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HEAVY CHARGED-PARTICLE STEREOTACTIC RADIOSURGERY: CEREBRAL ANGIOGRAPHY AND CT IN THE TREATMENT OF INTRACRANIAL VASCULAR MALFORMATIONS[1]

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Abstract

A method is described for stereotactic localization of intracranial arteriovenous malformations (AVM) and for calculating treatment plans for heavy charged-particle Bragg peak radiosurgery. A stereotactic frame and head immobilization system is used to correlate the images of multivessel cerebral angiography and computed tomography. The AVM is imaged by angiography, and the frame provides the stereotactic coördinates for transfer of this target to CT images for the calculation of treatment plans. The CT data are used to calculate the residual ranges and compensation for the charged-particle beam required for each treatment port. Three-dimensional coordinates for the patient positioner are calculated, and stereotactic radiosurgery is performed. Verification of the accuracy of the stereotactic postitioning is obtained with computer-generated overlays of the vascular malformation, stereotactic fiducial markers, and bony landmarks on orthogonal radiographs immediately prior to treatment. Using these procedures, the accuracy of the repositioning of the patient at each of a series of imaging and treatment procedures is typically within 1 mm in each of three orthogonal planes.

Key Words: radiosurgery, AVM, stereotaxis, charged-particles, angiography, CT

INTRODUCTION

At the Lawrence Berkeley Laboratory (LBL), heavy charged-particle beams are used for the stereotactic radiosurgical treatment of intracranial vascular disorders, mainly arteriovenous malformations (AVMs) [4] [5] [6]. Beams of monoenergetic heavy charged-particles are characterized by the deposition of a large fraction of their energy at the end of their range–the Bragg ionization peak– and by the small angle of lateral scattering. The sharp lateral and distal edges of these beams and the increased dose in the Bragg peak are physical characterisistics which provide very precise means for localizing the dose within the target lesion while sparing adjacent, normal tissues [11] [12]. These favorable dose-distribution characteristics of charged-particle beams provide a great deal of flexibility in designing optimal treatment plans for intracranial lesions so that critical structures within the brain, such as the brainstem, are protected. At the same time, the accurate placement of such well-localized dose distributions requires very accurate imaging and treatment planning.

Treatment planning of intracranial vascular lesions using charged-particles presents a number of unique problems, when compared with conventional radiotherapy treatment planning. The size, shape, and location of the vascular lesion are determined most precisely by cerebral angiography; however, angiography does not determine the relationships of the AVM to surrounding brain structures, nor does it provide information to calculate the range of charged-particle beams. Computed tomography (CT) can be used for range calculations and to demonstrate relationships to adjacent anatomic structures, but does not delineate the AVMs precisely. Contrast-enhanced CT often highlights the AVM, but feeding and draining vessels and the nidus containing the abnormal vascular shunts are not well differentiated from one another.

The essential requirement of stereotaxis is to locate the target precisely in three dimensions, and to direct probes to the target from any direction [2]. Stereotactic localization is used in performing biopsies, surgery, and radiation therapy for brain lesions. Stereotactic irradiation has been developed for many different pathological conditions within the brain, including, for example, tumors, vascular abnormalities, and Parkinson's disease, and for a number of different radiation sources, e.g. gamma rays, x-rays and accelerated charged-particles [1] [4] [5] [6] [7] [8] [9] [14] [15] [16] [17] [18] [19]. Due to the energy deposition characteristics of photons, a large number of convergent ports or several continuous arcs are required in order to achieve adequate dose deposition centered on the target; this results in a large volume of normal brain tissue being exposed to radiation. The application of charged particles to the treatment of intracranial lesions provides the opportunity to tailor the dose distribution to the target while minimizing the volume of normal tissue irradiated and the integral dose to the remainder of the brain. It is possible to achieve excellent dose distributions using three to five ports (or more if desired). This requirement for relatively few treatment ports of stereotactically-directed beams of heavy charged-particles allows the capability of selecting those ports that spare completely certain critical brain structures.

In order to utilize fully the physical characteristics of the charged-particle beams for the safe and effective treatment of selected intracranial vascular lesions, the vascular target volume must be precisely defined and located within a reproducible 3-dimensional reference frame, the physical properties of the materials to be traversed by the beam must be accurately determined, and the patient must be positioned precisely with respect to the beam. The treatment planning procedure consists of a series of stages involving sequential stereotactic neuroradiological imaging studies, computer correlations among the different types of radiological imaging information, calculations of the dose distributions, and application of the output of these steps to the radiosurgical procedure.

Previous reports have described the stereotactic frame and head immobilization system that is used for all neuroradiological studies and the radiosurgical treatment [13] and the stereotactic apparatus for patient positioning during treatment [10]. In this report, we describe the imaging methods and computer-based calculations that are used to localize the intracranial target and to calculate dose distributions, and the methods by which this information and the computational results are applied to the radiosurgical procedure.

METHODS AND MATERIALS

Neuroradiological Imaging Procedures. The stereotactic frame and head immobilizer [13] have been constructed so that they are easily removed from and reapplied to the patient, i.e. the frame is not attached by means of studs or otherwise fixed to the bones of the skull. All neuroradiological procedures are performed with the patient held by the head immobilizer in the same position within the frame coordinate system, even though some days may elapse between studies. A CT study without contrast-enhancement is performed at the LBL EMI 7070 CT scanner for two reasons. First, the calibrations of the x-ray attenuation coefficients measured by CT to the energy loss measurements of the heavy-charged particles have been performed using this particular scanner. Although data from other scanners can be used, errors are minimized by using the same scanner and periodically checking on the measured CT values. Second, a noncontrast scan avoids errors in calculating particle ranges that can be introduced by high concentrations of iodine-containing contrast medium.

Prior to catheterization for cerebral angiography, scout films are taken to optimize patient/couch position, field size and radiographic exposure parameters. Based on information from previous diagnostic radiological studies, selected vessels are chosen that will characterize completely the arterial feeders, shunts, and regional blood flow through the AVM, although examination of the results of the stereotactic angiographic study can modify those choices. For each vessel complex studied, AP and lateral film sequences are taken of the flow of the contrast bolus through the AVM, with care taken to visualize completely the arterial-phase components. The AP and lateral film sequences are orthogonal, and the orientations of the X-ray tube and film relative to the frame are set up to reproduce as closely as possible the initial alignment of the patient at the accelerator treatment facility. Deviations from these positions are corrected in the computer correlation procedure described below.

A contrast-enhanced CT study is performed immediately following the angiographic procedure to help identify the distribution of the AVM compartments, the nidus, and the relationships to the critical neuroanatomical structures within the brain, and to determine the extent of neuropathological change prior to radiosurgery. This is used to guide the selection of entry portals for treatment and the potential dose distribution within adjacent CNS tissues.

Figure 1 illustrates lateral and AP projections of a stereotactic cerebral angiogram, carried out with the patient immobilized in the stereotactic frame. The contrast material is readily demonstrated and the abnormal vasculature of the AVM is localized within the brain. The vessels to be included within the radiosurgical treatment volume are outlined on both views. The fiducial markers are located on the stereotactic frame and define the reference frame. The fiducial markers on the sideplates are seen on the lateral projection; they are arranged as two sets of X's, one located on the left and one on the right of the patient's head. In the AP projection, the two sets of markers (short horizontal and vertical lines) are located on the frame anterior to and posterior to the patient's head. These fiducial markers are also readily identified on the axial CT scans of the patient taken in the frame immobilization system (Figure 2); they are visualized as two dots projecting from the edge of the sideplate on the patient's right side. The angiographic films and contrast CT images are used to outline the volume to be treated with the particle beam radiation. The clinical history of the disease, extent of neurologic deficit, patterns and volume of regional cerebral blood flow, and location of the diseased vessels in relation to critical areas of healthy tissue are all factors used in deciding upon the volume to be irradiated, and the directions of the beampaths.

Magnetic resonance imaging (MRI) scans are performed on all patients unless contraindicated. We have fabricated a second identical stereotactic frame except that the fiducial markers and all structural components are non-metallic. Stereotactic MRI has proven invaluable for localization of angiographically-occult AVMs. The use of stereotactic MRI in treament planning and neuroradiological imaging correlations is discussed in a separate paper (Phillips et al, in preparation).

Correlation Between Angiographic and CT Images. The stereotactic cerebral angiographic films provide the information on the size, shape and location of the AVM target to be treated, while the CT images provide detailed information regarding the physical characteristics of the tissues on a pixel-by-pixel basis, as well as information on the correlative neuroanatomy of the head and brain. A computer program is used to transfer the target outline from the angiographic films to the CT data in order to calculate the charged-particle treatment beam parameters. Using a digitizing pad, the reference markers are digitized in an established sequence, so that each may be correlated with its precise spatial coordinates on the frame. The target outline is then digitized, followed by digitization of prominent midplane bony landmarks, such as the anterior and posterior clinoid processes, the sella turcica, the frontal plates, the clivus, the inner table, and the internal occipital protuberance. This sequence of digitizations is carried out first for the lateral view, and then for the AP view.

Using geometric optics, the digitization program uses the positions of the fiducial markers as they appear on the radiographs in conjunction with their known positions on the stereotactic frame to calculate the relevant radiological imaging parameters. These parameters are the focus-to-film distance, the focus-to-object distance, and the position and angle of the central ray relative to the frame. Since the intracranial AVM target is identified on both the lateral and AP projections of the angiogram, the location of the target within the frame can be calculated, with magnification and angular orientation corrections being made simultaneously.

The noncontrast CT images are loaded onto the computer, and the coordinates of the ends of two of the wire reference markers (row, column, and CT slice number) are obtained. This information, along with the slice thickness (3 mm) and pixel size (0.78 mm), is used by the program to map each point of the digitized target contours onto the CT image data set. At each level of the angiographic image (along the cranial-caudal axis) that corresponds to a CT slice, the dimensions of the AP and lateral projections of the AVM are used as the major and minor axes of an ellipse. Thus, the AVM target volume in the CT image set is a series of ellipses of thickness equal to the slice separation, stacked one on top of the other. Occasionally, pronounced deviations of the true shape of the lesion from such elliptical contours are evident from CT or MRI images, such as when the AVM extends around a ventricle or closely follows the edge of some readily imaged structure within the brain, e.g. the corpus callosum. In these cases, the CT target contours are redrawn on the CT images to conform to the actual target geometry. Figure 2 illustrates the angiography-derived CT contours. The CT data and the the contours have been reformatted to provide views through the lesion in the coronal and sagittal planes. Comparison of the relative size, shape and location of the target volume on the CT images can be made with the target volume defined on the angiography films in Figure 1. In the upper left panel, the axial view, the two side plates are visible with the right side wires seen as two bright dots. The trapezoidal shapes at the bottom are the graphite support rods of the stereotactic frame. The thermoplastic mask holding the patient's head is visible around the outer contour of the head. The area of bright signal on the upper right corner of the coronal section is part of the flange holding together the front and back halves of the patient mask.

When information from the contrast-enhanced CT images is needed for treatment planning or localization purposes, for example in the case of angiographically-occult (cryptic) AVMs, mapping targets from one set of CT images to the other is accomplished in a similar manner.

Treatment Planning Calculations. The contours of the AVM target derived from the angiographic films and transferred to the noncontrast CT images are the basis for the stereotactic treatment planning procedure. The CT data and target contours are used to calculate the residual range and compensation for each treatment beamport. The helium-ion beam is extracted from the accelerator at a fixed energy (at the 184-inch Synchrocyclotron, 230 MeV/amu for a water-equivalent range of 32 cm; at the Bevatron, 165 MeV/amu for a water-equivalent range of 18 cm). The water-equivalent pathlength through the head is calculated for each beamport, and the amount of absorber necessary to place the distal edge of the spread-out Bragg peak at the distal edge of the lesion is obtained [3]. Inhomogeneities or irregularities in the tissue to be traversed or in the shape of the lesion are accounted for by the use of compensators, which adjust the placement of the distal portion of the peak to the lesion boundaries across the profile of the beam. The width of the spread-out Bragg peak for each beamport is calculated to provide maximal coverage of the lesion on all slices. Beam-shaping apertures, fabricated from a dense metal alloy, are designed to match the beam shape with the orthogonal angiographic projections of the AVM.

Patient Localization. The digitized angiographic images are also used to calculate the initial position of the patient positioning couch, and provide the basis of computer-generated overlays of the frame, target and midplane bony landmarks. The stereotactic radiosurgical method at LBL relies on the precise location of the target at the intersection of the charged particle beam and the isocenter of the specially-designed patient positioning system, ISAH [10]. When the stereotactic frame is mounted on ISAH, a known set of coordinates positions the center of the frame at the isocenter ("frame zero"). The computer program calculates the offset of the target from frame center and, using the ISAH coordinate set for "frame zero", calculates the coordinates that will place the center of the target at isocenter for beam delivery.

Final alignment of the patient (and thus, the intracranial AVM)is assured by means of lateral and AP x-ray films and the computer-generated overlay of the frame, skull and AVM target. Figure 3 illustrates the lateral and AP views of a computer-generated overlay, with stereotactic frame fiducial markers, AVM treatment target, and midplane landmarks clearly identifiable. The upper left and right panels demonstrate the relative orientation of these elements when the frame center is located at "zero postion", e.g., ISAH isocenter (notice the perfect alignment of the fiducial markers on the lateral view). The lower left and right panels demonstrate the relative orientations when the center of the target volume is located at ISAH isocenter ("treatment position"). The position of isocenter is denoted by the cross; it is located at the intersection of the fiducials in the "zero" view, and at the center of the target on the "treatment" view. The different geometry is clearly visible when viewing the fiducial markers; the changes in the relative positions of the midplane landmarks and target contour are not so obvious, but, nevertheless, are present in the image. The two separate target contours represent the contour both magnified (outer) and unmagnified (inner). These contours correspond to, respectively, the image of the AVM on the angiogram and the actual size of the beam-shaping aperture.

Once the neuroradiological imaging parameters, derived from the cerebral angiograms, have been used to obtain the spatial relationships of the AVM target and anatomical landmarks in relation to the stereotactic frame, the program can reconstruct the size and relative positions of these objects for any other set of imaging parameters. The stereotactic radiosurgical procedure is carried out with the center of the target (AVM) volume at the isocenter of the patient positoner. This fixes the positions of the AVM target, x-ray tube, and x-ray film relative to one another. Depending on the selection of ports to be used, the treatment alignment films will be right or left lateral, and AP or PA projections. This fixes the orientation of the AVM target to the midplane landmarks and the fiducial markers on the stereotactic frame. For the desired treatment geometry, the program calculates the projections and magnifications of the markers, AVM target and anatomical landmarks and produces a computer-generated image of all of them.

An x-ray tube, mounted on ISAH, is aligned so that the central ray of the x-ray beam, horizontal with respect to the room, is coaxial with the central axis of the charged-particle beamline and passes through the isocenter of ISAH. A set of cross-hairs that are aligned with the beam is placed opposite the ISAH isocenter from the tube and in front of a film cassette. A similar arrangement obtains for the vertical direction; in this case the central ray is not coaxial with the axis of the beam line, but intersects it and is perpendicular to it, i.e. it is coaxial with the vertical rotation axis.

Initially, when aligning the patient, the image of the cross-hairs on the localization radiograph is compared with the computer-generated cross-hair image, and corrections are made to the patient's position so that when the radiographic landmarks are aligned with the computer overlay, the two sets of crosshairs are coincident. When this coincidence is achieved, a final localization radiograph is obtained, and an image of the beam-shaping aperture is obtained superimposed on the skull radiograph by exposing the film with a charged-particle beam of very low intensity. This then is overlaid on the computer-generated image, and the size, shape and orientation of the beam-shaping aperture is compared to the actual treatment target, and the final alignment is achieved.

RESULTS AND DISCUSSION

The information obtained from the stereotactic imaging procedures is applied to the treatment procedure in three distinct ways: (1) in obtaining target isocenter coordinates for the patient positioner (ISAH), (2) in generating the computer overlay for the treatment positioning radiographs, and (3) in generating target contours on the CT slices.

The accuracy and precision of the patient positioner is 0.1 mm in translation and 0.1 degrees in rotation. Errors in patient positioning due to ISAH are negligible compared to patient motion within the thermoplastic patient mask. Differences in patient position from procedure to procedure are typically 3 mm or less. A large fraction of these repositioning differences is the result of differences in the geometry of the angiographic and the treatment patient couches, such as the relative vertical postions of the head unit and the couch upon which the shoulders and torso lie.

The computer-generated overlay is designed to correct the repositioning errors that result from differences in the application of the patient mask between the angiographic procedure and the treatment procedures. The magnification of the overlay matches precisely the magnification of the localization radiographs, and is easily verified by checking the correspondence of the fiducial markers. The alignment of the midplane bony landmarks is performed by the physician. The ease with which the alignment is performed is characteristic of each patient and the condition and radiographic appearance of these landmarks. Although the overlay does not contain the resolution and details of the original angiographic radiograph, the physician can compare the localization radiograph with it in order to resolve ambiguities that might arise in the digitization process. Care must be taken in using those landmarks that are not truly midplane; allowances need to be made for the relative positions of landmarks that lie outside of this plane and are subject to different amounts of divergence. Typically, two or three sets of lateral and AP localization radiographs are taken, with adjustments in ISAH coordinates made between each set, in order to obtain coincidence with the overlay. The orientation of the beam-shaping aperture is obtained by exposing the localization film to a very low intensity particle beam, so that the film is exposed by the charged particles that go through the aperture. The final errors in positioning of the patient are less than 1 mm.

The greatest problem in the use of the overlay with the localization films results from rotations of the patient's head from the position at the time of the angiographic procedure. Rotations of the head in left/right directions or in the up/down directions result in changes in the projected positions of the bony landmarks. If the bony landmarks are truly midplane, then the magnitude of these errors is not large, but can result in blurring of the desired landmarks, making the unambiguous correlation of the digitized landmarks with the film image difficult. If the landmarks are not exactly in the midplane, then the errors introduced by rotations are larger and it may be impossible to superimpose those landmarks on the overlay even though they are clearly identifiable. The magnitude and importance of these differences vary with each patient, both in the ease of identification of radiographic landmarks and in the cooperation of the patient in ensuring reproducible positions at each procedure. These differences can be eliminated by either rotating the patient positioner to compensate for the head rotation, or by removing the patient from the mask and repositioning the patient.

The correlation of the angiographic images with the CT images is necessary to calculate the physical parameters required to to provide a uniform dose distribution within the target lesion while minimizing radiation outside the lesion. Patient repositioning differences in the mask between the angiography and CT procedures will result in errors in the position of the target contours within the CT images. These errors result not in errors in the location of the delivered radiation as described above, but in the calculated range of the beam. Rotations of the head often result in negligible differences in the calculated range due to the curvature of the skull. Errors in the contour locations perpendicular to the direction of a beamport also result in range errors that are negligible. Positioning errors parallel to the direction of a beam port result in range errors equal in magnitude to the positioning error. The use of parallel opposed beams can reduce the importance of such errors, since the range of one beam will be increased and the other decreased.

Errors in the design of compensators to match the distal edge of the Bragg peak with the target contours will also occur as a result of patient positioning differences. In contrast to the errors described above, repositioning errors parallel to the beamport direction lead to no errors in compensator design, while repositioning errors perpendicular to the beamport direction can result in compensator design errors. However, the magnitude of such errors is small relative to the resolution of the compensation calculations, and these errors have no great effect on the design of the compensators.

As discussed in the method section, the use of two orthogonal angiographic projections results in elliptical CT target contours, and MRI and CT are used to correct for evident contradictions between such contours and the true shape of the lesion. Since the projections of the AVM as seen on angiography are the largest dimensions of the AVM, deviations from the true shape are most likely to result in the delivery of radiation to normal tissue adjacent to the AVM, rather than portions of the AVM being missed by the radiation.

SUMMARY AND CONCLUSIONS

Heavy charged-particle Bragg peak stereotactic radisurgery of intracanial vascular lesions offers unique advantages in dose localization, while at the same time placing great reliance on accurate calculations of dose distributions and patient positioning. At LBL, we have developed a series of computer programs that, in conjunction with a specially designed stereotactic frame and head immobilization system, allows us to make use of the imaging information available from several different neuroradiological imaging procedures, e.g. cerebral angiography, contrast CT, and noncontrast CT. The size, shape, and location of the volume containing the abnormal vessels to be irradiated are transferred from the angiographic films to a set of CT images for the calculations of treatment ports, dose distribution, and charged-particle beam parameters. Computer-generated overlays that duplicate the appearance of the stereotactic frame fiducial markers, the target, and selected midplane bony landmarks on radiographs taken in the treatment alignment are used to position the patient for the radiosurgical procedure.

This system has been used in the treatment thus far of over 300 patients with inoperable arteriovenous malformations. The treatment volumes have ranged from 0.1 cm^3 to 60 cm^3. The physical characteristics of the heavy charged-particle beams have been used to produce uniform dose distributions over the target volume while sparing adjacent healthy tissues in the brain and superficial structures.

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FIGURE CAPTIONS

Figure 1: Lateral and AP views of stereotactic angiogram of a 26 yr old patient with an intracranial arteriovenous malformation. The volume of the AVM is 60 cm^3. The region to be treated by means of heavy charged-particle radiosurgery is outlined in black on both views. The stereotactic frame contains fiducial markers which are seen as a series of dots and lines in an X pattern on the lateral view, and as short horizontal and vertical lines on the AP view.

Figure 2: Non-contrast CT images of the patient from Figure 1. The upper right panel and lower left panel are, respectively, coronal and sagittal reformatted images through the center of the AVM. The white contour lines in each image represent the borders of the AVM and are obtained from the angiographic projections as described in the text. On the axial view, the stereotactic sideplates and support rods are visible to the sides and bottom of the head. The wire fiducial markers are located on the sideplate as two bright spots.

Figure 3: Computer-reformatted image of the digitized angiographic films from Figure 1. This computer-generated overlay, used to align the patient for the radiosurgical procedure, contains the fiducial markers, the target contours, midplane bony landmarks, and the position of the isocenter of the patient positioner (denoted by the cross). The top two panels are the view when the stereotactic frame center is located at isocenter. The bottom two panels are the view when the patient has been moved so as to place the center of the lesion at isocenter. The two target contours on the lower panels are the target contour magnified to match the localization radiograph (outer contour), and the actual size of the beam-shaping aperture (inner contour).

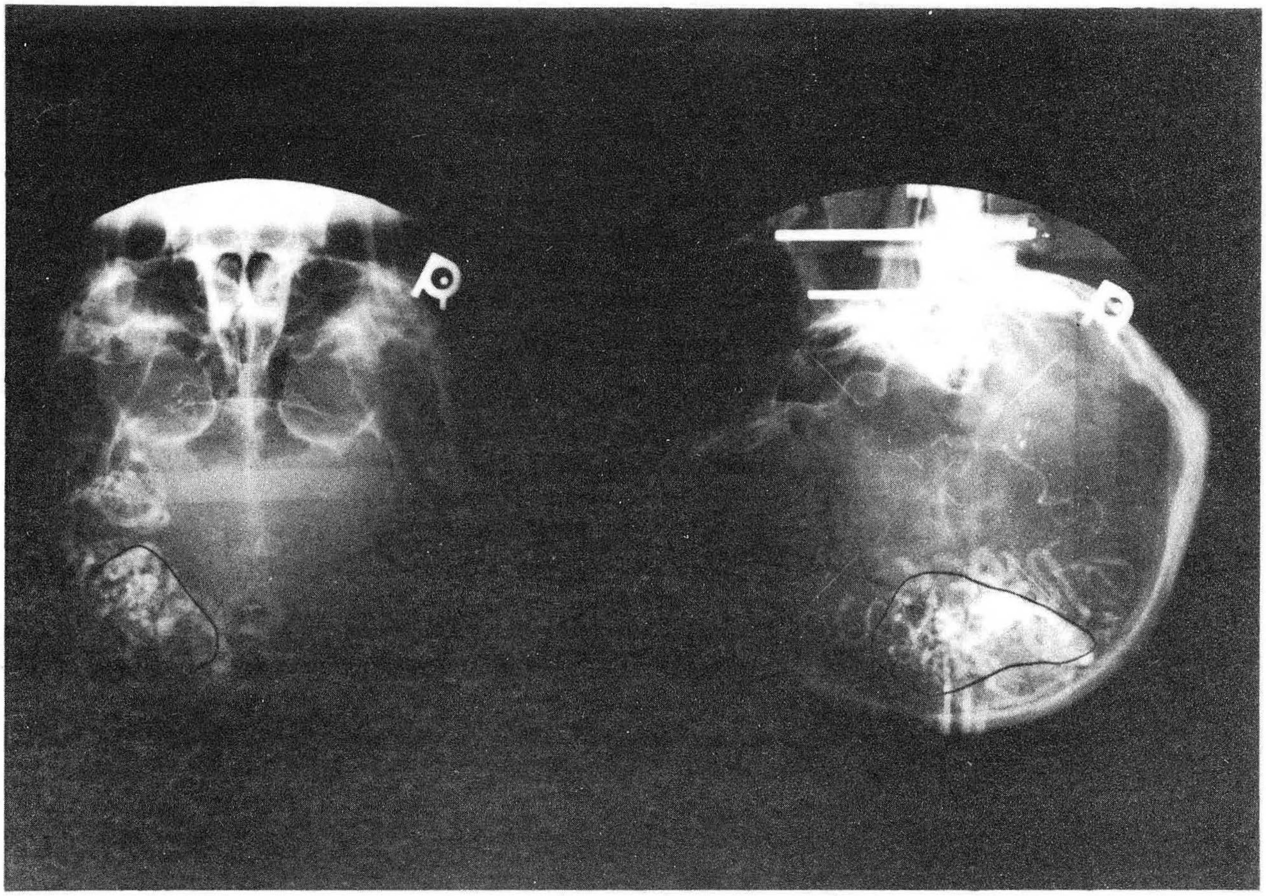

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Fig. 1

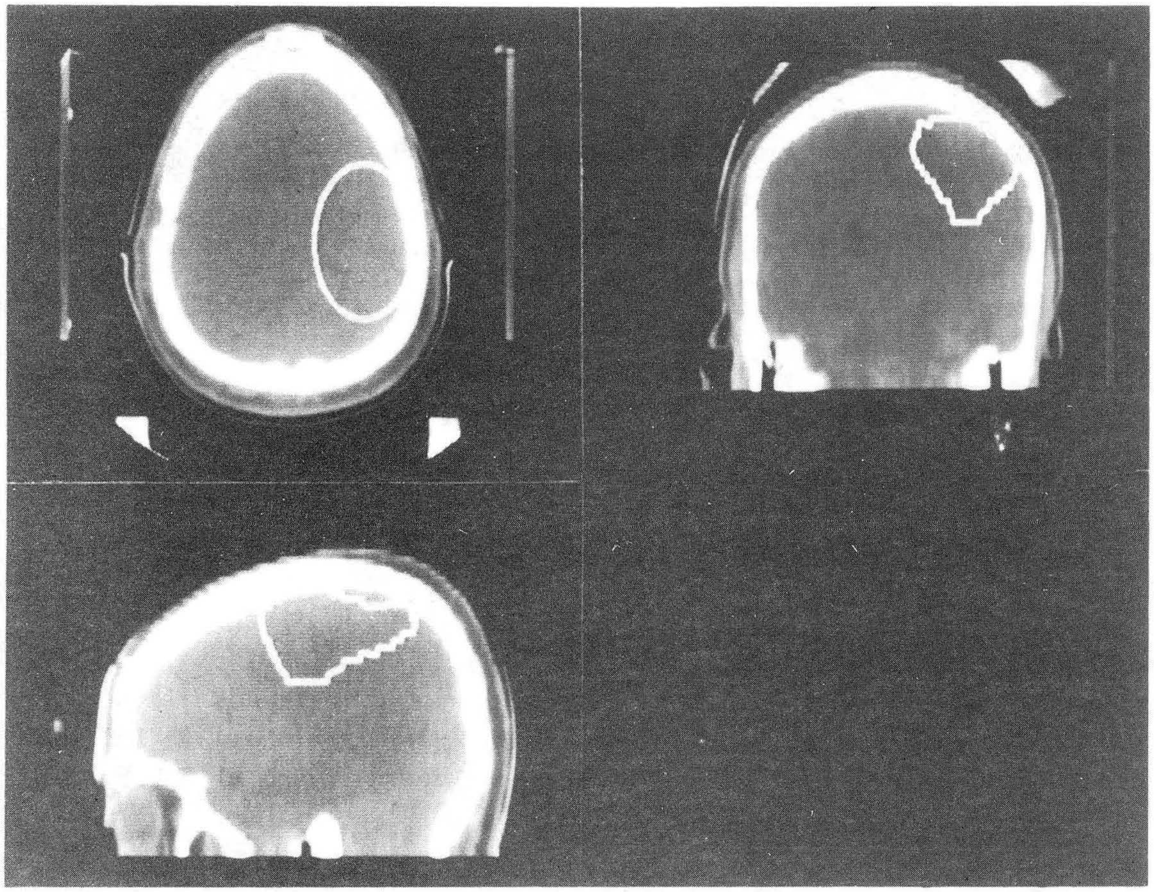

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Fig. 2

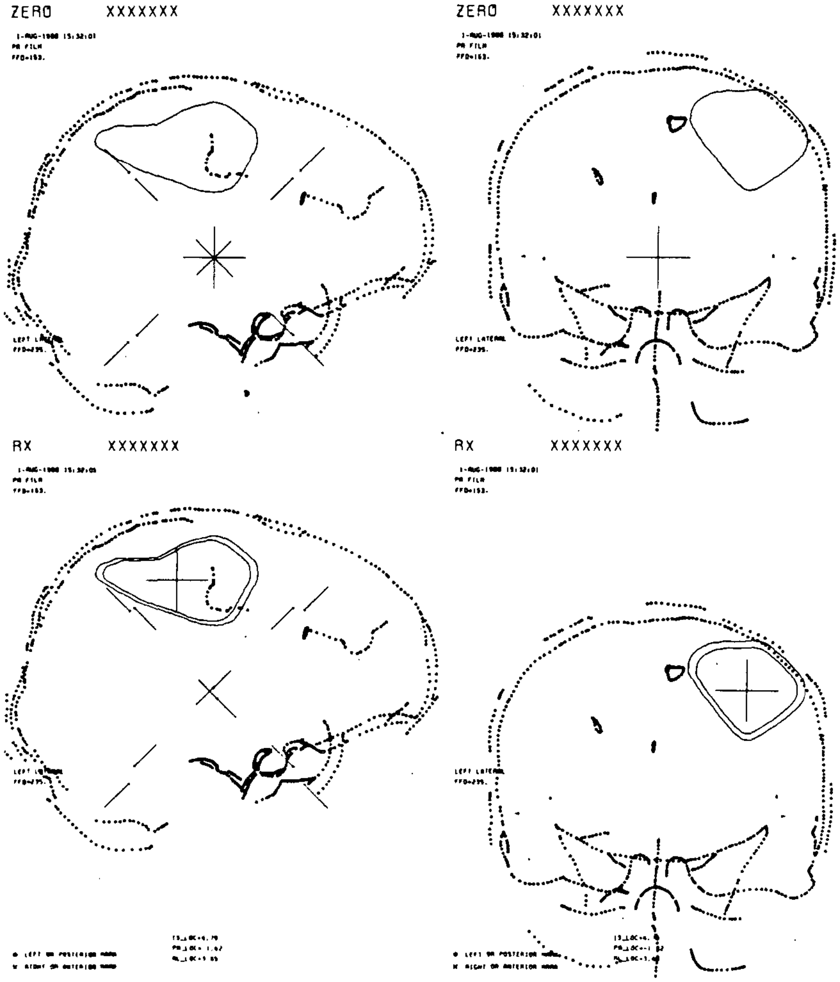

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Fig. 3

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