691613
361. Meyer JL, Verhey L, Xia P, et al. New technologies in the radiotherapy clinic. *Front Radiat Ther Oncol* 2007;40:1-17. PMID: 17641499
362. Meyer JL, Leibel S, Roach M, et al. New technologies for the radiotherapy of prostate cancer. A discussion of clinical treatment programs. *Front Radiat Ther Oncol* 2007;40:315-37. PMID: 17641517
363. Mignano JE, Engler MJ, Tsai JS, et al. Comparison of radiobiologic modeling for one- and two-isocenter dose distributions applied to ellipsoidal radiosurgery targets. *Int J Radiat Oncol Biol Phys* 2001 Mar 1;49(3):833-7. PMID: 11172967
364. Minn AY, Schellenberg D, Maxim P, et al. Pancreatic tumor motion on a single planning 4D-CT does not correlate with intrafraction tumor motion during treatment. *Am J Clin Oncol* 2009 Aug;32(4):364-8. PMID: 19398901
365. Molla M, Escude L, Nouet P, et al. Fractionated stereotactic radiotherapy boost for gynecologic tumors: an alternative to brachytherapy? *Int J Radiat Oncol Biol Phys* 2005 May 1;62(1):118-24. PMID: 15850911
366. Morgia G, De Renzis C. CyberKnife in the treatment of prostate cancer: a revolutionary system. *Eur Urol* 2009 Jul;56(1):40-2. Epub 2009 Feb 23. PMID: 19246151
367. Muacevic A, Wowra B, Kreth FW, et al. Radiosurgery in renal cell carcinoma. *J Neurosurg* 2003 Aug 1;99(2):441-2. PMID: 12924727
368. Muacevic A, Jess-Hempfen A, Tonn JC, et al. Clinical quality standards for gamma knife radiosurgery--the Munich protocol. *Acta Neurochir Suppl* 2004;91:25-32. PMID: 15707023
369. Muller K, Nowak PJ, Luyten GP, et al. A modified relocatable stereotactic frame for irradiation of eye melanoma: design and evaluation of treatment accuracy. *Int J Radiat Oncol Biol Phys* 2004 Jan 1;58(1):284-91. PMID: 14697450
370. Murphy MJ. Tracking moving organs in real time. *Semin Radiat Oncol* 2004 Jan;14(1):91-100. PMID: 14752737
371. Murphy MJ, Martin D, Whyte R, et al. The effectiveness of breath-holding to stabilize lung and pancreas tumors during radiosurgery. *Int J Radiat Oncol Biol Phys* 2002 Jun 1;53(2):475-82. PMID: 12023152
372. Murphy MJ, Chang SD, Gibbs IC, et al. Patterns of patient movement during frameless image-guided radiosurgery. *Int J Radiat Oncol Biol Phys* 2003 Apr 1;55(5):1400-8. PMID: 12654453
373. Murphy MJ. Intrafraction geometric uncertainties in frameless image-guided radiosurgery. *Int J Radiat Oncol Biol Phys* 2009 Apr 1;73(5):1364-8. PMID: 19084349
374. Murray B, Forster K, Timmerman R. Frame-based immobilization and targeting for stereotactic body radiation therapy. *Med Dosim* 2007;32(2):86-91. PMID: 17472887
375. Naff NJ. CyberKnife radiosurgery in neurosurgical practice. *Neurosurg Q* 2007 Dec;17(4):273-82.
376. Nagata Y, Matsuo Y, Takayama K, et al. Current status of stereotactic body radiotherapy for lung cancer. *Int J Clin Oncol* 2007 Feb;12(1):3-7. PMID: 17380434
377. Nakagawa K, Tago M, Shibata K, et al. Intercomparison of dose distribution between gamma knife and C-arm-mounted linac. *Radiat Med* 2003 Jul;21(4):178-82. PMID: 14514125

378. Nakaji P, Spetzler RF. Innovations in surgical approach: the marriage of technique, technology, and judgment. *Clin Neurosurg* 2004;51:177-85. PMID: 15571143
379. Nakamura JL, Verhey LJ, Smith V, et al. Dose conformity of gamma knife radiosurgery and risk factors for complications. *Int J Radiat Oncol Biol Phys* 2001 Dec 1;51(5):1313-9. PMID: 11728692
380. Nedzi LA. The implementation of ablative hypofractionated radiotherapy for stereotactic treatments in the brain and body: observations on efficacy and toxicity in clinical practice. *Semin Radiat Oncol* 2008 Oct;18(4):265-72. PMID: 18725114
381. Nguyen NP, Garland L, Welsh J, et al. Can stereotactic fractionated radiation therapy become the standard of care for early stage non-small cell lung carcinoma. *Cancer Treat Rev* 2008 Dec;34(8):719-27. PMID: 18657910
382. Nieder C, Pawinski A, Haukland E, et al. Estimating need for palliative external beam radiotherapy in adult cancer patients. *Int J Radiat Oncol Biol Phys* 2010 Jan 1;76(1):207-11. PMID: 19362788
383. Niranjan A, Lunsford LD. Radiosurgery: where we were, are, and may be in the third millennium. *Neurosurgery* 2000 Mar;46(3):531-43. PMID: 10719848
384. Niranjan A, Maitz AH, Kondziolka D, et al. Radiosurgery: Current techniques. *Tech Neurosurg* 2003;9(3):119-27.
385. Niranjan A, Maitz AH, Lunsford A, et al. Radiosurgery techniques and current devices. 2007;50-67.
386. Niranjan A, Maitz AH, Lunsford A, et al. Radiosurgery techniques and current devices. *Prog Neurol Surg* 2007;20:50-67. PMID: 17317976
387. Less invasive surgery for prostate cancer. *Harv Mens Health Watch* 2003 Dec;8(5):6-8
388. Proceedings of the 3rd Acta Oncologica Symposium on Stereotactic Body Radiotherapy, June 15-17, 2006, Copenhagen, Denmark. *Acta Oncol* 2006;45(7):771-994
389. Current world literature. Kidney cancer. *Curr Opin Urol* 2007 Sep;17(5):376-8
390. Update: minimal access surgery. *ANZ J Surg* 2007 Sep;77(9):792-5
391. Noda S, Lautenschlaeger T, Siedow MR, et al. Technological advances in radiation oncology for central nervous system tumors. *Semin Radiat Oncol* 2009 Jul;19(3):179-86. PMID: 19464633
392. Okunieff P, Petersen AL, Philip A, et al. Stereotactic Body Radiation Therapy (SBRT) for lung metastases. *Acta Oncol* 2006;45(7):808-17. PMID: 16982544
393. Onishi H, Kuriyama K, Komiyama T, et al. A new irradiation system for lung cancer combining linear accelerator, computed tomography, patient self-breath-holding, and patient-directed beam-control without respiratory monitoring devices. *Int J Radiat Oncol Biol Phys* 2003 May 1;56(1):14-20. PMID: 12694819
394. Orecchia R. Image-guided radiotherapy and hypofractionation in lung cancer. *J Thorac Oncol* 2007 May;2(5 Suppl):S42-S44. PMID: 17457233
395. Pan HC, Cheng FC, Sun MH, et al. Prediction of volumetric data errors in patients treated with gamma knife radiosurgery. *Stereotact Funct Neurosurg* 2007;85(4):184-91. PMID: 17389818
396. Pang LJ. Radiation oncology update. *Hawaii Med J* 2003 May;62(5):109-10. PMID: 12806792
397. Papiez L, Timmerman R. Hypofractionation in radiation therapy and its impact. *Med Phys* 2008 Jan;35(1):112-8. PMID: 18293568
398. Papiez L, Timmerman R, DesRosiers C, et al. Extracranial Stereotactic Radioablation: Physical Principles. *Acta Oncol* 2003;42(8):882-94. PMID: 14968949
399. Park C, Papiez L, Zhang S, et al. Universal survival curve and single fraction equivalent dose: useful tools in understanding potency of ablative radiotherapy. *Int J Radiat Oncol Biol Phys* 2008 Mar 1;70(3):847-52. PMID: 18262098
400. Parman CC. Stereotactic radiosurgery. *J Oncol Manage* 2004 Mar;13(2):7-8. PMID: 15180111

401. Pass H. The mets, the scalpels, and possibly the beams. *J Thorac Oncol* 2008 Nov;3(11):1211-2. PMID: 18978554
402. Pawlicki T, Cotrutz C, King C. Prostate cancer therapy with stereotactic body radiation therapy. *Front Radiat Ther Oncol* 2007;40:395-406. PMID: 17641522
403. Pennathur A, Luketich JD, Burton S, et al. Stereotactic radiosurgery for the treatment of lung neoplasm: initial experience. *Ann Thorac Surg* 2007 May;83(5):1820-4. PMID: 17462406
404. Petersch B, Bogner J, Dieckmann K, et al. Automatic real-time surveillance of eye position and gating for stereotactic radiotherapy of uveal melanoma. *Med Phys* 2004 Dec;31(12):3521-7. PMID: 15651635
405. Petrovich Z, Yu C. Frame-based and frameless stereotactic radiosurgery for intracranial and extracranial tumors. *Nowotwory* 2003;53(5):508-16.
406. Pishvaian AC, Collins B, Gagnon G, et al. EUS-guided fiducial placement for CyberKnife radiotherapy of mediastinal and abdominal malignancies. *Gastrointest Endosc* 2006 Sep;64(3):412-7. PMID: 16923491
407. Khrizman P, Small W, Jr., Dawson L, et al. The use of stereotactic body radiation therapy in gastrointestinal malignancies in locally advanced and metastatic settings. *Clin Colorectal Cancer* 2010 Jul;9(3):136-43. PMID: 20643617
408. Poll JJ, Hoogeman MS, Prevost JB, et al. Reducing monitor units for robotic radiosurgery by optimized use of multiple collimators. *Med Phys* 2008 Jun;35(6):2294-9. PMID: 18649461
409. Pollock BE. An evidence-based medicine review of stereotactic radiosurgery. *Prog Neurol Surg* 2006;19:152-70. PMID: 17033153
410. Pott PP, Scharf HP, Schwarz ML. Today's state of the art in surgical robotics*. *Comput Aided Surg* 2005 Mar;10(2):101-32. PMID: 16298921
411. Potters L, Timmerman R, Larson D. Stereotactic body radiation therapy. *J Am Coll Radiol* 2005 Aug;2(8):676-80. PMID: 17411904
412. Prabhu SS, Demonte F. Treatment of skull base tumors. *Curr Opin Oncol* 2003 May;15(3):209-12. PMID: 12778013
413. Prevost JB, Nuyttens JJ, Hoogeman MS, et al. Endovascular coils as lung tumour markers in real-time tumour tracking stereotactic radiotherapy: Preliminary results. *Eur Radiol* 2008 Aug;18(8):1569-76. PMID: 18389249
414. Prevost JB, Voet P, Hoogeman M, et al. Four-dimensional stereotactic radiotherapy for early stage non-small cell lung cancer: a comparative planning study. *Technol Cancer Res Treat* 2008 Feb;7(1):27-33. PMID: 18198921
415. Purdie TG, Moseley DJ, Bissonnette JP, et al. Respiration correlated cone-beam computed tomography and 4DCT for evaluating target motion in Stereotactic Lung Radiation Therapy. *Acta Oncol* 2006;45(7):915-22. PMID: 16982558
416. Quang TS, Wallner KE, Herstein PR, et al. Technologic evolution in the treatment of prostate cancer. Clinical, financial, and legal implications for managed care organizations. *Oncology (Huntingt)* 2007 Nov;21(13):1598-600, 1602. PMID: 18179049
417. Quinn AM. CyberKnife: a robotic radiosurgery system. *Clin J Oncol Nurs* 2002 May;6(3):149, 156. PMID: 11998608
418. Rassiah-Szegedi P, Salter BJ, Fuller CD, et al. Monte Carlo characterization of target doses in stereotactic body radiation therapy (SBRT). *Acta Oncol* 2006;45(7):989-94. PMID: 16982568
419. Ratto GB, Cafferata MA, Scolaro T, et al. Phase II study of combined immunotherapy, chemotherapy, and radiotherapy in the postoperative treatment of advanced non-small-cell lung cancer. *J Immunother (1991)* 2000 Jan;23(1):161-7. PMID: 10687149
420. Regine WF. Foreword: stereotactic radiosurgery - state of the art. *Technol Cancer Res Treat* 2003 Apr;2(2):77-8.

421. Regis J, Tamura M, Guillot C, et al. Radiosurgery with the world's first fully robotized Leksell Gamma Knife PerfeXion in clinical use: a 200-patient prospective, randomized, controlled comparison with the Gamma Knife 4C. *Neurosurgery* 2009 Feb;64(2):346-55. PMID: 19190462
422. Riboldi M, Baroni G, Spadea MF, et al. Robust frameless stereotactic localization in extra-cranial radiotherapy. *Med Phys* 2006 Apr;33(4):1141-52. PMID: 16696492
423. Rock JP, Ryu S, Yin FF. Novalis radiosurgery for metastatic spine tumors. *Neurosurg Clin North Am* 2004 Oct;15(4):503-9. PMID: 15450885
424. Rockhill JK. Advances in radiation therapy for oncologic pain. *Curr Pain Headache Rep* 2007 Aug;11(4):270-5. PMID: 17686390
425. Romanelli P, Chang SD, Koong A, et al. Extracranial radiosurgery using the CyberKnife. *Tech Neurosurg* 2003;9(3):226-31.
426. Romanelli P, Schweikard A, Schlaefler A, et al. Computer aided robotic radiosurgery. *Comput Aided Surg* 2006 Jul;11(4):161-74. PMID: 17060075
427. Romanelli P, Schaal DW, Adler JR. Image-guided radiosurgical ablation of intra- and extra-cranial lesions. *Technol Cancer Res Treat* 2006 Aug;5(4):421-8. PMID: 16866572
428. Rosahl SK, Roser F, Samii M. Renal metastasis. *J Neurosurg* 2002 Apr;96(4):804-5. PMID: 11990825
429. Rosenzweig KE, Amols H, Ling CC. New radiotherapy technologies. *Semin Surg Oncol* 2003;21(3):190-5. PMID: 14508852
430. Rosenzweig KE, Movsas B, Bradley J, et al. ACR appropriateness criteria on nonsurgical treatment for non-small-cell lung cancer: poor performance status or palliative intent. *J Am Coll Radiol* 2009 Feb;6(2):85-95. PMID: 19179235
431. Rousseau J, Gibon D. Optimizing for the Gamma knife. *Int J Radiat Oncol Biol Phys* 2000 Sep 1;48(2):613. PMID: 11012309
432. Rutten I, Deneufbourg JM. Radiotherapy in pediatric head and neck tumours. *Acta Otorhinolaryngol Belg* 2000;54(1):1-6. PMID: 10719587
433. Ryken TC, Meeks SL, Pennington EC, et al. Initial clinical experience with frameless stereotactic radiosurgery: analysis of accuracy and feasibility. *Int J Radiat Oncol Biol Phys* 2001 Nov 15;51(4):1152-8. PMID: 11704340
434. Samper PM, Lopez Carrizosa MC, Perez CA, et al. Impact of neoadjuvant hormonal therapy on dose-volume histograms in patients with localized prostate cancer under radical radiation therapy. *Clin Transl Oncol* 2006 Aug;8(8):599-605. PMID: 16952849
435. Sankaranarayanan V, Ganesan S, Oommen S, et al. Study on dosimetric parameters for stereotactic radiosurgery and intensity-modulated radiotherapy. *Med Dosim* 2003;28(2):85-90. PMID: 12804705
436. Sarfaraz M. CyberKnife robotic arm stereotactic radiosurgery. *J Am Coll Radiol* 2007 Aug;4(8):563-5. PMID: 17660122
437. Sasai K, Nagata Y, Hiraoka M. Is the linear-quadratic formula available in stereotactic radiosurgery or hypofractionated radiotherapy? The problem of the uncertainty of the alpha/beta ratio in the LQ formula. *Int J Radiat Oncol Biol Phys* 2000 Jul 1;47(4):1157-8.
438. Saunders JE. On stereotactic radiosurgery. *Hear J* 2007 Sep;60(9):70.
439. Savides TJ. EUS-guided fine-needle insertion of radiopaque fiducials: X marks the spot. *Gastrointest Endosc* 2006 Sep;64(3):418-9. PMID: 16923492
440. Saw CB, Chen H, Wagner H, Jr. Implementation of fiducial-based image registration in the Cyberknife robotic system. *Med Dosim* 2008;33(2):156-60. PMID: 18456167
441. Sawrie SM, Fiveash JB, Caudell JJ. Stereotactic body radiation therapy for liver metastases and primary hepatocellular carcinoma: normal tissue tolerances and toxicity. *Cancer Control* 2010 Apr;17(2):111-9. PMID: 20404794
442. Schefter TE, Kavanagh BD, Timmerman RD, et al. A phase I trial of stereotactic body radiation therapy (SBRT) for liver metastases. *Int J Radiat Oncol Biol Phys* 2005 Aug 1;62(5):1371-8. PMID: 16029795

443. Scheib SG, Gianolini S, Lomax NJ, et al. High precision radiosurgery and technical standards. *Acta Neurochir Suppl* 2004;91:9-23. PMID: 15707022
444. Schellenberg D, Quon A, Minn AY, et al. 18Fluorodeoxyglucose PET is prognostic of progression-free and overall survival in locally advanced pancreas cancer treated with stereotactic radiotherapy. *Int J Radiat Oncol Biol Phys* 2010 Aug 1;77(5):1420-5. PMID: 20056345
445. Schlaefer A, Fisseler J, Dieterich S, et al. Feasibility of four-dimensional conformal planning for robotic radiosurgery. *Med Phys* 2005 Dec;32(12):3786-92. PMID: 16475778
446. Schweikard A, Glosser G, Bodduluri M, et al. Robotic motion compensation for respiratory movement during radiosurgery. *Comput Aided Surg* 2000;5(4):263-77. PMID: 11029159
447. Schweikard A, Shiomi H, Adler J. Respiration tracking in radiosurgery. *Med Phys* 2004 Oct;31(10):2738-41. PMID: 15543778
448. Scorsetti M, Bignardi M. Conformal and stereotactic radiotherapy in hepatocellular carcinoma. *Ann Ital Chir* 2008 Mar;79(2):107-10. PMID: 18727272
449. Seki S, Kunieda E, Takeda A, et al. Differences in the definition of internal target volumes using slow CT alone or in combination with thin-slice CT under breath-holding conditions during the planning of stereotactic radiotherapy for lung cancer. *Radiother Oncol* 2007 Dec;85(3):443-9. PMID: 17981350
450. Senan S, Haasbeek NJ, Smit EF, et al. Stereotactic radiotherapy for centrally located early-stage lung tumors. *J Clin Oncol* 2007 Feb 1;25(4):464. PMID: 17264351
451. Seppenwoolde Y, Shirato H, Kitamura K, et al. 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* 2002 Jul 15;53(4):822-34. PMID: 12095547
452. Sharma A, Wong D, Weidlich G, et al. Non-invasive stereotactic radiosurgery (CyberHeart) for the creation of ablation lesions in the atrium. *Heart Rhythm* 2010 Jun;7(6):802-10. Epub 2010 Feb 13. PMID: 20156591
453. Shepard DM, Ferris MC, Ove R, et al. Inverse treatment planning for Gamma Knife radiosurgery. *Med Phys* 2000 Dec;27(12):2748-56. PMID: 11190958
454. Sherwood JT, Brock MV. Lung cancer: new surgical approaches. *Respirology* 2007 May;12(3):326-32. PMID: 17539834
455. Shibuya H, Tsujii H. The structural characteristics of radiation oncology in Japan in 2003. *Int J Radiat Oncol Biol Phys* 2005 Aug 1;62(5):1472-6. PMID: 16029809
456. Shirato H, Harada T, Harabayashi T, et al. Feasibility of insertion/implantation of 2.0-mm-diameter gold internal fiducial markers for precise setup and real-time tumor tracking in radiotherapy. *Int J Radiat Oncol Biol Phys* 2003 May 1;56(1):240-7. PMID: 12694845
457. Shirato H, Suzuki K, Sharp GC, et al. 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* 2006 Mar 15;64(4):1229-36. PMID: 16504762
458. Shirato H, Shimizu S, Kitamura K, et al. Organ motion in image-guided radiotherapy: lessons from real-time tumor-tracking radiotherapy. *Int J Clin Oncol* 2007 Feb;12(1):8-16. PMID: 17380435
459. Shiu AS, Chang EL, Ye JS, et al. Near simultaneous computed tomography image-guided stereotactic spinal radiotherapy: an emerging paradigm for achieving true stereotaxy. *Int J Radiat Oncol Biol Phys* 2003 Nov 1;57(3):605-13. PMID: 14529763
460. Shoshan Y, Wygoda M, Umansky F. Stereotactic radiosurgery and fractionated stereotactic radiotherapy: background, definitions, applications. *Isr Med Assoc J* 2005 Sep;7(9):597-9. PMID: 16190486

461. Shrieve DC, Klish M, Wendland MM, et al. Basic principles of radiobiology, radiotherapy, and radiosurgery. *Neurosurg Clin North Am* 2004 Oct;15(4):467-79. PMID: 15450882
462. Siddiqui F, Patel M, Khan M, et al. Stereotactic body radiation therapy for primary, recurrent, and metastatic tumors in the head-and-neck region. *Int J Radiat Oncol Biol Phys* 2009 Jul 15;74(4):1047-53. PMID: 19327895
463. Silvano G. New radiation techniques for treatment of locally advanced non-small cell lung cancer (NSCLC). *Ann Oncol* 2006 Mar;17 Suppl 2:ii34-ii35. PMID: 16608978
464. Singletary SE. Minimally invasive techniques in breast cancer treatment. *Semin Surg Oncol* 2001 Apr;20(3):246-50. PMID: 11523110
465. Siva S, MacManus M, Ball D. Stereotactic radiotherapy for pulmonary oligometastases: a systematic review. *J Thorac Oncol* 2010 Jul;5(7):1091-9. PMID: 20479693
466. Slotman BJ, Cottier B, Bentzen SM, et al. Overview of national guidelines for infrastructure and staffing of radiotherapy. ESTRO-QUARTS: work package 1. *Radiother Oncol* 2005 Jun;75(3):349-54. PMID: 15893832
467. Slotman BJ, Lagerwaard FJ, Senan S. 4D imaging for target definition in stereotactic radiotherapy for lung cancer. *Acta Oncol* 2006;45(7):966-72. PMID: 16982565
468. Smink KA, Schneider SM. Overview of stereotactic body radiotherapy and the nursing role. *Clin J Oncol Nurs* 2008 Dec;12(6):889-93. PMID: 19064382
469. Smit BJ. Radiosurgery in South Africa. *S Afr Med J* 2000 Apr;90(4):355-6. PMID: 10957916
470. Smith V, Chuang CF. The Cyberknife: practical experience with treatment planning and delivery. *Front Radiat Ther Oncol* 2007;40:143-61. PMID: 17641507
471. Snell JW, Sheehan J, Stroila M, et al. Assessment of imaging studies used with radiosurgery: a volumetric algorithm and an estimation of its error. Technical note. *J Neurosurg* 2006 Jan;104(1):157-62. PMID: 16509161
472. Soete G, Verellen D, Tournel K, et al. 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* 2006 Sep;80(3):371-3. PMID: 16914219
473. Solberg TD, Boedeker KL, Fogg R, et al. Dynamic arc radiosurgery field shaping: a comparison with static field conformal and noncoplanar circular arcs. *Int J Radiat Oncol Biol Phys* 2001 Apr 1;49(5):1481-91. PMID: 11286857
474. Solberg TD, Agazaryan N, Goss BW, et al. A feasibility study of 18F-fluorodeoxyglucose positron emission tomography targeting and simultaneous integrated boost for intensity-modulated radiosurgery and radiotherapy. *J Neurosurg* 2004 Nov;101(Suppl 3):381-9. PMID: 15537193
475. Solberg TD, Medin PM, Mullins J, et al. Quality assurance of immobilization and target localization systems for frameless stereotactic cranial and extracranial hypofractionated radiotherapy. *Int J Radiat Oncol Biol Phys* 2008;71(1 Suppl):S131-S135. PMID: 18406912
476. Solberg TD, Kavanagh BD, Medin PM. Stereotactic body radiation therapy: a new paradigm in radiotherapy management of cancer. *J Am Coll Radiol* 2008 May;5(5):673-7. PMID: 18442775
477. Song DY, Kavanagh BD, Benedict SH, et al. Stereotactic body radiation therapy. Rationale, techniques, applications, and optimization. *Oncology (Huntingt)* 1435 Jun;18(11):1419-30. PMID: 15609470
478. Sonke JJ, Rossi M, Wolthaus J, et al. Frameless stereotactic body radiotherapy for lung cancer using four-dimensional cone beam CT guidance. *Int J Radiat Oncol Biol Phys* 2009 Jun 1;74(2):567-74. PMID: 19046825
479. Sotiropoulou E, Stathochristopoulou I, Stathopoulos K, et al. CT-guided fiducial placement for CyberKnife stereotactic radiosurgery: an initial experience. *Cardiovasc Intervent Radiol* 2010 Jun;33(3):586-9. Epub 2009 Nov 12. PMID: 19908085

480. Spadea MF, Baroni G, Riboldi M, et al. Benefits of six degrees of freedom for optically driven patient set-up correction in SBRT. *Technol Cancer Res Treat* 2008 Jun;7(3):187-95. PMID: 18473490
481. St George EJ, Kudhail J, Perks J, et al. Acute symptoms after gamma knife radiosurgery. *J Neurosurg* 2002 Dec;97(5 Suppl):631-4. PMID: 12507110
482. Stancanello J, Berna E, Cavedon C, et al. Preliminary study on the use of nonrigid registration for thoraco-abdominal radiosurgery. *Med Phys* 2005 Dec;32(12):3777-85. PMID: 16475777
483. Steinke K. Lung tumors. *Recent Results Cancer Res* 2006;167:107-22. PMID: 17044300
484. Sterzing F, Herfarth K, Debus J. IGRT with helical tomotherapy--effort and benefit in clinical routine. *Strahlenther Onkol* 2007 Dec;183(Spec No 2):35-7. PMID: 18167007
485. Sterzing F, Schubert K, Sroka-Perez G, et al. Helical tomotherapy. Experiences of the first 150 patients in Heidelberg. *Strahlenther Onkol* 2008 Jan;184(1):8-14. PMID: 18188517
486. Storme G, Verellen D, Soete G, et al. From linac to tomotherapy: new possibilities for cure? *Adv Exp Med Biol* 2006;587:303-8. PMID: 17163173
487. Strassmann G, Vacha P, Braun I, et al. Methodology of continuous extracranial radiosurgery for lung cancer using EXOMIO 3-D CT simulation. *Strahlenther Onkol* 2004 Apr;180(4):241-4. PMID: 15057435
488. Strassmann G, Braun I, Kress O, et al. Accuracy of single-session extracranial radiotherapy for simple shaped lung tumor or metastasis using fast 3-D CT treatment planning. *Int J Radiat Oncol Biol Phys* 2006 Oct 1;66(2):576-82. PMID: 16965999
489. Suzuki O, Shiomi H, Nakamura S, et al. Novel correction methods as alternatives for the six-dimensional correction in CyberKnife treatment. *Radiat Med* 2007 Jan;25(1):31-7. PMID: 17225051
490. Taguchi H, Sakuhara Y, Hige S, et al. Intercepting radiotherapy using a real-time tumor-tracking radiotherapy system for highly selected patients with hepatocellular carcinoma unresectable with other modalities. *Int J Radiat Oncol Biol Phys* 2007 Oct 1;69(2):376-80. PMID: 17869660
491. Takayama K, Nagata Y, Negoro Y, et al. Treatment planning of stereotactic radiotherapy for solitary lung tumor. *Int J Radiat Oncol Biol Phys* 2005 Apr 1;61(5):1565-71. PMID: 15817363
492. Takeda A, Kunieda E, Shigematsu N, et al. Small lung tumors: long-scan-time CT for planning of hypofractionated stereotactic radiation therapy--initial findings. *Radiology* 2005 Oct;237(1):295-300. PMID: 16118151
493. Takeda A, Kunieda E, Takeda T, et al. Possible misinterpretation of demarcated solid patterns of radiation fibrosis on CT scans as tumor recurrence in patients receiving hypofractionated stereotactic radiotherapy for lung cancer. *Int J Radiat Oncol Biol Phys* 2008 Mar 15;70(4):1057-65. PMID: 17905527
494. Takeda A, Kunieda E, Sanuki N, et al. Dose distribution analysis in stereotactic body radiotherapy using dynamic conformal multiple arc therapy. *Int J Radiat Oncol Biol Phys* 2009 Jun 1;74(2):363-9. PMID: 19427552
495. Takeuchi H, Yoshida M, Kubota T, et al. Frameless stereotactic radiosurgery with mobile CT, mask immobilization and micro-multileaf collimators. *Minim Invasive Neurosurg* 2003 Apr;46(2):82-5. PMID: 12761677
496. Teh BS. Image-guided stereotactic body radiation therapy (SBRT): an emerging treatment paradigm with a new promise in radiation oncology. *Biomed Imaging Interv J* 2007;3(1):e5.
497. Thiel DD, Winfield HN. Robotics in urology: past, present, and future. *J Endourol* 2008 Apr;22(4):825-30. PMID: 18419224
498. Theodorou K, Platoni K, Lefkopoulos D, et al. Dose-volume analysis of different stereotactic radiotherapy mono-isocentric techniques. *Acta Oncol* 2000;39(2):157-63. PMID: 10859005

499. Theodorou K, Bazioglou M, Skouras T, et al. Linear accelerator-based stereotactic radiotherapy. Part I: rationale, techniques and future developments. *J BUON* 2000 Jan 1;5(2):209-18.
500. Thieke C, Malsch U, Schlegel W, et al. Kilovoltage CT using a linac-CT scanner combination. *Br J Radiol* 2006 Sep;79(Spec No 1):S79-S86. PMID: 16980687
501. Timmerman R, Papiez L, McGarry R, et al. Extracranial stereotactic radioablation: results of a phase I study in medically inoperable stage I non-small cell lung cancer. *Chest* 2003 Nov;124(5):1946-55. PMID: 14605072
502. Timmerman R, Papiez L, Suntharalingam M. Extracranial stereotactic radiation delivery: expansion of technology beyond the brain. *Technol Cancer Res Treat* 2003 Apr;2(2):153-60. PMID: 12680797
503. Timmerman R, Galvin J, Michalski J, et al. Accreditation and quality assurance for Radiation Therapy Oncology Group: Multicenter clinical trials using Stereotactic Body Radiation Therapy in lung cancer. *Acta Oncol* 2006;45(7):779-86. PMID: 16982540
504. Timmerman R, Abdulrahman R, Kavanagh BD, et al. Lung cancer: a model for implementing stereotactic body radiation therapy into practice. *Front Radiat Ther Oncol* 2007;40:368-85. PMID: 17641520
505. Timmerman R, Bastasch M, Saha D, et al. Optimizing dose and fractionation for stereotactic body radiation therapy. Normal tissue and tumor control effects with large dose per fraction. *Front Radiat Ther Oncol* 2007;40:352-65. PMID: 17641519
506. Timmerman RD, Park C, Kavanagh BD. The North American experience with stereotactic body radiation therapy in non-small cell lung cancer. *J Thorac Oncol* 2007 Jul;2(7 Suppl 3):S101-S112. PMID: 17603304
507. Timmerman RD, Kavanagh BD, Cho LC, et al. Stereotactic body radiation therapy in multiple organ sites. *J Clin Oncol* 2007 Mar 10;25(8):947-52. PMID: 17350943
508. Timmerman RD, Bizekis CS, Pass HI, et al. Local surgical, ablative, and radiation treatment of metastases. *CA Cancer J Clin* 2009 May;59(3):145-70. PMID: 19364702
509. Tobler M, Leavitt DD, Watson G. Optimization of the primary collimator settings for fractionated IMRT stereotactic radiotherapy. *Med Dosim* 2004;29(2):72-9. PMID: 15191751
510. Tonn JC. Microneurosurgery and radiosurgery--an attractive combination. *Acta Neurochir Suppl* 2004;91:103-8. PMID: 15707031
511. Tsai JS, Engler MJ, Rivard MJ, et al. A formalism for independent checking of Gamma Knife dose calculations. *Med Phys* 2001 Sep;28(9):1842-9. PMID: 11585215
512. Uematsu M, Shioda A, Suda A, et al. Intrafractional tumor position stability during computed tomography (CT)-guided frameless stereotactic radiation therapy for lung or liver cancers with a fusion of CT and linear accelerator (FOCAL) unit. *Int J Radiat Oncol Biol Phys* 2000 Sep 1;48(2):443-8. PMID: 10974460
513. Underberg RW, Lagerwaard FJ, Slotman BJ, et al. Benefit of respiration-gated stereotactic radiotherapy for stage I lung cancer: an analysis of 4DCT datasets. *Int J Radiat Oncol Biol Phys* 2005 Jun 1;62(2):554-60. PMID: 15890600
514. Underberg RW, Lagerwaard FJ, van Tinteren H, et al. Time trends in target volumes for stage I non-small-cell lung cancer after stereotactic radiotherapy. *Int J Radiat Oncol Biol Phys* 2006 Mar 15;64(4):1221-8. PMID: 16442240
515. Vaidya JS, Hall-Craggs M, Baum M, et al. Percutaneous minimally invasive stereotactic primary radiotherapy for breast cancer. *Lancet Oncol* 2002 Apr;3(4):252-3. PMID: 12067688
516. Van Houtte P. New potentials of radiotherapy in non-small cell lung cancer: stereotactic therapy and IMRT. *Curr Probl Cancer* 2003 Jan;27(1):60-3. PMID: 12569353

517. van der Voort van Zyp NC, Prevost JB, van der Holt B., et al. Quality of life after stereotactic radiotherapy for stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2010 May 1;77(1):31-7. PMID: 19864077
518. Varga PP, Bors I, Lazary A. Sacral tumors and management. *Orthop Clin North Am* 2009 Jan;40(1):105-23. PMID: 19064059
519. Vassiliev ON, Kry SF, Chang JY, et al. Stereotactic radiotherapy for lung cancer using a flattening filter free Clinac. *J Appl Clin Med Phys* 2009;10(1):2880. PMID: 19223837
520. Verbakel WF, Senan S, Cuijpers JP, et al. Rapid delivery of stereotactic radiotherapy for peripheral lung tumors using volumetric intensity-modulated arcs. *Radiother Oncol* 2009 Oct;93(1):122-4. Epub 2009 Jun 22. PMID: 19552979
521. Verellen D, Soete G, Linthout N, et al. Optimal control of set-up margins and internal margins for intra- and extracranial radiotherapy using stereoscopic kilovoltage imaging. *Cancer Radiother* 2006 Sep;10(5):235-44. PMID: 16854609
522. Videtic GM, Stephans K, Reddy C, et al. Intensity-modulated radiotherapy-based stereotactic body radiotherapy for medically inoperable early-stage lung cancer: excellent local control. *Int J Radiat Oncol Biol Phys* 2010 Jun 1;77(2):344-9. PMID: 19765913
523. Voynov G, Heron DE, Burton S, et al. Frameless stereotactic radiosurgery for recurrent head and neck carcinoma. *Technol Cancer Res Treat* 2006 Oct;5(5):529-35. PMID: 16981796
524. Vricella GJ, Ponsky LE, Cadeddu JA. Ablative technologies for urologic cancers. *Urol Clin North Am* 2009 May;36(2):163-78. PMID: 19406318
525. Wagner TH, Bova FJ, Friedman WA, et al. A simple and reliable index for scoring rival stereotactic radiosurgery plans. *Int J Radiat Oncol Biol Phys* 2003 Nov 15;57(4):1141-9. PMID: 14575847
526. Wagner TH, Meeks SL, Bova FJ, et al. Optical tracking technology in stereotactic radiation therapy. *Med Dosim* 2007;32(2):111-20. PMID: 17472890
527. Wakelee H, Langer C, Vokes E, et al. Cooperative group research efforts in lung cancer: focus on early-stage non-small-cell lung cancer. *Clin Lung Cancer* 2008 Jan;9(1):9-15. PMID: 18282352
528. Wakisaka M, Mori H, Hongo N, et al. Correlation of pathological finding with dose distribution in a case of intraocular choroidal melanoma treated by stereotactic radiosurgery. *Acta Oncol* 2000;39(5):639-42. PMID: 11093373
529. Wallen EM. Treatment for localized prostate cancer: surgical approaches. *N C Med J* 2006 Mar;67(2):146-8. PMID: 16752720
530. Wiegner EA, King CR. Sexual function after stereotactic body radiotherapy for prostate cancer: results of a prospective clinical trial. *Int J Radiat Oncol Biol Phys* 2010 Oct 1;78(2):442-8. Epub 2010 Feb 4. PMID: 20137864
531. Willoughby TR, Forbes AR, Buchholz D, et al. 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* 2006 Oct 1;66(2):568-75. PMID: 16887290
532. Wilt TJ, MacDonald R, Rutks I, et al. Systematic review: comparative effectiveness and harms of treatments for clinically localized prostate cancer. *Ann Intern Med* 2008 Mar 18;148(6):435-48. PMID: 18252677
533. Wu QJ, Chankong V, Jitprapaikularn S, et al. Real-time inverse planning for Gamma Knife radiosurgery. *Med Phys* 2003 Nov;30(11):2988-95. PMID: 14655946
534. Wu QJ, Thongphiew D, Wang Z, et al. The impact of respiratory motion and treatment technique on stereotactic body radiation therapy for liver cancer. *Med Phys* 2008 Apr;35(4):1440-51. PMID: 18491539
535. Wu QJ, Wang Z, Kirkpatrick JP, et al. Impact of collimator leaf width and treatment technique on stereotactic radiosurgery and radiotherapy plans for intra- and extracranial lesions. *Radiat Oncol* 2009;4. PMID: 19159471

536. Wulf J, Haedinger U, Oppitz U, et al. Stereotactic radiotherapy for primary lung cancer and pulmonary metastases: a noninvasive treatment approach in medically inoperable patients. *Int J Radiat Oncol Biol Phys* 2004 Sep 1;60(1):186-96. PMID: 15337555
537. Wunderink W, Mendez RA, Vasquez Osorio EM, et al. Target coverage in image-guided stereotactic body radiotherapy of liver tumors. *Int J Radiat Oncol Biol Phys* 2007 May 1;68(1):282-90. PMID: 17448881
538. Wurm RE, Gum F, Erbel S, et al. Image guided respiratory gated hypofractionated Stereotactic Body Radiation Therapy (H-SBRT) for liver and lung tumors: Initial experience. *Acta Oncol* 2006;45(7):881-9. PMID: 16982554
539. Xiao Y, Papiez L, Paulus R, et al. Dosimetric evaluation of heterogeneity corrections for RTOG 0236: stereotactic body radiotherapy of inoperable stage I-II non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2009 Mar 15;73(4):1235-42. PMID: 19251095
540. Yaeger TE. Accuray company advertising successful prostate cancer treatments with CyberKnife (CK). *Int J Radiat Oncol Biol Phys* 2009 Feb 1;73(2):638-9. PMID: 19147032
541. Yin FF, Ryu S, Ajlouni M, et al. Image-guided procedures for intensity-modulated spinal radiosurgery. Technical note. *J Neurosurg* 2004 Nov;101 Suppl 3:419-24. PMID: 15537199
542. Yin FF, Wang Z, Yoo S, et al. Integration of cone-beam CT in stereotactic body radiation therapy. *Technol Cancer Res Treat* 2008 Apr;7(2):133-9. PMID: 18345702
543. Yousefi S, Collins BT, Reichner CA, et al. Complications of thoracic computed tomography-guided fiducial placement for the purpose of stereotactic body radiation therapy. *Clin Lung Cancer* 2007 Jan;8(4):252-6. PMID: 17311689
544. Yu C, Shepard D. Treatment planning for stereotactic radiosurgery with photon beams. *Technol Cancer Res Treat* 2003 Apr;2(2):93-104. PMID: 12680789
545. Zamzuri I, Idris NR, Mar W, et al. Early Malaysian experience on the use of head and neck localizers in the precision radiotherapy of intra and extra cranial sites for first 28 cases. *Med J Malaysia* 2006 Dec;61(5):621-5. PMID: 17623965
546. Zimmermann F, Wulf J, Lax I, et al. Stereotactic body radiation therapy for early non-small cell lung cancer. *Front Radiat Ther Oncol* 2010;42:94-114. PMID: 19955796
547. Practice guideline for the performance of stereotactic body radiation therapy. In: American College of Radiology (ACR). ACR practice guideline. Reston (VA): American College of Radiology (ACR); 2006. p. 995-1002
548. Palacio M. Chart smart: linear accelerators. King of Prussia (PA): ADVANCE Newsmagazines/Merion Publications, Inc.; 2 p. Also available: http://enterprise-imaging-radiology-management.advanceweb.com/sharedresources/advanceforioa/resources/DownloadableResources/AR090105_p56ChartSmart.pdf
549. Direx Systems. 510(k) summary. AccuChanger. K043409. Rockville (MD): U.S. Food and Drug Administration (FDA); 2005 May 5. 6 p. Also available: <http://www.fda.gov/cdrh/pdf4/K043409.pdf>
550. Direx Systems. 510(k) summary for AccuLeaf. K040553. Rockville (MD): U.S. Food and Drug Administration (FDA); 2004 Apr 1. 5 p. Also available: <http://www.fda.gov/cdrh/pdf4/K040553.pdf>
551. Elekta Limited. Summary of safety and effectiveness for the beam modulator. K042794. Rockville (MD): U.S. Food and Drug Administration (FDA); 2005 Jan 31. 5 p. Also available: <http://www.fda.gov/cdrh/pdf4/K042794.pdf>
552. Accuray. 510(k) summary of safety and effectiveness for CyberKnife® Robotic Radiosurgery System. K072504. Rockville (MD): U.S. Food and Drug Administration (FDA); 2007 Sep 4. 4 p. Also available: <http://www.fda.gov/cdrh/pdf7/K072504.pdf>

553. Elekta Limited. 510(K) summary. Medical linear accelerator accessory, IYE. K082122. Rockville (MD); U.S. Food and Drug Administration (FDA); 2008 Jul 18. 4 p. Also available: <http://www.fda.gov/cdrh/pdf8/K082122.pdf>
554. Varian Medical Systems. 510(k) summary. Medical charged particle radiation therapy system. K071992. Rockville (MD); U.S. Food and Drug Administration (FDA); 2007 Aug 15. 5 p. Also available: <http://www.fda.gov/cdrh/pdf7/K071992.pdf>
555. Elekta Instrument AB. 510(k) summary. Radionuclide radiation therapy system. K063512. Rockville (MD); U.S. Food and Drug Administration (FDA); 2007 Mar 5. 5 p. Also available: <http://www.fda.gov/cdrh/pdf6/K063512.pdf>
556. BrainLAB AG. 510(k) summary of safety and effectiveness for m3 (micro-Multileaf Collimator). K020860. Rockville (MD); U.S. Food and Drug Administration (FDA); 2002 Jun. 5 p. Also available: <http://www.fda.gov/cdrh/pdf2/K020860.pdf>
557. Mitsubishi Heavy Industries, Ltd. 510(k) premarket notification database. Accelerator, linear, medical. K072047. [internet]. Rockville (MD); U.S. Food and Drug Administration (FDA); 2008 Nov 10 [accessed 2008 Nov 24]. [1 p]. Available: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=25401>
558. Siemens Medical Solutions USA. 510(k) summary for the microMLC. K032790. Rockville (MD); U.S. Food and Drug Administration (FDA); 2003 Oct 2. 5 p. Also available: <http://www.fda.gov/cdrh/pdf3/K032790.pdf>
559. MRC Systems GmbH. 510(k) summary of safety and effectiveness for multileaf collimator. K030609. Rockville (MD); U.S. Food and Drug Administration (FDA); 2003 Feb 21. 5 p. Also available: <http://www.fda.gov/cdrh/pdf3/K030609.pdf>
560. Varian Medical Systems. 510(k) summary for the medical charged particle radiation therapy system. K081188. Rockville (MD); U.S. Food and Drug Administration (FDA); 2008 Jul 14. 4 p. Also available: <http://www.fda.gov/cdrh/pdf8/K081188.pdf>
561. BrainLAB AG. 510(k) summary of safety and effectiveness for ExacTrac 3rd party. K072046. Rockville (MD); U.S. Food and Drug Administration (FDA); 2007 Oct 17. 5 p. Also available: <http://www.fda.gov/cdrh/pdf7/K072046.pdf>
562. Varian Medical Systems. 510(k) summary for imaging accessory to medical linear accelerator. K042720. Rockville (MD); U.S. Food and Drug Administration (FDA); 2004 Oct 29. 4 p. Also available: <http://www.fda.gov/cdrh/pdf4/K042720.pdf>
563. Siemens Medical Solutions USA. 510(k) summary for ONCOR Avant-Garde with COHERENCE workspaces. K031764. Rockville (MD); U.S. Food and Drug Administration (FDA); 2003 Sep 5. 6 p. Also available: <http://www.fda.gov/cdrh/pdf3/K031764.pdf>
564. Siemens Medical Solutions USA. 510(k) summary for ONCOR Expression TM with COHERENCETM Workspaces. K06226. Rockville (MD); U.S. Food and Drug Administration (FDA); 2006 Mar 15. 7 p. Also available: <http://www.fda.gov/cdrh/pdf6/K060226.pdf>
565. Siemens Medical Solutions USA, Inc. 510(k) summary and statement for ARTISTE MV SA. K072485. Rockville (MD); U.S. Food and Drug Administration (FDA); 2007 Dec 27. 4 p. Also available: <http://www.fda.gov/cdrh/pdf7/K072485.pdf>
566. Elekta Limited. 510(k) summary. Medical linear accelerator (with patient imaging). K051932. Rockville (MD); U.S. Food and Drug Administration (FDA); 2005 Aug 12. 5 p. Also available: <http://www.fda.gov/cdrh/pdf5/K051932.pdf>
567. TomoTherapy. 510(k) safety and effectiveness summary. Medical charged particle radiation therapy. K082005. Rockville (MD); U.S. Food and Drug Administration (FDA); 2008 Jul 7. 5 p. Also available: <http://www.fda.gov/cdrh/pdf8/K082005.pdf>
568. TomoTherapy. Summary of safety and effectiveness. Radiation therapy system. K060912. Rockville (MD); U.S. Food and Drug Administration (FDA); 2006 Apr 19. 6 p. Also available: <http://www.fda.gov/cdrh/pdf6/K060912.pdf>

569. TomoTherapy. Safety and effectiveness summary. Radiation therapy system. K042739. Rockville (MD): U.S. Food and Drug Administration (FDA); 2004 Nov 3. 6 p. Also available: <http://www.fda.gov/cdrh/pdf4/K042739.pdf>
570. TomoTherapy. 510(k) safety and effectiveness summary. Radiation therapy system. K013673. Rockville (MD): U.S. Food and Drug Administration (FDA); 2001 Nov 3. 6 p. Also available: <http://www.fda.gov/cdrh/pdf/K013673.pdf>
571. Radionics Software Applications. 510 (k) summary of safety and effectiveness. Mini multi-leaf collimator (MMLC VR1). K993594. Rockville (MD): U.S. Food and Drug Administration (FDA); 1999 Dec 15. 4 p. Also available: <http://www.fda.gov/cdrh/pdf/K993594.pdf>
572. Accuray CyberKnife stereotactic radiosurgery system. [Web site]. Sunnyvale (CA): Accuray, Inc.; 2006 [accessed 2006 Feb 15]. [various]. Available: <http://www accuray.com>
573. BrainLAB AG. [Web site]. Westchester (IL): BrainLAB AG; [accessed 2008 Nov 21]. [various]. Available: http://www.brainlab.com/scripts/website_english.asp
574. Direx Group. [Web site]. Canton (MA): Direx Systems Corp.; [accessed 2008 Nov 21]. [various]. Available: <http://www.direxgroup.com>
575. Elekta AB. [Web site]. Stockholm, Sweden: Elekta AB (Publ); [accessed 2008 Nov 21]. [various]. Available: <http://www.elekta.com>
576. Mitsubishi Heavy Industries, Ltd. [Web site]. Tokyo: Mitsubishi Heavy Industries, Ltd. (MHI); [accessed 2008 Nov 21]. [various]. Available: <http://www.mhi.co.jp/en/index.html>
577. Integra Radionics. [Web site]. Burlington (MA): Integra Radionics; [accessed 2008 Nov 21]. [various]. Available: <http://www.radionics.com>
578. Company profile: Siemens Medical Systems, Inc. [internet]. Iselin (NJ): Siemens Medical Systems, Inc.; [accessed 1999 Jul 12]. [2 p]. Available: http://www.usa.siemens.com/About_Siemens/OperatingCompanies/SiemensMedicalSys.htm
579. TomoTherapy. [Web site]. Madison (WI): TomoTherapy Incorporated; [accessed 2008 Nov 21]. [various]. Available: <http://www.tomo therapy.com>
580. Varian Medical Systems. [Web site]. Palo Alto (CA): Varian Medical Systems, Inc.; [accessed 2008 Nov 21]. [various]. Available: <http://www.varian.com>
581. Hahn E. (Elekta, Inc.). Personal communication. 2010 Jan 6. 7 p
582. Hedgspeth L. (Tomotherapy, Inc. Madison, WI). Personal communication. 2010 Jan 11. 5 p
583. Thomes CJ. (Director Corporate Accounts, Accuray Incorporated). Personal communication. 2010 Jan 6. 10 p
584. Berkowitz D, Huntzinger C, Schulz R. (Varian Surgical Sciences, Palo Alto CA). Personal communication. 2010 Jan 15. 10 p
585. Benedict SH. SBRT: technical issues for clinical implementation of an SBRT program. In: 23rd annual meeting of the American Academy of Pain Medicine; February 7-10, 2007; New Orleans, LA. Glenview (IL): American Academy of Pain Medicine (AAPM); 2007. Also available: <http://aapm.confex.com/aapm/2007am/techprogram/S1237.HTM>