RADIATION THERAPY IN BRAIN DISEASES

Brain tumors will occur in nearly 200,000 Americans in 2005. About 170,000 people will develop brain metastases from other cancers, and another 20,000 will develop primary brain tumors. Radiation Therapy (RT) has been used in the treatment of brain tumors for more than 50 years. RT has proven to be effective at prolonging survival in many patients, and can be curative. RT works by damaging the DNA of tumor cells, rendering them incapable of cell division. The limiting factor in RT has been normal tissue tolerance. Conventional RT has involved giving small doses of radiation to the brain over 5 to 6 weeks. This concept of giving small doses over time is called fractionation. It permits relative sparing of normal tissues, which are capable of repairing the radiation damage when the dose is fractionated. Tumors are less able to repair such damage, due to more rapid growth rates, and more primitive repair mechanisms.

Recent years have witnessed the development of new technologies which deliver higher doses of radiation to the target, while minimizing dose to surrounding normal tissues. These technologies have relied on CT, MRI, and PET Scan imaging with computer assisted targeting systems to precisely deliver high doses of radiation. The term Stereotactic Radiosurgery (SRS) has been coined to describe these systems. SRS is capable of giving large doses to small volumes with minimal damage to surrounding normal tissue. In contrast to a 6 week course of daily RT, SRS can be performed in one day. Various SRS systems have been devised, including Gamma Knife (GK), X-Knife, and Cyberknife. GK, with a 40 year clinical history, has the longest proven record by far. GK has been used successfully in the treatment of numerous brain diseases, including tumors and benign conditions.

The following is an overview of some of the applications of RT and SRS in various brain tumors and benign conditions.

BRAIN METASTASES

Brain metastases result from the spread of tumor cells thru the blood stream to the brain. It is estimated that about 170,000 people will develop brain metastases in 2005 in the United States. This number has increased markedly since 1972, when about 30,000 were found to have brain metastases. The advent of CT, MRI, and PET Scan technologies have dramatically increased the detection of these tumors. In addition, with better control of primary tumors, cancer patients are living longer to develop new problems. Historically, the most common treatment of brain metastases has been Whole Brain Radiation Therapy (WBRT) given daily for 2 to 5 weeks. The general prognosis in patients with brain metastases, is poor, as shown in the following table published in the New England Journal of Medicine in 1990 :

TREATMENT	MEDIAN SURVIVAL
No Treatment	1 month
Steroids	2 months
Whole Brain Radiation Therapy (WBRT)	3-6 months

(NEJM, 1990 ; 332 : 494)

The following series are representative results with WBRT from the medical literature :

BRAIN METASTASES
RESULTS WITH WBRT

AUTHORS	#PTS	DOSE	MEDIAN SURVIVAL
Cox	68	30 Gy	4 months
Giaccone	41	30 Gy	11 months
Carmichael	61	30 Gy	7 months
Ryan	122	30 Gy	3.3 months
Bergquist	32	30 Gy	3 months
Postmus	22	30 Gy	5 months
Johnstone	28	30 Gy	2 months
Broadbent	474	30 Gy	4 months

These data are in patients with multiple brain metastases, where the burden of metastatic disease is high. In patients with solitary brain metastases, survival times are significantly longer, and some patients may be cured. In patients with Stage IV non-small lung cancer, and a solitary brain metastasis, 20% 5 year survival has been achieved, usually with management consisting of resection of the brain metastasis followed by WBRT. Chemotherapy may improve survival figures further.

The use of SRS in patients with brain metastases is increasing. Tumor control rate of the treated brain metastases is high, in the range of ~ 95%. However, survival benefits remain controversial because of patients dying of uncontrolled distant metastases, or new brain metastases outside of the SRS field. The basic problem is one of microscopic disease throughout the brain, and in the rest of the body. While SRS has excellent results in the treatment of the lesion in question, new disease develops outside of the SRS treatment field. Therefore, survival benefits with SRS have not been clearly demonstrated, except in cases of minimal metastatic burden. There does appear to be a survival benefit in patients with solitary brain metastasis. Adding WBRT to SRS decreases the risk of intracranial relapse, and may improve survival, as shown in a recent intergroup study involving GK Centers at Pittsburgh, Mayo Clinic, UCSF, Dallas, and Atlanta. The following data were reported :

TREATMENT	#PTS	RECURRENT BRAIN METASTASES	5 YEAR SURVIVAL
Whole Brain XRT + GK	65	19%	26%
GK	51	47%	18%
p-value	-	0.004	NSD

(IJROBP, 1994 ; 28 : 798)

The reason for the decreased risk of recurrent brain metastases with the addition of WBRT is that microscopic disease outside of the GK volume is treated.

Notably, similar results have been reported with surgical resection of solitary brain metastases + WBRT. The following table is representative of the literature :

SOLITARY BRAIN METASTASES
RESULTS WITH SURGICAL RESECTION + WBRT

		BRAIN RECURRENCE			MED. SURV. Mo.		
AUTHOR	#PTS	XRT	No XRT	P-Value	XRT	No XRT	P-Value
Dosoretz	34	50%	52%	NSD	8	10	NSD
Smalley	85	21%	85%	NA	21	12	0.02
De Angelis	98	45%	65%	0.03	21	14	NSD
Hagen	33	50%	52%	NSD	8	10	NSD
Armstrong	64	47%	38%	NSD	10	14	NSD
Skibber	34	32%	72%	NA	18	6	0.002
Patchell*	95	18%	70%	0.001	11	10	NSD

*Randomized Trial

(Devita et al : Principles and Practices of Oncology, 6th Edition, 2001 pgs. 2662)

Devita et al, concluded from this data, "it remains unclear whether all patients who undergo surgical resection should also receive adjuvant radiotherapy."

SRS has achieved very similar results to surgery. The following data have been reported with GK and X-Knife :

BRAIN METASTASES
RESULTS WITH GK

AUTHOR	#PTS	RECURRENCE	MORBIDITY	MORTALITY	MEDIAN SURVIVAL
Seung	55	0%	7.0%	0%	8 months
Shiau	100	7%	4.0%	0%	11 months
Kim	77	13%	4.4%	0%	10 months
Steiner	100	3%	nr	0%	10 months
Flickinger	116	15%	4.0 %	0%	9 months
Fukuoka	130	7%	4.6%	0%	6 months
Kihlstrom	235	6%	nr	0%	9 months
Rand	56	0%	nr	0%	nr
Somaza	23	9%	nr	0%	9 months
Coffey	26	0%	nr	0%	10 months
Schoegl	97	6%	1%	nr	6 months
Gerosa	225	12%	3.9%	nr	9 months

BRAIN METASTASES
RESULTS WITH X-KNIFE

AUTHOR	#PTS	RECURRENCE	MORBIDITY	MORTALITY	MEDIAN SURVIVAL
Mehta	40	18%	0%	0%	7 months
Engenhart	69	6%	3%	nr	9 months
Alexander	248	11%	3%	nr	9 months
Valentino	139	14%	nr	nr	13 months
Auchter	122	14%	0%	nr	12 months
Joseph	120	6%	4%	nr	8 months
Shirato	39	8%	0%	nr	9 months
Breneman	84	25%	2%	nr	11 months
Cho	73	20%	8%	nr	8 months

These data compare quite favorably to surgery. Surgical resection of brain metastases results in ~ 20% recurrence at the primary site, and carries ~ 10% mortality risk, not to mention significant morbidity risk. The following comparative results have been reported in a recent literature review :

BRAIN METASTASES
TREATMENT OUTCOME

TREATMENT	#PTS	RECURRENCE	MORBIDITY	MORTALITY	MONTHS SURVIVAL
Gamma Knife	946	6.0%	3.6%	0.0%	8.9 months
X-Knife	1,081	10.1%	14.7%	0.3%	8.5 months
Surgery	1,719	17.5%	9.9%	9.6%	8.1 months

Based on all of the above data, multiple institutions, including UCSF, UCLA, UVA, and the University of Pittsburgh advocate using SRS alone in the management of brain metastases. This spares the patient potential morbidity of WBRT. In addition, SRS + WBRT does not add significantly to survival. Only the incidence of new brain metastases is decreased. Occasionally, WBRT is used because of the multiplicity of lesions. The following series show the impact of WBRT when combined with SRS or surgery :

BRAIN METASTASES
LOCAL TREATMENT +/- WBRT

AUTHOR	#PTS	TREATMENT	FREEDOM FROM BRAIN PROGRESSION	SURVIVAL
Pirzkall	158	SRS	-	5.0 mo.
	78	SRS + WBRT	-	6.5 mo.
Sneed	62	SRS	8.3 mo.	11.3 mo.
	43	SRS + WBRT	15.9 mo.	11.1 mo.
Patchell*	46	Surgery	6.0 mo.	9.9 mo.
	49	Surgery + WBRT	50.6 mo.	11.0 mo.
RTOG 9508*	70	WBRT	-	6.7 mo.
	69	SRS + WBRT	-	5.3 mo.
Chougule*	36	SRS	-	7 mo.
	37	SRS + WBRT	-	5 mo.
	31	WBRT	-	9 mo.
Sneed	983	WBRT	-	14.0 mo.
		SRS + WBRT	-	15.2 mo.
Andrews*	164	WBRT	-	6.5 mo.
	167	SRS + WBRT	-	4.9 mo.

*Randomized Trials

GLIOBLASTOMA MULTIFORME (GBM)

The most aggressive primary brain tumor is Glioblastoma Multiforme (GBM). About 5,000 people will be diagnosed with GBM in the United States in 2005. The standard of care for treatment of GBM in the United States has been to give involved field fractionated RT for 6 weeks. In recent years, many treatment centers added a radiation boost to the tumor bed with I-125 Implant, or SRS (LINAC or GK). The following data summarizes the radiation literature, with involved field RT +/- Boost :

GBM
RESULTS WITH RT +/- BOOST

AUTHOR	#PTS	RT – DOSE	BOOST	SURVIVAL
Barker	301	60 Gy	none	11 mo.
Fiorell	68	60 Gy	none	14 mo.
Loeffler	40	60 Gy	none	10 mo.
Nelson*	466	64.8 Gy	none	13 mo.
		72 Gy	none	
		76.8 Gy	none	
		82 Gy	none	
Loeffler	35	60 Gy	I-125	27 mo.
Scharfen	106	60 Gy	I-125	22 mo.
Laperriere**	140	50 Gy	none	13.2 mo.
		50 Gy	I-125	13.8 mo.
Loeffler	49	60 Gy	LINAC	20 mo.

GBM
RESULTS WITH RT +/- BOOST

AUTHOR	#PTS	RT – DOSE	BOOST	SURVIVAL
Kondziokola	64	60 Gy	GK	26 mo.
Sakaria	115	60 Gy	LINAC	24 mo.
Shrieve	78	60 Gy	GK	20 mo.
Prisco	17	60 Gy	LINAC	21.4 mo.
	15	60 Gy	none	11.4
Nwokedi	31	60 Gy	GK	25 mo.
	33	60 Gy	none	13 mo.
Buatti	11	60 Gy	LINAC	17 mo.
Gannett	30	60 Gy	LINAC	14 mo.
Van Kampen	35	54 Gy	LINAC	10 mo.
Mehta	31	54 Gy	LINAC	10 mo.
Baumert	17	60 Gy	LINAC	20 mo.
Mark	110	50 Gy	GK	24 mo.
Souhami**	203	60 Gy	none	14 mo.
		60 Gy	LINAC or GK	

*RTOG randomized trial employing radiation dose escalation with concurrent BCNU Chemotherapy. No significant survival advantage was found with dose escalation to 81.6 Gy. The dose was given at 1.2 Gy BID. Radiation toxicity occurred in 1.3-6.8% of the patients, and correlated with increasing dose.

**Canadian randomized trial examining XRT +/- I-125 Implant Boost. No significant survival benefit was seen.

***RTOG randomized trial employing XRT + BCNU +/- SRS Boost. No significant survival advantage was found. It is now thought that the advantage seen in the retrospective studies was due to patient selection bias.

In conclusion, involved field fractionated RT to 60 Gy has been shown to improve survival in GBM to about 12 months. A large RTOG randomized bid dose escalation trial to 82 Gy failed to demonstrate a survival benefit. Brain toxicity increased from 1.3% to 6.8% with increasing dose. This is especially significant because the median survival in this 4 armed trial was about 12 months. With longer median survival, the risk of brain necrosis would likely increase. Multiple retrospective series employing SRS Boost suggested an improvement in median survival to about 24 months. However, another randomized trial by the RTOG failed to confirm these results. The RTOG recently conducted another dose escalation trial in which patients receive 2 Gy qd up to 84 Gy. This trial was recently closed to patient accrual. Finally, a Canadian randomized trial found no benefit to XRT +/- I-125 Boost.

In summary some investigators advocate SRS Boost, while others argue for fractionated dose escalation, and others for systemic treatment. It is a situation where reasonable people can disagree. The currently available evidence now indicates that improved survival in GBM will not come from radiation dose escalation or SRS. Hopefully, new Chemotherapy or Biologic Treatment will provide the answers in this difficult disease.

SRS has been used in the treatment of recurrent GBM. The following data are representative of the literature.

RECURRENT GLIOBLASTOMA MULTIFORME
RESULTS WITH SRS

AUTHOR	#PTS	BOOST-DOSE	SURVIVAL
Cho	71	17 Gy	11 mo.
Shrieve	86	13 Gy	10 mo.
Chamberlain	20	-	7 mo.
Lederman	14	6 Gy	14 mo.
Hudes@	20	30 Gy	10 mo.

@ - Fractionated SRS, i.e. 30 Gy in 10 fractions

Systemic chemotherapy has proven to be of significant benefit in Grade III Astrocytomas, but not yet in GBM. However, a recent Meta-Analysis suggested a modest survival improvement, even in GBM (Cancer, 1993 ; 71 : 2585). Temodar may be more active against high grade gliomas than recent standard regimens such as PCV. Yung reported the results of 525 patients with malignant glioma treated with Temodar (Seminar Oncol, 2000 ; 27 : 27-34). Disease progression was delayed, and quality of life improved. Macdonald reported the results of a phase II trial, in which 225 GBM patients were randomized to receive Temodar vs. Procarbazine (Seminar Oncol, 2001 ; 28 : 3-12). The Temodar group had significantly improved 6 month progression free and overall survival. Stupp et al, reported the results of a recent Phase III randomized trial in which 573 GBM patients were randomized to received XRT vs. XRT + Temodar (JCO, 2004 ; 22 [14S] : 1s). The 2 year survival was 8% with XRT alone, vs. 26% with XRT + Temodar ($p < 0.001$).

MENINGIOMA

Meningiomas develop from arachnoidal cells in the meninges, or the lining of the brain. They tend to be slow growing tumors, but can be aggressive with life threatening potential. About 5,000 people will develop Meningiomas in the United States in 2005. The standard treatment has been surgical resection. Complete surgical resection results in good long-term control. SRS has been used with results which appear to be comparable to surgery. RT has also been used, with less favorable tumor control rates. The following tables have been reported in recent literature reviews comparing GK, X-Knife, Surgery, and RT in the treatment of Meningiomas :

MENINGIOMA
TREATMENT OUTCOME

TREATMENT	#PTS	RECURRENCE	MORBIDITY	MORTALITY
GK	637	6.0%	3.7%	0%
X-Knife	301	10.8%	9.7%	1.2%
Complete Resection	3,698	15.1%	24.7%	8.8%

FRACTIONATED RT RESULTS IN MENINGIOMA

AUTHOR	#PTS	TUMOR %PROGRESSION	SURVIVAL 5-YRS	10-YRS
Vendrely	156	21%	75%	45%
Pourel	45	25%	85%	85%
Barbaro	54	32%	-	68%
Winkler	67	32%	82%	70%
Maire	91	-	71%	40%
Forbes	31	24%	76%	-
Miralbell	25	0%	100%	-
Petty	12	25%	75%	-
Milosevic	59	67%	28%	-
Goldsmith	117	23%	89%	77%
Goldsmith	23	52%	48%	-
Haie-Meder	32	50%	64%	-
Shimizu	21	75%	67%	-

The standard fractionated RT dose has been 54 Gy in 30 fractions. Complications have been minimal. Some series have reported a worse prognosis with Malignant Meningiomas, though this is not a universal finding. GK results compare favorably to surgery and RT as shown below :

GK RESULTS IN MENINGIOMA
5-YEAR FOLLOW-UP

AUTHOR	#PTS	%DECREASED OR UNCHANGED	TUMOR %PROGRESSION	%COMPLICATIONS
Subach	62	90%	8%	8%
Kurita	25	96%	4%	4%
Pendl	78	96%	4%	5%
Hodes	20	100%	0%	5%
Hudgins	100	90%	nr	2%
Nicolato	50	98%	2%	6%
Tanaka	30	93%	2%	3%
Steiner	151	89%	11%	0%
Pendl	37	92%	8%	7%
Duma	34	100%	0%	4%
Kondziolka	50	96%	4%	6%
Mark*	279	86%	14%	17%

The standard GK radiation dose is 12 Gy in 1 fraction to the tumor margin.

We presented our experience with G) for progressive, or recurrent meningiomas at the 1996 Annual Meeting of the American Society of Therapeutic Radiology and Oncology (IJROBP, 1996 ; 36 [1] : 255). In 50 tumors treated, 46%(23/50) decreased by follow-up MRI. The other 27 were stable. There were no cases of tumor progression. Follow-up ranged from 3-48 months. We updated this experience, and presented the data at the American Association of Neurological Surgeons Meeting in Toronto, Canada, in 4/01. In 279 Meningiomas, with 6 year follow-up, tumor control rate was 86%. With respect to complications, 17% of patients developed symptomatic edema needing steroids, with 3% requiring surgical intervention.

PITUITARY ADENOMA

Pituitary tumors are generally slow growing tumors, but because of their location adjacent to the optic chiasm and cavernous sinus can cause severe visual deficits. They can also cause a wide array of hormonal deficits. About 2,000 people will be diagnosed with Pituitary tumors in the United States in 2005. Surgery has been the mainstay of treatment. When resection is subtotal, RT is frequently added. Primary SRS with GK has been reported with favorable results. The following table is representative of the medical literature.

PITUITARY ADENOMA
TREATMENT OUTCOME

TREATMENT	#PTS	% TUMOR PROGRESSION	TREATMENT PANHYPPIT.	TREATMENT MORTALITY
Microsurgery (Complete Resection)	8,494	12%	15%	0.6%
Microsurgery + RT (Subtotal Resction)	1,006	11%	49%	1.3%
GK	257	0.5%	18%	0%
XRT	188	23%	nr	0%
X-Knife	90	nr	nr	0%

ARTERIOVENOUS MALFORMATION (AVM)

Arteriovenous Malformations (AVM) are congenital abnormal blood vessels which are prone to bleed. The risk of hemorrhage, is ~ 2-4% per year, with ~ 1% annual mortality risk. Management options include observation, embolization, surgical resection and SRS with GK or X-Knife. The following results are representative of the medical literature :

AVM
TREATMENT OUTCOMES

TREATMENT	#PTS	%OBLITERATION	%REBLEED	%MORBIDITY	%MORTALITY
Surgery	2,722	94.7%	-	11.7%	4.4%
X-Knife	971	60.0%	9.9%	7.9%	2.4%
Gamma Knife	1,628	78.7%	3.4%	3.1%	1.2%
Embolization	1,085	3.3%	nr	8.8%	1.5%
Observation	-	N/A	40% at 25 yrs	Significant	25% at 25 years

ACOUSTIC NEUROMA

Acoustic Neuromas are slow growing tumors which form on CN VIII. They can cause progressive hearing loss, decreased balance, headaches, and rarely death. Management options include Surgical Resection, Stereotactic Radiosurgery (SRS), fractionated SRS, and Intensity Modulated Radiation Therapy (IMRT). SRS can be delivered either via GK or X-Knife. The following data is a literature review comparing surgery and GK :

ACOUSTIC NEUROMA
GAMMA KNIFE VS. MICROSURGERY

	GAMMA KNIFE	MICROSURGERY
Acute CN VII palsy	2.3%	36.0%
Chronic CN VII palsy	0%	9.0%
Useful Hearing Preserved	58.0%	39.0%
Acute CN V Numbness, Tingling	5.8%	9.0%
Chronic CN V Numbness, Tingling	1.7%	nr
CSF Leak	0%	9.2%
Hydrocephalus	0%	2.3%
Mortality	0%	1.1%
Hospitalization Days	0.5	10.5
ICU Days	0	2.4
Loss of Work Days	5	60

The Gamma Knife data on more than 1,000 patients were summarized by Prasad et al (J Neurosurg, 2000 ; 92 : 745), and Van Roijen et al (Acta Neurochir, 1997 ; 139 : 942). The surgical data on more than 1,000 patients were summarized by Samii et al (Neurosurg, 1997 ; 40 : 11).

TRIGEMINAL NEURALGIA

Trigeminal Neuralgia (TN), is a pain syndrome which effects about 10,000 people per year in the United States. It is a severe pain condition, which effects the 5th Cranial Nerve. Patients classically describe the pain, as intermittent sharp, stabbing, shooting, electric shocks. They will often rate the pain at 10/10, with 10 being the worst they can imagine. Some patients report suicidal ideation. The pain is thought to be caused by a blood vessel coming into contact with the 5th Cranial Nerve root as it enters the brainstem. Management options include, medical management, glycerol rhizotomy, radiofrequency rhizotomy, balloon compression, open surgery with microvascular decompression, and Stereotactic Radiosurgery (SRS). SRS can be delivered via Gamma Knife or X-Knife technology. Taha and Tew reported the following surgical results in an extensive literature review in 1996 (Neurosurgery, 1996 ; 38[5] : 865-871) :

TRIGEMINAL NEURALGIA
OUTCOME BY TREATMENT

Treatment	#Pts	Initial Pain Relief	Pain Recurrence	Numbness
Glycerol Rhizotomy	1,217	91%	54%	60%
Radiofrequency Rhizotomy	6,205	98%	23%	98%
Balloon Compression	759	93%	21%	72%
Open Surgery (MVD)	1,417	98%	15%	2%
Partial Rhizotomy	250	92%	18%	100%
*Medical	-	70%	75%	-
*SRS (Gamma Knife)	435	90%	11%	15%

Patients undergoing GK have frequently been treated with all of the other techniques, so that the 90% pain relief results have been achieved in a difficult patient population. We presented a combined institutional experience at the 10th International Meeting of the Leksell Gamma Knife Society, in Squaw Valley, CA in 4/00. We reported the results of 435 patients with Trigeminal Neuralgia treated with Gamma Knife. With a median follow-up of 31 months, 92% of the patients reported an excellent (no pain, no medications), or good (mild pain, tolerable medication dosage) result. In this same series, 47 patients have undergone retreatment for persistent, or recurrent pain. 81% have reported an excellent or good result. The following data are representative of the literature :

TRIGEMINAL NEURALGIA
OUTCOME WITH SRS

Author	#Pts	Initial Pain Relief	Pain Recurrence	Numbness
Petit	112	77%	16%	nr
Pollock	117	57%	2%	25%
Kondziolka	220	86%	30%	10%
Rogers	54	96%	nr	10%
Young	110	95%	3%	3%
Mehta	250	75%	11%	3%

The Gamma Knife protocol has called for delivering 87 Gy to the CN V entry root zone, while limiting the 20% IDL to the anterior surface of the brainstem. The Gamma Knife System has an accuracy of 0.4 mm.

PARKINSON'S DISEASE AND ESSENTIAL TREMOR

Parkinson's Disease is classified as a functional brain disorder, characterized by a number of neurologic deficits including shaking or tremors of the arms and legs. Essential tremor is a far more common disorder, limited just to tremors. The tremors can result in severe compromise of quality of life to the point where patients are unable to feed themselves, hold a cup of coffee, or write. Management options for tremors have included supportive care, medical management, Radiofrequency (RF) thalamotomy, Deep Brain Stimulation (DBS), and Stereotactic Radiosurgery (SRS). The following results have been reported with SRS (GK) :

PARKINSONIAN AND ESSENTIAL TREMOR
RESULTS WITH SRS

INSTITUTION	#PTS	EXCELLENT RESPONSE	COMPLICATIONS	F/U
Northwest	27	88%	0%	6 months
Good Samaritan	158	88%	1.5%	52 months
Hidaka Hospital	53	80%	0%	24 months
Shanghai	6	100%	0%	5 months
Univ. of Pittsburgh	12	83%	0%	12 months

These results with GK have been obtained with a protocol usually calling for a dose of 130-140 Gy to the VIM nucleus. The outcomes appear to be comparable to RF and DBS. Niranjan et al, reported the following results in 36 patients treated with RF, DBS, or SRS, at the University of Pittsburgh (Stereotact Funct Neurosurg 1999 ; 72 : 178-194) :

PARKINSONIAN AND ESSENTIAL TREMOR
RESULTS WITH RF, DBS, OR SRS

TREATMENT	#PTS	EXCELLENT RESPONSE	F/U
RF	13	85%	12 months
DBS	11	91%	12 months
SRS	12	83%	12 months

Serious complications with SRS have been reported with doses in the 200 Gy range, or when simultaneous bilateral thalamotomies are performed (Arch Neurol, 2001 ; 58 : 1995-2002).

THE FUTURE

Current research in cancer emphasizes targeted therapy against vascular, molecular, and even genetic targets of tumors. A vaccine was recently developed, and then proven to be effective at preventing certain forms of cervix cancer. We are entering the dawn of a new age in medicine. Tumor cell vaccines, antibodies, and repair of genetic alterations may one day be routine. In seeking treatment, patients would be well advised to be seek care not only at facilities where state of the art technologies for their condition exist, but also where promising research for the cures of tomorrow is being conducted. Cedars Sinai Medical Center is such a place.