

Optimization of Dose Distribution for High Dose Rate Intraluminal Therapy

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= Abstract =

The use of high dose rate remote afterloading system for the treatment of intraluminal lesions necessitates the need for a more accurate of dose distributions around the high intensity brachytherapy sources, doses are often prescribed to a distance of few centimeters from the linear source, and in this range the dose distribution is very difficult to assess.

Accurated and optimized dose calculation with stable numerical algorithms by PC level computer was required to treatment intraluminal lesions by high dose rate brachytherapy system. The exposure rate from sources was calculated with Sievert integral and dose rate in tissue was calculated with Meisberger equation.

An algorithm for generating a treatment plan with optimized dose distribution was developed for high dose rate intraluminal radiotherapy. The treatment volume becomes the locus of the constrained target surface points that is the specified radial distance from the source dwelling positions.

The treatment target volume may be alternately outlined on an x-ray film of the implant dummy sources. The routine used a linear programming formulism to compute which dwell time at each position to irradiate the constrained dose rate at the target surface points while minimizing the total volume integrated dose to the patient.

The exposure rate and the dose distribution to be confirmed the result of calculation with algorithm were measured with film dosimetry, TLD and small size ion chambers.

Key words : Intraluminal brachytherapy, Dose optimization, Sievert integral, Meisberger equation, Linear programming formulism.

INTRODUCTION

The high dose rate remote afterloading system for the treatment of intraluminal lesions needs a accuracy and optimization of dose distributions around the high intensity brachytherapy sources. The dose distribution to a distance of few centimeters from the linear source is very difficult to

evaluation^{1,2)}.

The recent developments in afterloading treatment techniques require numerically stable algorithms for a reliable three dimensional dose optimization^{3,4,5)}. The afterloading irradiator consists of a high activity radioactive source mounted at the end of a wire. The wire travels inside a catheter that has been inserted inside the patient^{6,7)}.

The exposure rate at a reference point in air was calculated with Sievert integral formula and dose rate calculation was performed with the Meisberger polynomial program.

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The radioactive source may be programmed to dwell for specified times at specific points along the pathway inside the catheter. This system permits selection of dwell positions and dwell times to achieve a desired dose distribution. Our purpose is to generate these plans quickly and automatically with minimal input, as the planning must be done after the placement of the catheters in the patient and before actual treatment can commence.

Linear programming is a mathematical technique for problems requiring optimization and solution methods are well developed. Linear programming has been applied to radiation therapy in previous reports, all of which are too numerous to cite here. We will follow the ideas developed in two prior reports on applications to planning implants^{5,6}.

By fixing the dwell positions and letting the dwell time be variables, our problem fits into the linear programming formalism.

The exposure rate and the dose distribution to be confirmed the result of calculation with algorithm were measured with film dosimetry, TLD and a PTW 0.1 cm³ ion chamber in a small water phantom in a distance of 10cm from the source.

MATERIALS AND METHODS

1. Dose distribution

Exposure rate distribution around a linear brachytherapy source can be calculated using the Sievert integral^{8,9,10}. The method consists of dividing the line source into small elementary sources and applying inverse square law and filtration corrections to each. Consider a source of active length L(cm) and filtration t(cm). The exposure rate I at a point P(x,y) contributed by the whole source elements

$$I(x, y) = \frac{A\Gamma}{Ly} \int_{\theta_1}^{\theta_2} \exp(-\mu t \sec \theta) d\theta \quad (1)$$

Where A and Γ are the activity (mCi) and exposure rate constant ($R * cm^2/hr * mCi$) of the unfiltered source and μ is the effective attenuation coefficient(cm^{-1}) for the filter, and θ is the angle

between the point and perpendicular distance,y (cm), on the active length axis^{11,12,13}.

The Sievert integral gives the exposure rate distribution in air and considers only the inverse square law and filtration effects. When a source is implanted in the tissue, one needs to consider, in addition, attenuation as well as scattering in the surrounding tissue. The exposure rate calculated at a point in tissue can then be converted into absorbed dose rate by using the appropriate roentgen-to-rad factor.

We used Meisberger's formula to calculate absorbed dose in tissue. It's a third order polynomial formula to fit the average of their theoretical and all available experimental data^{14,15,16}.

The calculation of isodose rate in a water medium is performed with the personal computer. The calculation program uses the "Meisberger Polynomial" for radial distances lower than 10 cm from the sources as follow.

$$D(r) = \frac{A\Gamma}{r^2} P(r) \quad (2)$$

$$P(r) = A + Br + Cr^2 + Dr^3 \quad (3)$$

Source	Γ	A	B	C	D
Ir-192	4.66	1.0128	$5.02 * 10^{-3}$	$-1.18 * 10^{-3}$	$2.01 * 10^{-5}$
Au-198	2.32	1.0306	$-8.13 * 10^{-3}$	$1.11 * 10^{-3}$	$-1.60 * 10^{-4}$
Cs-137	3.26	1.0091	$-9.02 * 10^{-3}$	$-3.46 * 10^{-4}$	$-2.82 * 10^{-5}$
Co-60	12.8	0.9942	$-5.32 * 10^{-3}$	$-2.61 * 10^{-3}$	$1.33 * 10^{-4}$

For distances larger than 10 cm an exponential equation is introduced for the isodose calculation.

$$D(r) = \frac{A\Gamma}{r^2} P(10) \exp\{-\mu(r-10)\} \quad (4)$$

D is the absorbed dose rate in tissue(cGy), A is activity (Ci), Γ is exposure rate constant ($R * cm^2/hr * mCi$), r is radial distance(cm) and μ is attenuation coefficient (cm^{-1}) for tissue.

This program allows to calculate points and wire sources, the maximum number of sources is 50. The isodose distribution can be displayed in different planes, sagittal, frontal and transversal.

2. Algorithm for dose optimization

Inspecting several numerical algorithms for

solving linear equation systems, we found a type of optimization problem similar to the problem of finding the appropriate dwell times in afterloading treatment planning. This type of problem is called Linear programming system. It consists of a system of linear constraints which can be used to specify lower and upper limits for both the dwell times and the dose values^{17,18,19)}. The optimization criterion can be used to specify weight factors for both dose and dwell time homogeneity^{20,21,22)}.

The algorithm, which is used for the solution of linear programming system problem, is the Simplex algorithm. It starts with the search for a feasible point, a combination of dwell times which fulfills all linear constraints, and minimizes the value of the objective function until an optimum is found^{5,18)}.

The coordinates of a finite number of possible dwell positions on a catheter are evenly spaced along the catheter as provided by the afterloading machine and have been restricted to a specified region of interest. These coordinates may be found from orthogonal x-ray films taken of the implant. Numbering all dwell positions on all catheters 1 through n, let t_i be the dwell time at the i th dwell position.

We mark the film indicating the beginning and end of the region of interest where the dose prescription is prescribed at the perpendicular distance from the catheter suitable margins which have been added to the tumor volume in indicating the region of interest. This is a matter of definition of target volume.

The points generated on the target volume margins are constraint points used in the algorithm and are enumerated 1 to m. Let the dwell time t_i at each dwell position be the unknown variable, let a_{ij} be the dose rate contribution from the i th dwell position to the j th constraint point, with D_j the total dose to the j th constraint point. Let Z be the numerical sum of all the dwell times, and TD is the specified target dose. Then the dwell times t_i can be found by solving the linear programming problem

$$\text{Minimize } Z = \sum_{i=1}^n t_i \quad (5)$$

Subject to the constraints

$$D_j = \sum_{i=1}^n a_{ij} t_i > TD, \text{ for all } j = 1 \text{ to } m \quad (6)$$

$$t_i > 0, \text{ for all } i = 1 \text{ to } n$$

The last constraint, that t_i is a positive number, is implicit in the linear programming formalism and is not formally written. The problem as formulated will have, in general, an infinite number of solutions. An optimal solution is one for which no other choices of dwell times will result in a smaller value of Z , the sum of the dwell times in this case, and still satisfy the requirements of all the constraints, i.e., that all constraint points receive at least the target dose (TD). There may be more than one optimal solution, but all will necessarily have the same value of Z . An optimal solution can be found by using the Simplex method^{5,22)}.

In the first place, minimizing the sum of the dwell times will minimize the integral dose to the patient. The total dose integrated over the volume of the patient is directly proportional to the total time the source is in the patient. Minimizing the time the source is in the patient will minimize the integrated dose. If there were no constraint points, then the sum Z would simply be zero. The constraint points, however, prevent such a trivial solution. The optimal solution calls for the smallest possible treatment time, while the constraint points enforce a floor on the dose at each constraint point. The solution will tend to lower the dose at each constraint point as much as possible, driving the solution in the direction of a uniform dose distribution on the target surface. We have not considered nonlinear approaches to this problem such as minimizing²³⁾

$$Z = \sum_{j=1}^m (D_j - TD)^2 \quad (7)$$

Because we want to force the dose to be at least target dose (TD) every where inside the target volume. A least squares fit of Eq.(7) with-

out constraints on the dose as above in Eq.(5) would not guarantee the target dose of TD at all constraint points, and the solution would also allow negative times. Nonlinear techniques with constraints will require an order of magnitude more computer time for solution for the same number of variables and constraints.

Such points are called nonbinding constraints as their presence will have no effect on the solution.

The solution times for the Simplex method increase exponentially with the size of the problem. Spending the computer time to eliminate constraint points inside the volume might in fact save more time in solving the problem and would certainly seem to be necessary when employing nonlinear techniques.

The algorithm doesn't necessarily produce a time at every dwell position. Spreading the times out over all the dwell positions may give a more uniform dose distribution in the interior of the volume near the catheter.

Consequently, there are some values in averaging the dwell times over a few neighboring dwell positions. A concentration of time in a small area will result in higher doses near that area, but on the other hand, using less dwell positions makes operation of the equipment easier and less error prone. This program has been implemented on IBM/PC compatible computers running MS-DOS. It accepts up to 100 dwell positions and 50 dose reference points. The personal computer has a 4MB RAM with the numerical coprocessor and printer.

The measurement of dose rates were performed in a standard water phantom with 0.1 cc water proofed ion chamber and TLD dosimeters

RESULTS

1. Dose distribution from source

Exposure dose rate calculations in the vicinity of the high activity sealed linear sources are performed with a computer. Fig. 1 is shown the exposure dose rate distribution for sealed point

source to be calculated by the Sievert Integral formula (Eq.1), and to be measured with film dosimetry. The exposure dose rate for radial direction is much larger than that for length along to source axis because of sealed materials and self absorption (Fig. 2).

The exposure dose rate is difference between the near and far field from the sources. There is

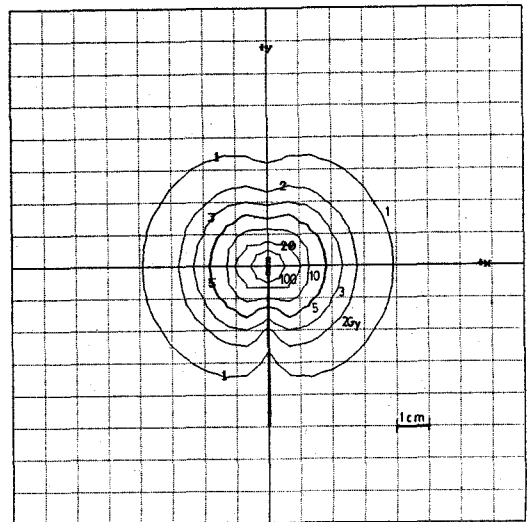


Fig. 1. Isodose curves around a 10Ci Iridium-192 short line source (0.6mm ϕ \times 3.5mm active length) with 120 sec dwell times. Dose plotted are 1, 2, 3, 5, 10, 20 and 100Gy

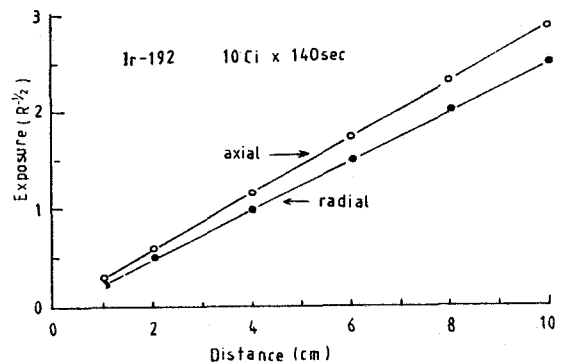


Fig. 2. Plot of exposure dose of 10Ci Ir-192 source as a function of radial and axial distance from short line source with 0.6mm ϕ \times 3.5mm active length.

a $1/r$ dependency for short radial distances against the active length of the source, where as for long radial distances against the active length of the source there is a $1/r^2$ dependency of the dose rate.

Figure 3 is shown the exposure rate for both direction from the linear source as a function of distance. The exposure dose rate distribution is a good correspondence between calculation and measurement, even as the formula considers neither absorption nor stray effects.

Figure 4 compares the radial exposure rate distribution of 3cm active length with that of a iridium-192 point source. Whereas the curve for the point source represents an inverse square law function, the linear source curve was obtained using the Sievert integral. It is evident from the figure that for the linear source, the exposure rate is less than that predicted by the inverse square law, especially at points close to the source. This is as expected since the photons reaching these points from the source extremities travel larger distances and suffer oblique filtration which is greater than the radial wall thick-

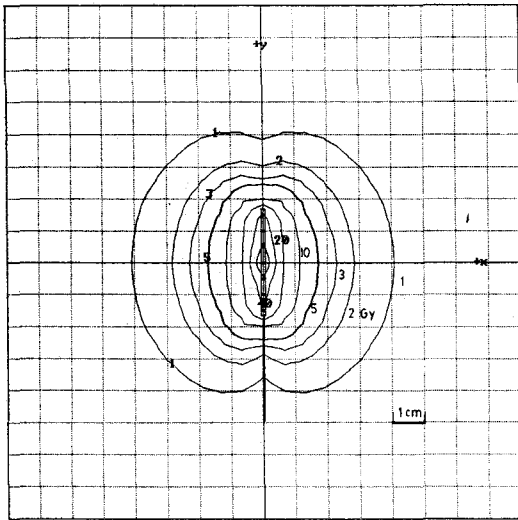


Fig. 3. Dose distribution of 10Ci Ir-192 linear source with same dwell times at 7 points into 3cm intraluminal catheter. Dose plotted are 1, 2, 3, 5, 10, 20, 40 and 60Gy.

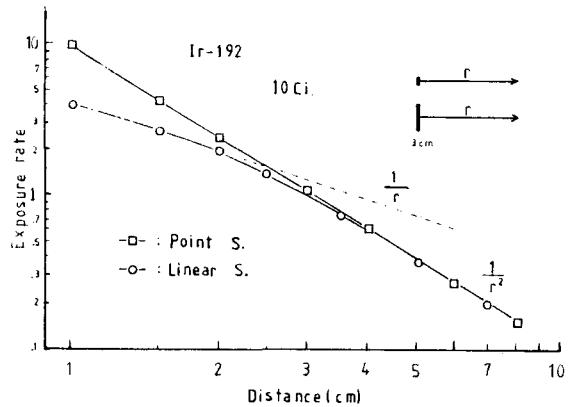


Fig. 4. Plot of exposure rate to radial distance from 10Ci Ir-192 source as a function of radial distance for point source and linear source with 3cm active length.

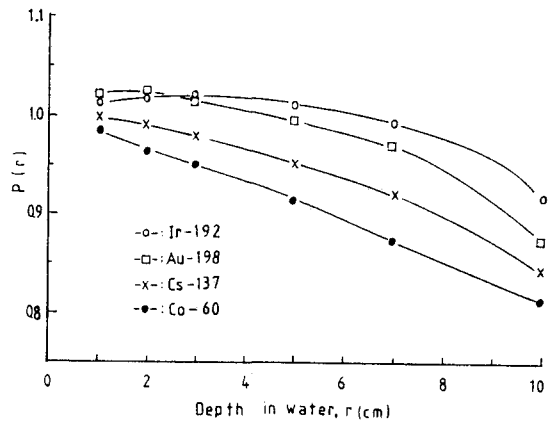


Fig. 5. Attenuation correction factor in water as a function of distance for a point source. curves are calculated by Equation 3.

ness. As the distance is increased, these effects of the linear source approach those of the pointsource and its exposure rate curve approaches inverse square law.

The absorbed dose rate in a water is calculated by Meisberger Polynomial (Eq.2), for radial distances shorter than 10 cm from the sources.

Figure 5 shows the absorbed dose curves calculated by Eq.3 at short distances, the attenuation of the primary photons is very much compensated for by the contribution of scattered photons with the result that the exposure in water is almost equal to the exposure in air at

the same point. However, tissue attenuation overtakes scattering at larger distances.

For cobalt sources, the net reduction is about 1% per cm of intervening tissue up to $5\text{cm}^{2,3)}$.

The consequences of activity deviations data on the isodoses of the linear array of 11 sources are demonstrated the activity range of 7.5% error in the dose distribution. As the dose gradient is much more steep close to the sources, the error of the radial dose is smaller than in larger distances due to the $1/r^2$ dependency

2. Dose optimization of intraluminal catheter

For optimum dose distribution on target volume, film simulated was taken as anterior and lateral position, and then we decided target volum along the intraluminal catheter and pointed out the constraint positions along the target volum contour. The optimized dose was calculated by the Simplex equation (5),(6) and (7) with computer.

As an example of the method considers the problem of irradiating a intraluminal catheter, 5cm long to a dose of 5Gy at a radius of 2cm, we will assume that all possible dwell positions are separated by 0.5cm intervals along the 5cm length catheter, beginning with dwell position No. 1 at one end and ending with No. 11 at the other end. The solution was found by generating constraint points using the same interval of 0.5cm at a radius parallel to the length of the catheter. Figure 6 shows the resultant dose distributions for a $3.7 \times 10^{11}\text{Bq}(10\text{Ci})$ Ir-192 source of 11 dwell points and 11 constrained reference points.

We have noted that the solution tends to have a concentration of time at the dwell positions at the ends of each catheter which may be objectionable (table 1). The reason for this is that the constraint points perpendicular to the end points and at distance from constraint points are only irradiated by dwell positions inside the region of interest as we have restricted the dwell positions to the region of interest. The constraint point near the center of the region of interest receives radiation from both ends of the catheter,

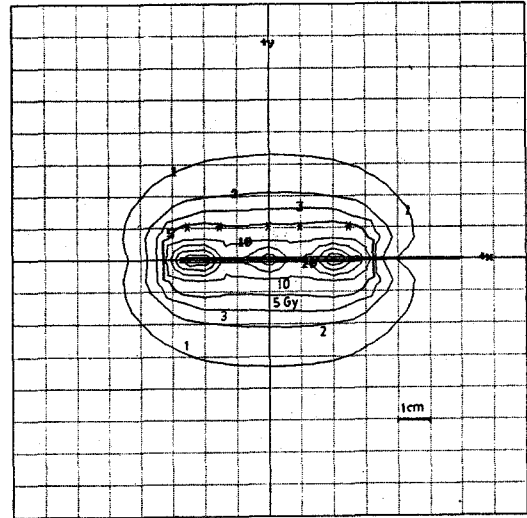


Fig. 6. Dose distribution under reference dose constraint at 1cm from source axis as 5Gy for intraluminal brachytherapy with 10 Ci Ir-192 source, the end dwell point times have been spread out over 11 dwell positions. Dose plotted are 1, 2, 3, 5, 10, 20, 30, 50 and 100 Gy.

Table 1. Solution for a 5cm long straight line catheter, with dwell positions every 0.5cm, to treat 5Gy to a constraint radius of 1cm, with a $3.7 \times 10^{11}\text{Bq}$ (10Ci) Ir-192 source, All times shown are in seconds

No	Dwell position			Dwell time sec	Constraint	
	x (cm)	y (cm)	z (cm)		radius (cm)	Dose (Gy)
1	-2.5	0	0	20	1	4.93
2	-2.0	0	0	13	1	4.99
3	-1.5	0	0	5	1	5.01
4	-1.0	0	0	4	1	5.00
5	-0.5	0	0	8	1	5.01
6	0.0	0	0	10	1	5.03
7	0.5	0	0	7	1	5.01
8	1.0	0	0	5	1	5.00
9	1.5	0	0	8	1	5.01
10	2.0	0	0	14	1	5.02
11	2.5	0	0	18	1	4.99

where—as a constraint point near the end only receives radiation from one direction. Consequent-

ly, the dwell time at the end has to be larger to boost the dose at the end constraint point to target dose. Because this larger time also contributes to constraint points near this same end, a decrease in time is needed in the area adjacent to the end.

3. Irregularly shaped optimization for a intraluminal catheter

The target volume for a single catheter can be alternately designed by outlining an irregular contour around the catheter in one or both of two orthogonal films. If we consider the line defined by a point on this contour to the point source of x-rays, we can find the point on this lines that comes closest to the catheter, which we will take as a constraint point. By generating such constraint point by considering even intervals around the contour on one or both films, we can define sufficient constraint points for solution by the above method, where the dose may now vary along the length of the catheter. In this case, to view the isodose curves, we generated the best plane through the catheter using least

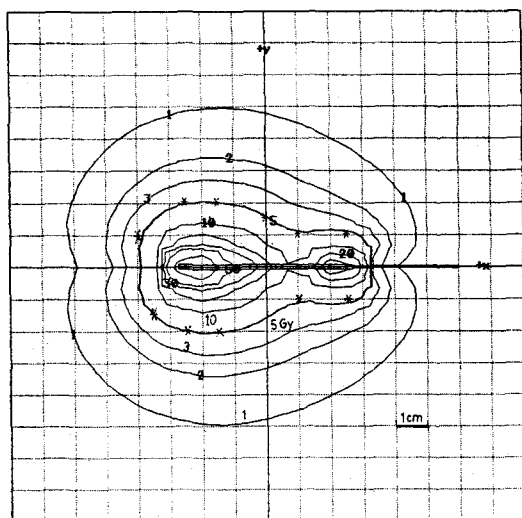


Fig. 7. Resultant of optimum dose distribution for an irregular volume with 1cm constraint points as dose of 5 Gy. Dose plotted are 1, 2, 3, 5, 10, 20, 30, 50 and 100Gy.

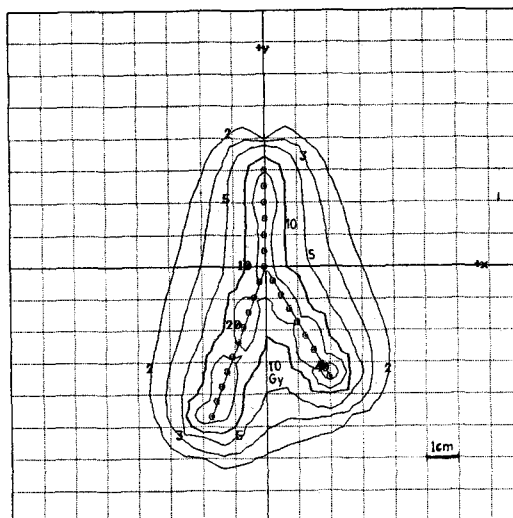


Fig. 8. Bronchial application dwell times, 10Gy isodose on constraint reference points at 0.6cm from catheter axis. Dose plotted are 2, 3, 5, 10, 20, 40 and 60Gy.

- : dwell position,
- * : dose reference point, constraint dose : 10Gy

squares. Figure 7 shows the resultant of optimized dose distribution for a pear shape target volume with 11 dwell points of Ir-192 source.

Figure 8 shows the optimization of dose distribution for the bronchial cancer with Iridium 192 source into linear bronchial catheter.

DISCUSSION

Using the activity of the radionuclide in the source as the method of specification suffers from a number of problems. It is difficult to determine the activity in a brachytherapy source, and different methods of determination may yield different values. Likewise, it is difficult for some radionuclide, to determine the exposure rate constant, especially for encapsulated sources. When activity and exposure rate are treated as separate parameters in the dose calculation, it is inevitable that attempts will be made to determine them with ever increasing accuracy. Not only is this wasted effort, from the viewpoint of brachytherapy, but it is inevitable that indepen-

dent choice of these parameters will in some cases be inappropriate, and lead to incorrect values of the desired quantity, exposure rate at the calibration point. For these reasons, activity is an unsuitable method of specifying brachytherapy sources.

Source strength specification in terms of the exposure rate at a specified distance does not suffer from the disadvantages mentioned above. Exposure rate is a measured quantity that can be directly traceable to a national standard. Dose rate in tissue, the quantity of interest in clinical dosimetry, is much more closely related to exposure rate than to the activity encapsulated in a source, and a knowledge of the exposure rate constant is unnecessary. The equivalent mass of radium is essentially the same as exposure rate specification since equality of exposure rate is used to define the equivalent mass of radium.

Specification in terms of equivalent mass of radium also facilitates the use of radium dosage tables for clinical dosimetry. However, the equivalent mass of radium is now of historical interest only, as radium substitutes replace radium sources. Although radium tables may still be of some utility in planning brachytherapy procedures, it is probable they will be replaced by more convenient computer generated planning aids. Radium tables should generally not be used for final dosimetric evaluation and computerized systems are used more and more to obtain dose distributions for individual patients on which clinical decisions are based.

It should be noted that both the radium equivalence method and the apparent activity method involve dividing exposure rate by the exposure rate constant to get the source strength and then multiplying by it to calculate the dose. Aside from the obvious redundancy, this manipulation of a dummy constant leads to the real possibility of error, especially since the division may be performed by the manufacturer, using one value, and the multiplication by the user, using another value.

Thus, the quantity exposure is in the process

of being phased out and the use of air kerma rate at a reference distance is recommended as the method of choice.

The dose rate at a specified distance is very difficult to measure accurately around sources and the quantity, although more directly related to clinically desired dose, would result in more variability errors among institutions^{14,15}.

Formulating the design of optimum dose distributions for a computer controlled afterloading device as a linear programming problem is successful in achieving a treatment plan for a specified target volume without requiring to locate constraint points or specify particular dwell positions. With this algorithm, it is only necessary for the constraint points to be generated so as to define the treatment volume, hence use of this method reduces the design of the implant problem to that of defining the target volume. The plan can then be arrived at automatically and fairly quickly after data entry with only a dose prescription at a distance required of the dose planners.

We have limited ourselves to considering an irregularly shaped volume found from contours drawn on film around a single catheter or volumes specified as the locus of all points at a given distance from the region of interest of all catheters. More sophisticated methods of defining a target volume would probably require construction of a volume from out lines in successive transverse computed tomography scans as described by Renner *et. al.*^{6,19,21,22}, since the out-lines would most likely have to relate somehow to the patient's particular anatomy. We will pursue that approach in the future only if the clinical problem proves to demand it.

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= 국문초록 =

고선량을 관내 방사선치료를 위한 종양선량분포의 최적화에 대한 연구

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원격조종 아프터로딩에 의한 고선량을 관내삽입조사는 체내 발생된 종양에 방사선원을 근접시켜 치료하는 방사선요법으로서 신속한 선량계산과 선량의 정확성 및 다양한 모양의 최적선량분포가 요구된다.

저자들은 크기가 작고 선량이 높은 고선량의 방사성동위원소에 대한 정확한 조사선량과 최적선량분포를 얻기 위하여 수학적인 컴퓨터 계산프로그램과 실측으로서 비교하였다.

고선량을 선원에 의한 방사선 조사선량과 조직내 흡수선량분포는 각각 Sievert적분식과 Meisberger의 다항식을 이용하여 작성하였다.

종양크기와 모양에 가장 알맞는 선량분포의 최적화를 실현하기 위하여 저자들은 치료기준점의 선량을 일정한 값으로 고정시키고 선원의 조사시간을 조정하는 선형반복 계산방정식을 이용하였다.

모형선원이 장착된 아프터로딩관을 삽입하고 조준엑스선으로 촬영하여 종양부위를 결정한 후 컴퓨터의 도움으로 아프터로딩관의 축과 평행한 등량곡선 또는 과일모양의 선량분포 및 기관지 모양의 등선량분포가 성취되도록 선량최적화를 시행하였고 선량계에 의한 실측치와 오차가 3%이하로 잘 일치하였다.