Development of Independent Target Approximation by Auto-computation of 3-D Distribution Units for Stereotactic Radiosurgery

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The stereotactic radiosurgery (SRS) describes a method of delivering a high dose of radiation to a small target volume in the brain, generally in a single fraction, while the dose delivered to the surrounding normal tissue should be minimized. To perform automatic plan of the SRS, a new method of multi-isocenter/shot linear accelerator (linac) and gamma knife (GK) radiosurgery treatment plan was developed, based on a physical lattice structure in target. The optimal radiosurgical plan had been constructed by many beam parameters in a linear accelerator or gamma knife-based radiation therapy. In this work, an isocenter/shot was modeled as a sphere, which is equal to the circular collimator/helmet hole size because the dimension of the 50% isodose level in the dose profile is similar to its size. In a computer-aided system, it accomplished first an automatic arrangement of multi-isocenter/shot considering two parameters such as positions and collimator/helmet sizes for each isocenter/shot. Simultaneously, an irregularly shaped target was approximated by cubic structures through computation of voxel units. The treatment planning method by the technique was evaluated as a dose distribution by dose volume histograms, dose conformity, and dose homogeneity to targets. For irregularly shaped targets, the new method performed optimal multi-isocenter packing, and it only took a few seconds in a computer-aided system. The targets were included in a more than 50% isodose curve. The dose conformity was ordinarily acceptable levels and the dose homogeneity was always less than 2.0, satisfying for various targets referred to Radiation Therapy Oncology Group (RTOG) SRS criteria. In conclusion, this approach by physical lattice structure could be a useful radiosurgical plan without restrictions in the various tumor shapes and the different modality techniques such as linac and GK for SRS.

Key Words: Stereotactic radiosurgery, Beam parameters, Target approximation, Dose evaluation

INTRODUCTION

Stereotactic radiosurgery delivers a high dose of radiation to the tumor at once and differs from radiotherapy, while the dose delivered to the surrounding normal tissue or critical organ should be minimized. Therefore, irradiating a tumor requires great accuracy making its planning very important.[1-4] Traditionally, in SRS based on a linear accelerator (linac) or gamma knife (GK), after radiosurgical planning acquires the patient's tumor image from the image devices such as CT, MRI, PET and SPECT etc, the contour of the tumor is defined on the image, and the planner organizes the treatment plan by controlling the beam parameters (i.e., isocenter position, number of isocenter, collimator size, arc start/stop angles and arc weighting). Subsequently, a dose value was calculated and a dose distribution of the tumor and the normal tissue is evaluated. Namely, the optimized plan is decided by repetitive work to combine the beam parameters and identify prescribed

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doses level in a tumor, which is usually called a trial and error method.[5-10] This requires a great deal of time, effort, and experience. Furthermore, the method is difficult because a 3-D spatial plan is more complicated than a 2-D plan and it is not easy to analyze quantitatively. In addition, it is quite difficult to fill up an irregular shaped tumor involving multiple isocenters /shots with various sizes in 3-D on a 2-D flat screen. Accordingly, many computer-aided techniques have been presented to determine the optimal treatment plan for an irregularly shaped tumor in SRS. For precise and efficient treatment planning, the researchers examined several techniques such as simulated annealing, genetic algorithm, and a heuristic algorithm.[11-14] Occasionally, these algorithms are used to mix between each other. In particular, packing of spheres proposed by Wu, Meeks and coworkers obtained data in an irregular shaped tumor using geometrical methods in GK and linac, and created an array of spheres within the tumor by considering the isocenter/shot position, the collimator/helmet hole size and relative weighting etc.[15-16] In addition, Suh and coworkers[17] approximated the tumor volume using a cylinder, and automatically packed the isocenters inside the cylinders. These techniques have some limitations, there are a limited number of tumor shapes, difficulties in finding the global optimum, time-consuming treatment planning and the conformity of repetitive treatment plan in identical situations.

The aim of this study was to determine an efficient method for a spherical dose arrangement considering the beam parameters (i.e., isocenter position, collimator size) in an irregularly shaped tumor. Finally, the spherical dose arrangement in an irregular shaped tumor was evaluated as a dose volume histogram (DVH), the volume of the prescription isodose surface divided by the target volume (ratio PITV) and maximum dose to prescription dose (ratio MDPD).[18,19]

MATERIALS AND METHODS

In stereotactic radiosurgery using linac and GK, a dose distribution is highly spherical converging into one isocenter/shot. In this study, one isocenter was modeled as a sphere, which is equal to the circular collimator size because the dimension of the 50% isodose level in the dose profile is similar to its size. It has advantages including a high isodose level and a steep dose gradient. Moreover, the multi-isocenter with a spherical dose distribution can be practiced an essential radiosurgical plan which is fast, easy and accurate. However, a tumor has diverse aspects and volume. The multi- isocenter used to cover the irregular tumor surface and confirm the characteristics of the different dose distribution using one isocenter. In stereotactic radiosurgery, the spheres packing within an irregularly shaped tumor are very important in designing an optimal treatment plan. The steps below showed the main points of this method for an irregularly shaped tumor.

Step one, isocenters of a smaller sphere size were first arrayed in order to approach an irregular tumor surface.

Step two, isocenters were selected to satisfy the prescription dose using a voxel as 3-D spatial unit.

Step three, three beam parameters such as the number of isocenter, isocenter position and collimator were considered. However, it was not considered to be a relative arc weighting and isocenter interval.

A detailed description of the planning procedure was discussed in the following sections.

1. Automatic multi-isocenter arrangement

In general, the tumor location within a patient was modeled in coordinates systems using frame and frameless methods in stereotactic radiosurgery. These methods provide the precise position and size of the tumor from diagnostic devices. In order to avoid a complex translation, the virtual targets in the coordinates system of this study were applied to the presented characteristics as a practical coordinates system (Eq. 1). Here, f and x_0, y_0, z_0 are the real coordinate system and origin in the images obtained by frame or frameless. f' and x_0', y_0', z_0' are a new coordinate system and origin in the study. The new coordinate system used to realize the sphere packing in the three dimensional space. The properties of the new and real coordinate system were identical. However, the origin coordinates differ from the origin of the frame or frameless coordinate system, and it only has a constant coordinate shift.

$$f(x_0, y_0, z_0) -> f'(x_0', y_0', z_0') \quad \text{.....(1)}$$

For a target volume obtained from the CT/MRI image devices etc, the largest and smallest coordinates can be used to generate the new coordinate system. The distance between the

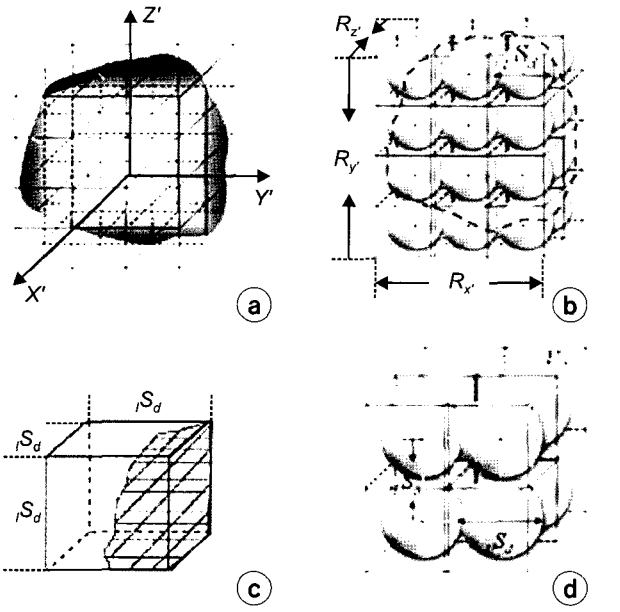

Fig. 1. Automatic arrangement algorithm of isocenters within the target. The V_c presents the volume of another cubic structure equal to eight cubes. (a) A rectangular parallelepiped was created from the characteristics of the tumor. (b) Multi-isocenters were packed into cubes. (c) A cube and tumor region consisted of voxel units. (d) Translation of the sphere with a different diameter based on a cubic structure.

largest and the smallest points can be calculated to obtain the center of the target volume in the new coordinate system (Eq. 2).

$$f_0' = (x_0', y_0', z_0') = \left[\frac{(x'_{\max} + x'_{\min})}{2}, \frac{(y'_{\max} + y'_{\min})}{2}, \frac{(z'_{\max} + z'_{\min})}{2}\right] \quad \text{.....(2)}$$

Continuously, automated multi-isocenter arrange -ment was determined using the following methods.

1) A rectangular parallelepiped was used to create cubes surrounding the tumor volume. The largest length of the lines, $L_{x'}, L_{y'}, L_{z'}$, connecting the two points $x'_{\max} / x'_{\min}$, $y'_{\max} / y'_{\min}$, $z'_{\max} / z'_{\min}$ at X', Y', Z' axes including the target contour, were calculated (Eq. 3). Each three lines $L(L_{x'}, L_{y'}, L_{z'})$ were extended by α, β, and γ as a multiplier of the spherical diameter. It named $R_{x'}, R_{y'}, R_{z'}$. Also, the $_IS_d$ is initially a sphere with a diameter equal to one line of cube (Eq. 4).

$$\begin{aligned} L_{x'} &= x'_{\max} + x'_{\min}, \\ L_{y'} &= y'_{\max} + y'_{\min}, \\ L_{z'} &= z'_{\max} + z'_{\min} \end{aligned} \quad \text{.....(3)}$$

$$\begin{aligned} R_{x'} &= L_{x'} + \alpha = a(\,_IS_d), \\ R_{y'} &= L_{y'} + \beta = b(\,_IS_d), \\ R_{z'} &= L_{z'} + \gamma = c(\,_IS_d) \end{aligned} \quad \text{.....(4)}$$

2) The rectangular parallelepiped is divided into cubic regions to an array isotropy spheres. Namely, the three lines R'_x, R'_y, R'_z are split in an initial spherical diameter (Eq. 5).

Here, the N_C is the number of divided cubes within the rectangular parallelepiped, and the R_S indicates each line on X', Y', Z' axes. The smaller spherical size is well approximated for an irregular tumor volume. In this sphere packing procedure, the smaller the size of the sphere the better it compasses the surface of an irregularly shaped tumor. Accordingly, this method considered the small diameter first.

$$N_C = \frac{R_S(R_{x'}, R_{y'}, R_{z'})}{_IS_d} \quad \text{.....(5)}$$

3) The number of divided partitions by spherical diameter, N_C, is either odd or even. Therefore, the starting section of the divided cubes progresses from the center to outside. The total section with an even spherical diameter progressed towards the positive and negative directions to the center, and when the total section is odd, it progresses towards the center.

4) Fig. 1 shows an automatic packing algorithm of the isocenters within the target in this method. The rectangular parallelepiped surrounds the tumor, which is divided into cubes, to determine the automatic packing of isocenters. The one cube has a single isocenter. The regions of the cube and tumor were composed of voxel units in three dimensional space, each cubes contained tumor fragments with different voxel counts. The voxel size was defined as $1 \times 1 \times 1$ mm^3, and a voxel ratio was determined as the voxel counts in the tumor area by the voxel counts in the cube area. The optimal locations of the isocenters were determined to deliver a high dose in the tumor, while a low dose was delivered in the tissue outside tumor, was selected by a specific voxel ratio that was calculated automatically (Eq. 6).

Table 1. The properties of the virtual targets and rectangular parallelepipeds as the target coverage relevant sphere packing.

Target	Length of the longest line on each axis			Covered rectangular (mm^3) (*width* × *length* × *height*)		Target volume (mm^3)
	X-axis (mm)	Y-axis (mm)	Z-axis (mm)	${}_{I}S_d$-5 mm	${}_{I}S_d$-8 mm	
1	17	17	16	20×20×20	24×24×26	2080
2	20	30	14	20×30×15	24×32×16	3338
3	21	21	27	25×25×30	24×24×32	5930
4	27	25	21	30×25×25	32×32×24	9912

Table 2. Parameters for the spherical dose model.

Collimator (cm)	S_1	S_2	S_3	S_4	S_5
1	0.320	7.430	0	0.020	2.520
2	0.232	7.009	0	0.032	1.606
3	0.257	9.575	0	0.036	1.071
Mean	0.249	7.019	0	0.029	1.927

$$\left[\frac{N_{tumor}}{N_{cube}}\right]_{The\ Number\ of\ Voxel} \times 100 \Leftrightarrow High\ DVH \quad \text{.....(6)}$$

Theoretically, the multi-isocenter arrangement depends on the cubic structure and a voxel on space. The cubic structure does not allow a superposition of the spheres to conform dose homogeneity in a target.

5) Eight spheres necessarily build another cubic structure that twice identifies the initial isocenter diameter (${}_{I}S_d$). The positions of the eight isocenters generally have eight coordinates bound by the two coordinates of $X_i'(x_1', x_2')$, $Y_j'(y_1', y_2')$, $Z_k'(z_1', z_2')$.

Extensions of the coordinates constitute another cubic structure. The characteristic of a cubic structure can be packed into one isocenter instead of eight isocenters. On the other hand, the initial spheres arrayed boundary regions between the tumor and normal tissue, remained for an approximation of the irregularly shaped tumor. Otherwise, the spheres were translated with different sizes with the exception of the boundary region. It was decreased a number of spheres. Whether is there are eight or one, the packing fraction to its cubes is physically identified as $4\pi\,{}_{I}S_d^3/3\,V_C$. V_C is the cube volume generated by eight spheres.

2. Application of virtual targets

The virtual targets and dose calculation algorithm were used to verify these optimization methods. In stereotactic radiosurgery using a linear accelerator, the dose distribution produced by the multiple non-coplanar arcs converged to one point, which is almost spherical at a high isodose level. In particular, the width of the dose distribution on the 50% isodose level is similar to the collimator diameter when multi-arcs were used. Therefore, the dose distribution of one isocenter was modeled as a sphere, and applied to the four virtual targets with various aspects.

The targets were each approximately 2080 mm^3, 3338 mm^3, 5930 mm^3 and 9912 mm^3. When applied to an initial sphere diameter (${}_{I}S_d$) of 5 mm and 8 mm, the rectangular parallelepiped coverage was built in two series per target. The detailed data is showed in Table 2. The irregularly shaped targets are largely divided by two types of 'simple' cases and 'complex' cases. The target model 1 and 4, as 'simple' cases, are combined with one or two of figures such as a triangular pyramid or prism, rectangular structure, and cylinder. The target models 2 and 3 as 'complex' cases are combined with three or more figures.

3. Dose calculation algorithm

After the arrangement was completed, a dose calculation algorithm based on the single isocentric dose model was used to analyze the dose distribution.[20] Treuer and coworker[21] proposed

Table 3. The results of the multi-isocenters arrangement within the virtual targets.

Target	5 mm $_{I}S_{d}$				8 mm $_{I}S_{d}$			
	Divided total cube #	Selected isocenter #	Limited voxel ratio (%)	Arrayed spherical diameter (mm)	Divided total cube #	Selected isocenter #	Limited voxel ratio (%)	Arrayed spherical diameter (mm)
1	64	21	35	5	18	11	10	8
2	72	49	10	5	24	14	15	8
3	150	71	10	5&10	36	25	10	8
4	150	89	20	5&10	48	32	20	8

Table 4. The dose volume information by the virtual target sphere packing automatic planning.

Target	5 mm $_{I}S_{d}$					8 mm $_{I}S_{d}$				
	Target volume 100%		Target volume 95%		Mean absorbed dose (%)	Target volume 100%		Target volume 95%		Mean absorbed dose (%)
	MDPD	PITV	MDPD	PITV		MDPD	PITV	MDPD	PITV	
1	1.89	1.87	1.64	1.35	77.25%	1.72	2.14	1.56	1.70	80.96%
2	1.67	2.03	1.47	1.47	82.74%	1.87	2.48	1.61	1.75	79.78%
3	1.75	2.05	1.64	1.37	83.20%	1.87	2.10	1.59	1.46	80.41%
4	1.85	1.64	1.72	1.17	81.24%	1.92	1.66	1.64	1.21	78.49%

a simplified empirical method based on the off-axis ratios, and the restricted tissue-axis ratio and weight function. Cho and coworkers[22] suggested a mathematical model based on various functions and beam data. In this study, the method was not considered to be a dose gradient because it utilized multi-isocenters, and applied to a spherical dose model, which fitted curves using a five coefficient based on the Cunningham model. It mainly considered with two parameters, the isocenter positions and collimator sizes.[23] The spherical dose model was developed for a standard of four arcs containing a single isocenter with equal arc spacing (e.g., 100^{0} arc with 45^{0} arc spacing). The dose calculation shows two separate analytic forms of Equation (7) and (8). We defined r is a radial distance from the isocenter, and C is the collimator diameter (5~35 mm).

1) When r is $\leq C/2$,

$$D = 1 - S_1 \times \exp\left[-S_2 \times \left(\frac{C}{2} - r\right) - S_3\left(\frac{C}{2} - r^2\right)\right] \quad \text{....(7)}$$

2) When r is $> C/2$,

$$D = S_4 + (1 - S_1 - S_4) \times \exp\left[-S_5 \times \left(r - \frac{C}{2}\right)\right] \quad \text{.....(8)}$$

Here, the S_i parameters are fitting parameters. (Table 2) This method used a cubic structure comprised of 5 mm and 8 mm dimensions to satisfy the irregular boundary lines between the target and normal tissue. Then, the different spheres to cubes contain the same packing fraction (approximately 52%). However, the isodose level range of spheres of 5 mm and 8 mm is different. Moreover, it is not one isocenter but a multi-isocenter that comprises a practical arrangement to target.

Finally, this study evaluated the tumor models that are separated into target volumes of 100% and 95%. This plan evaluation was based upon the dose-volume data from the

DVHs. The dose distribution for each sphere arrangement within the targets was evaluated with PITV and MDPD referred by the Radiation Therapy Oncology Group (RTOG) stereotactic radiosurgery criteria.

RESULTS

Four virtual targets were arrayed automatically into a multi-isocenter by the voxel ratio in the area of each cube, which is presented in Table 3. In the case if the selected 5 mm spherical diameter, the optimal voxel ratio to the irregularly shaped targets were 35%, 10%, 10%, 20%, 25%. In addition, in the case of the arrayed 8 mm spherical diameter, the optimal voxel ratio to the irregularly shaped targets were 10%, 15%, 10%, 20%, 20%. The summary dose-volume information for the four virtual targets is presented in Table 4 and Fig. 2. Both the 100% and 95% target volume were covered above 50% (of the maximum dose) of the isodose shell. In the 100% target volume applied both 5 mm and 8 mm $/S_d$, the mean prescription isodose level was 55%, with a mean prescription isodose level of 63.87% in the 95% target volume. The MDPDs (maximum dose by the prescription dose) were <2.0 and the PITVs (prescription isodose surface by the target volume) were <2.5 in all cases. In addition, PITVs by the 5 mm sphere differed approximately 0.02% to 0.45% from that of the PITVs by the 8 mm sphere in the target models. Namely, virtual targets packed as 5 mm sphere was better than dose conformity. The absorbed mean dose was greater than 77% of the maximum dose in the four targets.

DISCUSSION AND CONCLUSION

In this study, a cubic approximation for an irregular tumor was used to determine the optimal location of a multi-isocenter at the boundary region between the tumor and normal tissue. Each divided region depends on the number of voxels, which geometrically affects the decision on the cube placement and sphere packing surrounding the target. In solidstate physics, a lattice point like sphere has many crystal structures. The crystal structures are closely related to the arrangement of the isocenters, which has spherical dose distribution to one point within a target. This method was finally arrayed by spheres utilizing cubic structures with a relatively lower packing fraction for an irregular shaped target. Its structure is simple and translates easily, which is unlike a sphere size. The properties were applied to targets 3 and 4 with 5 mm spheres. The arrangement of the spheres produced a betterhomogeneity in the dose distribution within the target and included a high isodose level. This planning method selected a 5 mm and 8 mm initial sphere size for an irregular target surface. In all target cases, the dose distribution within target
was a well approximated target volume when arrayed with 5 mm spheres rather than with 8 mm spheres. Therefore, the smaller spheres closely approximate the target shapes but the

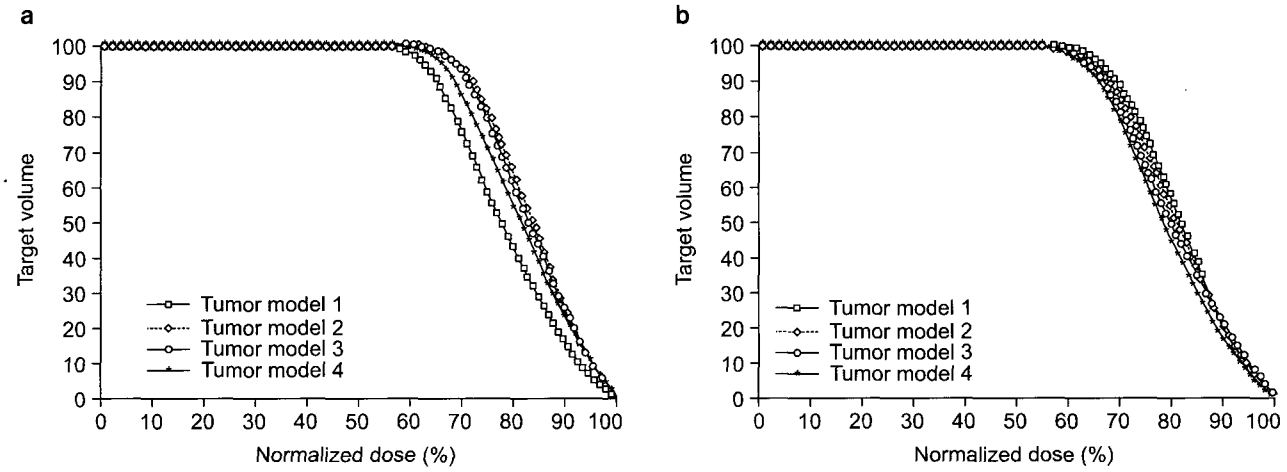

Fig. 2. DVHs for the virtual targets. (a) DVHs of the four irregular shaped targets arrayed by 5 mm spheres. (b) DVHs of the four irregular shaped targets arrayed by 8 mm spheres.

number of isocenters increase. In contrast, the 8 mm sphere arrangement had a generally lower voxel ratio for the selected spheres between the target and non target, and the number of isocenters was lower. Moreover, the interval of the isodose curves was tight. The planning method by a cubic approximation conformed to the arrangement of the isocenters satisfying the tumor shapes. This method only needs to determine a suitable cubic size considering the tumor volume, and can be lowed to a limited voxel ratio when the tumor surface has a deep flexibility or 'complex' cases. Therefore, these properties affect the number of isocenters located in a tumor. The divided cube regions included each isocenter where super- position of the isocenters was not allowed, which have a spherical dose distribution. As a result, the dose distribution within the tumor can achieve a homogeneous dose that meets the prescription dose. At least 95% of the target volume, which is the statistical method based on the voxel unit of the space, well satisfies the dose conformity and dose homogeneity to the targets relative to the RTOG radiosurgery plan guidelines. A technique for treatment planning optimization for linear accelerator radiosurgery was presented and verified for virtual targets. The optimization concentrated on the boundary region between a tumor and normal tissue, and overcame the problems of the previous technique based on the heuristic method. This method only considered two beam parameters such as the sphere location and diameter, which is commonly used in other modalities using spherical dose models. Namely, the treatment plan could be carried out fast, and was simple and applicable to other multiple isocenter radiosurgery techniques such as a Gamma Knife. Furthermore, a number of target shapes satisfied the dose distribution within the tumor referred to by the RTOG guideline. This method applied in a physical lattice structure easily provided information on the 3-D target volume and translated into different sphere sizes. In the arrangement of the small sphere, however, a number of spheres were consumed to cover the irregularly shaped tumor. In a simultaneous treatment plan for several targets in ROI, future work will involve constant voxel ratio using relative weighing, which is another common parameter in radiosurgical modality techniques.

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정위적 방사선 수술시 3차원적 공간상 단위분포들의 자동계산법에 의한 간접적 병소 근사화 방법의 개발

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정위적 방사선 수술은 한 번에 두 개내 병소에는 고선량의 방사선을 조사하면서, 주위 정상조직에는 최소한의 방사선이 조사되도록 시술하는 치료기법이다. 본 연구는 정위적 방사선 수술시 자동적 치료계획을 수행하기 위하여, 선형가속기와 감마나이프의 다수의 회전중심점을 이용하는 치료계획에 대한 물리적 격자구조에 기반한 새로운 방법을 개발하였다. 최적의 방사선 수술계획은 많은 빔관련 변수들의 조합으로서 만들어진다. 본 연구에서는 선형가속기와 감마나이프 수술시 빔 측면도의 50% 수준에서의 선량분포가 콜리메이터/헬멧의 구멍 크기와 일치하는 점을 이용하여 하나의 회전중심점을 중심으로 선량분포를 구형으로 모델화시켰다. 그리고, 다수의 회전중심점들은 병소내 위치와 크기를 고려한 정육면체 구조와 1×1×1 mm^3의 체적소 단위의 계산에 의해 자동적으로 배치시켰다. 이 기법에 의한 치료계획 방법은 선량체적히스토그램, 선량의 일치성, 선량의 균질성의 병소내 선량분포로서 평가되었다. 그 결과, 새로운 기법은 불규칙한 병소들에 대하여 프로그램 시스템에 의해 빠르게 다수의 회전중심점들을 배치시켰다. 또한, RTOG의 권고사항에 언급된 병소내 선량분포의 일치성, 균질성이 기준을 잘 만족하였고, 병소들은 50% 이상의 등선량 곡선 내에 포함되었다. 이와 같은 성과는 불규칙하게 형성된 병소와 선형가속기나 감마나이프와 같은 다른 치료 장치 기법들에서 특별한 제약없이 보편적으로 적용이 될 수 있을 것으로 생각된다.

중심단어: 정위적 방사선수술, 빔관련 변수, 병소재구성, 선량평가