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Invited articles

St. Joseph's Hospital and Barrow Neurological Institute stereotactic radiotherapy experience: comparison of Gamma Knife and CyberKnife

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The clinical utilisation of stereotactic radiotherapy continues to increase in breadth and scope within the medical community. However, no single standard treatment platform exists for the delivery of stereotactic radiotherapy treatments. This is because although there are several commercially available platforms capable of delivering stereotactic radiotherapy treatments, each platform has unique abilities and limitations. The most widely used stereotactic radiotherapy system for intracranial treatments is the Gamma Knife. The first image guided robotic stereotactic radiotherapy system enabling body stereotactic radiotherapy is the CyberKnife. Both are available at the Barrow Neurological Institute. We describe our experience with the complementary use of these two distinct treatment platforms. This permits us to make a meaningful comparison and to detail their contrasting advantages and disadvantages for state of the art for stereotactic radiotherapy.

Key words: stereotactic radiotherapy, Gamma Knife, CyberKnife, cranial tumours, extracranial tumours

Introduction

We present our stereotactic radiotherapy (SRT) comparison between the Gamma Knife (GK) installed at Barrow Neurological Institute (BNI) in 1997, and the CyberKnife (CK) installed at BNI in 2003, as a series of tables. Firstly though, we present a brief historical overview of SRT including the concept of skull mounted surgical guidance, radiotherapy methods using radium sources which pre-date SRT by several decades, SRT growth points and the American Society for Therapeutic Radiology & Oncology/American College of Radiology (ASTRO/ACR) definition of SRT.

Stereotactic defined

Chamber's English Dictionary of 1988 [1] defines the prefix stereo- as 'in composition, solid, hard, three-dimensional' and the word stereotactic as 'relating to the precise location of particular brain structures by three-dimensional survey'. Whereas *Dorland's Medical Dictionary* of 1988 [2] defines stereotactic (alternatively stereotaxic) as 'pertaining to or characterised by precise positioning in space; said especially of discrete areas of the brain that control specific functions'. With reference to radiotherapy probably the earliest use of the word stereotaxic was by Lars Leksell in 1951 [3] when he used it in conjunction with the term radiosurgery.

The adjective 'stereotactic' as applied to a fixation frame was referred to by Barton Guthrie & John Adler [4] when they described Robert Clarke's stereotactic frame for animal use, the last prototype of which was sold to Johns Hopkins University in 1920. Clarke was of the opinion that 'from its application to animals to its adaption to human surgery is a long step …. but … for my own part, I have no doubt that its application to human surgery will only be a question of time'. The term 'stereotaxic approach' was coined by Clarke at the beginning of the 20th century [5].

Concept of skull mounted surgical guidance

The concept of skull mounted surgical guidance was suggested in the 19th century. The Russian anatomist Zernov, using the anthropologic concept of craniotomy, designed a head frame on which were mounted a set of arcs that he used to map and measure human cerebral gyri. In 1887, Minor & Altuchov used the device on several patients to localise and remove cortical surface lesions. This combination of craniotomy and functional cerebral localisation proved adequate for finding gross intracranial pathologies but the patients died due to inadequate surgical and medical technology [6].

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Radium and radon for cranial therapy

By the end of the 1930s brain tumours had been treated by external beam radiotherapy, either using X-ray machines or teleradium machines termed radium bombs, or by several radium sources positioned on a cap or helmet worn by the patient and made of material such as leather or Colombia paste. Radium needles or radium tubes actually implanted within brain tissue (interstitial radium brachytherapy) were rare, although a few examples are recorded. One example is the attempt by Harvey Cushing as early as 1923, but he was not impressed with the results and did not pursue the method [7, 8].

Another example, in 1929, was by Sir Henry Souttar [9] surgeon to The London Hospital. He treated an angioma of the meninges where the skull flap had a central hole made so that radium needles could be withdrawn at the end of treatment. Six needles were used, each of 2 cm length and 2 mg radium activity. Souttar's conclusion was 'a new field of surgery is opening up before us, the limits of which it is impossible to see' [9].

However, neither Cushing nor Souttar used stereotactic head frames and it was not until the 1950s that such frames were introduced into radiotherapy practice, and then only for the limited application of radon seed implants to the pituitary. When artificially produced radionuclides became available after World War II for medical use, radon seeds were replaced in the 1960s by small ^{90}Yttrium rod sources. ^{90}Yttrium is a pure beta emitting radionuclide with a maximum energy of 2.25 MeV and a half-life of 64.2 hours [10]. Then came Lars Leksell, the Gamma Knife, linear accelerator based stereotactic radiotherapy using a head frame, and the CyberKnife: and the rest, as one might say, is now history.

Growth points in SRT

Table I lists the important growth points in SRT from Lars Leksell's original Gamma Unit of 1951 to the first clinical use, at Stanford University in 1994 of the CyberKnife.

Conformal SRT features

By the end of the 1980s the limitations of frame-based cranial SRT were becoming more apparent. The major challenge was increasingly seen as the development of a method to treat lesions using conformal SRT that would provide the following features. 1. Elimination of the need for frame fixation. 2. Ability to relate the identified lesion to radiographic markers and anatomical landmarks. 3. Allow for near real-time image acquisition and tracking.

It was realised that if these three features could be incorporated into a SRT system it would then be possible using SRT to deliver treatment to any location within the body and to compensate for body, organ and lesion motion during treatment. Also, fractionated treatment would be possible. This development was finally attained with the CyberKnife system [4, 22].

ASTRO/ACR guide to radiation oncology coding

The ASTRO/ACR Guide to Radiation Oncology Coding 2005 [23] defines SRT as the 'Delivery of an ablative level of radiation to a particular lesion, typically in the brain, with high precision. SRT is usually delivered in a high dose single fraction, through multiple fractions at smaller dose levels across days or weeks, or through hyper-fractionated dose multiple times in one day to minimise normal tissue damage'.

The Guidelines also define stereotactic body radiation therapy (SBRT) as a 'newly emerging radio-therapy treatment method to deliver a high dose of radiation to a target, utilising either a single dose or a small number of fractions with a high degree of precision within the body'.

Initially SRT was used only to treat intracranial lesions in a single fraction and was termed stereotactic radiosurgery (SRS). However, more recent SRT platforms have allowed this technique to be applied to all body sites and to be used in either a single or hypofractionated treatment regime and therefore SRS is more appropriately referred to as SRT or SBRT. We use SRT.

Table I. SRT growth points

Year	Author	SRT growth point
1951	Leksell	Description of technique & treatment of first patient: Stockholm [3]
1958	Larsson	185 MeV proton beam used for SRT: Uppsala [11]
1967	Leksell	First Gamma Unit patient treated [12]
1974	Larsson	Isocentric linear accelerators proposed as viable sources for SRT [13]
1975	Leksell	Second generation Gamma Unit developed [14]
1983	Betti	First linear accelerator modified for SRT: Buenos Aires [15, 16]
1985	Colombo	Non-coplanar converging arcs technique introduced clinically: Vicenza [17] and in Heidelberg by Hartmann [18]
1986	Lutz	First non-coplanar linear accelerator based SRT in North America: Harvard, Boston [19] and McGill, Montreal by Podgorsak [20, 21]
1991	Adler	Concept of the CyberKnife described [4]
1994	Adler	First intracranial lesion treated with CyberKnife [22]

Gamma Knife system

BNI is one of relatively few institutions which has both Gamma Knife and CyberKnife systems. Our Gamma Knife SRT patient workload is given in Table II. The CyberKnife system was installed later because of the limitation of frame based SRT with the Gamma Knife. These limitations are given in Table III and possible sources of inaccuracy for frame based SRT are indicated in Table IV. Figure 1 shows an example of a patient whom it was impossible to treat using the frame based Gamma Knife.

Table II. BNI Gamma Knife patients treated March 1997 to August 2004

Disease/condition	No. of cases
Metastatic to brain	715
Benign tumours	587
Glial tumours	405
Functional (Trigeminal neuralgia)	337
Vascular	149
Miscellaneous skull base	63
Total	2256

CyberKnife system

The ultimate solution to the problem of frame deformation would be to abandon the frame completely, applying fiducials directly to the cranium. With the CyberKnife system this is exactly what has been achieved, i.e., the abandonment of any necessity for a stereotactic frame. Our CyberKnife patient workload is given in Table V and CyberKnife features in Table VI. Table VII lists possible sources of inaccuracy in image guided frameless SRT.

Table V. BNI CyberKnife patients treated October 2003 to March 2005

Disease/condition	No. of cases
Intracranial	
Brain metastases	33
Malignant glial tumours	17
Meningiomas	33
Pituitary and acoustic	21
Other	17
Extracranial	
Head and neck	7
Spine	34
Lung	9
Other	7
Total	178

Table VI. CyberKnife features

- A new set of images is acquired and analysed at each independently targeted linear accelerator beam position/node
- A feedback loop between the robotic arm and the imaging system adjusts the targeting of the linear accelerator beam to compensate for patient or target movement during treatment: since with the
- CyberKnife, patient or target movement can be detected
- The interval between imaging acquisition and linear accelerator repositioning is 4-10 seconds
- A typical SRT case might be 6-30 Gy delivered to the PTV margin generated from 100-300 intersecting beams

Table III. Frame based SRT limitations

- There is pain at the pin sites and during the post-operative recovery. This requires an anaesthesiologist, a nurse and patient monitoring
- Some lesions are either impossible or extremely difficult to treat because of their location. This is due to technical limitations which can cause collisions of frame or patient with hardware
- Same day imaging is required
- Fractionated treatments are difficult and uncomfortable for the patient
- Unable to treat extracranial lesions
- Imaging during treatment is not possible
- Detection and analysis of patient or target movement during treatment is not possible

Table IV. Possible sources of inaccuracy in frame based SRT

- Errors associated with the steps of frame based SRT set-up [24]
  - Point selection
  - Vector calculations
  - Vernier settings
  - Mechanical coupling and adjustment
- Mechanical limitations of SRT frames: factors dependent upon the properties of the frame [25]
  - Rigidity and the perfect immobilisation of the patient's head within the reference frame
  - Mechanical properties of the frame's construction: engineering design and the materials used
  - Mechanical loads on the frame due to the weight of the patient's head and shoulders, possibly resulting in physical deformation of the frame
- Patient positioning errors due to positioning changes: supine to prone [25]

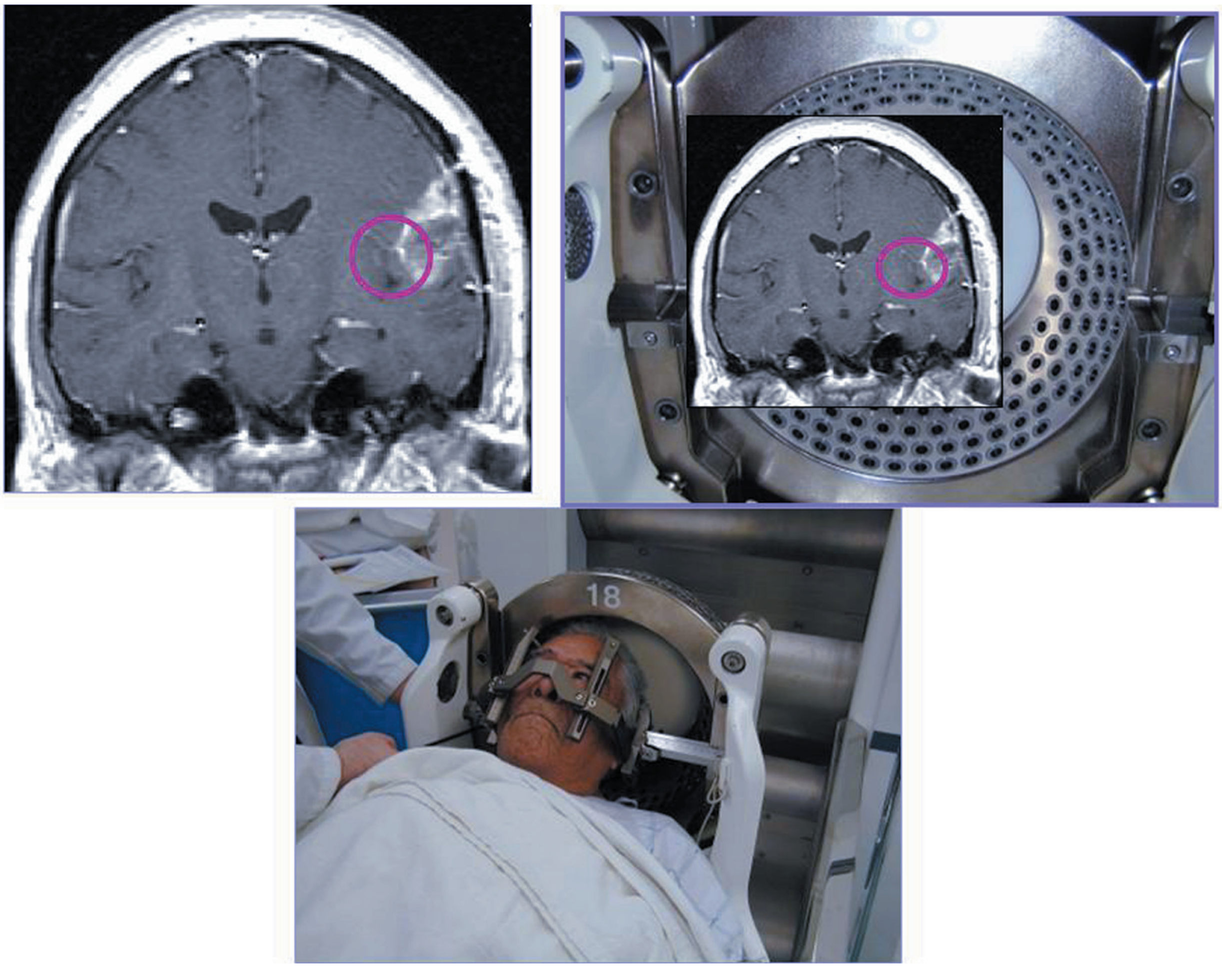

Figure 1. Example of a patient whose lesion could not be fully treated using the frame based Gamma Knife SRT system. This was due to location of the lesion and would have resulted in head frame collision with the collimator

Table VII. Possible sources of inaccuracy in image-guided frameless SRT

– Image data management
Registration and import of images into the treatment planning system
Fusion and scaling of MR, CT, angiography and PET images
– CT/MRI slice protocols
Image resolution
Geometrical fidelity of the images
Edge softening, blurring from reconstruction
Other operator dependent ambiguities in delineation of structures
Volumetric accuracy of scanner
– Beam delivery accuracy
Robotic positioning fidelity
Patient couch positioning and stability

Gamma Knife and CyberKnife comparisons: advantages and disadvantages

With the image-based frameless CyberKnife SRT system, its accuracy and precision has been reported by Chang et al [26] to have values within one voxel of the imaging study. Since then resolution results of less than 1 mm have been reported by Yu et al [27]. Errors affecting clinical accuracy are those relating to anatomical targeting, stereotactic localisation and treatment delivery. The achievable clinical accuracy for SRT for the different systems are given in Table VIII. Our assessment of the advantages and disadvantages of Gamma Knife and CyberKnife systems are listed in Table IX and Table X.

Table VIII. Achievable clinical accuracy for SRT systems [24, 25]

SRT system	Accuracy (mm)
CyberKnife	0.7
Gamma Knife	1.7
Gantry linear accelerator	2.0

Table IX. Advantages and disadvantages of Gamma Knife SRT

Advantages
– Evidence-based optimisation of dose response and outcomes based on more than 30 years of clinical experience
– Fast treatment planning
– Arteriovenous malformation (AVM) treatment is equivalent to SRT using CyberKnife without angiography image fusion
– Well established trigeminal neuralgia SRT with MRI images (CyberKnife requires a cisternogram)
– Same day therapy: treatment completed in less than one week
– System reliability and very little down time
Disadvantages
– Frame placement
– Staffing requirements: nursing and anaesthesiolog
– No real-time imaging: no intra-treatment motion compensation
– No extracranial applications, only limited to brain/skull SRT
– Fractionation impracticable
– Schedule flexibility is limited: inefficient time use during the treatment day
– Cost of replacement of ^{60}Cobalt sources every 5-6 years
– Old technology Limited on lesion size No inverse treatment planning No inhomogeneity corrections

Table X. Advantages and disadvantages of CyberKnife SRT

Advantages
– All body locations, both cranial and extracranial, can be treated
– Fractionation possible
– CT image-based treatment planning
– Ability to track and correct for patient or lesion movement
– Inverse treatment planning software
– No requirements for a frame or for anaesthesia, nursing or other ancillary staff
– Flexible sequential scheduling possible for patients
Disadvantages
– Evolving software. Image fusion and planning are time consuming
– Fiducial placement required for spine and body sites
– CT imaging requirement for treatment planning and motion tracking
– Immature clinical data and lack of clinical trials
– Unknown optimal dose-fractionation scheme
– Unknown optimal PTV for extracranial sites
– Scheduling coordination for treatment planning and delivery
– Inability to treat in manual mode without automated computer directed system
– Maintenance requirements

Conclusions

Now that at BNI we have both the CyberKnife and Gamma Knife systems we have assessed which are the optimum groups of patients for SRT using the two systems, Table XI. This is based on our findings presented in the previous tables of this paper.

Table XI. Preferred SRT workload subdivision between CyberKnife and Gamma Knife at BNI

CyberKnife	Gamma Knife
– Spines	– AVMs
– Extracranial sites	– Trigeminal neuralgia
– Perichiasmal	– Rapid treatments
– Cranial nerves	– Out-of-town patients
– Brain stem	
– Extreme intracranial locations	
– Patient preference	

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