

Appendix A. Literature search methods

A variety of approaches were used to identify relevant information for this report, including searches of peer-reviewed literature, grey 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 2008, Issue 4	www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	Through 2008, Issue 4	www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	Through 2008, Issue 4	www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	Through 2008, Issue 4	www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through November 2, 2008	OVID
Health Technology Assessment Database (HTA)	Through 2008, Issue 4	www.thecochranelibrary.com
MEDLINE	1950 through October 6, 2008	OVID
PreMEDLINE	Searched November 7, 2008	National Library of Medicine
U.K. National Health Service Economic Evaluation Database (NHS EED)	Through 2008, Issue 4	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\$ hemangiopericyoma\$ herpceptin laparoscop\$ mdl medulloblastoma\$ meningioma\$ neurocyoma\$ oligodendroglioma\$ pinealoma\$ pituitary plesiomorphic robot-assisted tumo?r\$ xanthoastrocyoma\$

Concept	Controlled vocabulary	Keywords
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
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

Electronic database searches

The following databases have been searched for relevant information.

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
11		

Part 2

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

Name	Date limits	Platform/Provider
Clinicaltrials.gov	Searched 11/13/08	www.clinicaltrials.gov
ECRI cross-search	Searched 11/6/08	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	URL
Centers for Medicare and Medicaid Services (CMS)	www.cms.gov

Appendix B. Included studies

Table 13. Studies included to address key question 3

Reference
<i>GI (colon, liver, pancreas)</i>
Dawson et al., (2006) ¹²²
Gunven et al., (2003) ¹²³
Hoyer et al., (2005) ¹²⁴
Hoyer et al., (2006) ¹²⁵
Katz et al., (2007) ¹²⁶
Kavanagh et al., (2006) ¹²⁷
Koong et al., (2004) ¹²⁸
Koong et al., (2005) ¹²⁹
Romero et al., (2006) ¹³⁰
Tse et al., (2008) ¹³¹
Wulf et al., (2006) ¹³²
<i>Head and neck</i>
Ahn et al., (2000) ⁵⁶
Chang et al., (2000) ⁵⁷
Chen et al., (2001) ⁵⁸
Chua et al., (2006) ⁵⁹
Chua et al., (2007) ⁶⁰
Douglas et al., (2004) ⁶¹
Douglas et al., (2008) ⁶²
Habermann et al., (2002) ⁶³
Hara et al., (2008) ⁶⁴
Katoh et al., (2008) ⁶⁵
Le et al., (2003) ⁶⁶
Low et al., (2006) ⁶⁷
Mori et al., (2006) ⁶⁸
Nijdam et al., (2007) ⁶⁹
Oda et al., (2006) ⁷⁰
Pai et al., (2002) ⁷¹

Reference
Ryu et al., (2004) ⁷²
Unger et al., (2005) ⁷³
Voynov et al., (2006) ⁷⁴
Wu et al., (2007) ⁷⁵
Xiao et al., (2001) ⁷⁶
Yau et al., (2004) ⁷⁷
<i>Kidney</i>
Beitler et al., (2004) ¹³⁷
Gerszten et al., (2005) ¹³⁸
Ponsky et al., (2007) ¹³⁹
Svedman et al., (2006) ¹⁴⁰
<i>Lung</i>
Aoki et al., (2007) ²¹
Baumann et al., (2006) ²²
Brown et al., (2007) ²³
Casamassima et al., (2008) ²⁴
Collins et al., (2007) ²⁵
Coon et al., (2008) ²⁶
Fritz et al., (2008) ²⁷
Gerszten et al., (2006) ²⁸
Guckenberger et al., (2007) ²⁹
Harada et al., (2002) ³⁰
Hodge et al., (2006) ³¹
Hof et al., (2007) ³²
Hof et al., (2007) ³³
Hoopes et al., (2007) ³⁴
Ishimori et al., (2004) ³⁵
Joyner et al., (2006) ³⁶
Koto et al., (2007) ³⁷
Le et al., (2006) ³⁸
Lee et al., (2003) ³⁹
Muacevic et al., (2007) ⁴⁰
Nakagawa et al., (2000) ¹¹⁸

Reference
Nuyttens et al., (2006) ⁴¹
Onimaru et al., (2008) ⁴²
Paludan et al., (2006) ⁴³
Pennathur et al., (2007) ⁴⁴
Ricardi et al., (2007) ⁴⁵
Scorsetti et al., (2007) ⁴⁶
Sinha et al., (2006) ⁴⁷
Song et al., (2005) ⁴⁸
Takeda et al., (2008) ⁴⁹
Timmerman et al., (2003) ⁵⁰
Uematsu et al., (2001) ⁵¹
Whyte et al., (2003) ⁵²
Wulf et al., (2004) ⁵³
Xia et al., (2006) ⁵⁴
Yoon et al., (2006) ¹¹⁹
Zimmermann et al., (2006) ⁵⁵
Multiple sites
DeSalles et al., (2004) ¹⁴⁴
Ernst-Stecken et al., (2006) ¹⁴⁵
Jereczek-Fossa et al., (2008) ¹⁴⁶
Nuyttens et al., (2007) ¹⁴⁷
Shioyama et al., (2005) ¹⁴⁸
Teh et al., (2007) ¹⁴⁹
Wulf et al., (2001) ¹⁵⁰
Ocular
Cohen et al., (2003) ⁷⁸
Dieckmann et al., (2006) ⁷⁹
Emara et al., (2004) ⁸⁰
Fakiris et al., (2007) ⁸¹
Furdova et al., (2005) ⁸²
Georgopoulos et al., (2003) ⁸³
Haas et al., (2002) ⁸⁴
Hirschbein et al., (2008) ⁸⁵

Reference
Langmann et al., (2002) ⁸⁶
Liscak and Vladyka, (2007) ⁸⁷
Miralbell et al., (2007) ⁸⁸
Modorati et al., (2008) ⁸⁹
Muacevic et al., (2008) ⁹⁰
Mueller et al., (2000) ⁹¹
Muller et al., (2005) ⁹²
Simonova et al., (2002) ⁹³
Woodburn et al., (2000) ⁹⁴
Zehetmayer et al., (2000) ⁹⁵
<i>Pelvis, sacrum, uterus</i>
Gerszten et al., (2003) ¹³³
Kim et al., (2008) ¹³⁴
Kunos et al., (2008) ¹³⁵
Molla et al., (2005) ¹³⁶
<i>Prostate</i>
Fuller et al., (2008) ¹⁴¹
King et al., (2008) ¹⁴²
Madsen et al., (2007) ¹⁴³
<i>Spine</i>
Benzil et al., (2004) ⁹⁶
Chang et al., (2007) ⁹⁷
Degen et al., (2005) ⁹⁸
Gagnon et al., (2007) ¹²⁰
Gerszten and Burton, (2008) ⁹⁹
Gibbs et al., (2007) ¹⁰⁰
Gwak et al., (2006) ¹²¹
Jin et al., (2007) ¹⁰¹
Rock et al., (2006) ¹⁰²
Ryu et al., (2001) ¹⁰³
Ryu et al., (2007) ¹⁰⁴
Ryu et al., (2008) ¹⁰⁵

Appendix C. Excluded studies

Table 14. Excluded studies

Reference	Exclusion reason
Kondziolka et al., (2000) ¹⁵⁴	Not a clinical study
Meeks et al., (2003) ¹⁵⁵	Treatment delivery
Murphy (2004) ¹⁵⁶	Not a clinical study
Derweesh and Novick, (2003) ¹⁵⁷	Not a clinical study
Yu and Shepard, (2003) ¹⁵⁸	Not a clinical study
King et al., (2003) ¹⁵⁹	Treatment delivery
Chang and Adler, (2001) ¹⁶⁰	Not a clinical study
Quinn, (2002) ¹⁶¹	Not a clinical study
Murphy et al., (2003) ¹⁶²	Treatment delivery
Schweikard et al., (2000) ¹⁶³	Treatment delivery
Klimo and Schmidt, (2004) ¹⁶⁴	Not a clinical study
Edens and Weber, (2004) ¹⁶⁵	Not relevant
Ryken et al., (2001) ¹⁶⁶	Treatment delivery
Chang and Adler (2001) ¹⁶⁷	Not a clinical study
Uematsu et al., (2000) ¹⁶⁸	No relevant outcomes
Welch and Gerszten, (2005) ¹⁶⁹	Not a clinical study
Schweikard et al., (2004) ¹⁷⁰	Treatment delivery
Gerszten and Welch, (2004) ¹⁷¹	Not a clinical study
Rock et al., (2004) ¹⁷²	Not a clinical study
Ryu et al., (2003) ¹⁷³	Less than 3 patients
Niranjan and Lunsford, (2000) ¹⁷⁴	Not a clinical study
Kelly, (2000) ¹⁷⁵	Not a clinical study
Herbert et al., (2003) ¹⁷⁶	Treatment delivery
Solberg et al., (2004) ¹⁷⁷	Not relevant
Bilsky, (2005) ¹⁷⁸	Not a clinical study
Shibuya and Tsujii (2005) ¹⁷⁹	Not relevant
Ding et al., (2005) ¹⁸⁰	Not a clinical study
Hevezi, (2003) ¹⁸¹	Not a clinical study

Reference	Exclusion reason
Holland (2001) ¹⁸²	Not a clinical study
Bese et al., (2006) ¹⁸³	Not a clinical study
Henderson et al., (2006) ¹⁸⁴	Not a clinical study
Hocht et al., (2005) ¹⁸⁵	Treatment planning
Bangalore et al., (2007) ¹⁸⁶	Not a clinical study
Jaffray et al., (2007) ¹⁸⁷	Not a clinical study
Takeuchi et al., (2003) ¹⁸⁸	Treatment delivery
Romanelli et al., (2006) ¹⁸⁹	Not a clinical study
Gibbs, (2006) ¹⁹⁰	Not a clinical study
Kresl, (2006) ¹⁹¹	Not a clinical study
Gerszten, (2007) ¹⁹²	Not a clinical study
Auberger et al., (2007) ¹⁹³	Not relevant
Holmes et al., (2008) ¹⁹⁴	Not a clinical study
Agazaryan et al., (2008) ¹⁹⁵	Treatment delivery
Brock (2007) ¹⁹⁶	Not a clinical study
Bayouth et al., (2007) ¹⁹⁷	Not a clinical study
Wagner et al., (2007) ¹⁹⁸	Not a clinical study
Fuss et al., (2007) ¹⁹⁹	Not a clinical study
Orecchia (2007) ²⁰⁰	Not a clinical study
Guckenberger et al., (2007) ²⁰¹	Treatment delivery
Shirato et al., (2007) ²⁰²	Not a clinical study
Chang et al., (2008) ²⁰³	Not a clinical study
Sterzing et al., (2007) ²⁰⁴	Not relevant
Chen et al., (2007) ¹⁴	Not a clinical study
Prevost et al., (2008) ²⁰⁵	Treatment delivery
Dilling and Hoffe (2008) ³	Not a clinical study
Lillard (2008) ²⁰⁶	Not a clinical study
Pollock (2006) ²⁰⁷	Not a clinical study
Pollock and Foote (2004) ²⁰⁸	Not a clinical study
Jawahar et al., (2004) ²⁰⁹	Not relevant
Fuss and Thomas (2004) ²	Not a clinical study
Hara et al., (2007) ²¹⁰	Not a clinical study

Reference	Exclusion reason
Cheshier et al., (2007) ²¹¹	Not relevant
De et al., (2005) ²¹²	Treatment delivery
Niranjan et al., (2007) ²¹³	Not a clinical study
Flickinger et al., (2007) ²¹⁴	Not a clinical study
Leskell (2007) ⁴	Not a clinical study
De Salles et al., (2008) ²¹⁵	Not relevant
Poll et al., (2008) ²¹⁶	Not a clinical study
Saw et al., (2008) ²¹⁷	Not a clinical study
Macdermed et al., (2008) ²¹⁸	Not a clinical study
Spadea et al., (2008) ²¹⁹	Treatment delivery
Yin et al., (2008) ²²⁰	Treatment delivery
Kriminski et al., (2008) ²²¹	Treatment delivery
Finn et al., (2007) ²²²	Not a clinical study
Romanelli and Adler (2008) ²²³	Not a clinical study
Wang et al., (2008) ²²⁴	Treatment planning
Buchgeister et al., (2007) ²²⁵	Not a clinical study
Cho et al., (2008) ²²⁶	Not relevant
Astrahan (2008) ²²⁷	Not a clinical study
Sahgal et al., (2008) ²²⁸	Not a clinical study
Jamal et al., (2008) ²²⁹	Not a clinical study
Theil and Winfield (2008) ²³⁰	Not a clinical study
Wu et al., (2008) ²³¹	Treatment delivery
Lindvall et al., (2008) ²³²	Not relevant
Kondziolka et al., (2008) ²³³	Not relevant
Solberg et al., (2008) ²³⁴	Quality Assurance
Lu et al., (2008) ²³⁵	Treatment planning
Merchant et al., (2008) ²³⁶	Not relevant
Heinzerling et al., (2008) ²³⁷	Treatment delivery
Solberg et al., (2008) ²³⁸	Not a clinical study
Kupferman and Hanna (2008) ²³⁹	Not a clinical study
Wakelee et al., (2008) ²⁴⁰	Not a clinical study
Chang et al., (2007) ²⁴¹	Not a clinical study

Reference	Exclusion reason
Prevost et al., (2008) ²⁴²	Treatment planning
Karampelas et al., (2008) ²⁴³	Not relevant
Park et al., (2008) ²⁴⁴	Treatment planning
Seki et al., (2007) ²⁴⁵	Treatment planning
De Pooter et al., (2007) ²⁴⁶	Treatment planning
Edler (2007) ²⁴⁷	Not relevant
Wilt et al., (2008) ²⁴⁸	Not relevant
Papiez and Timmerman (2008) ²⁴⁹	Not a clinical study
Cesaretti et al., (2008) ²⁵⁰	Not a clinical study
Hoogeman et al., (2008) ²⁵¹	Treatment delivery
Imura et al., (2008) ²⁵²	Treatment delivery
Sterzing et al., (2008) ²⁵³	Not relevant
Quang et al., (2007) ²⁵⁴	Not a clinical study
Fenwick et al., (2008) ²⁵⁵	Not relevant
Hoh et al., (2007) ²⁵⁶	Not a clinical study
Keiler et al., (2007) ²⁵⁷	Not relevant
Loeffler et al., (2003) ²⁵⁸	Not a clinical study
Ganslandt et al., (2003) ²⁵⁹	Not relevant
Ashamalla et al., (2003) ²⁶⁰	Treatment delivery
Shirator et al., (2003) ²⁶¹	Not relevant
Kitamura et al., (2003) ²⁶²	Treatment delivery
Onishi et al., (2003) ²⁶³	Treatment delivery
Timmerman et al., (2003) ²⁶⁴	Not a clinical study
Bourland and Shaw (2003) ²⁶⁵	Not a clinical study
Flickinger et al., (2003) ²⁶⁶	Not a clinical study
Kavanagh et al., (2003) ²⁶⁷	Not a clinical study
Heron et al., (2003) ²⁶⁸	Not a clinical study
Lomax et al., (2003) ²⁶⁹	Treatment planning
Classen et al., (2003) ²⁷⁰	Not relevant
Georg et al., (2003) ²⁷¹	Treatment delivery
Gardner et al., (2003) ²⁷²	Not a clinical study
Nakamura et al., (2003) ²⁷³	Not relevant

Reference	Exclusion reason
Borden (2002) ²⁷⁴	Not a clinical study
Hadinger et al., (2002) ²⁷⁵	Treatment planning
Yin et al., (2002) ²⁷⁶	Treatment planning
Kondziolka et al., (2002) ²⁷⁷	Not a clinical study
Francel et al., (2002) ²⁷⁸	Not relevant
Ganz (2002) ²⁷⁹	Not a clinical study
St. George et al., (2002) ²⁸⁰	Not relevant
Mack et al., (2002) ²⁸¹	Not relevant
(2002) ²⁸²	Not a clinical study
Leybovich et al., (2002) ²⁸³	Not relevant
(2002) ²⁸⁴	Not relevant
Kitamura et al., (2002) ²⁸⁵	Not relevant
O'Dell et al., (2002) ²⁸⁶	Not relevant
Kitamura et al., (2002) ²⁸⁷	Not relevant
Seppenwoolde et al, (2002) ²⁸⁸	Treatment delivery
Vaidya et al., (2002) ²⁸⁹	Not relevant
Bhatnagar et al., (2002) ²⁹⁰	Not relevant
Murphy et al., (2002) ²⁹¹	Treatment delivery
Demarco et al., (2002) ²⁹²	Not relevant
Bale and Sweeney (2002) ²⁹³	Not a clinical study
Lee et al., (2002) ²⁹⁴	Not relevant
Day (2002) ²⁹⁵	Not a clinical study
Rosahl et al., (2002) ²⁹⁶	Not a clinical study
Burton et al., (2002) ²⁹⁷	Not relevant
Gross and Engenhardt-Cabillic (2002) ²⁹⁸	Not a clinical study
Murphy et al., (2001) ²⁹⁹	Treatment planning
Fuss et al., (2004) ³⁰⁰	Not relevant
Chang and Timmerman (2007) ¹¹³	Not a clinical study
Chuang et al., (2007) ³⁰¹	Treatment delivery
Suzuji et al., (2007) ³⁰²	Treatment delivery
Cadman (2007) ³⁰³	Treatment planning
Ball and Withers (2007) ³⁰⁴	Not a clinical study

Reference	Exclusion reason
Cheung et al., (2007) ³⁰⁵	Treatment planning
Lindquist and Paddick (2007) ³⁰⁶	Not relevant
Taguchi et al., (2007) ³⁰⁷	Treatment delivery
Grills et al., (2007) ³⁰⁸	Treatment planning
Anatham et al., (2007) ³⁰⁹	Not relevant
No Authors Listed (2007) ³¹⁰	Not relevant
Mery et al., (2007) ³¹¹	Not a clinical study
No Authors Listed (2007) ³¹²	Not relevant
Cheshier et al., (2007) ³¹³	Not relevant
Sarfaraz et al., (2007) ³¹⁴	Not a clinical study
Dhanachai et al., (2007) ³¹⁵	More than 10 fractions
Kavanagh et al., (2007) ³¹⁶	Not a clinical study
Gibbs (2007) ³¹⁷	Not a clinical study
Pawlicki et al., (2007) ³¹⁸	Not a clinical study
Chang et al., (2007) ³¹⁹	Not a clinical study
Timmerman et al., (2007) ³²⁰	Not a clinical study
Timmerman et al., (2007) ³²¹	Treatment planning
Kavanagh et al., (2007) ³²²	Not a clinical study
Smith and Chuang (2007) ³²³	Not a clinical study
Meyer et al., (2007) ³²⁴	Not a clinical study
Abbas et al., (2007) ³²⁵	Not a clinical study
Chang and Roth (2007) ³²⁶	Not a clinical study
Bradley (2007) ³²⁷	Not a clinical study
Timmerman et al., (2007) ³²⁸	Not a clinical study
Aboulafia et al., (2007) ³²⁹	Not relevant
Pan et al., (2007) ³³⁰	Treatment delivery
Ganz (2007) ³³¹	Not a clinical study
Sherwood and Brock (2007) ³³²	Not a clinical study
Hinson et al., (2007) ³³³	Treatment delivery
Linthout et al., (2007) ³³⁴	Not relevant
Mazzei and Toole (2007) ³³⁵	Not a clinical study
Matsumoto et al., (2007) ³³⁶	Not relevant

Reference	Exclusion reason
Bogart (2007) ³³⁷	Not a clinical study
Huntzinger et al., (2007) ³³⁸	Not a clinical study
Murray et al., (2007) ³³⁹	Treatment delivery
Wunderink et al., (2007) ³⁴⁰	Treatment planning
Larre et al., (2007) ³⁴¹	Not relevant
Hiraoka et al., (2007) ³⁴²	Not a clinical study
Kunzler et al., (2007) ³⁴³	Treatment delivery
Nagata et al., (2007) ³⁴⁴	Not a clinical study
Timmerman et al., (2007) ³⁴⁵	Not a clinical study
Gerszten et al., (2007) ³⁴⁶	Not a clinical study
Lunsford et al., (2007) ³⁴⁷	Not a clinical study
Niranjan et al., (2007) ³⁴⁸	Not a clinical study
Kondziolka et al., (2007) ³⁴⁹	Not a clinical study
Yousefi et al., (2007) ³⁵⁰	Treatment delivery
Gaspar (2007) ³⁵¹	Not a clinical study
Brenner and Schwade (2007) ³⁵²	Not a clinical study
Lo et al., (2007) ³⁵³	Not a clinical study
Zamzuri et al., (2006) ³⁵⁴	Not relevant
Asamura (2006) ³⁵⁵	Not a clinical study
Bogart (2006) ³⁵⁶	Not a clinical study
Sciubba and Gokaslan (2006) ³⁵⁷	Not a clinical study
Storme et al., (2006) ³⁵⁸	Not a clinical study
Andrews et al., (2006) ³⁵⁹	Not a clinical study
Hogle (2006) ³⁶⁰	Not a clinical study
Muacevic et al., (2006) ³⁶¹	Treatment delivery
Kontrisoava et al., (2006) ³⁶²	Treatment planning
Steinke (2006) ³⁶³	Not relevant
Verellen et al., (2006) ³⁶⁴	Treatment planning
Fenwick et al., (2006) ³⁶⁵	Not a clinical study
Soete et al., (2006) ³⁶⁶	Treatment planning
Fuller et al., (2006) ³⁶⁷	Treatment delivery
Rassiah-Szegedi et al., (2006) ³⁶⁸	Treatment planning

Reference	Exclusion reason
Lax et al., (2006) ³⁶⁹	Treatment planning
Slotman et al., (2006) ³⁷⁰	Not a clinical study
Fuss et al., (2006) ³⁷¹	Treatment planning
Hansen et al., (2006) ³⁷²	Treatment delivery
Casamassima et al., (2006) ³⁷³	Treatment delivery
Korreman et al., (2006) ³⁷⁴	Treatment planning
Purdie et al., (2006) ³⁷⁵	Treatment delivery
Guckenberger et al., (2006) ³⁷⁶	Treatment planning
Wurm et al., (2006) ³⁷⁷	Not relevant
Timmerman et al., (2006) ³⁷⁸	Not a clinical study
Thieke et al., (2006) ³⁷⁹	Treatment planning
Strassmann et al., (2006) ³⁸⁰	Treatment delivery
Baisden et al., (2006) ³⁸¹	Treatment planning
Willoughby et al., (2006) ³⁸²	Not relevant
Samper et al., (2006) ³⁸³	Not relevant
Savides (2006) ³⁸⁴	Not a clinical study
Pishvaian et al., (2006) ³⁸⁵	Treatment delivery
Decker et al., (2006) ³⁸⁶	Not a clinical study
Bernier et al., (2006) ³⁸⁷	Not relevant
Romanelli et al., (2006) ³⁸⁸	Not relevant
Bauman et al., (2006) ³⁸⁹	Not relevant
McDermott et al., (2006) ³⁹⁰	Not relevant
Wallen (2006) ³⁹¹	Not a clinical study
Riboldi et al., (2006) ³⁹²	Treatment planning
Scemla et al., (2006) ³⁹³	Not a clinical study
Soisson et al., (2006) ³⁹⁴	Treatment planning
Silvano (2006) ³⁹⁵	Not a clinical study
Oldenberg (2006) ³⁹⁶	Not relevant
FitzGerald et al., (2006) ³⁹⁷	Not relevant
Kavanagh and Timmerman (2006) ¹⁵³	Not a clinical study
Singh et al., (2006) ³⁹⁸	Not a clinical study
Kavanagh et al., (2006) ³⁹⁹	Not a clinical study

Reference	Exclusion reason
Curtis and The (2006) ⁴⁰⁰	Not relevant
Ernst-Stecken et al., (2006) ⁴⁰¹	Not relevant
Snell et al., (2006) ⁴⁰²	Treatment planning
Shirato et al., (2006) ⁴⁰³	Not a clinical study
Underberg et al., (2006) ⁴⁰⁴	Treatment delivery
Nieder et al., (2006) ⁴⁰⁵	Treatment planning
Kommu et al., (2006) ⁴⁰⁶	Not relevant
Fritz et al., (2006) ⁴⁰⁷	Treatment delivery
Potters et al., (2005) ⁴⁰⁸	Not a clinical study
Kondziolka et al., (2005) ⁴⁰⁹	Not a clinical study
Isaksson et al., (2005) ⁴¹⁰	Not relevant
Schlaefer et al., (2005) ⁴¹¹	Treatment planning
Stancanello et al., (2005) ⁴¹²	Treatment planning
Mell and Mundt (2005) ⁴¹³	Not relevant
Dinka et al., (2005) ⁴¹⁴	Not a clinical study
Imura et al., (2005) ⁴¹⁵	Treatment delivery
Pott et al., (2005) ⁴¹⁶	Not relevant
Li and Ma (2005) ⁴¹⁷	Treatment planning
Laigle-Donadey et al., (2005) ⁴¹⁸	Not relevant
Mut et al., (2005) ⁴¹⁹	Not relevant
Livi et al., (2005) ⁴²⁰	Not relevant
Shoshan et al., (2005) ⁴²¹	Not a clinical study
Attia et al., (2005) ⁴²²	Not a clinical study
Takeda et al., (2005) ⁴²³	Treatment planning
Heros (2005) ⁴²⁴	Not a clinical study
Slotman et al., (2005) ⁴²⁵	Not relevant
Maarouf et al., (2005) ⁴²⁶	Not relevant
Fatigante et al., (2005) ⁴²⁷	Not relevant
Underberg et al., (2005) ⁴²⁸	Treatment delivery
El Hamri et al., (2005) ⁴²⁹	Not a clinical study
Dvorak et al., (2005) ⁴³⁰	Not a clinical study
Takayama et al., (2005) ⁴³¹	Treatment planning

Reference	Exclusion reason
Jin et al., (2005) ⁴³²	Treatment planning
El-Sherif et al., (2005) ⁴³³	Not a clinical study
Theodorou et al., (2000) ⁴³⁴	Treatment planning
Buatti et al., (2000) ⁴³⁵	Not a clinical study
Jozsef et al., (2000) ⁴³⁶	Treatment planning
Lee et al., (2000) ⁴³⁷	Treatment planning
Buatti et al., (2000) ⁴³⁸	Not relevant
Baser et al., (2000) ⁴³⁹	Not relevant
Rutten and Deneufbourg (2000) ⁴⁴⁰	Not relevant
Pollock et al., (2000) ⁴⁴¹	Not relevant
Ratto et al., (2000) ⁴⁴²	Not relevant
(2001) ⁴⁴³	Not relevant
Liu et al., (2001) ⁴⁴⁴	Not a clinical study
Nakamura et al., (2001) ⁴⁴⁵	Treatment planning
Chou et al., (2001) ⁴⁴⁶	Not a clinical study
Tsai et al., (2001) ⁴⁴⁷	Treatment planning
Dieckmann et al., (2001) ⁴⁴⁸	Treatment planning
Zhang et al., (2001) ⁴⁴⁹	Treatment planning
Singletery (2001) ⁴⁵⁰	Not relevant
Leavitt et al., (2001) ⁴⁵¹	Treatment delivery
Armstrong (2001) ⁴⁵²	Not a clinical study
Chin et al., (2001) ⁴⁵³	Not relevant
Alheit et al., (2001) ⁴⁵⁴	Treatment planning
Lind et al., (2001) ⁴⁵⁵	Not relevant
Friedman et al., (2001) ⁴⁵⁶	Treatment delivery
Huber et al., (2001) ⁴⁵⁷	Not relevant
Bance and Guha (2001) ⁴⁵⁸	Not a clinical study
Solberg et al., (2001) ⁴⁵⁹	Treatment planning
Fuss (2001) ⁴⁶⁰	Not a clinical study
Gottlieb (2001) ⁴⁶¹	Not relevant
Gottlieb (2001) ⁴⁶²	Not a clinical study
Mignano et al., (2001) ⁴⁶³	Treatment planning

Reference	Exclusion reason
Hu et al., (2000) ⁴⁶⁴	Not relevant
Shepard et al., (2000) ⁴⁶⁵	Treatment planning
Horstmann et al., (2000) ⁴⁶⁶	Not relevant
Mathews and Smith (2000) ⁴⁶⁷	Treatment delivery
Wakisaka et al., (2000) ⁴⁶⁸	Treatment planning
Friedman and Foote (2000) ⁴⁶⁹	Not a clinical study
Barnett et al., (2000) ⁴⁷⁰	Not a clinical study
Liao et al., (2000) ⁴⁷¹	Treatment planning
Rousseau and Gibon (2000) ⁴⁷²	Not a clinical study
Bridgewater and Spittle (2000) ⁴⁷³	Not relevant
Jeremic et al., (2000) ⁴⁷⁴	Not relevant
Smit (2000) ⁴⁷⁵	Not a clinical study
Kenai et al., (2005) ⁴⁷⁶	Treatment planning
Haedinger et al., (2005) ⁴⁷⁷	Treatment planning
Tonn (2004) ⁴⁷⁸	Not a clinical study
Muacevic et al., (2004) ⁴⁷⁹	Not a clinical study
Scheib et al., (2004) ⁴⁸⁰	Not relevant
Petersch et al., (2004) ⁴⁸¹	Treatment delivery
Song et al., ⁴⁸²	Not a clinical study
Nakaji and Spetzler (2004) ⁴⁸³	Not relevant
Guerrero and Li (2004) ⁴⁸⁴	Treatment planning
Hui et al., (2004) ⁴⁸⁵	Not relevant
Yin et al., (2004) ⁴⁸⁶	Treatment delivery
Foote et al., (2004) ⁴⁸⁷	Not relevant
Kondziolka et al., (2004) ⁴⁸⁸	Not a clinical study
Rock et al., (2004) ⁴⁸⁹	Not a clinical study
Shrieve et al., (2004) ⁴⁹⁰	Not a clinical study
Kawaguchi et al., (2004) ⁴⁹¹	Less than 3 patients
Tobler et al., (2004) ⁴⁹²	Treatment planning
Parman (2004) ⁴⁹³	Not a clinical study
Gerrard and Franks (2004) ⁴⁹⁴	Not relevant
Liu et al., (2004) ⁴⁹⁵	Treatment planning

Reference	Exclusion reason
Strassmann et al., (2004) ⁴⁹⁶	Treatment planning
Kunieda et al., (2004) ⁴⁹⁷	Treatment planning
Hermann et al., (2004) ⁴⁹⁸	Not a clinical study
Bogart (2004) ⁴⁹⁹	Not a clinical study
Muller et al., (2004) ⁵⁰⁰	Treatment delivery
(2003) ⁵⁰¹	Not a clinical study
Wu et al., (2003) ⁵⁰²	Treatment planning
Gibbons et al., (2003) ⁵⁰³	Not relevant
Kassaei et al., (2003) ⁵⁰⁴	Treatment delivery
Wagner et al., (2003) ⁵⁰⁵	Treatment planning
Chang and Lo (2003) ⁵⁰⁶	Not relevant
Shiu et al., (2003) ⁵⁰⁷	Treatment delivery
Nakagawa et al., (2003) ⁵⁰⁸	Treatment planning
Rosenzweig et al., (2003) ⁵⁰⁹	Not a clinical study
Coker (2003) ⁵¹⁰	Not a clinical study
Linskey and Johnstone (2003) ⁵¹¹	Not a clinical study
Ma et al., (2003) ⁵¹²	Not relevant
Gross et al., (2003) ⁵¹³	Treatment delivery
Pang (2003) ⁵¹⁴	Not a clinical study
Sankaranarayanan et al., (2003) ⁵¹⁵	Treatment planning
No Authors Listed (2003) ⁵¹⁶	Not relevant
Prabhu and Demonte (2003) ⁵¹⁷	Not relevant
Papiez et al., (2003) ⁵¹⁸	Not a clinical study
Petrovich and Yu (2003) ⁵¹⁹	Not relevant
Muacevic et al., (2003) ⁵²⁰	Not relevant
Regine (2003) ⁵²¹	Not a clinical study
Van (2003) ⁵²²	Not a clinical study
Salter et al., (2001) ⁵²³	Treatment delivery
Ebert et al., (2001) ⁵²⁴	Treatment planning
Theodorou et al. ⁵²⁵	Not a clinical study
Sasai et al., (2000) ⁵²⁶	Treatment planning
Dawood (2008) ⁵²⁷	Not a clinical study

Reference	Exclusion reason
Sahgal et al., (2008) ⁵²⁸	Treatment planning
Galvin and Bednarz (2008) ¹¹²	Quality Assurance
Meretoja et al., (2008) ⁵²⁹	Not relevant
Andrews (2007) ⁵³⁰	Not a clinical study
Naff (2007) ⁵³¹	Not relevant
Soltys and Gibbs (2007) ⁵³²	Not a clinical study
Senan et al., (2007) ⁵³³	Not a clinical study
Saunders (2007) ⁵³⁴	Not a clinical study
Lee (2007) ⁵³⁵	Not a clinical study
Rockhill (2007) ⁵³⁶	Not a clinical study
Rades and Schild (2007) ⁵³⁷	Not a clinical study
Sciubba et al., (2007) ⁵³⁸	Not a clinical study
Colombo et al., (2006) ⁵³⁹	Not a clinical study
Kondziolka et al., (2006) ⁵⁴⁰	Not a clinical study
Benedict et al., (2008) ⁵⁴¹	Not a clinical study
Takacs et al., (1999) ⁵⁴²	No full text

Appendix D. Personnel qualifications

Table 15. 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 2006¹¹⁴

Appendix E. Recommendations

Table 16. Recommendations for stereotactic body radiation therapy procedures

Procedure specifications	Accessory AC	Images QC	Treatment planning QC	Simulation and treatment	Follow-up
<ul style="list-style-type: none"> ✓ Treatment-delivery unit requires implementation of/adherence to QA program ✓ Mechanical tolerance must assure actual isocenter is within +/- 2mm 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 2006¹¹⁴

Appendix F. Currently marketed devices for SRS/SBRT

Table 17. Devices currently marketed for stereotactic radiosurgery

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 non-coplanar 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 – non-coplanar and non-isocentric; 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 6MV 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® Perfexion™	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 (2.33×10^{14} 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
MHI-TM2000 linear accelerator system	Mitsubishi	<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® shaped beam surgery	BrainLab AG	<ul style="list-style-type: none"> ✓ Beam delivery – static or dynamic Shaped Beam radiosurgery ✓ Beam energy – 6 MV (photon) Collimation – micro-multileaf ‘beam shaper’ ✓ Design – a high precision linac unit ✓ Dose delivery system – a computer controlled photon beam integrated with an automated photon beam shaping system ✓ Field size – 100 mm x 100 mm maximum ✓ Imaging – 3D reconstruction of patient’s anatomy as CT and MR images are fused automatically and allow incorporation of non-localized images. ✓ Output – 100- 800 MU/min ✓ Patient positioning/localization – ExacTrac positioning system and an automated patient positioning system ✓ Treatment Sessions – single and fractionated 	No	To plan, to perform and to document RS or SRT for lesions (i.e., AVMs), tumors, head and neck targets, functional disorders and extracranial indications	Spine, lung, liver, prostate, head, neck

Device name	Manufacturer/Distributor	Features	Dedicated to SRS	FDA indication	Extracranial indications presented on company web site
<p>Novalis TX™</p>	<p>BrainLab AG/ Varian Medical Systems</p>	<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 – 6-20MV/6-20MEV ✓ Collimation –Varian's HD120 MLC with 2.5 mm high-definition leaves ✓ Design – includes Adaptive Gating and On-Board Imager devices ✓ Field size – 22 x 40cm maximum ✓ Imaging – 3D CT scanner with 2D radiographic and fluoroscopic imaging capability combined with room-mounted X-ray imaging system for real-time imaging and motion management ✓ Output – 1,000 MU at 100 cm ✓ Patient positioning/localization – 6D Robotic Treatment Couch/room-based stereo x-ray with 2D-3D KV match and machine-based imaging and cone-beam CT (CBCT) 3D imaging and MV-BEV (beam's eye view) and True KV-fluoro ✓ Treatment Sessions – single and fractionated 	<p>Yes</p>	<p>Trilogy linac intended to provide SRS and precision RT for lesions, tumors and conditions anywhere in the body</p>	<p>Spine, lung, liver, prostate, head, neck</p>

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 5x5 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 non-coplanar ✓ 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 multileaf collimator ✓ Field size – 16cm x 21cm ✓ Imaging – 4D Adaptive™ IGRT technology ✓ Patient positioning/localization ✓ Treatment Sessions – single and fractionated 	No	Radiation therapy treatment of malignant neoplastic diseases	Spine, lung, liver, prostate, pancreas, head, neck

Device name	Manufacturer/Distributor	Features	Dedicated to SRS	FDA indication	Extracranial indications presented on company web site
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 – 6MV (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™		<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 – 6MV (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 from ⁵⁴³

- AVM Arteriovenous malformations
- IGRT Image guided radiation therapy
- LINAC Linear accelerator
- MEV Million electron volt
- MLC Multi-leaf collimator
- MU/min Monitor units per minute

MV	Megavole
NR	Not reported
RS	Radiosurgery
RT	Radiotherapy
SRS	Stereotactic radiosurgery
SRT	Stereotactic radiotherapy

Appendix G. Linac-based SRS/SBRT accessories

Table 18. 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 multileaf collimator with a generous 16 x 21cm field size. The field comprises 80 individually controlled leaves, each with a travel range of more than 21cm. 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 non-coplanar 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

Device name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA indications	Indications presented on company web site	Compatibility
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	Accessory x-ray collimator designed to be mounted on Varian Trilogy TX and Trilogy linacs and is intended to shape the x-ray field perimeter. HD 120 MLC provides higher resolution via finer width leaves (120) resulting in a modified treatment field from 40 cm to 22 cm in width.	No	Target volumes during RS and RT		Varian's Trilogy

Device name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA indications	Indications presented on company web site	Compatibility
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.		

Device name	Manufacturer/ Distributor	Description	Dedicated to SRS	FDA indications	Indications presented on company web site	Compatibility
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

HD High definition
 IMSRS Intensity modulated stereotactic radiosurgery
 MV Megavolts
 NR Not reported
 RS Radiosurgery
 RT Radiotherapy

Appendix H. Applicant's FDA 510K information

Table 19. Regulatory status of devices

Device name	Manufacturer/ Distributor	510(k) applicant	Substantial equivalence	Classification name	Product code(s)	510(k) number	Approval date
AccuChanger ⁵⁴⁴	Direx Systems Corporated	Direx Systems Corp.	Acculeaf ; Cranial stereotactic equipment k010065 Arplay/BrainLab ; Radionics XKnife*	Accelerator, Linear, Medical	IXI	K043409	5/05
AccuLeaf ⁵⁴⁵	Direx Systems Corporated	Direx Systems Corp.	BrainLab MMLC*	Accelerator, Linear, Medical	IXI	K040553	4/04
Axesse™	Elekta Inc.			Approval documentation requested from FDA and manufacturer			
Beam Modulator™ ⁵⁴⁶	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	1/05
CyberKnife® Robotic Radiosurgery System ⁵⁴⁷	Accuray Incorporated	Accuray Corporation	Predicate device	Medical charged particle radiotherapy device	IYE	K072504	9/07
Dynamic Micro Multileaf Collimator (DMMLC) ⁵⁴⁸	Elekta Limited	Elekta Limited	Predicate device	Medical Linear Accessory, IYE	IYE	K082122	8/08

Device name	Manufacturer/ Distributor	510(k) applicant	Substantial equivalence	Classification name	Product code(s)	510(k) number	Approval date
HD 120 MLC ⁵⁴⁹	Varian Medical Systems	Varian Medical Systems	Predicate device	Medical Charged Particle Radiation Therapy System	90 IYE	K071992	8/07
Leksell Gamma Knife® Perfexion™ ⁵⁵⁰	Elekta Inc.	Elekta Ltd.	Predicate device	Radionuclide radiation therapy system	IWB	K063512	3/07
m3® (micro-Multileaf Collimator) ⁵⁵¹	BrainLAB AG	BrainLAB AG	Predicate device	Accelerator, Linear, Medical	90 IYE	K020860	6/02
MHI-TM2000 ⁵⁵²	MHI Medical Systems/Hiroshima Machinery Works	Mitsubishi Heavy Industries, Ltd.	Trilogy; Hi-Art System	Accelerator, Linear, Medical	IYE	K072047	8/07
Micro MLC ⁵⁵³	Siemens Medical Solutions USA, Inc.	Siemens Medical Solutions	Predicate device	Accelerator, Linear, Medical	IXI	K032790	10/03
Moduleaf™ mini Multileaf Collimator ⁵⁵⁴	Siemens Medical Solutions	MRC Systems GmbH	Predicate device	Block, Beam Shaping, Radiation Therapy	90 IXI	K030609	3/03
Novalis® Shaped Beam Surgery ⁵⁵⁵	BrainLAB AG	BrainLAB AG	NR	Novalis Shaped Beam Surgery™ System	90 IYE and 90 MUJ	K002509	11/00

Device name	Manufacturer/ Distributor	510(k) applicant	Substantial equivalence	Classification name	Product code(s)	510(k) number	Approval date
Novalis TX™ ^{549,556-558}	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	7/08; 8/07; 10/07; 10/04
Oncor Artiste, Impression, Avant-Garde, and Expression ⁵⁵⁹⁻⁵⁶¹	Siemens Healthcare	Siemens Medical Solutions USA, Inc.	ONCOR linac family	Accelerator, Linear, Medical	IYE	Artiste – K072485 Avant-Garde – K031764 Expression – K060226	12/07; 3/06; 9/03
Synergy®S ⁵⁶²	Elekta	Elekta Limited	Predicate device	Medical Linear Accelerator Accessory 90 IYE	90 IYE	K051932	8/05
TomoTherapy® Hi-Art® ^{563- 566}	TomoTherapy, Inc.	Tomotherapy, Inc.	Varian Clinac 600*	Medical charged-particle radiation therapy system	MUJ	K082005 K060912 K042739 K013673	8/08; 4/06; 11/04; 1/02
Trilogy™ ⁵⁵⁶	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	7/08

Device name	Manufacturer/ Distributor	510(k) applicant	Substantial equivalence	Classification name	Product code(s)	510(k) number	Approval date
XKnife™MMLC™ ⁵⁶⁷	Radionics	Radionics		Radiotherapy beam shaping block	90 IYE	K993594 Asked Radionics to confirm	12/99

NR Not reported

* Purged from CDRH database

Appendix I. Manufacturer web sites

Table 20. Manufacturers

Company	Web site
Accuray Incorporated ⁵⁶⁸	http://www.accuray.com
BrainLAB AG ⁵⁶⁹	http://www.brainlab.com
Direx Systems Corp. ⁵⁷⁰	http://www.direxusa.com
Elekta Inc. ⁵⁷¹	http://www.elekta.com
MHI Medical Systems Inc. ⁵⁷²	http://www.mhi.co.jp/en/index.html
Radionics ⁵⁷³	http://www.radionics.com
Siemens USA ⁵⁷⁴	http://www.medical.siemens.com
TomoTherapy Incorporated ⁵⁷⁵	http://www.tomotherapy.com
Varian Medical Systems ⁵⁷⁶	http://www.varian.com

Appendix J. Facilities performing SRS/SBRT for extracranial solid tumors

Table 21. Facilities

Hospital name	State	City	Devices(s)	Treatment site(s)
University of Alabama Hospital	AL	Birmingham	Tomotherapy	Prostate, Spine
Gulf Coast Cancer Centers	AL	Foley	Novalis	Liver mets, Lung, Spine
Banner Good Samaritan Med Center	AZ	Phoenix	Tomotherapy	NS
Mayo Clinic Hospital	AZ	Phoenix	NR	NS
Scottsdale Healthcare-Osborn	AZ	Scottsdale	Novalis	Breast, Liver, Lung, Pancreas, Prostate, Rectal, Spine
Scottsdale Healthcare-Shea	AZ	Scottsdale	Novalis	Breast, Liver, Lung, Pancreas, Prostate, Rectal, Spine
St. Joseph's Hospital and Med Center	AZ	Phoenix	CyberKnife	Abdomen, Chest, and Spine
University Medical Center	AZ	Tucson	Novalis	Liver and other extracranial locations
Cedars-Sinai Medical Center	CA	Los Angeles	NR	Lung, Spine
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, Spine
CyberKnife Centers of San Diego - Encinitas	CA	Encinitas	CyberKnife	Liver (primary and mets), Lung (primary and mets)
CyberKnife Centers of San Diego – San Diego	CA	San Diego	CyberKnife	Liver (primary and mets), Lung (primary and mets)
CyberKnife of Southern California at Vista	CA	Vista	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate, Spine
Eisenhower Medical Center	CA	Rancho Mirage	NR	Prostate, Spine
El Camino Hospital	CA	Mountain View	Novalis	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
Hoag Memorial Hospital Presbyterian	CA	Newport Beach	Tomotherapy	Liver Mets, Lung Mets, Spine
John Muir Medical Center, Walnut Creek	CA	Walnut Creek	Novalis	Breast, Colon, Liver, Liver Mets, Lung Mets, Prostate, Spine
Long Beach Memorial Medical Center	CA	Long Beach	Tomotherapy	Pelvis, Prostate
Los Robles Hospital and Medical Center	CA	Thousand Oaks	NR	Spine
Miller Children’s Hospital	CA	Long Beach	Tomotherapy	NS
Northridge Hospital Medical Center	CA	Northridge	Trilogy	Spine
Pomona Valley Hospital Medical Center	CA	Pomona	Trilogy	Prostate and other extracranial sites
Saint Agnes Medical Center	CA	Fresno	Novalis	NS
Sharp Grossmont Hospital	CA	La Mesa	Tomotherapy, 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	NS
UCSF Medical Center	CA	San Francisco	CyberKnife	Lung, Pancreas, Prostate, Spine
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
Poudre Valley Hospital	CO	Fort Collins	NR	NS
Rocky Mountain CyberKnife Center	CO	Boulder	CyberKnife	Lung
CyberKnife Center at Stamford Hospital	CT	Stamford	CyberKnife	Kidney, Liver, Lung, Pancreas, Prostate, Spine
Hartford Hospital	CT	Hartford	Trilogy	NS
Saint Francis Hospital and Med Center	CT	Hartford	CyberKnife	Liver, Lung, Pancreas

Hospital name	State	City	Devices(s)	Treatment site(s)
Christiana Care Health System	DE	Wilmington	CyberKnife	Kidney, Liver, Pancreas, Pelvis, Prostate, Spine, Spine Mets
MedStar-Georgetown Medical Center	DC	Washington	CyberKnife	Kidney, Liver (primary and mets), Lung, Spine
Washington Hospital Center	DC	Washington	Trilogy	NS
Baptist Hospital of Miami	FL	Miami	Tomotherapy	Bone, Breast, Lung, Prostate
Bethesda Memorial Hospital	FL	Boynton Beach	Trilogy	Kidney, Liver, Lung, Pancreas, Spine
Blake Medical Center	FL	Bradenton	CyberKnife	Spine
Broward General Medical Center	FL	Fort Lauderdale	CyberKnife, Trilogy	Liver, Lung, Pancreas, Spine
Cancer Care Centers of Brevard	FL	Melbourne	CyberKnife	Liver, Lung, Pancreas, Prostate
Capital Regional Medical Center	FL	Tallahassee	Tomotherapy	Prostate
Central Florida Regional Hospital	FL	Sanford	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis, Prostate, Spine
CyberKnife Cancer Center	FL	Jacksonville	CyberKnife	Liver (primary and mets), Pancreas, Prostate, Spine
CyberKnife Ctr at No.FL Radiation Oncology	FL	Gainesville	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate, Spine
CyberKnife Center of Miami	FL	Miami	CyberKnife	Bladder, Breast, Gynecologic, Liver, Lung, Pancreas, Prostate
CyberKnife Center of Palm Beach	FL	Palm Beach Gardens	CyberKnife	NS
Doctors Hospital	FL	Coral Gables	Tomotherapy	Bone, Breast, Lung, Prostate
Florida Hospital	FL	Orlando	Trilogy	NS
H. Lee Moffitt Cancer Center	FL	Tampa	Tomotherapy, Novalis	NS
Jackson Health System	FL	Miami	CyberKnife	Breast
Jupiter Medical Center	FL	Jupiter	CyberKnife, Trilogy	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
Mayo Clinic Jacksonville	FL	Jacksonville	NR	NS
Memorial Hospital of Jacksonville	FL	Jacksonville	CyberKnife	Liver, Lung, Pancreas, Prostate, Spine
Mount Sinai Medical Center	FL	Miami Beach	Trilogy	NS
North Broward Medical Center	FL	Deerfield Beach	CyberKnife, Trilogy	Liver, Lung, Pancreas, Spine
Orlando Regional Medical Center	FL	Orlando	Tomotherapy, Novalis	Liver, Lung, Spine
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
Emory Crawford Long Hospital	GA	Atlanta	Trilogy	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
Saint Alphonsus Regional Medical Center	ID	Boise	Novalis	Liver, Lung, Prostate, Spine
Advocate Christ Medical Center	IL	Oak Lawn	CyberKnife	Lung, Pancreas, Prostate, Spine Mets
Advocate Good Samaritan Hospital	IL	Downers Grove	CyberKnife	Liver, Lung, Pancreas, Prostate, Spine
Advocate Lutheran General Hospital	IL	Park Ridge	Tomotherapy	Bone Mets, Gynecologic, Pancreas, Prostate
CyberKnife at Community Cancer Center	IL	Normal	CyberKnife	Spine and malignant tumors (primary and mets)
Edward Hospital	IL	Naperville	Trilogy	Lung, Prostate
Evanston Northwestern Healthcare	IL	Evanston	Novalis	Spine

Hospital name	State	City	Devices(s)	Treatment site(s)
Loyola University Medical Center	IL	Maywood	Novalis	NS
Northwest Community Hospital	IL	Arlington Heights	CyberKnife	Liver, Pancreas, Spine
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
University of Chicago Medical Center	IL	Chicago	Trilogy	Metastatic treatment
Univ of IL Medical Center at Chicago	IL	Chicago	Trilogy	Metastatic treatment
Clarian Health Partners	IN	Indianapolis	Novalis	NS
Community Hospital	IN	Munster	CyberKnife, Trilogy	Liver, Lung, Pancreas, Spine
CyberKnife Center St. Catherine Hospital	IN	East Chicago	CyberKnife	Liver Mets, Lung, Pancreas, Spine
CyberKnife of Indianapolis	IN	Indianapolis	CyberKnife	Bone, Liver, Lung, Pancreas, Pelvis, Prostate, Spine
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 Hospital	IN	Fort Wayne	CyberKnife	Liver, Lung, Pancreas, Pelvis, Spine
St. Mary's Medical Center of Evansville	IN	Evansville	Novalis, Tomotherapy	NS
St. Vincent Indianapolis Hospital	IN	Indianapolis	Novalis	Liver, Lung, and Prostate
St. Vincent Jennings Hospital	IN	North Vernon	Novalis	Liver, Lung, and Prostate
St. Vincent Randolph Hospital	IN	Winchester	Novalis	Liver, Lung, and Prostate
Clarinda Regional Health Center	IA	Clarinda	Novalis	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
Mercy Medical Center	IA	Cedar Rapids	Tomotherapy	Prostate
Mercy Medical Center-Des Moines	IA	Des Moines	NR	Spine
Menorah Medical Center	KS	Overland Park	CyberKnife	NS
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, Spine
Central Baptist Hospital	KY	Lexington	NR	Spine
CyberKnife Ctr W. Jefferson Med Center	LA	Marrero	CyberKnife	Liver, Lung, Pancreas, Spine
Lafayette General Med Center	LA	Lafayette	CyberKnife	Liver, Lung, Pancreas, Prostate, Skeletal, Spine
Mary Bird Perkins Cancer Center	LA	Baton Rouge	Tomotherapy, Novalis	Prostate, Liver, Spine
Rapides Regional Medical Center	LA	Alexandria	Trilogy	NS
Slidell Memorial Hospital	LA	Slidell	Trilogy	NS
York Hospital	ME	York	Trilogy	NS
Anne Arundel Medical Center	MD	Annapolis	Novalis	Spine
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	Liver, Lung, Pancreas, Prostate, Skeletal Mets, Spine
Johns Hopkins Hospital	MD	Baltimore	Tomotherapy	Spine
Maryland Regional Cancer Care	MD	Rockville	Novalis	Liver, Lung, Prostate, Spine
Memorial Hospital at Easton Md	MD	Easton	NR	Spine
Peninsula Regional Health System	MD	Salisbury	Trilogy	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
Sinai Hospital of Baltimore	MD	Baltimore	CyberKnife	NS
St. Agnes HealthCare	MD	Baltimore	Tomotherapy	NS
University of Maryland Medical Center	MD	Baltimore	Trilogy	NS
Baystate Medical center	MA	Springfield	NR	NS
Beth Israel Deaconess Medical Center	MA	Boston	CyberKnife	Liver, Lung, Pancreas, Prostate, Spine
Boston Medical Center	MA	Boston	CyberKnife	NS
Brigham and Women's Hospital	MA	Boston	NR	Lung, Prostate, Spine
Children's Hospital Boston	MA	Boston	Novalis	NS
Lahey Clinic Hospital	MA	Burlington	Trilogy	Liver, Lung, Pancreas, Spine
Lowell General Hospital	MA	Lowell	Synergy	Prostate, Spine
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, Spine
UMass Memorial Medical Center	MA	Worcester	NR	NS
Bay Regional Medical Center	MI	Bay City	Tomotherapy	NS
Beaumont Hospital - Royal Oak	MI	Royal Oak	Synergy	Breast, Lung, Pancreas, Prostate
CyberKnife Radiosurgery/ St. Joseph Mercy	MI	Ann Arbor	CyberKnife	Liver, Lung, Pancreas, Prostate
Henry Ford Hospital	MI	Detroit	Trilogy, Novalis	Adrenal, Liver, Lung, Pancreas, Spine
Karmanos Cancer Center	MI	Detroit	Tomotherapy	Lung, Prostate
McLaren Regional Medical Center	MI	Flint	Tomotherapy	NS
MidMichigan Medical Center-Midland	MI	Midland	NR	Kidney, Liver, Lung Mets, Prostate, Spine

Hospital name	State	City	Devices(s)	Treatment site(s)
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	Nasal, spine and other extracranial sites
St. Mary's of Michigan	MI	Saginaw	CyberKnife, Tomotherapy	Liver, Lung, Prostate, Spine
Abbott Northwestern Hospital	MN	Minneapolis	Trilogy	Pancreas
St. Cloud Hospital	MN	Saint Cloud	Synergy	NS
St. Joseph's Hospital and Med Center	MN	Saint Paul	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis, Prostate, Spine
St. Luke's Hospital	MN	Duluth	NR	NS
Mississippi Baptist Medical Center	MS	Jackson	CyberKnife	Liver, Lung, Pancreas, Spine
Barnes-Jewish Hospital	MO	Saint Louis	NR	Gynecologic, Lung Mets
Ellis Fischel Cancer Center	MO	Columbia	Trilogy	NS
Research Medical Center	MO	Kansas City	NR	Liver, Pancreas
Saint Francis Medical Center	MO	Cape Girardeau	NR	NS
Saint John's Radiosurgery Center	MO	Springfield	CyberKnife	Liver, Lung, Pancreas, Spine Mets
Saint Louis University Hospital	MO	Saint Louis	CyberKnife	Prostate, Spine
Saint Luke's Hospital of Kansas City	MO	Kansas City	Novalis	Spine and other extracranial sites
Southeast Missouri Hospital	MO	Cape Girardeau	Novalis	NS
SSM DePaul Health Center	MO	Bridgeton	Tomotherapy	Spine and other extracranial sites
St. Anthony's Medical Center	MO	Saint Louis	Trilogy	Lung, spine and other extracranial sites
St. Luke's Hospital	MO	Chesterfield	Trilogy	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
Benefis Healthcare System	MT	Great Falls	CyberKnife	Lung, Pancreas, Prostate, Spine
Kalispell Regional Medical Center	MT	Kalispell	Trilogy	NS
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, Spine
Banner Churchill Community Hospital	NV	Fallon	Tomotherapy	NS
Renown Regional Medical Center	NV	Reno	Tomotherapy	Bone, Breast, Colon, Gynecolog., Lymph Nodes, Throat, Rectal, Pancreas, Stomach
Dartmouth-Hitchcock Medical Center	NH	Lebanon	Trilogy	Lung
Elliot Hospital	NH	Manchester	NR	Prostate, Spine
Huggins Hospital	NH	Wolfeboro	NR	NS
Capital Health System at Mercer	NJ	Trenton	CyberKnife	Gynecologic, Lung, Pancreas, Spine
CentraState Healthcare System	NJ	Freehold	NR	Liver, Lung, Spine
Christ Hospital	NJ	Jersey City	NR	NS
Community Medical Center	NJ	Toms River	Tomotherapy	NS
Cooper Health System	NJ	Camden	CyberKnife	Bone (primary/mets), Liver, Lung, Pancreas, Prostate, Spine
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	Kidney, Lung, Pancreas, Prostate, Spine

Hospital name	State	City	Devices(s)	Treatment site(s)
Riverview Medical Center	NJ	Red Bank	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate, Spine
Robert Wood Johnson Univ Hospital	NJ	New Brunswick	NR	NS
Robert Wood Johnson Univ Hosp	NJ	Hamilton	NR	NS
Saint Barnabas Medical Center	NJ	Livingston	Tomotherapy, CyberKnife	Prostate and other extracranial sites
University of Medicine -University Hospital	NJ	Newark	Tomotherapy	NS
Valley Hospital	NJ	Ridgewood	Tomotherapy	NS
Presbyterian Hospital	NM	Albuquerque	NR	Lung, Spine (primary and mets)
CyberKnife Center of New York	NY	Johnson City	CyberKnife	Liver, Lung, Pancreas, Prostate, Spine
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, Novalis	Bone Mets, Lung, Pelvis, Prostate, Skin, Spine (primary/mets)
Mount Sinai Hospital	NY	New York	Novalis	Liver, Lung, Spine
New York-Presbyterian Hospital	NY	New York	CyberKnife	Spine
North Shore University Hospital	NY	Manhasset	Novalis	Liver, Lung, Prostate, Spine
Northern Westchester Hospital	NY	Mount Kisco	Trilogy	NS
Roswell Park Cancer Institute	NY	Buffalo	Trilogy	Breast, Liver, Lung, Pancreas, Prostate, Spine
St. Peter's Hospital	NY	Albany	Novalis	Liver, Lung, Spine
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, Nasal, Pancreas, Prostate, Spine

Hospital name	State	City	Devices(s)	Treatment site(s)
Winthrop-University Hospital	NY	Mineola	CyberKnife	NS
Carolinas Medical Center	NC	Charlotte	Novalis	NS
Carolinas Med Center-NE	NC	Concord	NR	Spine and other malignant tumors (primary and mets)
Columbus Reg Healthcare System	NC	Whiteville	NR	NS
Duke University Hospital	NC	Durham	Novalis TX	Liver, Spine
Grace Hospital	NC	Morganton	Novalis	NS
Mission Hospitals	NC	Asheville	CyberKnife	Kidney, Liver, Lung, Pancreas, Spine
North Carolina Baptist Hospital (Wake Forest University Baptist Medical Center)	NC	Winston-Salem	NR	Lung
University of North Carolina Hospitals	NC	Chapel Hill	CyberKnife	NS
Blanchard Valley Health system	OH	Findlay	NR	Spine
Cleveland Clinic Foundation	OH	Cleveland	Novalis	Kidney, Liver, Lung, Spine
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
Jewish Hospital	OH	Cincinnati	Trilogy	NS
Mercy Medical Center	OH	Canton	Trilogy	NS
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, Spine

Hospital name	State	City	Devices(s)	Treatment site(s)
Summa Health System	OH	Akron	Novalis	NS
University Hospital	OH	Cincinnati	Lexar	NS
University Hospitals Case Medical Center	OH	Cleveland	CyberKnife, Novalis	Liver, Lung, Pancrease, Prostate, Spine
Univ Hosp Geauga Regional Hospital	OH	Chardon	CyberKnife, Novalis	Liver, Lung, Pancrease, Prostate, Spine
Deaconess Hospital	OK	Oklahoma City	Tomotherapy	Prostate
Hillcrest medical Center	OK	Tulsa	CyberKnife	NS
Mercy Health Center	OK	Oklahoma City	CyberKnife	NS
Oklahoma CyberKnife LLC	OK	Tulsa	CyberKnife	Lung, Spine
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, Pancrease, Prostate, Spine
Legacy Emanuel Hospital and Health center	OR	Portland	Novalis	Breast, Liver, Lung, Prostate, Spine
OHSU Hospital	OR	Portland	Trilogy, Novalis	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	Lung Mets
Frankford Hospital	PA	Philadelphia	Trilogy	Prostate
Geisinger Medical Center	PA	Danville	Trilogy	Lung
Hahnemann University Hospital	PA	Philadelphia	NR	Spine
Hamot Medical Center	PA	Erie	Trilogy	NS
Hospital of the Univ of PA	PA	Philadelphia	Trilogy, Oncor, Synergy	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
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 CyberKnife Center	PA	Havertown	CyberKnife	Liver, Lung, Pancreas, Pelvis, Prostate, Skeletal, Spine
Pennsylvania Hospital	PA	Philadelphia	Trilogy, Oncor	NS
Pocono Medical Center	PA	East Stroudsburg	NR	NS
Reading Hospital and Medical Center	PA	West Reading	Trilogy	Kidney, Liver, Lung, Pancreas, Spine
St. Luke's Hospital - Bethlehem Campus	PA	Bethlehem	Trilogy	Lung, Spine
St. Luke's Miner's Memorial Hospital	PA	Coaldale	Trilogy	Lung, Spine
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, Cybknife	NS
UPMC Presbyterian	PA	Pittsburgh	Trilogy	NS
UPMC Shadyside Hospital	PA	Pittsburgh	Trilogy	NS
Western Pennsylvania Hospital	PA	Pittsburgh	XKnife	Lung
Rhode Island Hospital	RI	Providence	Trilogy	Breast, Kidney, Liver, Lung, Pancreas, Pelvis, Prostate, Skin, Spine
MUSC Medical Center	SC	Charleston	Tomotherapy	Abdomen, Prostate
Roper Hospital	SC	Charleston	CyberKnife	Liver, Lung, Pancreas, Prostate, Spine
Sanford Univ of SD Medical Center	SD	Sioux Falls	Novalis	NS
University of Tennessee Medical Center	TN	Knoxville	CyberKnife	NS
Wellmont Bristol Regional Med Center	TN	Bristol	CyberKnife	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
Baptish Health system	TX	San Antonio	CyberKnife	Spine
Baylor Medical Center at Garland	TX	Garland	CyberKnife	NS
Baylor University Medical Center	TX	Dallas	CyberKnife	NS
CyberKnife/Brackenridge Hospital	TX	Austin	CyberKnife	Liver (primary and mets), Pancreas, Prostate, Spine
East Texas Medical Center Tyler	TX	Tyler	CyberKnife	Lung, Pancreas, Prostate, Spine
Kingwood Medical Center	TX	Kingwood	CyberKnife	Spine
Methodist CyberKnife Center, San Antonio	TX	San Antonio	CyberKnife, Tomotherapy	Spine
Methodist Hospital	TX	San Antonio	CyberKnife	Spine and other extracranial sites
North Cybpress Medical Center	TX	Cypress	NR	Kidney, Liver/Lung Mets, Lung, Pancreas, Pelvis, Prostate
Richardson Regional Medical Center	TX	Richardson	Novalis	Liver, Lung, Prostate, Spine
Spring Branch Medical Center	TX	Houston	NR	Adrenals, Liver, Lung, Pancreas, Pelvis, Prostate
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, Spine
Univ of Tx M. D. Anderson Cancer Center	TX	Houston	NR	Lung and Spine
Univ of Tx Southwestern Medical Center	TX	Dallas	CyberKnife	Prostate and other extracranial sites
Walls Regional Hospital	TX	Cleburne	CyberKnife	Liver, Lung, Pancreas, Prostate, Spine
Primary Children's Medical Center	UT	Salt Lake City	Trilogy	NS
Carilion Medical center	VA	Roanoke	CyberKnife	NS
Carilion New river Valley Medical Center	VA	Christiansburg	CyberKnife	NS
Centra Health	VA	Lynchburg	Trilogy	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
CJW Medical Center	VA	Richmond	Trilogy	NS
Inova Fairfax Hospital	VA	Falls Church	NR	Skeletal
Riverside Regional Medical Center	VA	Newport News	Synergy	NS
University of Virginia Medical Center	VA	Charlottesville	Tomotherapy	Liver, Lung, Paraspinal, Spine
VCU Health System	VA	Richmond	Tomotherapy	NS
Harborview Medical Center	WA	Seattle	NR	Spine
Multicare Health System	WA	Tacoma	Trilogy	NS
Southwest Washington Medical Center	WA	Vancouver	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis, Spine
St. Joseph Hospital	WA	Bellingham	Tomotherapy	Gastronintestinal, Gynecologic, Prostate
Swedish Health Services	WA	Seattle	CyberKnife, Synergy	NS
Swedish Medical Center	WA	Seattle	CyberKnife, Synergy	NS
University of Washington Med Center	WA	Seattle	Tomotherapy	NS
Virginia Mason Medical Center	WA	Seattle	NR	Prostate
St. Mary's Medical Center	WV	Huntington	CyberKnife	Kidney, Liver, Lung, Pancreas, Pelvis, and Spine
Appleton Medical Center	WI	Appleton	CyberKnife, Tomotherapy, Trilogy	NS
Aurora Medical Center	WI	Kenosha	CyberKnife	Lung, Pancreas, Spine
Aurora Memorial Hospital of Burlington	WI	Burlington	CyberKnife	Lung, Pancreas, Spine
Aurora St. Luke's Medical Center	WI	Milwaukee	CyberKnife	Lung, Prostate, Spine
Columbia St. Mary's - Columbia Campus	WI	Milwaukee	Trilogy	Breast, Kidney, Liver, Lung, Pancreas, Pelvis, Prostate, Skin, Spine
Saint Joseph's Hospital	WI	Marshfield	Trilogy	NS
St. Vincent Hospital	WI	Green Bay	Trilogy	NS

Hospital name	State	City	Devices(s)	Treatment site(s)
Theda Clark Medical Center	WI	Neenah	CyberKnife, Tomotherapy	NS
University of Wisconsin Hosp	WI	Madison	Tomotherapy	NS
Waukesha Memorial Hospital	WI	Waukesha	CyberKnife	NS

NR Not reported

NS Reported extracranial but not specific to sites

Appendix K. Ongoing clinical trials

Table 22. Ongoing clinical trials

Condition	Study design	Intervention	Primary outcome measures	Secondary outcome measures	Estimated enrollment	Planned duration	Location
Breast Cancer, Metastatic ⁵⁷⁷	Non-randomized; efficacy study	HSBRT	OS, DFS	CRR, chemical and radiobiological response, QoL	80	December 2000 - ongoing	Rochester, NY
Cholangio-carcinoma Klatskin Tumor Biliary Tract cancer ⁵⁷⁸	Non-randomized, safety study	External beam radiation and CyberKnife radiosurgery boost and capecitabine	Evaluate acute toxicities, MTD of CyberKnife boost	LCR, regional control, radiographic response, delayed and long-term toxicities, DSS, OS	11	October 2007 - October 2011	San Francisco, CA
Kidney Cancer ⁵⁷⁹	Treatment	Coventional surgery; neoadjuvant therapy; SRS	MTD, toxicity	DFS, LP, DF, DSS	20	January 2007 - January 2012	Cleveland, OH
Kidney Cancer ⁵⁸⁰	Treatment	SRS	MTD	OS, DFS, LP, DF	32	February 2007 - February 2012	Cleveland, OH
Lung Cancer ⁵⁸¹	Non-randomized	SRS (CyberKnife)	MTD, symptoms and radiographic responses	NR	60	March 2000 - ongoing	Stanford, CA
Lung Cancer ⁵⁸²	Randomized; Safety and Efficacy Study	SRT vs. Primary Resection	LC, RC, QoL; treatment costs	OS; QALY; total costs	960	August 2008 - December 2013	Amsterdam, Netherlands
Metastatic cancer ⁵⁸³	Treatment	SRS	NR	NR	10 - 25 within 2 - 3 years	February 1999 - ongoing	Richmond, VA

Condition	Study design	Intervention	Primary outcome measures	Secondary outcome measures	Estimated enrollment	Planned duration	Location
Non-Small Cell Lung Cancer ⁵⁸⁴	Treatment, Efficacy Study	CyberKnife SRS	CRR, LCR, PFS, OS	QoL, procedures related outcomes	156	April 2006 – July 2013	Pittsburgh, PA
Pancreatic Cancer ⁵⁸⁵	Treatment	gemcitabine hydrochloride, oxaliplatin, adjuvant therapy, hypofractionated radiation therapy, neoadjuvant therapy, SRS	CRR	Toxicity, time to progression, time to death, perioperative morbidity and mortality, rate of R0 resections, histologic response rate	29	May 2006 - NS ¹	Munich, Germany
Prostate Cancer ⁵⁸⁶	Treatment; Efficacy Study	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 ⁵⁸⁷	Treatment	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 Villager, OH; Westlake, OH; Middleburgh Heights; OH
Prostate Cancer ⁵⁸⁸	Treatment; Efficacy Study	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

Condition	Study design	Intervention	Primary outcome measures	Secondary outcome measures	Estimated enrollment	Planned duration	Location
Spinal Metastases ⁵⁸⁹	Randomized; Safety/Efficacy Study	Low Dose SRS vs. High Dose SRS	Estimate pain control rate, function, QoL	LCR	72	September 2007 - September 2011	St. Louis, MO
Unspecified Adult Solid Tumor ⁵⁹⁰	Treatment	SRS	MTD, MD	Radiographic response rate, median time to progression, toxicity, cause of death	48	June 2002 - ongoing	Winstom-Salem, NC

CRR	Clinical Response Rate
DF	Distant Failure
DFS	Disease-free survival
DSS	Disease specific survival
F	Female
HSBRT	Hypofractionated Stereotactic Body Radiotherapy
LCR	Local Control Rate
LF	Local Failure
LP	Local Progression
M	Male
MD	Minimum Dose
MTD	Maxium Tolerated Dose
OS	Overall Survival
PFS	Progression Free Survival
QALY	Quality adjusted Life Years
QoL	Quality of Life
RC	Regional Control
SRS	Stereotactic Radiosurgery
SRT	Stereotactic Radiotherapy

Appendix L. Results for key question 3

Table 23. Non-randomized comparison studies

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Douglas et al., (2008) ⁶²	USA	Salivary gland	Gamma Knife/NR	Non-randomized comparison (Gamma Knife boost vs. neutron RT alone) alone controls)	n = 34, n = 61 neutron RT alone controls	Neutron RT (median dose, 11.98 neutron Gray (nGy); n = 11 gamma knife group and 48% of controls had surgical resection prior to NRT	Median: 20.5 (Range: 4-55) Median controls: 56.5	Local failure rate; Kaplan- Meier estimated local control	Skin reactions, mucositis, oral candidiasis observed in all patients in both groups. RTOG grade 3 to 4 toxicities similar in both groups. Radiation- induced necrosis observed in 3 gamma knife boost patients and resolved by 30 months post-treatment.

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Chua et al., (2007) ⁶⁰	China	Nasopharyngeal Carcinoma	SRS - Varian Clinac 600C (6-MV linac); GGI - Royal Marsden Gold Grain Implantation Gun MKIII (Associated Surgical Products, Bristol, UK)/NR	Non-randomized comparison (Gold grain implantation (GGI) vs. SRS)	n = 74 (37 each group)	97.3% primary RT (median dose 67 Gy); n = 9 prior chemotherapy using cisplatin concurrently with RT with or without adjuvant chemotherapy.	Median 41.5 (SRS) vs. 42 (GGI)	Local control	SRS group Brain necrosis, cranial neuropathy, pituitary insufficiency, GGI group Moderate - severe headaches, development of palatal fistula, neuroendocrine complications (n = 5)
Gagnon et al., (2007) ¹²⁰	USA	Breast cancer spinal metastases	CyberKnife/NR	Non-randomized Comparison (SRT versus conventional EBRT)	n = 18 cases, n = 18 controls	n = 17 prior RT to the spinal region	Range: 1-24	Activity; pain	Acute toxicities; no reports of higher than Grade 2 toxicity for either group.
Guckenberger et al., (2007) ²⁹	Switzerland	NSCLC or pulmonary metastatic lesions	NR/NR	Non-randomized comparative study (Hypofractionated SBRT (3-8 fractions) vs. 1 fraction SRS)	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

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Nijdam et al., (2007) ⁶⁹	USA & The Netherlands	Tonsillar fossa (TF) and soft palate (SP) tumors	CyberKnife/NR	Non-randomized comparison (IMRT plus Brachytherapy (BT) boost vs. IMRT plus CyberKnife SRS. Neck dissection was performed for nodal-positive (N+) patients.)	n = 103 IMRT + BT, n = 9 IMRT + CyberKnife	NR	12 for MRT+SRS; 60 for IMRT + BT patients	Tumor response; disease- free survival; overall survival	SRS patients and BT patients had similar severity of pain and difficulty swallowing post-treatment; QOL was similar for both groups
Furdova et al., (2005) ⁸²	Slovakia	Uveal melanoma	NR/NR	Non-randomized comparison (Brachytherapy or SRS vs. enucleation)	n = 145: 33 brachytherapy, 87 enucleation, 25 combined technique (8 had SRS)	Combined techniques include SRS, photocoagula- tion, transpupillar thermotherapy	3 month intervals	Survival	Cataract; glaucoma; rubeosis iridis
Yau et al., (2004) ⁷⁷	Hong Kong	Persistent naso- pharyngeal carcinoma	Brachytherapy (MicroSelectron: Nucletron) with iridium 192 SRT (Siemens Mevatron MX-2, a 6 MV linac)/NR	Non-randomized comparison (Brachytherapy boost vs. SRT boost)	n = 45: 24 brachytherapy, 21 SRT boost	All prior RT	Median: 38.4 (Range: 1.2-99.6)	Tumor response; local failure	Mild transient soft tissue necrosis in the nasopharynx
Cohen et al., (2003) ⁷⁸	United Kingdom	Uveal melanoma	Gamma Knife/NR	Non-randomized comparison	SRS n = 78, Enucleation n = 118	None	SRS Median: 38 (Range: 1-120) ; Median enuclea- tion 23	Metastasis -free survival; disease- free interval	NR

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Georgopoulos et al., (2003) ⁸³	Austria	Uveal melanoma	RU, GK (Elekta), Linac (6MV Linac, Sturme 43, General Electric Medical System, Paris France)/NR	Non-randomized comparison (ruthenium-106 radioactive plaque brachytherapy (RU) vs. fractionated high-dose gamma knife stereotactic teletherapy (GK) vs. fractionated linear accelerator-based stereotactic teletherapy)	n = 74 RU, n = 58 GK, n = 79 linac	NR	RU: 55 +/- 36 (12-202) GK: 47 +/- 18 (11-86) Linac: 29 +/- 12 (11-54)	Tumor thickness; local tumor control	Flat scar
Langmann et al., (2002) ⁸⁶	Austria	Uveal melanoma	Gamma Knife/NR	Non-randomized Comparison (High dose vs. low dose SRS)	n = 64	n = 29 surgery	Range: 12-79	Tumor response	Neovascular glaucoma

Table 24. Prospective single group studies

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Fuller et al., (2008) ¹⁴¹	USA	Prostate cancer	CyperKnife/NR	Prospective single group	n = 10	Concurrent distribution of high dose rate brachytherapy	2 week, 4 week, 8 week, and 4 month followup done	Early PSA response	No urinary obstruction observed to date, mild and transient rectal toxicity; no acute rectal bleeding observed
Katoh et al., (2008) ⁶⁵	USA	Adrenal tumors	Linac/NR	Prospective single group	n = 9	None	Median: 16 (Range: 5-21)	Disease progression; local failure	No decline in hormone level, tumor related flank pain
King et al., (2008) ¹⁴²	USA	Localized prostate cancer	CyberKnife/NR	Prospective single group	n = 41	None	Median: 33	PSA response, QoL	Late urinary and rectal toxicity
Muacevic et al., (2008) ⁹⁰	Germany	Uveal melanoma	CyberKnife/ Nonisocentric inverse treatment planning algorithm	Prospective single group	n = 20	n = 1 prior brachytherapy	Mean: 13 (Range: 6-22)	Local tumor control	Decrease in visual acuity; no patient needed enucleation due to tumor growth or treatment-induced complications

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Tse et al., (2008) ¹³¹	Canada	Unresectable hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (IHC)	NR/NR	Prospective single group	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
Aoki et al., (2007) ²¹	Japan	Primary lung or mets	Mitsubishi EXL-20TP 10-MV standard linac/NR	Prospective single group	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

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Chang et al., (2007) ⁹⁷	USA	Spinal mets	21EX linac/NR	Prospective single group	n = 63	n = 35 prior RT (Median: 33 Gy, Range: 30-54); n = 29 prior surgical spine procedure	Median: 21.3 (Range: 0.9-49.6)	Tumor response; survival time; pain relief	Grade 3 neurological function; no cases of grade 4 neurological toxicity were reported; no grade 3 or 4 neurological toxicity reported to date; grade 3 nausea, vomiting and diarrhea; grade 3 dysphagia and trismus; grade 3 noncardiac chest pain; radiation-induced hyperpigmentation of the skin
Collins et al., (2007) ²⁵	USA	Stage 1 lung cancer or single lung metastases	CyberKnife/NR	Prospective single group	n = 24	n = 17 prior conventional thoracic radiation; 25% of patients concurrent systemic therapy	Range: 6-30)	Tumor response	Transient chest wall discomfort; pneumothorax after fiducial placement; grade III pneumonitis
Gibbs et al., (2007) ¹⁰⁰	USA	Spinal mets	CyberKnife/NR	Prospective single group	n = 74	n = 50 prior radiotherapy, n = 11 prior chemo, n = 3 prior surgery, n = 4 prior other treatment	Mean: 9 (Range: 0-33)	Symptom response	Severe myelopathy
Hof et al., (2007) ³²	Germany	Pulmonary mets	NR/Pencil beam algorithm for dose calculation	Prospective single group	n = 61	N/A	Median: 14 (Range: 1.5-82)	Local control	Grade 1, 2, 3 toxicities

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Hof et al., (2007) ³³	Germany	Early stage lung cancer	Siemens Mevatron Linac/ Pencil beam algorithm for dose calculation	Prospective single group	n = 42	N/A	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) ³⁴	USA	NSCLC	NR/NR	Prospective single group	n = 58	N/A	Median: 42.5 (Range: 27-61)	Local failure; regional progression; metastatic dissemination	NR
Jin et al., (2007) ¹⁰¹	USA	Localized spine mets	Novalis/NR	Prospective single group	n = 196	Prior chemo and chemo after SRT	Post treatment assessment: 2	Pain relief	Treatment well tolerated; no reports of serious treatment complications related to short-term radiation toxicity
Koto et al., (2007) ³⁷	Japan	Stage 1 NSCLC	Varian Clinac 23EX/NR	Prospective single group	n = 31	N/A	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
Liscak and Vladyka, (2007) ⁸⁷	Czech Republic	Uveal melanoma	Gamma Knife Model B/NR	Prospective single group	n = 81	Enucleation	Minimum 10	Survival; local tumor control	Secondary glaucoma

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Madsen et al., (2007) ¹⁴³	USA	Localized prostate cancer	NR/NR	Prospective single group	n = 40	None	Median: 41 (Range: 12-60)	PSA levels	Acute: rectal discomfort, constipation, diarrhea, tenesmus Late: proctitis, occasional blood, rectal discomfort, frequent stools, constipation, diarrhea
Miralbell et al., (2007) ⁸⁸	Spain	Ocular melanoma	Novalis/NR	Prospective single group	n = 5	None	36-48	Tumor response	NR
Muacevic et al., (2007) ⁴⁰	Germany	Lung tumors	CyberKnife/Nonis ocentric inverse planning algorithm	Prospective single group	n = 15	N/A	2 month intervals	NR	Pneumothorax; nausea; pneumonitis
Nuyttens et al., (2007) ¹⁴⁷	The Netherlands	Mets (para-aortic or pelvic lymph nodes, abdominal wall, muscle tissue, rib, retroperitoneal fat, local recurrences in pelvis, neck)	CyberKnife/NR	Prospective single group	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	Acute: transient grade 1 lymphedema in leg, grade 1 abdominal pain, nausea, and diarrhea, grade 1 dermatitis; Late: grade 1 rectal bleeding, chronically painful grade 2 subcutaneous fibrosis, grade 1 diarrhea, grade 2 pain in surgical scar on belly

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Ponsky et al., (2007) ¹³⁹	USA	Renal	NR/NR	Prospective single group	n = 3	Partial or radical nephrectomy 8 weeks after RS	Mean: 12.8 (Range: 12-14)	Tumor response	None reported
Ricardi et al., (2007) ⁴⁵	Italy	NSCLC	NR/NR	Prospective single group	n = 43	N/A	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) ⁴⁶	Italy	NSCLC	Linac/NR	Prospective single group	n = 43	NR	Median: 14 (Range: 6-36)	Actuarial survival; morbidity	Acute and late grade I or grade II
Dawson et al., (2006) ¹²²	Canada	Hepatocellular carcinoma, intrahepatic cholangiocarcinoma, liver metastases	Elekta Synergy/ NR	Prospective single group	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) ¹⁴⁵	Germany	Lung cancer, thyroid cancer	Novalis/Dose calculation done by pencil beam algorithm	Prospective single group	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 design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Gerszten et al., (2006) ²⁸	USA	Spinal lung metastases	CyberKnife/NR	Prospective single group	n = 77	n = 70 external beam RT	Median: 12 (Range: 6 to 40)	Long-term radiographic response; Long-term radiographic control	NR
Gwak et al., (2006) ¹²¹	South Korea	Recurrent sarcoma, recurrent breast cancer	CyberKnife/NR	Prospective single group	n = 3	Prior surgical decompression with metallic fusion followed by conventional radiation therapy	Mean: 13.3	Treatment response	Grade 1 headache
Hodge et al., (2006) ³¹	USA	NSCLC	Tomotherapy Hi-Art/NR	Prospective single group	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) ¹²⁵	Denmark	Colorectal metastases	Siemens Primus or Varian Clinac 2100/2300/NR	Prospective single group	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

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Kavanagh et al., (2006) ¹²⁷	USA	Liver mets	Linac 6-15 MV/Doses calculated with tissue heterogeneity correction algorithms	Prospective single group	n = 36	None	Median: 19 (Range: 6-29)	In-field local control	Intrahepatic progression; pyloric stenosis; gastritis; grade 3 soft tissue toxicity; skin redness; pain; subcutaneous tissue breakdown
Le et al., (2006) ³⁸	USA	NSCLC or mets	CyberKnife/NR	Prospective single group	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) ⁴¹	The Netherlands	Early stage lung cancer	CyberKnife/NR	Prospective single group	n = 20	N/A	Median: 4 (Range: 2-11)	Tumor response	Intrathoracal pain
Romero et al., (2006) ¹³⁰	The Netherlands	Primary liver tumors and mets	Siemens Primus linac/NR	Prospective single group	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 transperase (GGT) grade 3; asthenia grade 3
Svedman et al., (2006) ¹⁴⁰	Sweden	Primary and metastatic renal cell carcinoma	Linac 6MV/NR	Prospective single group	n = 30	n = 26 nephrectomy; n = 2 interferon alpha; n = 2 tamoxifen	Median: 52 (11-66)	Local tumor response (primary); toxicity, pain, and survival (secondary endpoint)	Cough, fatigue, skin rash, ocal pain, one patient died - cannot be ruled out may have been treatment related

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Wulf et al., (2006) ¹³²	Germany	Primary liver cancer and hepatic mets	NR/Dose distribution calculated based on a pencil beam algorithm	Prospective single group	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) ¹¹⁹	South Korea	Thoracic (38 primary or 53 metastatic)	NR/NR	Prospective single group	n = 91	NR	Median: 14 (Range: 4-56)	Overall response	None greater than RTOG toxicity criteria grade 2 were observed.
Xia et al., (2006) ⁵⁴	USA & China	Stage 1 or Stage 2 NSCLC	Gamma-knife (30 rotary conical surface Cobalt 60); NR	Prospective single group	n = 43	N/A	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 (hypodynamia, anorexia, naupathis, and vomiting); grade 1 neutropenia; late radiation induced local fibrosis

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Zimmerman et al., (2006) ⁵⁵	Germany	Stage 1 NSCLC	NR; NR	Prospective single group	n = 68	N/A	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
Gerszten et al., (2005) ¹³⁸	USA	Renal cell carcinoma metastatic to spine	CyberKnife/NR	Prospective single group	n = 48	n = 42 prior EBRT; n = 31 prior nephrectomy; n = 5 open decompressive surgery	Median: 37 (Range: 14-48)	Pain assessment, tumor response	NR
Hoyer et al., (2005) ¹²⁴	Denmark	Pancreatic cancer	Siemens Primus or Varian Clinac/ NR	Prospective single group	n = 22	None	2-34	Toxicity; tumor response; overall survival; progression free survival	Severe mucositis or ulceration of stomach or duodenum; ulcer perforation of stomach
Koong et al., (2005) ¹²⁹	USA	Locally advanced pancreatic cancer	CyberKnife/NR	Prospective single group	n = 19	IMRT and 5-FU	Median: 5.3	Acute GI toxicity; tumor response; overall survival	Symptomatic duodenal ulcers

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Molla et al., (2005) ¹³⁶	Spain	Gynecologic tumors	Novalis/NR	Prospective single group	n = 16	n = 15 hysterectomy; n = 4 concomittant chemo; n = 3 para-aortic irradiation	Median: 12.6 (Range: 6-26)	Toxicity	Abdominal pain grade 1, grade 3 rectal bleeding
Muller et al., (2005) ⁹²	The Netherlands	Uveal melanomas	NR/NR	Prospective single group	n = 38	None	Mean: 25 (Range: 10-36)	Primary: acute toxicity, local control; Secondary: survival after 5 & 10 years local control	Acute: hyperemia, irritation tears, chemosis, light flashes, mononuclear diplopia, floaters, metamorphopsia, loss of hair or lashes, fatigue; Late: neovascular glaucoma, retinopathy, optical neuropathy, dry eye, subretinal bleeding
Shioyama et al., (2005) ¹⁴⁸	Japan	Lung and liver tumors	Varian Clinac 21 Ex /NR	Prospective single group	n = 20	None	1-15	Accuracy of fixation; local tumor response; survival and local rates calculated by Kaplan-Meier method; toxicities	MCI-CTC grade 2 complications

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Song et al., (2005) ⁴⁸	USA	Lung tumors	NR/Tissue maximum ratio calculation algorithm	Prospective single group	n = 17	N/A	Median: 14	Tumor response; toxicity	Fatigue; mild rib pain & tenderness; rib fracture; nonproductive cough; dyspnea; bronchial stenosis; collapse
Douglas et al., (2004) ⁶¹	USA	Minor or major salivary gland tumors with base of skull invasion	Gamma Knife/NR	Prospective single group	n = 8	Prior neutron radiotherapy	Median: 21.5	Tumor response	Grade 2 toxicities, persistent nausea (5 months duration), vertigo, delayed fatigue reaction
Ishimori et al., (2004) ³⁵	Japan	Solitary lung cancer	Varian Clinac 2300 C/D/NR	Prospective single group	n = 9	N/A	Range: 2-17	Local response - complete response; partial response; no change; progressive disease	Radiation induced pneumonitis
Koong et al., (2004) ¹²⁸	USA	Locally advanced pancreatic cancer	CyberKnife/NR	Prospective single group	n = 15	n = 2 conventional chemo-radiotherapy; n = 1 chemo	Median: 5	Overall survival; local control	Diarrhea; nausea; abdominal pain
Wulf et al., (2004) ⁵³	Germany	NSCLC or pulmonary mets	NR; Pencil beam algorithm or Collapsed cone algorithm for treatment plans	Prospective single group	n = 61	Metastases – prior chemo, pneumonectomy	NSCLC Median: 11 (Range: 2-61); Metastases Median: 9 (Range: 2-37)	Local tumor control; local failure	Mild pain; fever; chills; focal pneumonitis; slight temporary erythema; focal fibrosis

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Gerszten et al., (2003) ¹³³	USA	Sacrum	CyberKnife/NR	Prospective single group	n = 18	n = 15 prior EBRT	NR	Pain improvement	No acute radiation toxicity or new neurological deficits occurred
Lee et al., (2003) ³⁹	South Korea	Primary and metastatic lung tumors	NR/NR	Prospective single group	n = 28	NR	Median: 18 (Range: 7 to 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.
Timmerman et al., (2003) ⁵⁰	USA	Stage 1 NSCLC	NR/NR	Prospective single group	n = 37	NR	Median: 15.2 (Range: 2-30)	Partial tumor response; complete response; toxicity; disease-free survival rate and overall survival rate (Kaplan-Meier)	Worsening shortness of breath; nonproductive cough; worsening pulmonary infiltration; worsening fibrotic changes; grade 3 hypoxemia; Symptomatic radiation pneumonitis

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Whyte et al., (2003) ⁵²	USA	Primary lung cancer and mets	CyberKnife/ Nonisocentric inverse-planning algorithm	Prospective single group	n = 23	n = 1 right lower lobectomy	Mean: 7 (Range: 1-26)	Complete tumor response; Partial tumor response; Stable; Progressive; Death of non-treatment related causes	Pneumothoraces; exacerbation of underlying chronic obstructive pulmonary disease
Harada et al., (2002) ³⁰	Japan	Lung tumors	NR/NR	Prospective single group	n = 18	n = 1 prior RT	Median: 9 (Range: 5-15)	Overall response rate	Pneumonitis
Uematsu et al., (2001) ⁵¹	Japan	Stage 1 NSCLC	FOCAL unit (combination of linac, CT scanner, X-ray simulator, carbon table)/NR	Prospective single group	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 small atelectases,
Ryu et al., (2001) ¹⁰³	USA	Spinal lesions	CyberKnife/NR	Prospective single group	n = 5	n = 4 radiotherapy, n = 1 chemo, n = 5 open resection, n = 3 surgical resection, n = 1 vertebroplasty, n = 1 embolization	Range: 3-48	Disease progression	None reported

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Wulf et al., (2001) ¹⁵⁰	Germany	Lung and liver	NR/NR	Prospective single group	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) ¹¹⁸	Japan	Thoracic neoplasms	Megavoltage computed tomography assisted SRS/NR	Prospective single group	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.
Woodburn et al., (2000) ⁹⁴	USA	Choroidal melanoma	Gamma Knife/NR	Prospective single group	n = 11	None	Median: 6 (Range: 2-19)	Tumor control and response	Vitreous hemorrhage resulted in sudden temporary loss of vision, decreased visual acuity, dry eye

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Zehetmayer et al., (2000) ⁹⁵	Austria	Uveal melanoma	Gamma Knife/NR	Prospective single group	n = 62	None	Median: 28.3 (Range: 12-51)	Local tumor control	Acute & subacute side effects: eyelash loss, exudative retinal detachment, uveitis Late side effects: lens opacities, secondary glaucoma, neovascular glaucoma, retinopathy, optic neuropathy, corneal epithelial defects, vitreous hemorrhage, secondary enucleation

Table 25. Retrospective studies

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Casamassima et al., (2008) ²⁴	Italy	NSCLC or mets	Elekta Synergy/ Pencil beam algorithm for dose calculation	Retrospective	n = 104	Metastases prior chemo	Median: 13.88 (Range: 1.37-49.4)	Overall survival (Kaplan-Meier method); tumor response	Acute lung toxicity; dysphagia
Coon et al., (2008) ²⁶	USA	NSCLC, recurrent disease, or solitary lung mets	CyberKnife/NR	Retrospective	n = 51	NR	Median primary and recurrent cancer: 11 (Range: 2-24); Median mets: 12 (Range: 2-24)	Complete response; partial response; stable disease; disease progression	Grade 2 radiation pneumonitis; exacerbation of preexisting COPD
Fritz et al., (2008) ²⁷	Germany	Stage 1 NSCLC	Elekta Precise Sli/NR	Retrospective	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
Gerszten and Burton, (2008) ⁹⁹	USA	Spinal lesions	CyberKnife/NR	Retrospective	n = 486	n = 337 lesions prior EBRT	Range: 3-49	Pain improvement; overall long-term tumor control	NR

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Hara et al., (2008) ⁶⁴	USA	Nasopharyngeal carcinoma	CyberKnife/NR	Retrospective	n = 82	All EBRT; n = 70 concurrent/ adjuvant chemo; n = 3 neoadjuvant chemo	Median: 40.7 (6.5 - 144)	Overall survival, freedom from local progression, freedom from nodal relapse, freedom from local regional relapse, freedom from distant metastases, freedom from relapse - Kaplan-Meier method	Transient facial numbness, retinopathy, carotid aneurysm, temporal lobe necrosis
Hirschbein et al., (2008) ⁸⁵	USA	Orbital	CyberKnife/ Non-isocentric inverse “dose-planning” algorithm	Retrospective	n = 16	n = 4 prior surgery; n = 1 RT; n = 3 chemo; n = 3 steroids	Mean 7 (Range: 2- 15)	Tumor response, visual acuity	Transient nausea; herpes Zoster
Jereczek-Fossa et al., (2008) ¹⁴⁶	Italy	Breast, lung, head and neck, urologic, gynecologic, gastrointestinal, CNS, other primaries	Linac (6-18 MV, used for 3D-CRT and SRT)/NR	Retrospective	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

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Kim et al., (2008) ¹³⁴	South Korea	Pelvic recurrence from rectal carcinoma	CyberKnife/NR	Retrospective	n = 23	Prior lower anterior resection, abdomino-perineal resection; adjuvant chemo; concurrent chemo-radiotherapy; 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
Kunos et al., (2008) ¹³⁵	USA	Squamous cell carcinoma of the vulva	CyberKnife/NR	Retrospective	n = 3	n = 3 prior pelvic radiation for vulvular cancer	At least 2	Tumor response	No skin, urinary, or gastrointestinal toxicities were observed during course

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Modorati et al., (2008) ⁸⁹	Italy	Uveal melanoma	Gamma Knife/NR	Retrospective	n = 78	None	Median: 31.3 (IQR: 17.6-60.6)	Survival rate; local tumor control; eye retention rate; visual acuity	Minor cutaneous bleeding, subconjunctival hemorrhage, small transient retinal hemorrhages, exudative retinopathy, neovascular glaucoma, radiogenic retinopathy, vitreous hemorrhages, radiogenic optic neuropathy, cataract, bulbar phtthisis
Onimaru et al., (2008) ⁴²	Japan	NSCLC	NR/treatment planning made with Focus or Xio calculation algorithm: 31 Clarkson, 10 Superposition	Retrospective	n = 41	N/A	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
Ryu et al., (2008) ¹⁰⁵	USA	Spinal mets	NR/NR	Retrospective	n = 49	n = 16 prior chemo	Median 6.4 (Range: 6- 30)	Assessment of pain; tumor control	NR

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Takeda et al., (2008) ⁴⁹	Japan	Lung cancer	NR/Radiation doses calculated by using a superposition algorithm with heterogeneity correction	Retrospective	n = 50	N/A	Median: 30.4 (12-73.8)	Opacity changes; tumor recurrence	Degenerative and fibrous tissues
Brown et al., (2007) ²³	USA	Stage 1 NSCLC and lung metastases	CyberKnife/NR	Retrospective	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
Fakiris et al., (2007) ⁸¹	USA	Uveal melanoma	Gamma Knife/NR	Retrospective	n = 19	None	Median: 40 (Range: 7-81)	Primary: tumor control; Secondary endpoints: overall survival and free from distant mets analyzed by Kaplan-Meier; Other endpoints: tumor response & complications	Worse visual acuity; vitreous hemorrhage; vitreitis and conjunctivitis

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Katz et al., (2007) ¹²⁶	USA	Limited hepatic metastases	NR/NR	Retrospective	n = 69	Most 1 or more prior courses of chemo; concurrent chemo permitted	Median: 14.5, Mean: 15.2 (Range: 3.6-37)	Local control; regional failure; distant failure; toxicity; disease progression; actuarial overall survival, progression-free survival (Kaplan-Meier)	Fatigue; nausea; grade 1 or 2 elevation of liver function tests
Pennathur et al., (2007) ⁴⁴	USA	NSCLC; or pulmonary mets	CyberKnife/ Nonisocentric inverse planning algorithm	Retrospective	n = 37	N/A	Median 9 (Range: 7-15)	Complications; clinical response rates; time to progression (local and overall); overall survival	Pneumothorax from fiducial placement
Ryu et al., (2007) ¹⁰⁴	USA	Spinal mets	Novalis/NR	Retrospective	n = 177	NR	Median: 6.4 (Range: 0.5-49.3)	Average overall survival	Neurological deterioration; motor weakness
Teh et al., (2007) ¹⁴⁹	USA	Spine, bone, soft tissue/organ, and lymph node	Novalis/NR	Retrospective	n = 80	Prior RT; n = 1 prior surgery for sacral nerve neuroma	NR	Pain relief; symptom control; tumor response	NR

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Wu et al., (2007) ⁷⁵	China	Locally persistent or recurrent nasopharyngeal carcinoma	Commercial stereotactic radiotherapy system using Elekta linac/NR	Retrospective	n = 90	Primary radiation therapy: n = 34 Persistent – Median: 70 Gy (Range: 50-86), n = 56 Recurrent – Median: 70 Gy (Range: 60-80)	Median: 20.3 (Range: 4.9-77.5)	Tumor response, local failure free survival, progression free survival, distant metastasis free survival, disease specific survival (Kaplan-Meier method)	Naso-pharyngeal mucosal necrosis, massive hemorrhage on nasopharynx, brain stem necrosis, temporal lobe necrosis
Baumann et al., (2006) ²²	Sweden	Stage 1 NSCLC	Linac/NR	Retrospective	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; atelectases; grade 3-4 toxicity
Chua et al., (2006) ⁵⁹	China	Nasopharyngeal carcinoma (NPC)	Varian Clinac 600C/NR	Retrospective	n = 48	n = 4 surgery; n = 7 external RT; n = 48 radical RT	Median: 54	Tumor response, overall survival	Brain necrosis, pituitary insufficiency, cranial neuropathy, osteo-radionecrosis, mucosal necrosis, trismus, carotid aneurysm

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Dieckmann et al., (2006) ⁷⁹	Austria	Uveal melanoma	6 MV Linac based/NR	Retrospective	n = 158	None	Median: 33.4 (Range: 3-85)	Local tumor control	Opticopathy, retinopathy, neovascular glaucoma, cataract, visual acuity decline
Joyner et al., (2006) ³⁶	USA	Mets or Recurrence NSCLC	Linac/NR	Retrospective	n = 9	N/A	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
Low et al., (2006) ⁶⁷	Singapore	Local recurrent or persistent NPC	Linac Siemens KD2/NR	Retrospective	n = 36	EBRT prior	Median: 50.9 (8.8-105.7)	Overall survival, local control, disease-free survival - Kaplan-Meier method	Palatal fibrosis, trismus <2 cm, cranial nerve palsies, temporal lobe necrosis, osteo-radionecrosis of skull base
Mori et al., (2006) ⁶⁸	Japan	Adenoid cystic carcinoma	Gamma Knife/NR	Retrospective	n = 12	n = 9 prior conventional fractionated radiotherapy; n = 7 prior chemo	Median: 18 (Range: 3-55)	Local result, distant failure	NR
Oda et al., (2006) ⁷⁰	Japan	Recurrent epipharyngeal carcinoma	Gamma knife/NR	Retrospective	n = 14	Prior conventional fractionated radiotherapy and chemo	Median: 15 (Range: 2-47)	Control rate, survival rate, relapse	NR

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Paludan et al., (2006) ⁴³	Denmark	Stage 1 NSCLC	NR/DVH parameters calculated by use of a pencil beam algorithm	Retrospective	n = 28	N/A	Median: 6.7 (Range: 2.1-7.5)	Dyspnea development	NR
Rock et al., (2006) ¹⁰²	USA	Residual spinal: mets, sarcoma, multiple myeloma/plasmacytoma, or giant cell tumor	Novalis/NR	Retrospective	n = 18	n = 18 surgery	Median: 7 (4-36)	Neurological stability or improvement	None reported
Sinha et al., (2006) ⁴⁷	USA	Bilateral primary lung cancer	NR/NR	Retrospective	n = 10	n = 1 prior resection of lesion	Mean: 20.7, Median: 18.5 (Range: 7-42)	Tumor response	Grade 1 and 2 complications
Voyvoy et al., (2006) ⁷⁴	USA	Recurrent squamous cell carcinoma of head and neck	CyberKnife/NR	Retrospective	n = 22	All prior full dose irradiation; in some cases further irradiation with low dose rate brachytherapy, high dose rate brachytherapy, or IMRT for recurrent tumors	Median: 19 (Range: 11-40)	Local control, cause specific survival, overall survival (Kaplan-Meier), symptom relief, acute, late toxicity	Grade 2 and 3 mucositis

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Degen et al., (2005) ⁹⁸	USA	Spinal	CyberKnife/NR	Retrospective	n = 51	n = 38 lesions prior irradiation	Mean: 11.5 (Range: 1.2-22.5)	Neurological deficits; tumor control rate	Diarrhea; lethargy; paresthesias; wound dehiscence; increased nocturia; self- limited dysphagia
Unger et al., (2005) ⁷³	Austria	Olfactory neuroblastoma	Gamma Knife/NR	Retrospective	n = 14	n = 2 previous surgery (craniotomy); all prior endoscopic sinus surgery	Median: 58 (Range: 13-128)	Tumor response, quality of life (Karnovsky Indices)	Mild and transient headache and dizziness
Beitler et al., (2004) ¹³⁷	USA	Renal cell carcinoma	NR/NR	Retrospective	n = 9	n = 1 prior nephrectomy	Median: 26.7	Survival calculated by Kaplan-Meier method	Nausea, vomiting, glandular atypia in the stomach
Benzil et al., (2004) ⁹⁶	USA	Spinal mets (cervical, thoracic, lumbar, or sacral)	Novalis/The CT images localized using body marker or head and neck algorithms	Retrospective	n = 31	Prior radiation therapy	Generally every 3 months	Treatment related toxicity; neurological improve- ment; pain relief	Neurological deterioration; radiation necrosis; transient radiculitis; mild transient laryngitis; death related to disease progression
DeSalles et al., (2004) ¹⁴⁴	USA	Metastatic disease (lung, renal cell, breast, or colon)	Novalis/NR	Retrospective	n = 14	n = 7 spine surgery; n = 12 RT; n = 9 chemo	Mean: 6.1 (Range: 1- 16)	Morbidity; tumor response	None reported

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Emara et al., (2004) ⁸⁰	Canada	Juxtapapillary choroidal melanoma	Varian 2100C/NR	Retrospective	n = 28	None	Median: 18.5 (Range: 5- 37)	Treatment failure; patient survival (Kaplan- Meier method)	Cataract development, radiation retinopathy, maculopathy, optic neuropathy, neovascular glaucoma, vitreous hemorrhage, retinal detachment developed or worsened, corneal ulceration, alopecia, punctal canalicular stenosis, enucleation necessary
Ryu et al., (2004) ⁷²	USA	Squamous cell carcinoma; mucoepidermoid carcinoma, adenoid cystic carcinoma, adenoma, basal cell carcinoma all in the head and neck	Novalis/NR	Retrospective	n = 13	Prior treatments: combined modalities of surgery, radiotherapy, and chemotherapy	Median: 8 (Range: 6-16)	Precision and accuracy of the radiosurgery; local tumor control; tumor response; pain relief; symptom improvement	Acute side effects: mild mucositis, skin irritation depending on tumor location

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Gunven et al., (2003) ¹²³	Sweden	Recurring liver metastases of colorectal cancer (CRC)	Linac/NR	Retrospective	n = 4	Prior surgical resection	10-101	Tumor sizes and evolution; tumor regression	Epigastric pain; slight diffuse mucosal redness
Le et al., (2003) ⁶⁶	USA	Nasopharyngeal carcinoma	CyberKnife and frame-based system; 4 or 6 MeV linac/NR	Retrospective	n = 45	EBRT 66 Gy; chemo	Median: 35 (Range: 4-85)	Local control, freedom from nodal relapse, freedom from distant metastasis, progression free survival and overall survival - Kaplan-Meier Method	No acute toxicities; late - cranial nerve zoster, transient V2 or V3 numbness, cranial nerve III paresis and asymptomatic temporal lobe necrosis, asymptomatic temporal lobe necrosis alone

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Haas et al., (2002) ⁸⁴	Austria	Choroidal melanoma	Gamma Knife/NR	Retrospective	n = 32	NR	Median: 38 (Range: 6-81); 25 patients Median: 46 (Range: 24-81)	Visual Acuity	Intraretinal hemorrhage; retinopathy; macular edema; capillary nonperfusion; exudates; cotton wool spots; microvascular degeneration; proliferative radiation retinopathy with neovascularization of the retina or optic disc; iris neovascularization with progression to neovascular glaucoma
Habermann et al., (2002) ⁶³	Austria	2 cylindric cell carcinomas, 2 adenocarcinomas, 2 malignant neuroblastomas, 1 squamous cell carcinoma, 1 amelanotic melanoma all in the nasal cavity or paranasal sinuses infiltrating skull base	GammaKnife/NR	Retrospective	n = 8	Prior surgery	Range: 2-53	Tumor response	none observed

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Pai et al., (2002) ⁷¹	Taiwan	Recurrent nasopharyngeal carcinoma (NPC)	Linac-based accelerator with 10 Mv photon/NR	Retrospective	n = 36	All prior RT (64.8 Gy to 81.6 Gy, Median dose: 72 Gy)	Median: 26.7 months	Total response rate; overall local control rate; overall survival; disease-free survival	Frequent nose bleeding; asymptomatic skull base destruction; nasopharyngeal necrosis
Simonova et al., (2002) ⁹³	Czech Republic	Uveal melanoma	Gamma Knife/NR	Retrospective	n = 75	None	Median: 32 (Range: 10-74)	Local disease control	Secondary neovascular glaucoma; enucleation; corneal damage; optic nerve damage; damage to iris; vitreous hemorrhage
Chen et al., (2001) ⁵⁸	Taiwan	Nasopharyngeal carcinomas	KD-S Siemens/NR	Retrospective	n = 11	Prior conformal radiotherapy and/or chemotherapy (radiation Range: 60-80 Gy)	5 to 31	Tumor response	Epistaxis
Xiao et al., (2001) ⁷⁶	China	Recurrent or residual nasopharyngeal carcinoma	Linac-based SRS	Retrospective	n = 50	Prior conventional radiotherapy	Median: 20 (10-49)	Tumor response	Cellulitis of the nasopharynx, oropharynx, and parapharyngeal soft tissues, acute radiation otitis media

Study	Country	Cancer type	Instrumentation/ Algorithms	Study design	Study size	Prior or concurrent treatment	Length of follow-up (months)	Outcomes measured	Adverse events
Ahn et al., (2000) ⁵⁶	South Korea	Head and neck tumors; nasopharynx cancer, lacrimal gland adenoid cystic carcinoma, orbital lymphoma, skull base recurrence of maxillary sinus adenoid cystic carcinoma	Clinac 600C (Varian Association, Palo Alto, CA)/NR	Retrospective	n = 21	Conventional external radiation therapy; chemotherapy	Median: 28 (Range: 3-45)	Tumor response, local control rates, survival rates	Mucosal necrosis
Chang et al., (2000) ⁵⁷	Taiwan	Recurrent NPC	NR/NR	Retrospective	n = 15	Prior external radiotherapy	Median: 42	Overall survival	Varying degree of hearing impairment and trismus
Mueller et al., (2000) ⁹¹	Germany	Uveal melanomas	Gamma Knife/NR	Retrospective	n = 35	None	Range: 11-20	Tumor control; visual acuity	Radiation retinopathy, edema of optic nerve, optic atrophy, worsening of preexisting cataract