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Optimization of Stereotactic Radiosurgery Treatment Planning

Introduction

Gamma knife, which uses stereotactic radiosurgery, is extensively used to treat a wide range of cancers. This therapy satisfies our needs by destroying locus as a result of enough radiation, while avoiding unnecessary damage to the surrounding tissue and organs. In the field of medicine, we can get optimal results if the dosage inside average tumor reaches above 50% .

Our model, during the whole treating course, is considered as a bulk composed of a group of isodose curves, which have the same center, inside the tumor. Guaranteeing the safety of surrounding tissues, we only take into account the volume relationship between the tumor and what 50% isodose curve encompasses. Through discrete digital calculating, we can decide optimal shots, locations, beam channels' diameters and all these parameters make 50% isodose curve coincide with tumor's contour. We also analyzed more difficult situations (see **Figure 0**). The small ball stands for the critical tissue, which must be outside the curve surface enclosed by a certain dosage curve.

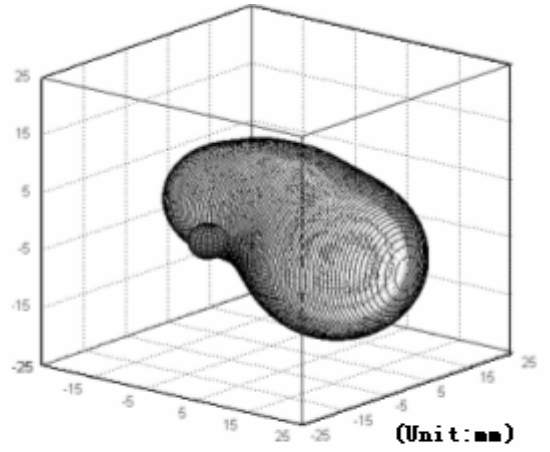

Figure 0.

Perspective view of the tumor.

We designed a computer program to deal with varieties of tumors' shapes, which can be produced through continuous curve surface's equation or discrete data. Applying geometrical and physical laws, this treating course can be simulated as a sphere-packing problem. Tumor's external is imagined to be firm and mustn't be protruded by 50% isodose curve. When the requests of volume, dosage and gradient are met, packing will stop.

Analysis of the Problem

According to clinic request, an optimal therapy planning must conform to rules as follows:

- A "conformity" goal: High-dosage area should approximately coincide with the

tumor's volume.

- A "homogeneity" goal: Dosage distribution should be homogeneous as much as possible, that is, energy gradient inside the volume of tumor must be small.
- "Decrease" goals: Dosage outside tumor must be decreased to minimum.
- Gradient goals: Ensure low dosage gradient inside tumor and high enough gradient on the edge.
- Safety goals: If there're significant critical organs, we must see to it that dosage on them is lower than the safe value.

Therefore, we must consider how to protect surrounding normal tissues, as well as how to effectively destroy locus area. Furthermore, we must prevent critical tissues from being damaged by radiations. So proper choice of shot-related parameters, including number of isocenters, locations and beam channels' diameters has become very important, Only in this way can we get optimal dosage curve surface in line with tumor surface.

Considering factors above, our algorithm should solve these problems well.

- Damage will be done to normal brain cells each time, so we should guarantee that shots are as few as possible.
- In order to form the largest volume covered, we need more radiation and beam channels of longer diameters.
- In order to lower the dosage gradient of target volume, we need beam channels of longer diameters.
- In order to bring down the damage done to critical organs, we can't produce shots near them. Meanwhile, choice of small-size beam channels is also essential.

The most difficult problem we met is that there's not a perfect therapeutic plan, and many requirements are even contradicted conflict with each other, especially about shots and target volume. Target volume is the function of shots. The more shots are, the bigger the target volume is. But our model requires that shots are as few as possible and target volume is as big as possible.

Assumptions and Hypothesis

- Tumor's position, contour can be precisely detected.
- Critical organs' position, contour and volume can be precisely detected.
- We assume the thickness of tissues involved can be neglected.
- Minimum effective therapy dosage is 50% of maximum, that is, volumes which receive dosage less than 50%, with exception of critical organs, will not be damaged.
- Tolerance dose of critical organs is lower than that of normal tissues, so we can just give it 30% of maximum dosage.
- Tolerance dose of different critical organs is identical.
- Distribution of 201 radiation sources is homogeneous on the helmet, so these 201 beams intersect at the isocenter and form a sphere.
- Radiating time is always the same, and the maximum dosage, too.
- Bad cells inside tumor are also distributed homogeneously so therapeutic effect of identical

dosage is the same.

- Media are also homogeneous outside tumor.
- There's no normal tissue inside tumors, and they are all tumor cells.

Table 1. Symbols used.

Symbol	Unit	Definition
U	Gy	total dosage value of a point
U_N	Gy	overall tolerable dosage of a normal tissue
U_C	Gy	overall tolerable dosage of an critical tissue
s	mm	beam channel's diameter
F^2	dimensionless	modification factor
TMR	dimensionless	tissue 's maximum ratio
OAR	dimensionless	off-axis ratio
C	dimensionless	constant which changes radiation exposure time into dosage
OF	dimensionless	output factor
ω	dimensionless	power amount distributed to a shot
η	dimensionless	Packing ratio
λ	mm	side length of volume element
N	1	number of radioactive sources
N_T	1	Volume elements' number contained in a shot area
N_D	1	Volume elements' number contained in half-dosage volume
M	1	number of shots

Structure of radioactive source

Gamma knife is composed of 201 colbat-60 distributed on a semi-sphere. Each one of them has individual longitude and altitude. They form 201 radioactive cones and there is a shot of largest intensity at the peak. More details acquired in **Figure 1.**

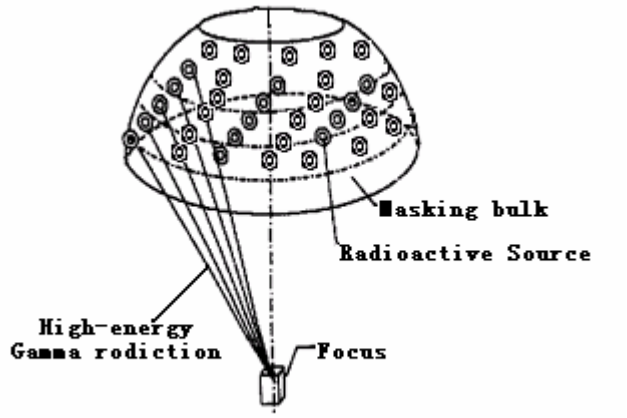

Figure 1. Illustration of radioactive source

Model of Dosage Calculation

Ideal model dosage calculation is to employ Monte Carlo's method applicable to radiating field of any shape, energy distribution of any radiation, inhomogeneity of any medium which we

can calculate dosage distribution via simulating physical course of interaction between photon and media. In order to be suitable for clinic application, we assume that the media are homogeneous for practical use. In this way the energy space's diffusion mode formed by the main interaction between radiation and media (that is, there's no edge effect), so it is practicable to the calculation of any point in the media. Based on this case, we use Rapid searching algorithm in combination with Monte Carlo's method to calculate dosage.

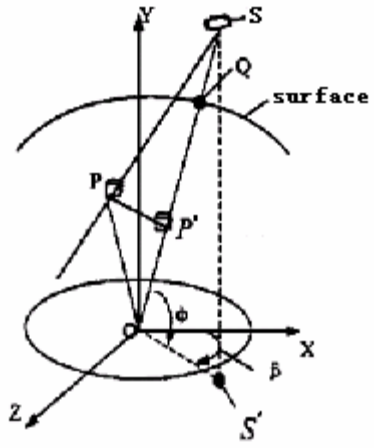

Figure 2. Illustration of single source irradiating.

Let's have a look at **Figure 2**, *O* is the focus of radiation, which is also the semi-spherical masking bulk's center. ϕ is single source *S*" altitude on the masking bulk, β is the longitude. *OS* is axis of radiating field with the definite length of *A*. The vertical line from *P* to *OS* interlaces *OS* at *P'*, *Q* is the interlacing point of *OS* and surface. *S'* is the vertical interlacing point from *S* to *XOZ* plane. Thus the absorption dosage of any point *P(X, Y, Z)* is:

$$\mathrm{D}_p\left(X,Y,Z\right)=C\times U_{OF}\left(s\right)\times U_{TMR}\left(s,d_p\right)\times U_{OAR}\left(r_p,s,d_p\right)\times F^2 \qquad (1)$$

In this formula, r_p is the distance from *P* to axis; d_p is the distance from the projection of *P* to the radiating field's axis to surface. According to Figure 2, we can calculate:

$$r_p=PP'==\sqrt{\left(X^2+Y^2+Z^2\right)-\left(X\cos\phi\cos\beta+Z\cos\phi\sin\beta+Y\sin\phi\right)^2} \qquad (2)$$

$$d_p=A-SSD-\left|\overline{OP'}\right|=A-SSD-\left(X\cos\phi\cos\beta+Z\cos\phi\sin\beta+Y\sin\phi\right) \qquad (3)$$

We can get the value of *TMR* and *OAR* at point *P* by referring to scientific tables, (we give *C* the value 1 because of the same radiating time) and then the absorption dosage of this point under the condition of single source and single shot can be calculated.

When many sources are radiating, the dosage we get is total amount when all sources radiate at the same time. According to formula（1）, we know that the total dosage at point *P* is:

$$D\left(\mathrm{X},\mathrm{Y},\mathrm{Z}\right)=\sum_{\mathrm{j}=1}^{N}C_j\times U_{OF_j}\left(s\right)\times U_{TMR}\left(s,d_j\right)\times U_{OAR}\left(r_j,s,d_j\right)\times F^2 \qquad (4)$$

$j=1,...,N,N=100$, j is the number of radiating sources.

When the number of shots is *M*, the total dosage at point *P* is:

$$U\left(X,Y,Z\right)=\sum_{i=1}^{M}\omega_i D_i\left(X,Y,Z\right) \qquad (5)$$

$i = 1,...,M$, ω_i is the power weight distributed to the shot which ranks i in sequence.

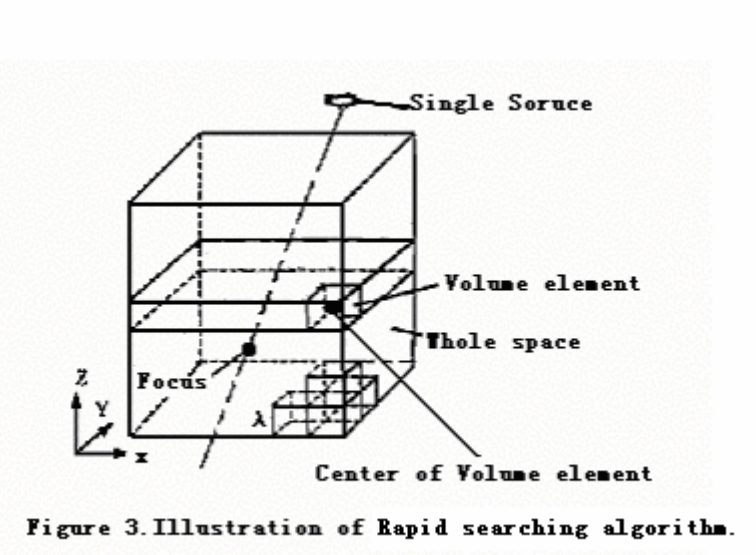

Figure 3. Illustration of Rapid searching algorithm.

Considering the whole *3D* space, we used Rapid Searching Algorithm, and its steps are as follows:

1. We cut the *3D* space whose center is the isocenter, and then we get many small cubic volume elements whose side length is λ. Suppose it can be divided into $a \times b \times c$ elements.
2. According to the request, we can work out the value of λ. If λ meets error requirement, we can substitute dosage of the center for that of other points in this volume element.

3. With formula（5）and step λ, work out the dosage value of every volume element. To calculate $a \times b \times c$ times is needed. In this way, we can get the distribution of spacial dosage. Changing the value of λ, we will get dosage of different accuracy.

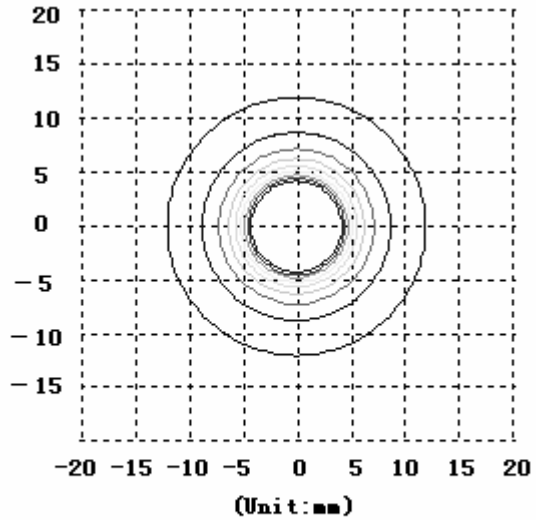

Figure 4.a x-z Plane
λ = 0.5, s= 8, ■= 1.

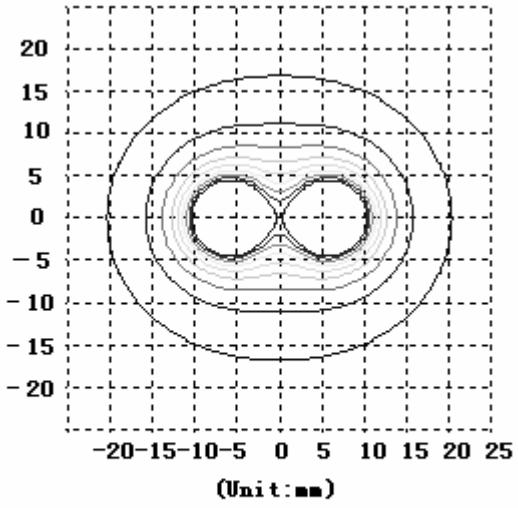

Figure 4.b x-z Plane
λ = 0.5, s= 8, ■= 2.

Suppose λ=0.5mm, dosage distribution section's illustration when we give it 1 shot and that when we give 2 are as follows, and we can see 9 isodose curves (from 10% to 90%). In **Figure 4.b**, distance between two shots' centers is 12mm.

Judgment of Dosage Gradient in Shot Areas

We can obtain from both practical analysis and computer-simulating results that gamma radiations are focused through rotation of 201 cones and then form a high-dosage area encompasses the focus. The area's dosage intensity gradually weakens from focus to edges in the way of isocenter circle and the weakening sharpness is related to size of the beam channel. In this way, we can get the half-dosage curve's width and sharpness degree of each beam channel. More details can be obtained from **Table 2**.

Table 2: (Unit: mm)
Half-dosage curve's width and Sharpness degree

Beam channel's radius	Half-dosage curve's width	Sharpness degree
4	6.1	3.6
8	11.5	7.5
14	19.5	11.8
18	24.7	12.2

We conclude from **Table 2** that relationship between sharpness degree and beam channel's radius is positive proportion. The smaller size a beam channel has, the more concentrated the dosage is and the quicker the edge dosage weakens, that is, the higher gradient shot area has; on the contrary, the lower gradient in the shot area is. Thereby, beam channels of bigger size are better.

Damage to Normal Tissues

We can attain overall absorption dosage at any point such as *P(X, Y, Z)* from the foregoing:

$$U(X,Y,Z)=\sum_{i=1}^{M}\omega_i D_i(X,Y,Z)$$

According to assumptions, we can find a point $P_{NORMAL}(X,Y,Z)$ within normal tumor, and then know whether normal tissues are damaged. Of course, we must adopt different paces in different conditions.

1. If $U(X,Y,Z)\geq U_{\mathrm{N}}$, we need to adjust shots, locations and sizes of beam channels.

2. If $U(X,Y,Z) \le U_{\mathrm{N}}$, that's OK.

Our goal is to make damage to outer tissues slightest, that is, tissues near the contour must be damaged slightest. So highest dosage gradient near the contour must be guaranteed. We indicate it in discrete method:

$$\max\{U(X,Y,Z)-U(X+\lambda,Y+\lambda,Z+\lambda)\} \tag{6}$$

Note that (X,Y,Z) is coordinate of a point on the contour.

Damage to Critical Tissues

Critical tissues can be precisely detected according to assumptions, that is, $P_{CRITICAL}(X,Y,Z)$ within critical tissues is definite. First, we must guarantee that the maximum value of damage to critical tissues must be smaller than $U_{c.}$ Second, we make the maximum value smallest. Namely, with regard to $P(X,Y,Z) \in P_{CRITICAL}(X,Y,Z)$:

$$\min\left(\max\{U_{CRITICAL}(X,Y,Z)\}\right) \tag{7}$$

$$\max\{U(X,Y,Z)\} \le U_{\mathrm{C}} \tag{8}$$

Calculation of Volume-packing Ratio

After cutting the whole space into volume elements, total volume surrounded by any contour can be measured by number of volume elements in it. We can also say that total volume is equal to product of λ^3 and number of volume elements. When we know the contour, computer will search in *3D* space with the step of λ and work out $N_{T.}$ Likewise, we can work out $N_{D.}$ So packing-ratio η can be represented as below:

$$\eta = \frac{N_D \times \lambda^3}{N_T \times \lambda^3} \times 100\% = \frac{N_D}{N_T} \times 100\% \tag{9}$$

Number of Shots and Original Value of Shots

As far as an isocenter is concerned, the original value of *s* is undoubtedly given a value as big as possible. And its original position is any point which satisfies the conditions below:

1. Half-dosage curve will not exceed the tumor;
2. 30% isodose curve will not cover critical tissues.

When there's no condition-satisfied point, decrease *s* and then search. Suppose the number of isocenters for a certain tumor $M \in [1,15]$. When diameter of the beam channel *s* and position of it

changes, *M's* value constantly changes. Suppose isocenters is $P_{F_i}(X,Y,Z)$, and then:

$$s \in \{4,8,14,18\}, \quad P_{F_i}(X,Y,Z) \in Shot\ Area, \quad i \in [1,M]$$

So we can define *M* using formula below:

$$M = f(X,Y,Z,s) \tag{10}$$

Namely, shots are determined by isocenters' locations and beam channels' diameters.

Model Design

Taking into account dosage gradient, damage to normal tissues, damage to critical tissues and packing ratio, we get the following discrete model to ascertain reasonable number of shots, locations and beam channel's diameters.

$$\min \quad M = f(X',Y',Z',s)$$

$$s.t \begin{cases} \eta > 90\% \\ U_{NORMAL}(X'',Y'',Z'') < U_N \\ U_{CRITICAL}(X''',Y''',Z''') < U_C \\ P(X',Y',Z') \in Shot\ Area \\ P(X'',Y'',Z'') \in Normal\ Tissue \\ P(X''',Y''',Z''') \in Critical\ Tissue \\ s \in \{4,8,14,18\}. \end{cases}$$

Steps implemented by computer are as follows:

1. add a isocenter $P(X',Y',Z')$;
2. move any isocenters $P(X',Y',Z')$ by step λ, making *s.t* met: if $max\{\eta\}<90\%$, then go to step1;
3. move any isocenters $P(X',Y',Z')$, till $max\{\eta\}$;

Algorithm ends, present plan is optimal..

Model Modification

For we have cut the whole *3D* space into small volumes, calculation amount is very tremendous especially when λ is small. Considering these factors, we can properly simplify the running course of our program. Accordingly, running time will reduce on basis of guaranteeing accuracy. These aspects below may be what we should pay attention to:

- Diminish the value range of M, based on tumor's contour.
- We also diminish the value range of $P(X',Y',Z')$ according to tumor contour, critical tissues' contour, corresponding sharpness degree and half-dosage curve's width. The final changed range is S_1.
- Choose some points on contour's curve, and these points' assembly will take the place of contour curve.

S_2 stands for the assembly of points in normal tissues; S_3 stands for assembly of points in critical tissues, if there's no critical tissue, S_3 is empty.

The original model will be altered into the following formula:

$$\min \quad M = f(X',Y',Z',s)$$

$$s.t\begin{cases}\eta > 90\% \\ U_{NORMAL}(X'',Y'',Z'') < U_N \\ U_{CRITICAL}(X''',Y''',Z''') < U_C \\ P(X',Y',Z') \in S_1 \\ P(X'',Y'',Z'') \in S_2 \\ P(X''',Y''',Z''') \in S_3 \\ s \in \{4,8,14,18\}. \end{cases}$$

Model Application

We supposed an irregular complicated tumor after outputting discrete data in MATLAB. And there's a critical tissue near the concave place. You can get the general situation from **Figure 0.** $\lambda=0.5mm$, the size of containing box is $100\times100\times100$. Consequently, we can work out the number of volume elements-----64807.

Table 3. Illustration of optimizing process

shots	Volume elements' number contained in half-dosage volume	Packing ratio
1	42493	65.6%
2	52556	81.1%
3	57030	88.0%
4	59686	92.1%

We can see from this table that packing-ratio will increase more slowly when shots' number increases. When shots' number reaches 5, the packing ratio will increase quite slightly and the computer program will neglect it automatically. Finally we got 4 isocenters. More details are in **Table 4.**

Table 4. Isocenters

	1	2	3	4
Isocenter's coordinate $P_i(X,Y,Z)$	(-6，11，-2)	(0，-12，0)	(5，-4，1)	(5，3，1)
Beam channel's diameter $S_i(mm)$	14	8	4	4

In order to justify validity of the model, we pick up 3 sections and they are z=0, x=5, y=5 separately. The charts of them are as follows:

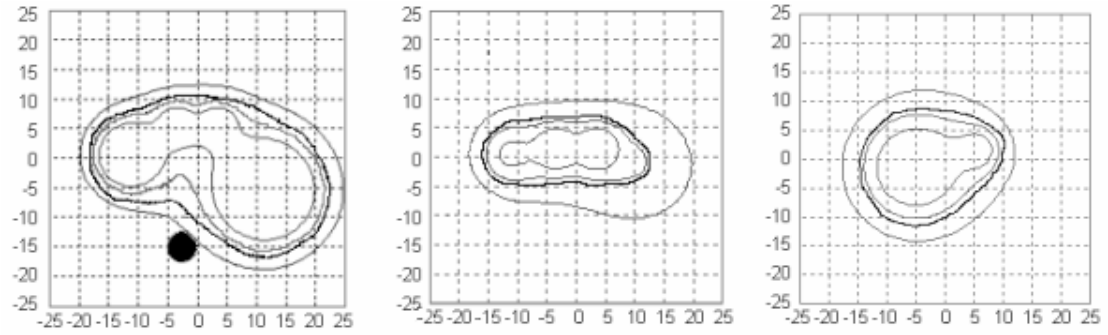

Figure 5.a x-y Plane λ=0.5, ■=4, z=0.

Figure 5.b y-z Plane λ=0.5, ■=4, x=5.

Figure 5.c x-z Plane λ=0.5, ■=4, y=5.

This chart shows: 50% isodose curve doesn't exceed target volume and 30% isodose curve does not cover critical tissues. Moreover, it also tells us the distribution regularity of isodose curves. Inside the tumor, they are dense; while outside the tumor, they gradually become sparser, rapider in weakening, and larger in gradient. So selection of isocenters is reasonable and valid.

Error Analysis

Selection of the initial point in this model constitutes a problem. When the number of isocenters increases, this model chooses any random point in line with conditions within tumor volume as the initial one. Therefore, this model is random to some extent, which leads to incomplete results as a result of improper choice of the initial point. We solved this problem by calculating several times so as to get the best solution.

Sensitivity Analysis

This model is not designed for a shape-designated tumor, and it considers tumors of any shape even shapes simulated from discrete data. Consequently, it is applicable to tumors of any shape.

To determine our model's stability, we choose different values of U_C and U_N， It doesn't hinder our attainment of the best solution, although the best solution would be different if we choose different maximum dosage.

At the same time, we also consider different OF， F^2 and C, and then get corresponding best

solution. In practical use, the model can be adjusted to application, by given different factors.

Strengths and Weaknesses

This model can arrive at above 90% or any given proportion's therapeutic area for tumors of any shape, but it won't damage normal cells, furthermore, it protects surrounding critical cells. It implement realizes good therapeutic effect on the basis of adequate safety.

The shape of tumor can be given by any curve surface's equation, or by discrete data similar to CT images in clinic practice, and tumor's contour can be very complex. In this way, it has extensive range of application. In the course of simulating sphere-packing in the whole area, to calculate the accurate shots, position and beam channels' diameter makes therapeutic error smaller, suitable for manipulation in practical treatment.

We think that there's no perfect plan for a practice, and the best plan got from model is based on contemplations of the balance between therapeutic area and shots, and it is, to some extent, affected by random original points, which is the most serious flaw.

To different contours and critical tissues, we need to change the value of λ according to the error allowed, which will inevitably influence the executive results.

Time complexity of this algorithm is not large, but large quantities of time are still needed. Therefore, selection of original points and moving of shots also require improving.

Conclusion

Our model has solved the problem of shots, dosage gradient and packing- ratio's calculation, so it's suitable for clinic application. However, some other factors need to be considered in further modifications.

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