A PHYSICS PROTOCOL FOR INTERSTITIAL IRRADIATION OF BRAIN TUMORS USING Ir-192

A Thesis

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by

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ABSTRACT

There is agreement that gliomas in the vicinity of the third ventricle and medial temporal lobe and small infiltrating tumors in the hemispheres cannot be removed by surgical excision. Conventional external irradiation alone has proven unsatisfactory in the case of cerebral midline gliomas. In contrast to conventional irradiation, stereotaxic interstitial implantation with Ir-192 wires offers the objective of affecting a local tumor regression while the surrounding neuronal structures are protected from radiation necrosis. In cases of stereotaxic irradiation of small tumors, CT makes possible a precise determination of tumor volume and permits localization of the target point and therapy probe with a high degree of accuracy, thereby facilitating exact volume/dosage calculations and keeping penetration through healthy brain sections to a minimum. This protocol was undertaken to optimize the use of the Brown-Roberts-Wells Stereotaxic System to provide accurate parameters for implantation and computerized dosimetry. A skull phantom provided by the BRW system was used in conjunction with a GE 9800 CT scanner and a Capintec RT 110 treatment planning computer to generate the data and illustrate possible errors that may be encountered during an actual implantation and its related dose calculations.

INTRODUCTION

Intrinsic tumors of the central nervous system, the majority of which are gliomas, are peculiar because they rarely spread beyond the central nervous system (CNS). All gliomas are malignant, being locally invasive and complete removal is not usually possible. Despite advances that have been made in neurosurgery and radiotherapy, CNS tumors are associated with a high degree of mortality. Certain tumors, such as lower grade CNS tumors, are less likely to spread throughout the CNS. Posterior fossa tumors and spinal cord tumors are less likely to spread into the brain.

This predisposition to remain contained in the cerebrospinal area would imply that irradiation could successfully control these tumors. Despite high doses and large fields, external beam megavoltage irradiation has been ineffective in arresting glioblastoma multiforme. Glioblastoma is a general term for neoplasms containing neurological cells. The neurological cells are non-neuronal cells, such as supportive cells, and they include oligodendroglia, astrocytes, and ependymal cells. Glioblastoma multiforme is the most malignant of all gliomas, (primary brain tumors) it is a rapidly growing fatal tumor of the cerebral hemispheres and is composed of undifferentiated cells. The modern term for this category of tumor is astrocytoma grade 3 or 4 (4 being the most malignant).

The three major non-neural brain cells and their cancer:

1. Astrocytes - astrocytoma
2. Oligodendrocytes - oligodendroglioma
3. Ependyma - ependymoma

The astrocytes are the largest neuroglial cells and are star shaped. These have numerous outward radiating processes that end on blood vessels and are called perivascular feet. These perivascular feet cover most of the outer surface of the brain capillaries and contribute to the blood- brain-barrier that selectively restricts the passage of chemotherapeutic agents into the brain. The oligodendrocytes form sheaths around nerve fibres (axons) in the CNS only and not in the peripheral nervous system. The ependymal cells form the epithelial lining of the brain ventricles and central canal of the spinal canal. Tumors involving these cells tend to spread into the cerebrospinal fluid.

Gliomas make up 50% of all primary brain tumors and gliobastomas comprise over 50% of all gliomas. They occur most frequently between the ages of 40-60, and currently there are no known causes of human gliomas.

Treatment dose is determined by the tumor's histological type, radioresponsivness, anatomic site, and level of tolerance. Treatment fields are determined by the anatomic extent of the tumor and the potential areas of spread. Total tumor doses (external beam only) range from 5,000-7000 cGy in 6-8 weeks with daily fractions of 150-200 cGy each. Doses in excess of 7,000 cGy have not resulted in curability of grade IV tumors. Reduced fields are advised when the

whole brain doses reach 3,500-4000 cGy in children, 5000 cGy in young adults, and 5,000-6,000 cGy in adults.

Age is an important factor in the treatment of gliomas. The tumors may be more radiosensitive in very young children, but the tolerance levels are less; therefore, the therapeutic ratio is the same although smaller doses are used. Young children with malignant gliomas seem to exhibit a better survival than older persons with the same disease. More than 50% of patients with grade IV glioblastomas will not exceed a survival period of six months, and virtually all will not survive beyond two years. For lesser grade tumors the survival is better, with the median survival improvimg with an increase in dose from 5,000-7,000 cGy. See table I. In view of this, hyperthermia, intratumoral and intra-arterial chemotherapy (systemic chemotherapy having a limited effect), and interstitial irradiation have been suggested. Because radiation therapy has been the most effective modality against malignant brain tumors and because necrosis of normal brain has prevented the delivery of more than 6,000-7,000 cGy at conventional dose rates (200 cGy/min), interstitial irradiation becomes a logical treatment for brain tumors.

The advantage of interstitial irradiation is thus twofold: radiation delivered at low dose rates, often 1 cGy/minute, and intratumoral placement of sources with rapid reduction in dose in the proximity of normal tissue. Implying that low dose irradiation is advocated because the therapeutic ratio between neoplastic tissue and normal tissue is enhanced by low dose rate irradiation.

TABLE I

ESTIMATED SURVIVAL FOR THE MORE COMMON BRAIN TUMORS

	Percent Survival	
	5-year	10-year
Astrocytoma		
Grade I (cerebellar)	90 - 100	85 -100
Grade I (all sites)	50 - 60	30 - 40
Grade II	16 - 46	0 - 10
Grade IV	0 - 10	0 - 1
Ependymoma	40 - 55	35 - 45
Oligodendroglioma	50 - 80	20 - 30

Therapeutic doses of radiation at low dose rates can be delivered over several days with relative sparing of normal tissue, whereas to avoid necrosis of normal tissue the same total dose given at high dose rates must be divided into multiple fractions delivered over several weeks. Thus the reasons for the relative sparing of normal brain tissue with low dose rate implants can be summarized:

1. Normal tissue repairs sublethal damage more efficiently than neoplastic tissue.
2. There is a larger hypoxic fraction in tumor than in normal tissue, which makes reoxygenation more important in the tumor, and low dose rate irradiation requires a lower oxygen enhancement ratio than high dose rate irradiation to achieve the same cell kill.
3. Continuous irradiation causes synchronization of tumor cells in G_2 and M, which may also apply to normal tissue cells.

The potential uses of brachytherapy for the treatment of intracranial neoplasia were recognized as early as 1912 when Hirsch inserted a radium-loaded probe through the nasal cavity into the sella turcica of a patient with acromegaly. Hirsch continued to use the technique, and for over four decades had great success in treating pituitary adenomas and craniopharyngiomas[2]. Around 1950, neurosurgeons began using stereotactic techniques, (A 3-D arrangement of spatial coordinates to give an accurate reproduction of organs/sources/tumor), to implant sources into the brain. Stereotaxy was not new even then; the first head frame had been

designed by Horsley and Clarke in 1908. Although other frames were designed contemporarily, stereotactic surgery was not opted for until the work of Leksell in the late 1940s [2]. The Brown-Roberts-Wells stereotactic system is a modern version of the Leksell idea.

The BRW system used in conjunction with a CT scanner has revolutionized the use of interstitial brachytherapy for brain tumors. Until the introduction of the CT scanner, tumors were localized and doses were planned on the basis of films obtained by pneumoencephalography, angiography, and nuclear scanning. In addition to providing a more exact preoperative estimation of the size, consistency, and location of the tumor, the CT scan has made dosimetric calculations much more accurate. This accuracy is achieved when the stereotactic system (BRW) is used with a CT scanner to achieve precise implantation of the source probe and the coordinates obtained thereof which permit reliable dose calculations.

The BRW stereotaxic system was designed to be worn during head scanning in a CT body scanner. The frame produces reference points in each CT section that allow anatomic information from that section to be related to the frame. This approach eliminates the need to obtain sections which are equally spaced, mutually parallel, or parallel to the base of the frame. In addition it eliminates the necessity of centering the frame in the scanner gantry or restricting rotation of the frame with respect to the gantry. The most recent version of the BRW system utilizes a programmable

micro-computer (Epson FX 20) for data processing. This important modification creates a stereotaxic system which is dependent on the CT scanner only for identification of the target and the localizing rods. (Refer to fig., 1) All subsequent data processing can be performed away from the CT scan area, making this BRW system a versatile and efficient unit.

The accuracy and efficiency of this technique is directly related to the variables and parameters employed in all aspects of the procedure. In order to be able to optimize our methods each variable must be consistently defined, and the source from which the parameters are obtained should be verified and compared wih other sources. One variable is the clinical aspects of the disease, its histology, stage, and extent, based on which the referring physician and radiation oncologist can prescribe a dose and modality of treatment (refer to Table II). The other major variables include a precise delivery of the prescribed dose to the tumor volume. This is accomplished by the radiation physicist who can accurately determine the placement of the radioactive sources, and the computer dosimetry involved that can provide verification of the dose rate delivered.

It is the object of this thesis to accurately define the necessary protocol, using available information on the BRW stereotaxic system, the CT scanner, Ir-192 source data, computer algorithms, and actual computer dosimetry. The information available is reported in original form, followed by a discussion of

possible variation for the specific application for Ir-192 implants for brain tumors.

TABLE II

INDICATIONS FOR STEREOTACTIC INTERSTITIAL 4

IMPLANT OF BRAIN TUMORS

Malignant supratentorial glioma

Tumor size 6cm. or less average dimension

Karnofsky 70 or greater

Tumor stable or shows response to external radiation

Informed consent

MATERIALS AND METHODS

All procedures and measurements reported in this thesis were made utilizing the Brown-Roberts-Wells CT Stereotaxic System, General Electric 9800 CT Scanner at Our Lady of the Lake Regional Medical Center, and the Capintec RT 110 Treatment Planning Computer at the Mary Bird Perkins Cancer Center.

The BRW stereotaxic system consists of five functional components: a head ring, a localizing system, an arc guidance system (includes Epson FX computer), a phantom simulator, and a floor stand. These five components are operated as follows:

1. Head Ring: The head ring is fixed to the cranium by vertical graphite epoxy posts with plastic and steel pins. The graphite posts do not introduce artifacts, and the head ring is worn throughout the scanning and stereotaxic procedure.

2. Localizing system: The localizing system incorporates vertical and diagonal graphite rods, and is attached to the head ring during scanning. In each CT scan slice, the rods of the localizing system produce marks that indicate the spatial coordinate relationship of that section to the head ring. After completion of the scan, the localizing system is removed from the head ring, and the arc guidance system is installed.

3. Arc Guidance System: This system consists of a base ring, a rotatable ring, and a perpendicular arc (Fig. 3). Contained within the base ring are three mounting studs which unidirectionally fix the base ring accurately to the head ring. The rotatable ring surrounds the base ring and allows the arc to undergo a 360^{o}

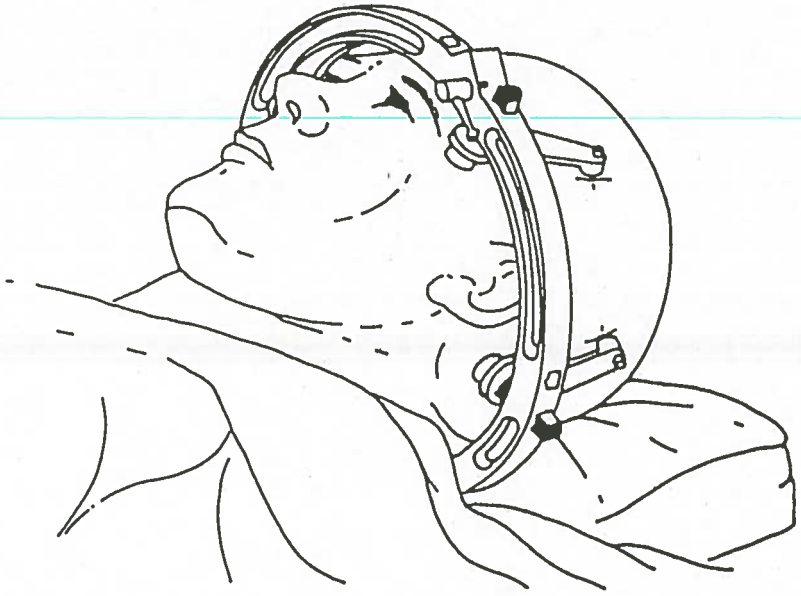


FIGURE 1. Head holder ring affixed to the patient

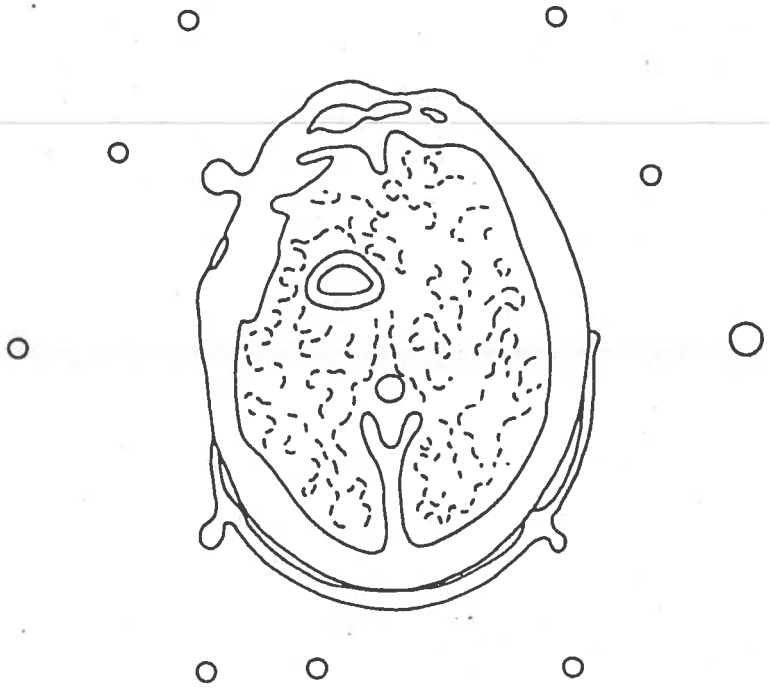


FIGURE 2. Scan and localizing reference points

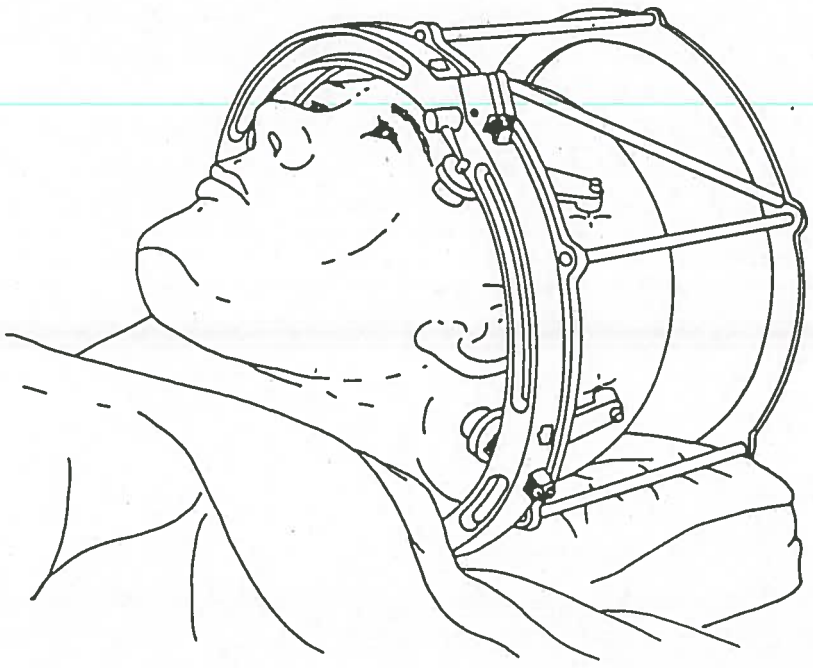
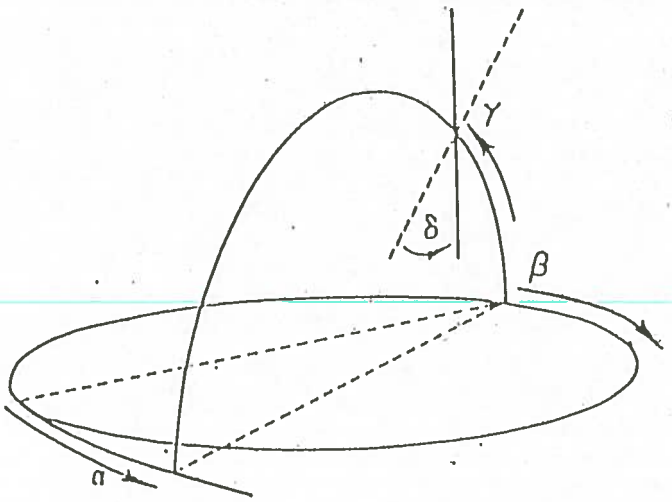


FIGURE 3. Head holder and localizing rods.

rotation, attached to this rotatable ring is the perpendicular arc. The rotatable ring also contains a slot which permits the perpendicular arc to pivot through a second arc of 30^{o}. Located upon the perpendicular arc is a radial slide which moves through 180^{o} along the archway of the perpendicular arc. Additionally the radial slide contains a sleeve which pivots about the axis pin of the arc. This sleeve holds various guidance and surgical instruments. The ability to combine the 360^{o} base ring rotation and the 30^{o} pivot rotation of the arc with the 180^{o} movement of the slide on the arc and the 90^{o} pivot of the sleeve is the unique improvement of the BRW system (Refer to Fig. 4). This combination of angles are computed by the portable micro computer which generates the coordinates of the entry and target points within the sphere of the guidance arc. The geometry of this system is explained in combination with the computer algorithm used for calculations of the coordinates.

4. Phantom Simulator: During the initial developments of this system, the accuracy of the target coordinates was determined postoperatively with a CT scan showing a spot of air density at the point of biopsy. With this method a problem arises if the lesion was too firm for the entrance of the biopsy probe or if the lesion was cystic which would considerably displace the air bubble from the original target. The BRW system for which this protocol was developed circumvented this problem by using the phantom simulator. The phantom consists of a base ring and a moveable pointed tip, called the 'dummypoint'. This dummy point can be be oriented with



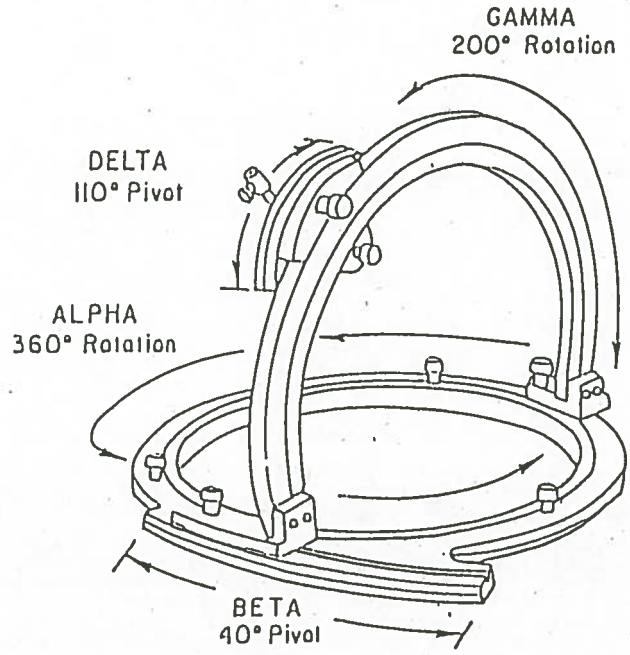


FIGURE 4. Angular movements of the BRW system

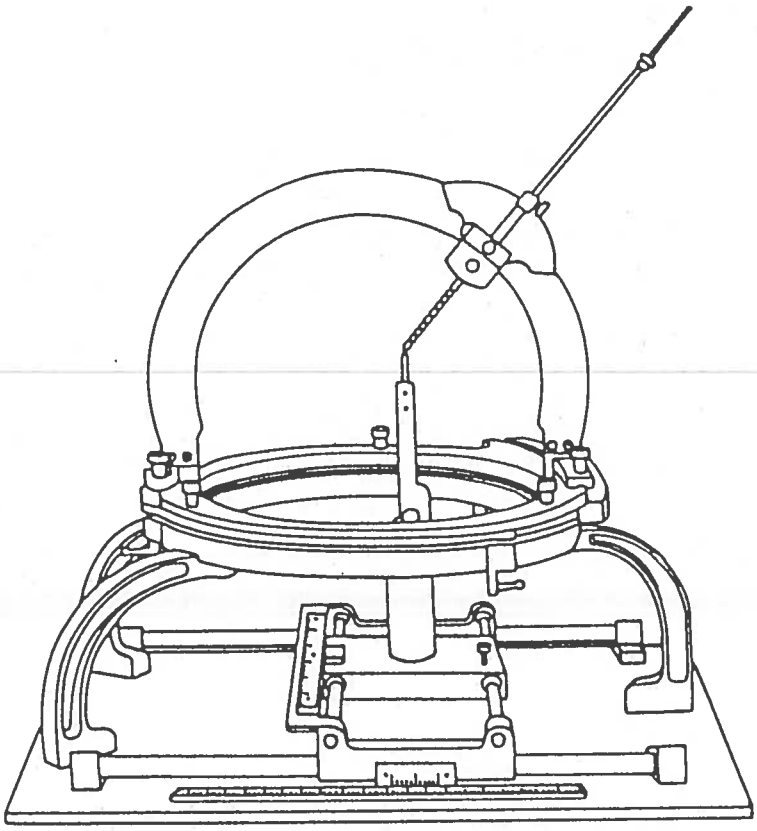


FIGURE 5. Phantom simulator

the appropriate x, y, and z coordinates which are etablished from the computer output for the coordinates of the target or entry point chosen from the arc guidance system. After entry of the localizing data obtained from the scan (tumor coordinates) and the entry point coordinates obtained from the phantom simulator, the computer calculates the frame settings (angles) and the distance to the target from the entry point. After this is completed, the arc system is placed on the base ring of the phantom. Thus placed the arc system will have the same relationship to the dummy point as the anatomical entry point or target has to the head ring fixed to the patient. This enables one to check the accuracy, direction, and depth of the dummy point before attempting to reach the anatomical target in the patient.

5. Floor Stand: This allows precision positioning of the head for standard functional neurosurgical targets obtained by ventriculography. Verniers allow movement of the base ring in vertical and horizontal directions. By proper of coupling these axes one can define a vertical anterior-posterior line through the midline of the brain. Additionally the floor stand has standard X-ray film cassete holders attached, such that targets can be identified intraoperatively with standard ventriculography.

The software for the BRW system computer utilizes data from the x and y coordinates of the central CT pixel of the nine localizing rods and the targets identified on the CT scan. Using mathematical manipulation of matrices and vector addition the two-dimensional coordinates are transformed to three-dimensional coordinates (x, y,

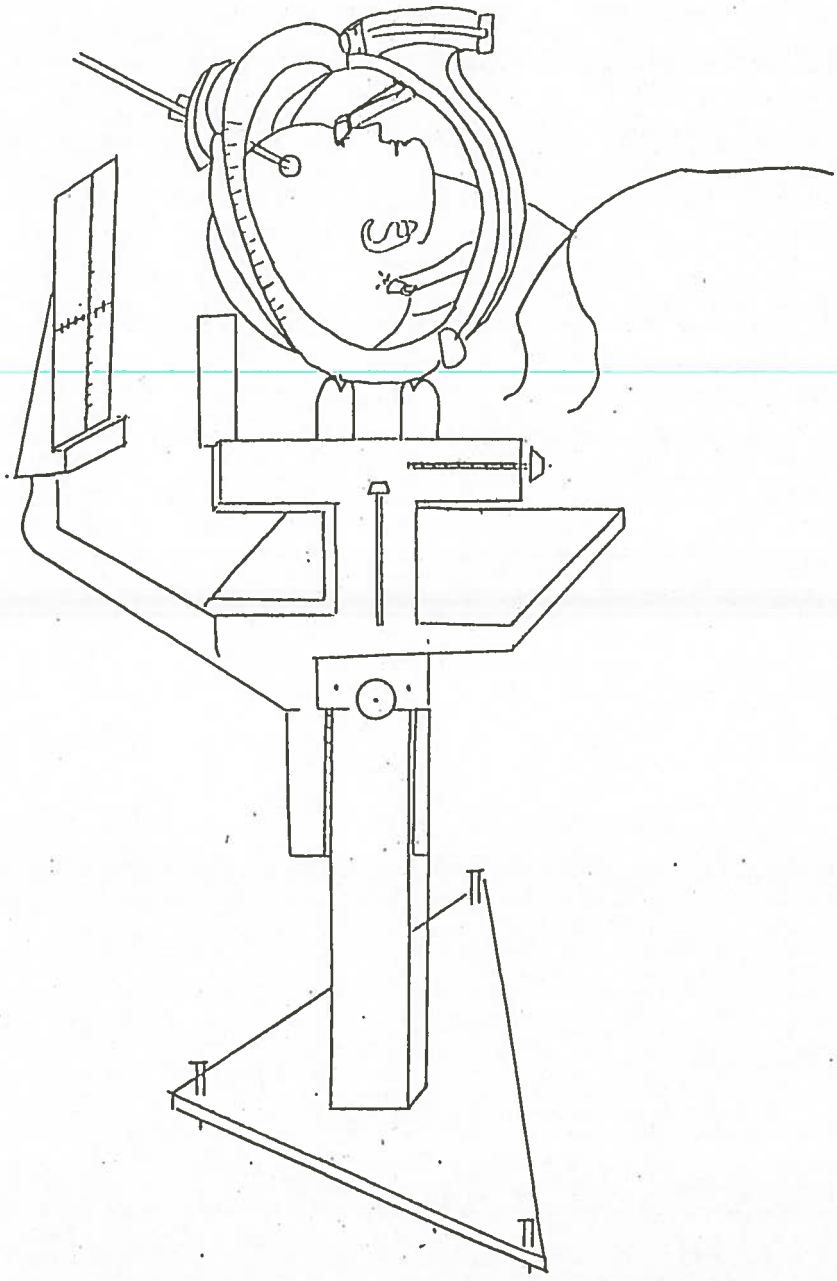


FIGURE 6. Floor stand

and z), relating the position of the localizing rods and the targets to a plane with its vertical height referenced to the base ring which is fixed only to the skull. Once the x, y, and z coordinates of the target are computed, the design of the arc system allows a course and distance to be plotted between any two points in space. Generally, these two points represent the entry point on the skull and the target. The software used on the Epson FX 20 does allow for multiple entry and target points. (A detailed explanation of software alogorithm follows later in this protocol).

At this stage it is advised that the actual operators manual for the BRW system be referred to for sterilization procedure and the restrictions that apply. (The manual is supplied along with a video tape for care and instructions. It cannot be over emphasized that the manufacturers procedure for sterilization of the components be strictly adhered to. Improper use of sterilization techniques could result seizure of vernier precision components, and possible destruction of the carbon fiber components of the BRW system.

At the begining of the implant procedure the head ring is fixed to the skull to provide a constant reference plane. The graphite localizing system is attached to the base ring, and the patient is scanned. Note that the angled graphite rods will appear as elipses on the CT scan slices (refer to Fig. 7). As mentioned previously these points in each scan allow anatomic information from that section to be referenced with respect to the localizing rods. The radiotherapist and neurosurgeon upon visualization of the tumor geometry can determine the length and number of sources. The x and

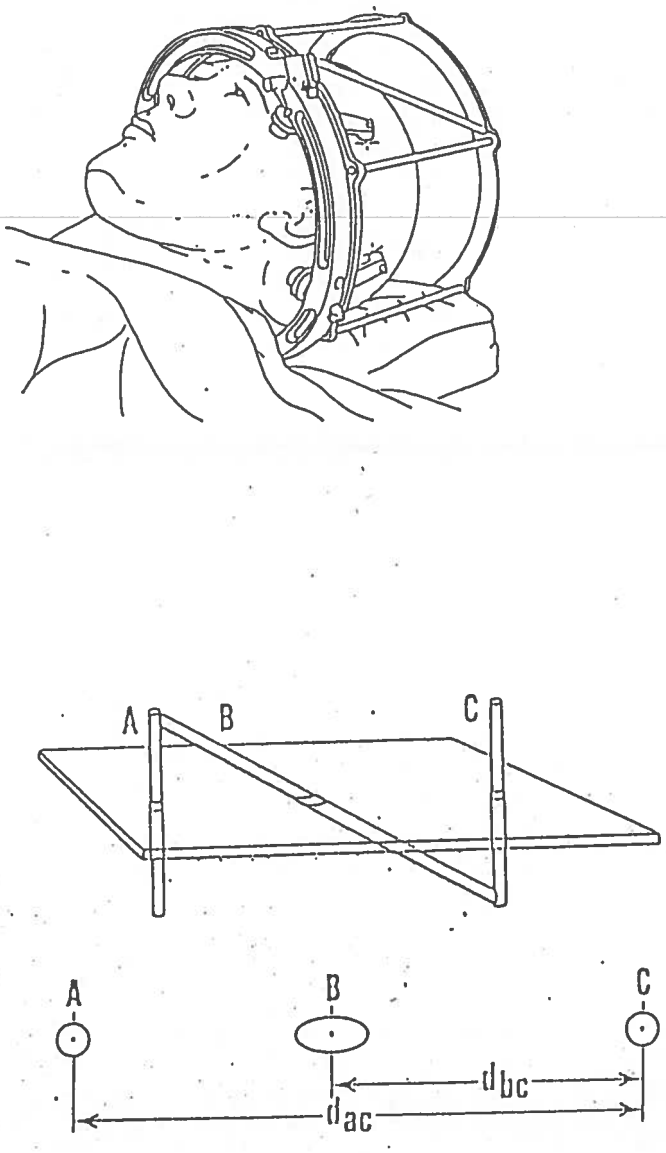


FIGURE 7. Localizer ring with angled rods yielding elliptical reference points.

y coordinates are read from the scanner console, the tip and end of each source placement must be obtained using precise cursor control (GE 98000 = ball type cursor, Siemens = digitizer pen), and entered into the portable computer. It is advised that a system of obtaining hard copies of the coordinates as they appear on the scanner screen be employed to eliminate any transcription error and to provide a permanent record on paper. (This can be achieved by using a Polaroid video graphics copier, or if a system printer is interfaced with the CT scanner, as provided by the manufacturer.

The localizing ring is now removed and the patient is prepared for the operating room. The patient is taken to the operating room with the head ring on as it was affixed before the CT scans. This ring must not be moved until the entire procedure is over. The slightest movement of the head ring with respect to the skull would result in an in consistent reference plane for implant entry, and the entire series of scans must be repeated as a set.

The coordinates obtained from the scans are entered into the portable computer (Epson FX 20). Based on this information appropriate arc guidance settings (alpha, beta, gamma & delta) are calculated by the computer to permit accurate catheter placement within the tumor through a desired entry point on the skull (refer to fig 4). The accuracy of these coordinates should be verified using the phantom simulator. This is done by manually adjusting the phantom verniers to the data provided by the computer. Next the arc guidance system is placed on the phantom simulator and its angles and vernier scales are adjusted to the same computer output

coordinates. Upon completion of all adjustments if the pointer on the phantom simulator exactly coincides with the probe on the arc guidance system, the placement of the catheters in the patient's skull will be reproduced with the same accuracy (refer to Fig 5).

Thus having eliminated the possiblity of incorrect implantation due to mechanical errors, the patient is readied for the actual procedure. The floor stand is used for positioning the patient on the operating table (refer to Fig. 6). The arc guidance system is now affixed to the head ring on the patient (refer to Fig.8). The guidance system is adjusted according to the previously computed coordinates, and entry to the skull is achieved with a closed technique using a twist drill. Following each drill opening the catheter for that particular set of coordinates is inserted. Upon completion of the appropriate suturing tecnique and the recovery procedure, the patient is scanned again (CT) to determine correct placement of the catheters.

The catheters are now loaded with 'dummy' wires (stainless steel wires of the same diameter and length as the ^{192}Ir wires) and mutually perpendicular radiographs are obtained to ensure correct placement of the sources within the catheters. The source length and orientation obtained from the mutually perpendicular radiographs should be compared with the length and orientation obtained from the CT computed data. Any error detected should not exceed 4%. The dummy wires are then replaced by active lengths of the ^{192}Ir wire. Following this, treatment planning dosimetery is implemented to determine the dosage to the tumor volume. Based on this dosage, in

cGy/hour, the radiotherapist can prescribe the amount of total time for the implant.

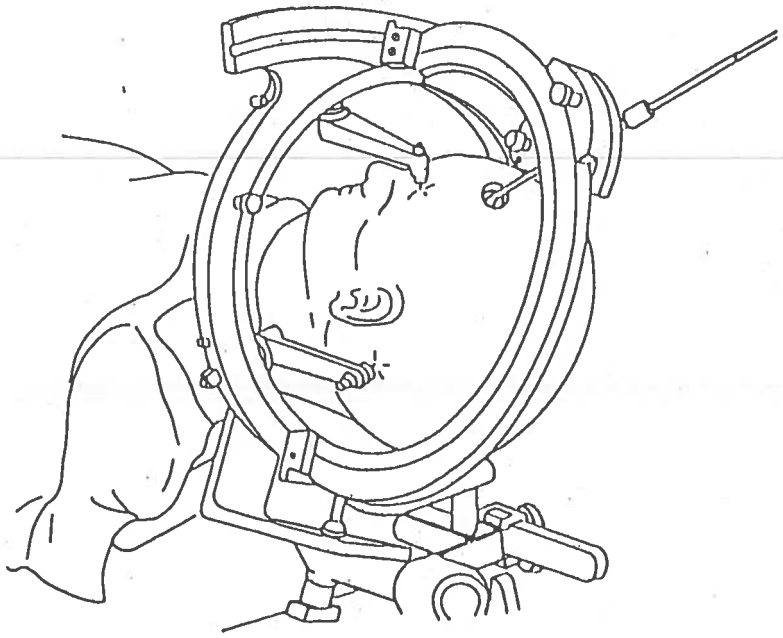


FIGURE 8. Arc guidance system affixed to head ring on the patient.

BIBLIOGRAPHY

American Cancer Society. Clinical Oncology. ACS. Press, 1983.

Agnew Jeanne. Linear Algebra with Applications. Monterey Ca: Wadsworth Pub Co., 1978.

Attix, Frank H. Radiation Dosimetry. New York: Academic Press, 1969.

Bernstein, Mark. "Interstitial Irradiation of Brain Tumors: A Review." Neurosurgery, 9, (1981), 741-750.

Bouchard, Jean. Radiation Therapy of Tumors and Diseases of the Nervous System. Philadelphia: Lea and Febiger, 1966.

Bouzaglou, Armand. "Stereotactic Interstitial Implantation of Brain Tumors." Endocurietherapy/Hyperthermia Oncology, I (1985), 99-112.

Brown, R A. "A Computerized tomography-computer graphics approach to stereotaxic localization." J. Neurosurgery., 50, (1979), 715-720.

Brown, R A. "A Stereotactic Head Frame for use with CT Body Scanners". Invest. Radiol., 14, (1979), 300.

Brown, Russell A. "Stereotaxic Frame and Computer Software for CT-Directed Neurosurgical Localization." Invest. Radiol., 15, (1980), 308-312.

Capintec Inc. Cap-Plan: Linear Implants. Ramsey NJ: 1981.

Chang, C H. "Comparison of Postoperative radiotherapy and Combined Postoperative Chemotherapy in the Multidisciplinary Management of Malignant Gliomas." Cancer, 52, (1983), 997-1007.

Ching, Clifton L. "Dose Inhomogeniety in Interstitial Implants using I-125 Seeds." Int. J. Radiation Oncology Biol. Phys., 5, (1979), 419-425.

Csanda, Andre. "Early and Late Brain Edema following High Dose Irradiation." INSERM Symposium, 12 (1979), 137-147.

Findley, David. "Routine Quality Control of Ir-192 Sources: Results of 46 Months of Surveillance." Int. J. Radiation Oncology Biol. Phys., 11 (1985), 1727-1730.

Fletcher, Glibert H. Textbook of Radiotherapy. Philadelphia: Lea and Febiger, 1978.

Gutin, Phillip H. "Permanent and Removable Implants for the Brachytherapy of Brain Tumors." Int. J. Radiation Oncology Biol. Phys., 7, (1981), 1371-1381.

Heilbrun, M P., Roberts, T S., Apuzzo, M.L.J., et al. "Preliminary Experience with Brown-Roberts-Wells (BRW) Computerized Tomographic Stereotaxic Frame". J. Neurosurgery, 1982. (Submitted in July).

Hilaris, Basil S. A Manual for Brachytherapy. New York: National Cancer Institute Press, 1970.

Johns, Harold Elford., et al. The Physics of Radiology. Springfield: Charles C. Thomas, 1983.

Johnson, Sheldon A. MD. (personal communication 1986).

Khrishnaswamy, V. "Dose Distributions about ^{137}Cs Sources in Tissue." Radiology, 105, (1972), 181-184.

Kline, Robert W. "Computer Dosimetry of Ir-192 Wire." Medical Physics, May (1985), 634-637.

Kubricht, William S. M.M.Sc. (personal communication, 1986).

Landry, Danny. PhD. (personal communication, 1986).

MacKay, Alexander R. "Computed Tomography-directed Stereotaxy for Biopsy and Interstitial Irradiation of Brain Tumors: Technical Note." Neurosurgery, 11, (1982), 38-42.

Malhotra, O P. Pure Mathematics. New Delhi: S. Chand & Co., 1976.

Marinello, G. "Comparitive Dosimetry between Iridium Wires and Seed Ribbons." Int. J. Radaition Oncology Biol. Phys., 11 (1985), 1733-1739.

Maruyama, Yosh. "Implantation of Brain Tumors with Cf-252." Therapeutic Radiology, 152, (1984), 177-181.

Mesiberger, Leo. "The Effective Attenuation in Water of the Gamma Rays of Gold 198, Iridium 192, Cesium 137, Radium 226, and Cobalt 60." Radiology, 90, (1968), 953-957.

Mullan, Sean. Essentials of Neurosurgery. New York: Springer Publishing Co., 1968.

Mundinger, F. "Treatment of Small Cerebral Gliomas with CT-Aided Stereotaxic Curietherapy." Neuroradiology, 16, (1978), 564-567.

Murphy, D J. "A ^{192}Ir Nomogram System for Single Plane Implants." Int. J. Radiation Oncology Biol. Phys., 12, (1986), 267-270.

Ostertag, B. "Radiation Effects of Iridium-192 Implants in the Cat Brain." Nuclear-Medizin, 21 (1982), 99-105.

Paul, J M. "Uniformity of Dose Distributipn in Interstitial Implants." Endocurietherapy/Hyperthermia Oncology, 2 (1986), 107-118.

Quimby, Edith H. Dosage Calculations in Radiation Therapy. New York: Columbia University Press.

Rockwell, Theodore. Reactor Shielding Design Manual. United States Atomic Energy Commision. 1958.

Rossman, Kent J. "Stereotactic Afterloading Iridium Implants in Treatment of High-Grade Astrocytomas."

Scanlon, Paul W. "Radiotherapy of Intracranial Astrocytomas: Analysis of 417 Cases Treated form 1960 through 1969." Neurosurgery, 5, (1979), 301-308

Shalek, Robert J. Implant Dosimetry. Houston: Unive. of Texas Press, 1967.

Subramania, Jayaraman. "An Overview of Errors in Line Source Dosimetry for Gamma-Ray Brachytherapy." Medical Physics, May (1983), 871-875.

Tuma, Jan J. Engineering Mathematics Handbook. New York: McGraw Hill, 1979.

Walker, Michael. "An Analysis of dose-Effect Relationship in the Radiotherapy of Malignant Gliomas." Int. J. radaition Oncology Biol. Phys., 5 (1979), 1725-1731.

Waltregny, Alain. "Experimental Interstitial Irradiation (Iridium -192) EEG Aspects." INSERM Symposium, 12 (1979), 131-135.

TABLE X

EFFECTS OF ENCASEMENT ON IRIDIUM WIRE

Length of wire = 1cm (0.436mg Eq ^{226}Ra)

	Unencapsulated	Vinyl (0.01mm)	Vinyl + Steel (0.02mm)
	cpm	cpm	cpm
1.	148,647	147,629	146,613
2.	147,511	148,623	146,421
3.	149,771	148,339	146,775
AVG	148,643	148,197	146,603

99.67 % transmission through vinyl & 98.63 % through vinyl + steel

cpm through 0.5 cm Pb = 13,185, 8.87 % transmission through 0.5cm Pb

All readings with GM tube and counter. Source at 1 cm from detector. Background cpm (19) corrected in all readings.