HISTORICAL REVIEW

Dynamic Radiosurgery at the Toronto - Bayview Regional Cancer Centre, 1988-2007

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ABSTRACT: Dynamic radiosurgery was first developed in Montreal and was subsequently adopted at the Toronto-Bayview Regional Cancer Centre in 1988. At that time radiosurgery was in its infancy in Canada. The opportunity of offering highly conformal radiation treatments for intracranial targets presented numerous technical challenges notably in the area of quality assurance. This review chronicles the development of radiosurgery at the Toronto-Bayview Regional Cancer Centre and summarises the successes and failures of the program over the following two decades.

RÉSUMÉ: La radiochirurgie dynamique au Bayview Regional Cancer Centre de Toronto de 1988 à 2007. La radiochirurgie dynamique a été mise au point à Montréal et a ensuite été établie au Bayview Regional Cancer Centre de Toronto en 1988, au moment où la radiochirurgie était encore à ses débuts au Canada. La possibilité d'offrir des traitements de radiothérapie en très haute adéquation avec la tumeur intracrânienne ciblée offrait de nombreux défis techniques notamment dans le domaine du contrôle de la qualité. Cette revue raconte l'évolution de la radiochirurgie au Bayview Regional Cancer Centre de Toronto et résume les succès et les échecs du programme au cours des deux décennies suivantes.

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Dynamic radiosurgery is an eloquent iteration of linac based radiosurgery which was developed in Montreal in the 1980's by Podgorsak and colleagues[1]. Conventional linear accelerator based radiosurgery typically delivers radiation by moving the linear accelerator gantry through a series of arcs with the treatment couch in a fixed position. Treatment is temporarily interrupted whilst the gantry and couch positions are adjusted for each arc. Unlike conventional linear accelerator based radiosurgery, dynamic radiosurgery exploits the ability to move both the linear accelerator gantry and the treatment couch simultaneously without interruption thereby reducing the treatment time for the patient. This Canadian invention was adopted at the Odette Cancer Centre (named the Toronto-Bayview Regional Cancer Centre at that time) and the first patient in Ontario to undergo radiosurgery was treated there on the 15th September 1988[2]. Over the following two decades, dynamic radiosurgery at the Odette Cancer Centre underwent a number of clinically significant improvements and, in the early years, provided a national resource for radiosurgery referrals. The program was decommissioned in 2007 and the last patient was treated on 5th July that year. This article reviews the history of dynamic radiosurgery at the Odette Cancer Centre including the challenges presented by this innovative technology, the successes and failures of the program, as well as the considerable efforts made by staff which previously may have gone unrecognized.

Technological Innovation

The first important technical advance in the application of dynamic radiosurgery at the Odette Cancer Centre was the use of an X-ray beam with the flattening filter removed from the linear accelerator's collimator[3]. Removing the beam flattener resulted in a substantial increase in radiation dose rate with a corresponding reduction in the beam on treatment time for the patient. Beam-on time for a typical single iso-centre was around four minutes. In the 1980's linear accelerators were not manufactured with the capability to remotely remove the flattening filter from the beam. Although it required a little over half an hour's incremental linear accelerator preparation time to physically dismantle, remove and replace the beam flattener afterwards, this innovation paved the way to the possibility of treating multiple and irregular targets[4] with fractionated

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prescriptions without subjecting patients to inordinately long treatment times. The concept of delivering radiosurgery using radiation dose rates in excess of 600cGy/min was met with stunned silence when first reported at a conference in London, England, in 1991. In order to make available a high dose rate beam on a linear accelerator that was also used for conventional radiation treatments, a number of engineering modifications were required[5]. A beam flattener removal system was designed and built (Figure 1), modifications to the parameters of the couch rotation speed required a speed reduction gearbox, and mechanical locks were added to the lateral and longitudinal motions of the couch. Electronic systems were designed and built to synchronize couch and gantry drives over a wide range of gantry speeds and to interlock operation of the linear accelerator to a number of predefined operating conditions (radiosurgery or conventional treatment modes). Some of the modifications were subsequently incorporated in the construction of replacement radiosurgery capable linear accelerators by the manufacturer.

Quality assurance has always been a concern in the delivery of radiation treatments. The recent history of the speciality of radiation oncology has unfortunately demonstrated opportunities to under and overdose patients not least because of limitations in the programming of software controlling treatment delivery using FDA approved equipment. In the case of the OBT frame, it was soon appreciated that the system used to define co-ordinates based on the mid saggital plane introduced the possibility of accidently reversing positive and negative co-ordinates particularly if the target was close to the midplane. To overcome this, a device was built to provide a digital readout of the couch position using optical encoders. These readings, which represented the actual manually set-up target co-ordinates, could then be checked against the radiosurgery plan and any discrepancies identified before treatment was delivered.

Due to the ongoing need to provide end to end testing of the radiosurgery system to ensure quality assurance, the Odette Cancer Centre machine shop designed and built a dedicated anthropomorphic acrylic (Lucite) phantom named Lucy[6]. This was used to confirm the accuracy of machine alignments and patient dosimetry. The commercial rights to Lucy were sold to Sandstrom Trade and Technology Inc. in the 1990's. Lucy is currently available from Standard Imaging Inc. (Middleton, WI, USA) and is still manufactured in Canada.

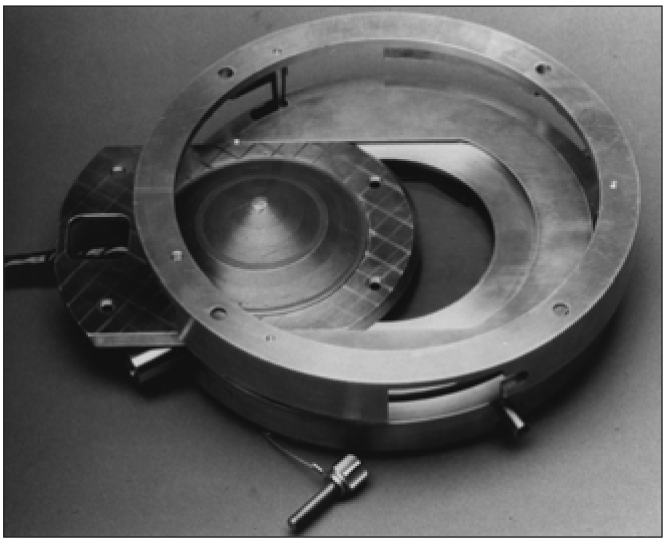

Figure 1: The removable beam flattener.

The radiosurgery treatment planning software was originally written to run under the Microsoft DOS (Figure 2). At that time, planning was a collaborative effort involving physicists and medical staff with the exclusion of radiation therapy dosimetrists who normally plan patients' radiation treatment. Following the introduction of versions of Microsoft Windows supporting a graphical user interface, it was decided to recompile the planning software to run under Windows and train dosimetrists to become involved in the process of planning patients for radiosurgery. Accordingly the original software code was purchased from CMI (Montreal, QC, Canada) and recompiled to run under Windows NT.

Radiosurgery is a complex multidisciplinary treatment. In order to better inform patients of the procedure, an educational video for patients was recorded onsite in 1990.

Arteriovenous Malformations

Between 1989 and 2005, 342 patients with arteriovenous malformations (AVMs) were treated with linear accelerator-based stereotactic radiosurgery at the Odette Cancer Centre. The planning for these treatments was based on cerebral angiography and dynamic computed tomogram (CT) scanning. The OBT stereotactic frame used for these procedures is not magnetic resonance imaging (MRI) compatible. The MRI scanning was obtained in many cases and reviewed to achieve a better understanding of the AVM architecture, but the MRI scan was not directly utilized in the planning process.

Our results for the first 50 patients were published in 1997[7]. A prediction algorithm, the obliteration prediction index (OPI), was developed from this review and published in collaboration with the University of Sheffield[8]. The MRI scans of this same cohort of patients were used by Dr. Richard Farb in the development of real-time auto triggered MR angiography[9]. Dr. Yuri Andrade-Souza, then a fellow in the division of neurosurgery, analyzed the outcome for certain specific groups of patients. Those with deep, central arteriovenous malformations were shown to be less likely to have obliteration of their AVM and to be subject to more frequent complications[10]. Patients with arteriovenous malformations in the vicinity of the rolandic fissure who had successful obliteration of their AVM with radiosurgery had easier control of epileptic seizures than they did prior to treatment[11]. We examined two outcome prediction systems for the treatment of arteriovenous malformations and compared them to the OPI. Using the radiosurgery-based AVM score (RBAS), we compared our results to the gamma knife radiosurgery units at the University of Pittsburgh and at the Mayo Clinic[12]. The outcome in all three centers was found to be comparable. We analyzed our experience with pediatric patients[13] and looked at factors that influence patients' satisfaction[14]. We found that the most important factor was freedom from neurological deficit rather than successful obliteration. We also reviewed our experience

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Figure 2: Michael Schwartz and Peter O'Brien planning dynamic radiosurgery in the early years. (Note the tape reader for importing CT images, the three button mouse and 386 PC complete with Packard Bell monitor).

with those patients who required more than one radiosurgical treatment for obliteration of their AVM[15].

The Sunnybrook radiosurgery unit has been a participant in the University of Toronto Brain Vascular Malformation Study Group since its inception and many of our patients have been treated with more than one modality of treatment. We examined the effect of endovascular treatment of AVMs prior to radiosurgery[16]. We found that embolization reduced the probability of successful obliteration with radiosurgery. A physical experiment found that the reason for this worse outcome was attenuation of the dose of radiation to the AVM[17]. Two recent publications from the group have reported the effect of multimodality management on patients with posterior fossa and occipital lobe arteriovenous malformations[18,19].

At the present time, a report of the effect of angioarchitecture on outcome is in preparation. This latter report combines the Sunnybrook experience with the experience at the gamma knife unit at the Toronto Western Hospital where patients with arteriovenous malformations have been treated since September, 2005. We have found that high flow lesions with fistulous connections between the arterial and venous systems are less likely to occlude with radiosurgery than AVMs with glomerular architecture and slower flow.

Brain Metastases

Although the dynamic radiosurgery program was initiated with the intent of primarily offering treatment to patients with AVM's, the first patient to undergo radiosurgery on the 15th September 1988 was treated for a recurrent brain metastasis. At the time the idea of using such a sophisticated treatment in a group of patients commonly perceived to be pre-terminal was met with astonishment. Objections raised when the original radiosurgery protocol was submitted to the hospital REB included the concern that patients subjected to such high doses of radiation were bound to succumb shortly thereafter from uncontrolled nausea and vomiting. Of course such concerns were not supported by the published data. Brain metastases are often attractive radiosurgical targets given their near spherical shape. The clinicians advocating radiosurgery had made an attempt to identify the subset of patients with recurrent brain metastases most likely to benefit from additional treatment[20]. In 1988 there were no phase I data available to support the choice of an appropriate dose prescription. Consequently the original dose of radiation[21] was selected as falling in the middle of the range of doses that had been reported in the treatment of brain metastases at that time. There also remained the problem of how best to define the location of the prescribed dose. Since dynamic radiosurgery could be considered to be a form of moving beam or "arc" therapy it was decided to adopt the specification of dose at the centre of rotation as recommended for moving beam therapy in ICRU report 29 section 3.3.2. In the 1980's there were no generally accepted constraints for dose inhomogeneity across the target. Nevertheless, as ICRU report 29 recommended stating the maximum and minimum target absorbed doses if there was more than 10% variation in dose across the target, it was decided that coverage of the target by the 90% isodose surface represented a reasonable compromise between ICRU recommendations at the time and the need to exploit the steep radiation dose penumbra that was, after all, the main attraction of radiosurgery.

Once radiosurgery had been established in the treatment of brain metastases at the Odette Cancer Centre the investigators sought to obtain accreditation with the RTOG in order to participate in that group's proposed Phase I study of radiosurgery in the management of recurrent brain metastases. Following successful accreditation, the department's own protocol was placed on hold and between October 1992 and February 1994 and patients were entered on RTOG protocol 90-05[22]. In 1995 it was decided to capitalize on the introduction of high radiation dose rates and the capability to treat multiple and irregular targets. The original in-house radiosurgery protocol was modified for fractionated radiosurgery and the investigators parted company with the RTOG. Fractionation was seen as potentially the most promising means of improving the therapeutic ratio for radiosurgery in the treatment of malignant tumours. By then Brenner, Hall and colleagues had published a look-up table of fractionated radiosurgery regimens that were considered equivalent in terms of acute normal tissue tolerance to single dose prescriptions[23]. Fortunately that table included the single dose prescription which had been in use at the Odette Cancer Centre previously. REB approval was obtained and the first fractionated radiosurgical treatment for recurrent brain metastases was delivered at the Odette Cancer Centre on the 18th January 1996[24]. A three fraction protocol was introduced in 2003.

The treatment of recurrent brain metastases with dynamic radiosurgery was based on same day as treatment CT imaging using a diagnostic CT scanner. Although a dedicated wide bore planning CT unit was commissioned at the Odette Cancer Centre in 1996, patients continued to be imaged using diagnostic equipment. As was the case with other early adopters of highly conformal radiation treatments it became apparent that there could be disagreement between planners about target

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delineation. In addition, the methodology used to acquire images of brain metastases could influence the final selection of the radiosurgery plan. These concerns were confirmed in a prospective study which explored the effects of the dose of contrast agent and the timing of image acquisition[25]. These findings emphasized the importance of using a standardized protocol at all steps in the procedure in order to generate a valid prospective clinical database. Over the years this database has been used to explore the effects of fractionation[24] as well as local control rates in treating recurrent metastases at previously operated sites[26]. With continued follow-up it now known that fractioned dynamic radiosurgery can, in selected patients with recurrent brain metastases, provide ten year survivor rates that compares favourably with surgical resection at presentation[27].

Acoustic Neuromas and other pathologies

Radiosurgery was presented as an alternative to surgical resection for selected patients with acoustic neuromas from 1991 onwards. With the acquisition of a relocatable GTC stereotactic headframe in the mid 1990's however, patients were thereafter generally offered fractionated stereotactic radiotherapy rather than a single dose treatment[28]. In later years, the availability of a Gamma Knife® unit in Toronto provided an alternative source of radiosurgery. The last treatment for an acoustic neuroma with dynamic radiosurgery at the Odette Cancer Centre took place on 4th September 1997. Because of the clinicians' prevailing view that single dose treatments alone potentially offered an inferior therapeutic ratio compared to fractionated therapy[29], relatively few patients with primary malignant tumours, base of skull meningiomas or pituitary tumours underwent dynamic radiosurgery. The exceptions included patients for whom radiosurgery was provided as conformal "boost" as part of a fractionated radiotherapy prescription. As a result, the Odette Cancer Centre managed to avoid much of the morbidity experienced elsewhere for single dose treatments, especially in patients previously irradiated.

Conclusions

Radiosurgery was the first example of highly conformal external beam radiation therapy using a photon beam to be introduced in North America and remains in general use today. The Odette Cancer Centre was the second Canadian centre and the first in Ontario to commission and develop the technique further using a linear accelerator based system. By selecting Podgorsak's dynamic iteration, it was feasible to provide radiosurgery using equipment that remained capable of delivering conventional radiotherapy as well as fractionated radiosurgery during regular working hours without requiring a linear accelerator dedicated to radiosurgery alone. In the case of dynamic radiosurgery at the Odette Cancer Centre, staff likely had a more detailed understanding of the 'nuts and bolts' of the system than would be the case with a commercial turn key solution. On the downside, an opportunity to financially exploit the inhouse development of the anthropomorphic phantom Lucy was probably lost. The Odette Cancer Centre still offers radiosurgery using the Radionics 'X' Knife® system. Treatments take much longer because the beam flattener remains in place and require a step and shoot technique (multiple short arcs rather than a single continuous arc). Radiosurgery is delivered at the end of the working day and is capped at one procedure per day. Fractionated radiosurgery is no longer offered.

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