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Development of a Stereotactic Device for Gamma Knife Irradiation of Small Animals

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Objective : The authors developed a stereotactic device for irradiation of small animals with Leksell Gamma Knife® Model C. Development and verification procedures were described in this article.
Methods : The device was designed to satisfy three requirements. The mechanical accuracy in positioning was to be managed within 0.5 mm. The strength of the device and structure were to be compromised to provide enough strength to hold a small animal during irradiation and to interfere the gamma ray beam as little as possible. The device was to be used in combination with the Leksell G-frame® and KOPF® rat adaptor. The irradiation point was determined by separate imaging sequences such as plain X-ray images.
Results : The absolute dose rate with the device in a Leksell Gamma Knife was 3.7% less than the value calculated from Leksell Gamma Plan®. The dose distributions measured with GAFCHROMIC® MD-55 film corresponded to those of Leksell Gamma Plan® within acceptable range. The device was used in a series of rat experiments with a 4 mm helmet of Leksell Gamma Knife.
Conclusion : A stereotactic device for irradiation of small animals with Leksell Gamma Knife Model C has been developed so that it fulfilled above requirements. Absorbed dose and dose distribution at the center of a Gamma Knife helmet are in acceptable ranges. The device provides enough accuracy for stereotactic irradiation with acceptable practicality.

KEY WORDS : Stereotactic device · Gamma Knife Model C · Absolute dose · Dose distribution.

INTRODUCTION

Radiosurgery has been accepted as a resonable alternative to craniotomy in treatment of intracranial neurological diseases. However, it is also generally accepted that radiosurgery is not satisfactory in treatment of primary malignant brain tumors such as high grade glioma.[5,7] Various researches are undergoing to improve the effectiveness of radiosurgery in treatment of high grade glioma. Radiation sensitizer and/or radiation protectors are being investigated to increase the ratio of irradiated energy to tumor than to surrounding normal tissue. Combined approaches such as chemo-radiation therapy or gene-radiation therapy are also have been tried.[9-11] As a test tool for these researches, animal experiments are essential and these experiments require special tools to irradiate small animals. Several stereotactic devices have been developed for this purpose, but they are usually complex to use and/or expensive.[4,8] In this study, the authors developed a stereotactic device to irradiate small animals such as a rat or a mouse with a commercially available radiosurgery machine, Leksell Gamma Knife® Model C (Elekta AB, Stockholm, Sweden).

There are contradictory design requirements for this stereotactic device. It must be strong enough to hold a small animal in case awakening from anesthesia during irradiation. At the same time the distortion of the gamma rays caused by the device must be as small as possible. The compromising points should be found in the design procedure. Regarding the accuracy of the device, it must be accurate and precise within an error range of less than 1.0 mm.[6,12,16] Because the mechanical accuracy of a Gamma Knife is usually less than 0.5 mm, the mechanical accuracy of the fixation device was required to be less than 0.5 mm. Design, test output, and real application data of the stereotactic device are given in this article.

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MATERIALS AND METHODS

Design and manufacture

The compromising points between device strength and minimum beam distortion were obtained by designing the device with aluminum and making the portion of the device which comes into the radiation field as little as possible. Fig. 1 shows the schematic design of the device. The ear plugs were used to locate the rat to a desired position and KOPF® Rat Adaptor (David Kopf Instruments, Tujunga, California, USA) was used to fix the rat. Scales on the ear bars were in millimeters in order to provide mechanical accuracy of 0.5 mm. When an animal was irradiated, the device was fixed to a Leksell G-frame® (Elekta Instruments AB, Stockholm, Sweden) and the G-frame was set on the automatic positioning system of Leksell Gamma Knife® Model C. The mid point of the two ear plugs corresponded to the point of x=100.0, y=100.0, and z=120.0 of the Leksell G-frame stereotactic coordinate system.

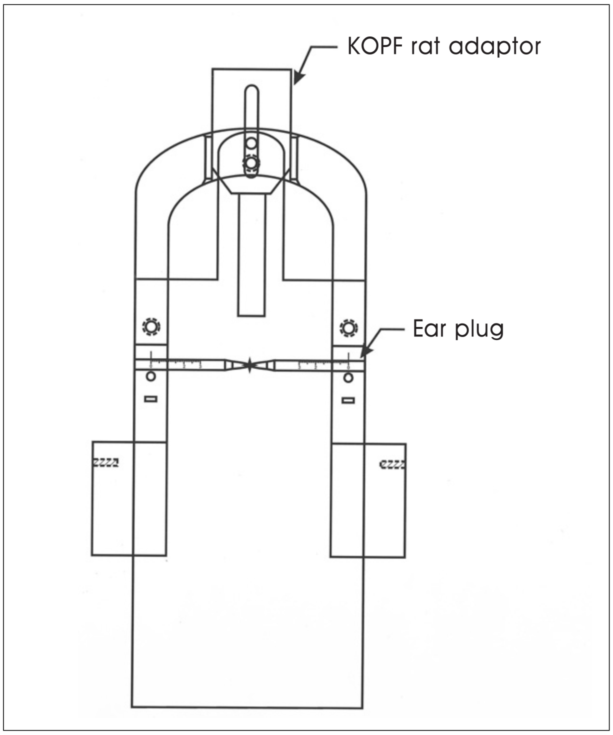

Fig. 1. A schematic design drawing of the stereotactic device developed in this study. It is designed to be used in combination with a KOPF® rat adaptor and Leksell G-frame®.

Absolute dose measurement

Some parts of the device were located inside the radiation field when the device was set on the Gamma Knife helmet. These parts caused distortion in the radiation distribution and decrease in the absorbed dose. To measure the diminution of the absolute absorbed dose, a small water phantom of size similar to a rat head was made (Fig. 2A). An ion chamber (Capintec® PR05P, Capintec, Inc. Ramsey, New Jersey, USA) was put at the center of the phantom and connected to an electrometer (PTW® UNIDOS, PTW Freiburg GmbH, Germany). The phantom was fixed to the device and plain X-ray images were obtained in two perpendicular directions. The irradiation point was chosen to be the center of the ion chamber cavity using the treatment planning program of Gamma Knife (Leksell Gamma Plan®, V5.34, Elekta Instruments AB, Stockholm, Sweden) (Fig. 2B). The left figure of Fig. 2B is an xz-plane image and the right figure is an yz-plane image. White ellipsoids are 50% iso-dose lines formed by a single iso-center of the 18 mm helmet.

Dose distribution

Basically, a Gamma Knife helmet is in a shape of a half sphere with a cut top. The shape of the iso-dose surface at

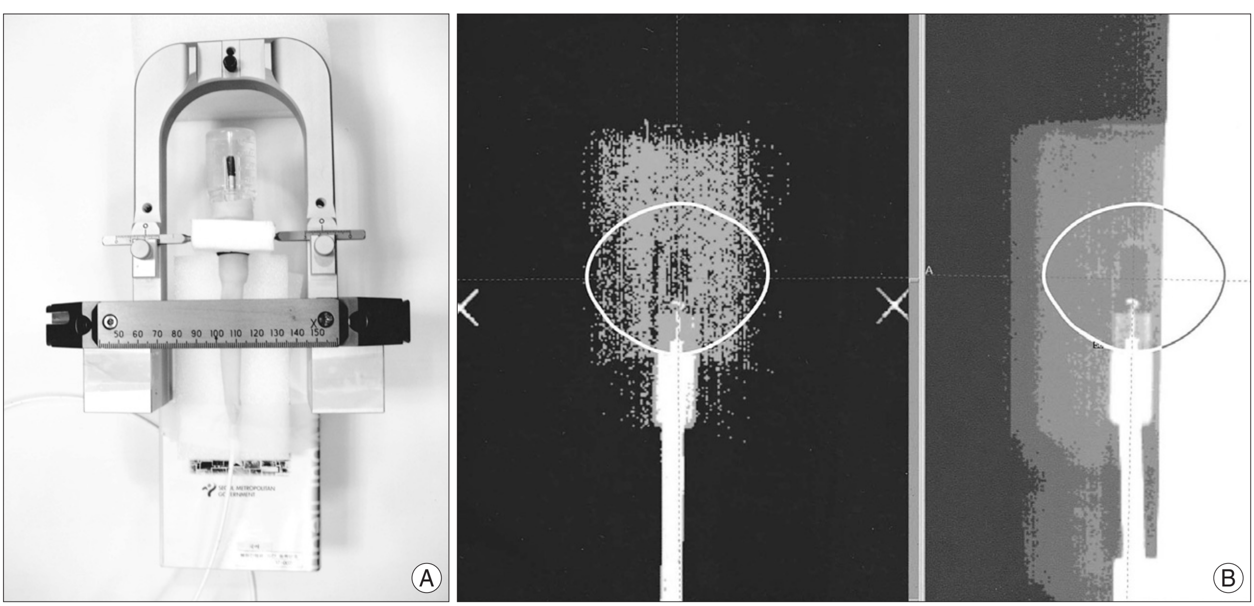

Fig. 2. A : A picture showing a small phantom installed at the stereotactic device and Leksell G-frame® to measure the absolute dose at the center of an 18 mm helmet of a Gamma Knife® model C. B : Amplified images of the plain X-rays of the phantom pictured in A. The center of the ion chamber cavity is chosen to be coincided with the center of irradiation. Left figure is the anterior-posterior image and the right is the lateral image.

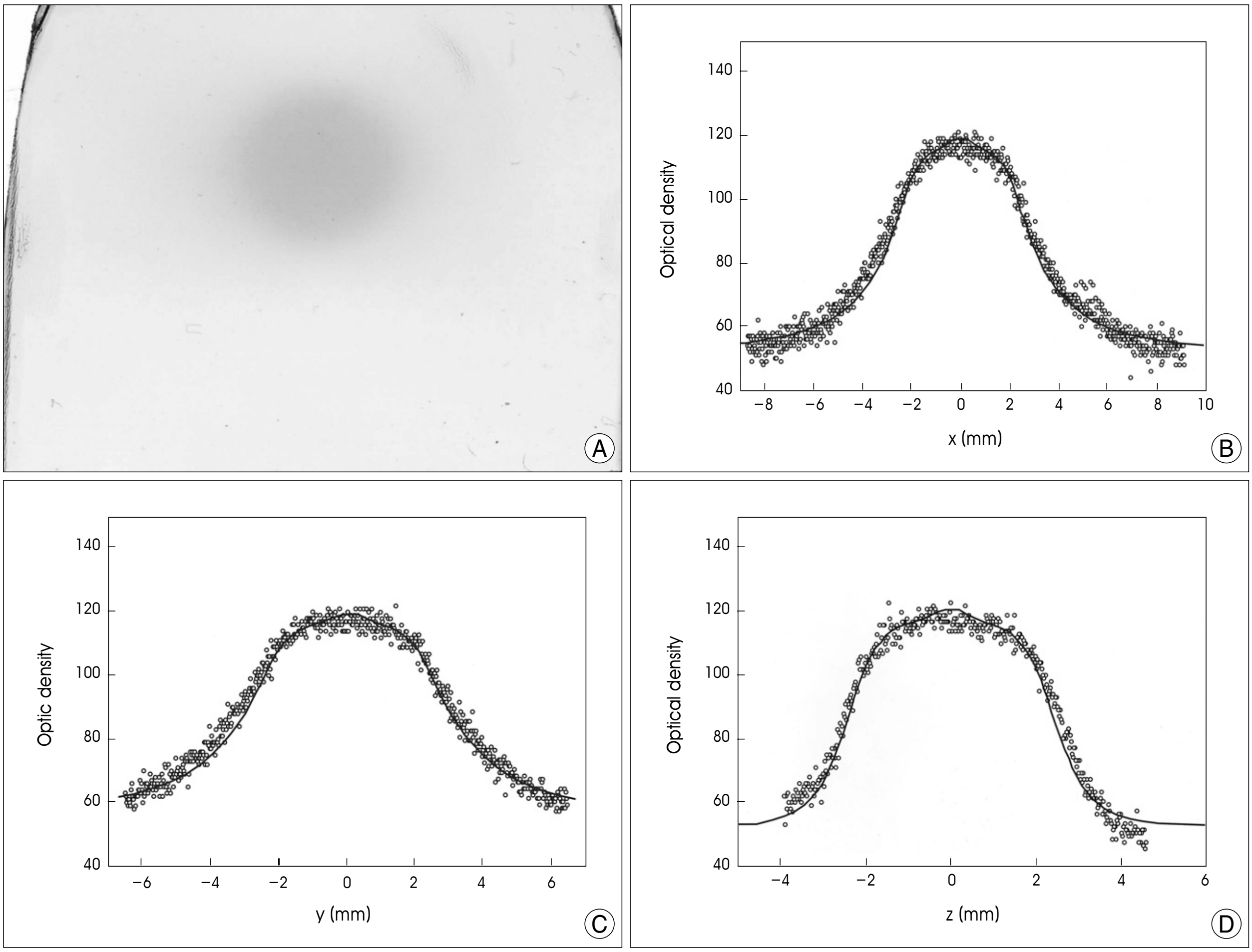

Fig. 3. A : The scanned image of a radiochromic film obtained along the zx-plane of the Gamma Knife at z=111. The upper side of the picture is to the vertex and the right side is to anterior direction. B : Beam profile obtained along the x-axis of a Gamma Knife. C : Beam profile along the y-direction. D : Beam profile along the z-direction. The solid lines in B, C, and D are dose distributions in each direction provided by Leksell Gamma Plan®.

the irradiation point of a Gamma Knife, the center of the helmet, is not a sphere. Instead, it resembles a compressed sphere similar to an ellipsoid with short axis in the z-direction of the Gamma Knife stereotactic space. The z-direction corresponds to the cranio-caurdal direction. This iso-dose shape is affected by the introduction of the stereotactic device into the radiation field. Because only small portion of the 201 radiation sources of the Gamma Knife is blocked by the device, we can expect the change in dose distribution is not so important. In order to check the distortion in dose distribution, the beam profiles in the xy-plane, yz-plane, and zx-plane were measured using radiochromic films. GAFCHROMIC® MD-55 radio-chromic dosimetry films (ISP Technologies Inc., Wayne, Jew Jersey, USA) were cut in a rounded rectangular shape and irradiated by 30 Gy at the center of a 4 mm Gamma Knife helmet. Irradiated films were scanned and analyzed by a free image analysis software, Osiris version 4.19 (University Hospital of Geneva, Swiss).

Application in a rat experiment

The stereotactic device introduced in this article was used in a series of rat irradiation experiments with Gamma Knife. Human glioma cells were stereotactically seeded into a rat brain. After a certain period of time, a tumor grown in the rat brain was checked with MR scanning. When there was a sufficient size of tumor, gene therapy and Gamma Knife radiosurgery were performed separately or in combination.

Just before fixation of the rat to the device, MR images of the rat brain were taken. Because the rat brain is too small to generate enough MR signals with a head coil adapted for the Leksell G-frame, the MR images were taken with smaller coils without the Leksell MR indicators. As a result, the MR images could not be used with Leksell Gamma Plan. So, the irradiation point was determined by plain X-ray images taken in two directions perpendicular to each other. The location of the tumor in the rat brain is measured with the MR images taken before frame application. The location of the burr hole which was made to seed the tumor cells into the rat brain was identified in the plain X-ray images and the irradiation point was determined by calculating the tumor position from the burr hole using the information obtained in MR images.

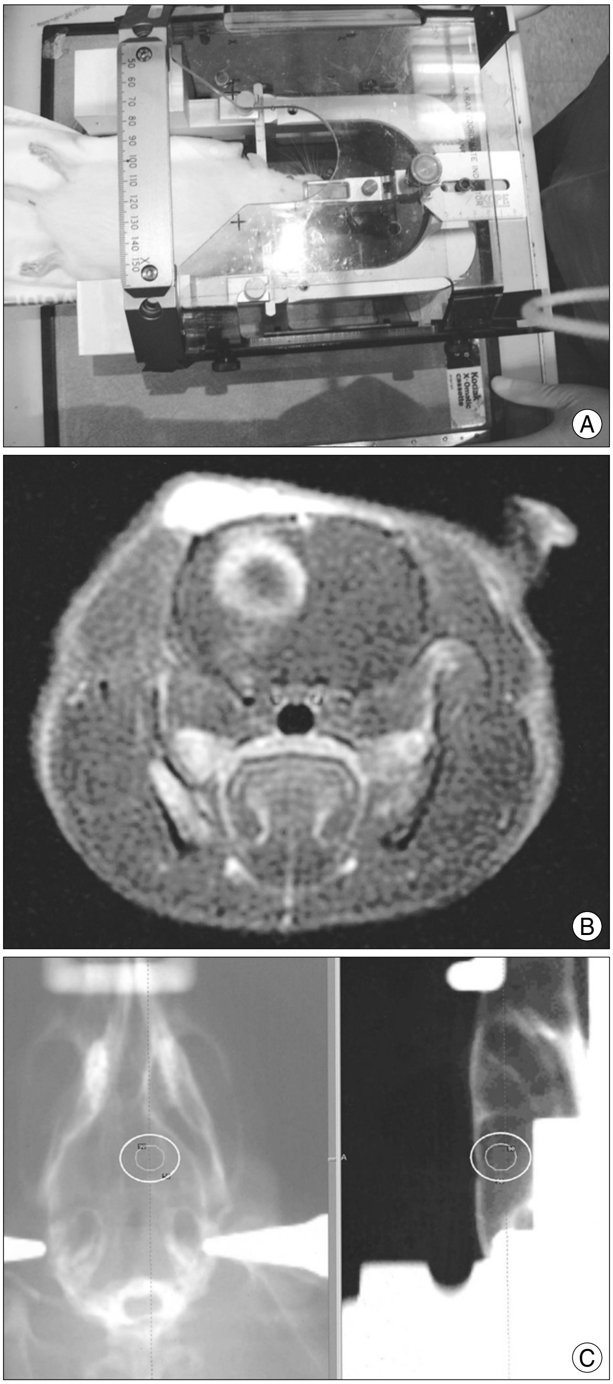

Fig. 4. A : A rat is mounted on the stereotactic device. The angiography indicator is applied to take plain X-ray images for localization. B : A magnetic resonance image of a rat brain taken just before irradiation. The tumor is enhanced at the right hemisphere of the brain. C : Amplified images of the plain X-rays of the rat pictured in A. The irradiation point was determined together with these images and the magnetic resonance images. Left figure is the anterior-posterior image and the right is the lateral image.

RESULTS

Absolute dose measurement

The small water phantom described in the Materials and Methods section was irradiated with the 18 mm helmet of Gamma Knife and measured dose was compared with that of Gamma Plan. The value provided by Gamma Plan took into account the size of the phantom by measuring the distance from the center to the surface with a special skull measurement device provided by the Gamma Knife manufacturing company. Measured dose at the center was 1.637 $\pm$0.018 Gy per minute and it is 3.7% less than the value provided by Leksell Gamma Plan (1.70 Gy/min).

Dose distribution

Fig. 3A is the scanned image of the irradiated film obtained in the zx-plane of the Gamma Knife at the point x=100, y=100, and z=111. Z=111 was chosen because the irradiation point for a rat experiment described in the following section is near Bregma point which is 9 mm forward from the Lambda point.[14] Fig. 3B, C, D show the beam profiles along the x, y, and z-direction, respectively. As shown in Fig. 3, the beam profiles obtained with the stereotactic device are well correspond to dose distributions provided by the Leksell Gamma Plan in the range of higher than 50%.

Application in a rat experiment

Fig. 4A shows a rat fixed in the stereotactic device for Gamma Knife irradiation. The Leksell angiography indicator (Elekta Instruments AB, Stockholm, Sweden) is applied to the Leksell G-frame to take plain X-ray images in order to determine the irradiation point.

Fig. 4B shows a T1 weighted enhanced axial MR image of a tumor formed in the right hemisphere of the rat brain. The MR images were taken in prone position. Fig. 4C shows the location of the irradiation point determined in plain X-ray images. The left figure of Fig. 4C is an xz-plane image and the right figure is an yz-plane image. White ellipsoids are 50% iso-dose lines formed by a single iso-center of the 4 mm helmet of Gamma Knife. Maximum 20 Gy was irradiated to a rat with the 4 mm helmet. The radiological and biological outcome of this experiment will be published in separate papers.

DISCUSSION

The absorbed dose rate of the Gamma Knife obtained with the stereotactic device was 1.637$\pm$0.018 Gy per minute which is 3.7% less than the dose provided by Leksell Gamma Plan. This value is reasonable and could be expected because about ten of the 201 sources of a Gamma Knife were blocked by the device. Difference of 3.7% from the calculated value is somewhat better than 14% smaller value of the stereotactic device of Im et al.[8] Because of thicker plates and heavy materials, the device of Im et al.[8] showed larger decrease in absolute dose measured at the center of the device. Furthermore, the PTW Model 31006 Pinpoint Chamber (PTW, Germany) with sensitive volume of 0.015 cm^3 is too small to measure absolute dose because of its small charge accumulation volume[1,3,15]. On the other hand, this chamber is too big to measure the absolute dose of the 4 mm helmet of Gamma Knife as Im et al. did in their measurements.[8] Due to the small ionizing volume of the 4 mm helmet, the 18 mm helmet is usually used to measure absolute dose of a Gamma Knife.[2,13,17]

The dose distribution inside the stereotactic device well corresponds to dose distribution of Leksell Gamma Plan in the region of 50% or higher. However, it is a little bit wider in the range, around 30-40% region. Because the difference is less than 5% and mainly the upper portion of the beam profile that is higher than 50% is important in animal experiments, this difference is in an acceptable range.

A stereotactic device developed in this study is very simple and easy to use. Because of this simplicity of the structure, there are several points to be handled carefully in actual use. First, the position of the irradiation point should be determined by imaging before irradiation. If the device has a kind of localization tools to reproduce the stereotactic position of the tumor seeding point such as that of Im et al.[8], it might not be necessary to take images before irradiation. However, it is more desirable to take stereotactic images before irradiation due to two main reasons. One of them is that tumor growth is not centered at the tumor seeding point in general. It may grow in any direction from the seeding point and irradiation to the seeding point might not hit the center of the tumor. The other is that the posture of the rat can be different in irradiation procedure from that of seeding procedure even though we use the same stereotactic devices in seeding procedure and irradiation. According to our experience, positioning of a rat strongly depends on the person who sets the rat. Therefore, it is desirable to check the target point for each rat irradiation. Combination of MR images and plain X-ray images were used in determination of the irradiation point. The burr hole could be identified in both set of images. But, determination of the target point was not simple because posture of the rat was not the same in imaging procedures. Because of the weak signal in the MR head coil for Gamma Knife imaging, the stereotactic MR images could not be obtained. Computed tomography imaging was not tried because severe artifact caused by the ear plugs was expected. More studies are necessary to determine the irradiation point for more accuracy and simplicity.

CONCLUSION

A stereotactic device for irradiation of small animals with Leksell Gamma Knife Model C has been developed and absorbed dose and dose distribution at the center of the device have been shown in acceptable ranges. With careful imaging procedures to determine the irradiation point, this device can be used in a series of rat irradiation experiments.

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