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Conceptual Source Design and Dosimetric Feasibility Study for Intravascular Treatment: A Proposal for Intensity Modulated Brachytherapy

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Purpose: To propose a conceptual design of a novel source for intensity modulated brachytherapy.

Materials and Methods: The source design incorporates both radioactive and shielding materials (stainless steel or tungsten), to provide an asymmetric dose intensity in the azimuthal direction. The intensity modulated intravascular brachytherapy was performed by combining a series of dwell positions and times, distributed along the azimuthal coordinates. Two simple designs for the beta-emitting sources, with similar physical dimensions to a ^{90}Sr/Y Novoste Beat-Cath source, were considered in the dosimetric feasibility study. In the first design, the radioactive and materials each occupy half of the cylinder and in the second, the radioactive material occupies only a quater of the cylinder. The radial and azimuthal dose distributions around each source were calculated using the MCNP Monte Carlo code.

Results: The preliminary hypothetical simulation and optimization results demonstrated the 87% difference between the maximum and minimum doses to the lumen wall, due to off-centering of the radiation source, could be reduced to less than 7% by optimizing the azimuthal dwell positions and times of the partially shielded intravascular brachytherapy sources.

Conclusion: The novel brachytherapy source design, and conceptual source delivery system, proposed in this study show promising dosimetric characteristics for the realization of intensity modulated brachytherapy in intravascular treatment. Further development of this concept will center on building a delivery system that can precisely control the angular motion of a radiation source in a small-diameter catheter.

Key Words: Intensity modulation, Intravascular brachytherapy, MCNP

Introduction

Recently, intravascular brachytherapy has received considerable attention for the prevention of restenosis of both coronary and peripheral blood vessels. It has been shown that radiation can substantially reduce the problem of restenosis after angioplasty.[1~10)] Several techniques have been developed for the delivery of low dose radiation to the site of restenosis. Two major approaches are a temporary implant using a catheter-based delivery system and a permanent implant using radioactive stents.[11)] In a catheter-based delivery system, the radiation source is introduced to the proper position through a catheter; it stays there for the amount of time needed to deliver the prescribed dose to the target and then is retracted. A radioactive stent is permanently placed in the obstructed vessel in a permanent implant system. Both gamma and beta emitters have been used in catheter-based radiation delivery systems, whereas radioactive stents have primarily used beta emitters only.

Two major issues arise with the current systems. The first is the centering of the radiation source in the coronary vessel and the effect of off-centering on the dose distribution in catheter-based radiation delivery systems. The effect of off-centering is

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significant for both photon and beta emitters because of the short distances to dose prescription points. The short range of beta particles in tissue further alters the resulting dose distribution with even a slightoff-centering of thedelivery catheter. Amols *et al* have shown that a centering offset of 0.5 mm within a 3 mm artery can cause a dose asymmetry b y a factor that ranges from 2 to 3 for both beta-emitting (^{32}P and ^{90}Sr) andgamma-emitting (^{192}Ir) sources.[12] Radioactive liquid- filled balloons wouldappeartoavoidoff-centeringissueby evenlydistributing the liquid source within the balloon. However inflation of the balloon leads to restricted blood flow through the vessel, thus leading to ischemia and vessel spasms and thus negating the potential advantage. The recently introducedhelicalballoon has theadvantageofhavingadequatesource centering while allowing minimal blood flow. The second major issue involves the inhomogeneous composition and geometric asymmetry of an atherosclerotic plaque. A common assumptionfor radiation dose calculation and delivery in intravascular brachytherapy has been thatthetargetconsistsofahomogeneous medium equivalent to water that is azimuthally symmetric with respecttothelongaxis ofasource.Sinceastenotichumanbloodvessel often is lined with atheromatous plaques of heterogeneous composition,[13~19] the radiation dose distribution delivered can be significantly different from that calculated or prescribed. Furthermore, the asymmetric distribution of residual plaques can create a more heterogeneousdose distribution. Such significant discrepanciesin dose distribution can introduce relatively large uncertainties in thelimitsofthedosewindowforeffective andsafeapplication ofintravascular brachytherapy,andconsequentlyinthe clinical evaluation of the efficacy of intravascular brachytherapy.

Currently, noradiation dose delivery system forintravascular brachytherapy completely overcomes the issues of dose asymmetry due to radiation source off-centering and the heterogeneous composition of an atheromatous plaque. We propose a concept for an intensity modulated brachytherapy delivery system that potentially solves dose asymmetry problems associated withexistingintravascular brachytherapydeliverysystems. The proposed systemcan provide anazimuthally asymmetricdose distribution using different combinationsofsource orientations and source dwell times. Source orientation and dwell times are optimized to deliverthedesireddose distributiontoan appropriate radiation targetobtained from imaging devices such as an intra vessel ultrasound scan (IVUS).

Materials and Methods

1. Source design

Traditionally, sealed brachytherapy sources are designed to provide azimuthally symmetric dose distributions. In principle, symmetric sources cannot provide the heterogeneous radiation intensitythatisrequired to producean optimal dose distribution through the heterogeneous andasymmetric target thatisfairly commoninintravascular brachytherapytreatments. Basedonthis consideration, a design for a brachytherapy source, named the intensity modulationbrachytherapysource(IMBS),isintroduced. Unlike other sources, the brachytherapy source consists of two parts, a radioactive part ineitheronehalf(π in azimuthal angle) or one fourth ($1/2\,\pi$ in azimuthal angle)ofthesourceandthe shielding materialintheremainder of the source (Fig. 1). An azimuthally asymmetric dose distribution can beobtainedfrom this source by using different combinationsofazimuthal source positions and sourcedwelltimes.Source positions anddwelltimes are optimized to deliver the desired dose distribution to an appropriate radiation target obtained from IVUS images. This source design can potentiallybe extendedtootherconventional brachytherapy applications.

2. Monte Carlo calculation

A Monte Carlo calculation is performed to obtain the dose distribution in water for theproposedbrachytherapy source. A general-purpose photon/electron/neutron transport code developed attheLosAlamosNationalLaboratory(MCNPVersion 4c)isusedinthisstudy.MCNPutilizesthecondensed-history

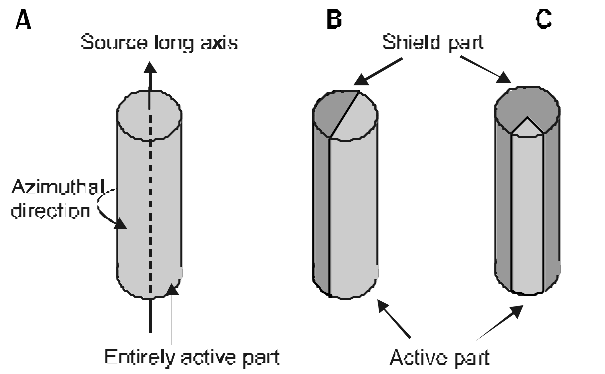

Fig. 1. General view of brachytherapy source: (A) conventional source-designed to give azimuthally symmetric dose distribution, (B,C) partially shielded source-designed to give azimuthally asymmetric dose distribution; dose optimization is obtained by optimizing dwell positions and dwell times.

approach of Integrated Tiger Series (ITS) version3.0forelectron transport.[20] MCNP has recently been used in medical physics as well as many other areas such as nuclear physics, nuclear engineering, and material science.

A ^{90}Sr/Y betasource that is similar to a Novoste Beta-Cath (Novoste Corporate, Norcross, GA, USA) source is assumed in thissimulation. Inthebeta-cath system, the source is a cylindrical train of12or16sourceseeds,eachhaving dimensions of0.64 mmindiameterand 2.5mminlength, and proximal/distal gold markers. Each seed contains ^{90}Sr/Y mixed with fired ceramic encapsulated in a 0.04 mm stainless steel wall. In this study,

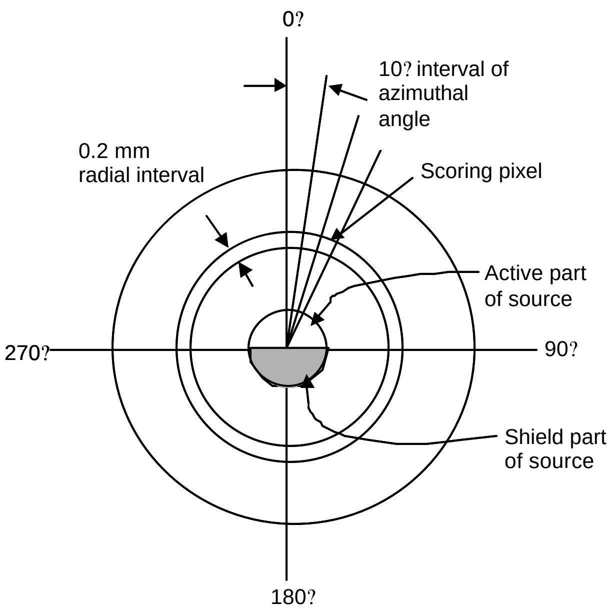

Fig. 2. MCNP calculation geometry.

however, the source assumed is a cylinderhavingdimensions of 0.68 mm in outer diameter (including 0.04 mm thick stainless steel wall) and 2.5 mm in length. The calculation geometry is shown inFig.2.Thecalculation pixelwas chosenin a cylindrical coordinate with radial intervalof 0.2mmand10° azimuthal angle. The calculationwasperformedto6 mm radial distance for only half ofacirclebecauseoftheazimuthalsymmetry.Itis important to choose an appropriate shielding material to obtain an asymmetricdosedistribution adequate forintensity modulation. Both stainless steel and tungsten were used in the computer simulationtodeterminewhich one providedtheoptimalshielding within the sourcesize and geometric constraints. Emitting beta spectrumissimplified into6 energy binsof0.125,0.25,0.5,1.5, 2.0, and2.27 MeVs.Probabilitiesused for energybins are 0.167, 0.158, 0.0875, 0.033, 0.01875, and 0.00625 respectively. Summarized is detail information for Monte Carlo calculation in Table 1. Bremsstrahlung x-ray production from thebetarays ofthesourceisestimatedtobeinsignificant.For1MeVelectron (average energy of ^{90}Y is 934keV),radiation yieldintungsten material is about 6%. In the one fourth oftheradiationsource case (x-ray production is higherinonefourthdesignthanone half), wecanassume 3 electrons enterintotungsten shield when 1 electron headstonon-shielddirection. Conservativelyassuming 100% of energy is absorbed within shield, x-ray production is approximately $3\times0.06=0.18$, that is, 18% of 1 electron energy heading to non-shield direction. If we assume an isotropic distribution of x-ray intensity, the energy fluence to each quadrant is4.5%.Consideringmuch longer penetrationofx-rays compared t o electrons, real energydeposition by x-rays isexpected to be insignificant within the range of interest. Therefore, we have ignored theenergydeposition by the bremsstrahlung x-rays

Table 1. Parameters Used for MC Calculation

Mode	Spectrum: MeV	Spectrum: Probability	Material and weight fraction: Water	Stainless steel	Tungsten	Al.Oxide	History
Electron	0.125 0.25 0.5 1.5 2.0 2.27	0.167 0.158 0.0875 0.033 0.01875 0.00625	H 0.11 O 0.89	Si 0.01 Cr 0.17 Mg 0.02 Fe 0.68 Ni 0.12	W 1.0	Al 0.71 O 0.89	6 million

in our analysis.

3. Dose optimization

As an example of dose optimization, we consider an off-center placement of a source. As shown in Fig. 3, the source is placed 0.75 mm off center in a 3 mm diameter vessel. Optimization is performed to provide a dose as uniform as possible at 2 mm distance from the center of the vessel. This is the recommended dose prescription point for the Novoste system. Dose optimizations should be performed in three-dimensional geometry. We, however, consider only a two-dimensional geometry for this feasibility test because dose contribution in longitudinal direction is relatively insignificant. In principle, a minimum of four dose calculation points (D_1, D_2, D_3, and D_4) are needed to obtain four dwell times (t_1, t_2, t_3 and t_4) as shown in Fig. 3, where t_j is the optimized dwell time for dwell position with which source part is heading to point j (j = 1, 2, 3, and 4). Therefore, the problem can be as simple as 4 linear equations with 4 unknowns like

$$D_i = \sum_{j=1}^{4} D_0 \, R(\gamma_i) \, A(\gamma_i, \phi_{i,j}) \, t_j \quad \text{for } i = 1,\ 2,\ 3, \text{ and } 4 \quad \cdots\cdots(1)$$

where

D_0 = dose rate at radius of 1 mm through azimuthal angle 0^o,

$R(\gamma)$ = relative radial dose distribution at radius γ through azimuthal angle 0^o,

γ_i = radius from the center of source to the dose calculation point i,

$A(\gamma, \phi)$ = azimuthal dose distribution at angle ϕ and radius γ, and

ϕ_{ij} = azimuthal angle between point i and the source with dwell position j.

Our problem can even be simplified further to 3 linear equations with 3 unknowns because of the symmetry of the geometry (i.e., $t_2 = t_3$). It may be possible to solve an inverse matrix directly when it is well conditioned. However, in practice, as the number of dwell positions increases, iterative methods can be applied. The optimization routine optimizes the dwell positions in the azimuthal direction. Intuitively, an optimal solution will result from an infinite number of dwell positions, but this is not practical. We arbitrarily constrained the optimization to four dwell positions for practical reasons.

Results

1. Monte Carlo calculation

The relative dose distributions through azimuthal angle at a radius of 1, 2, 3, and 4 mm from the center of the source are shown in polar coordinates in Fig. 4 through 7. Results for a one-half-radioactive source (hereafter, we will call π source) with a stainless steel (SS) shield and a tungsten (W) shield are shown in Fig. 4 and 5, respectively. Fig. 6 and 7 show results for a one-fourth-radioactive source (hereafter, we will call 1/2π

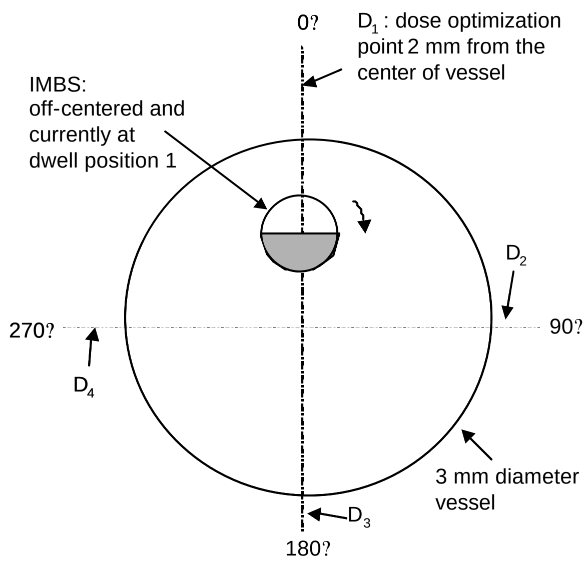

Fig. 3. Dose optimization geometry.

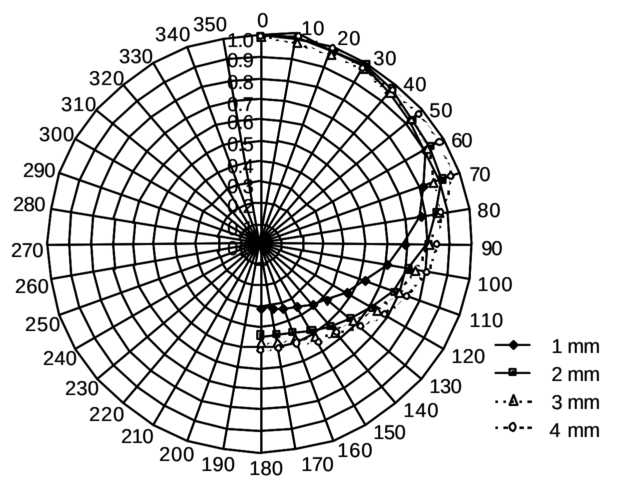

Fig. 4. Relative azimuthal dose distribution at bisector plane in polar coordinate by distances from the center of the source: π source with stainless steel shield.

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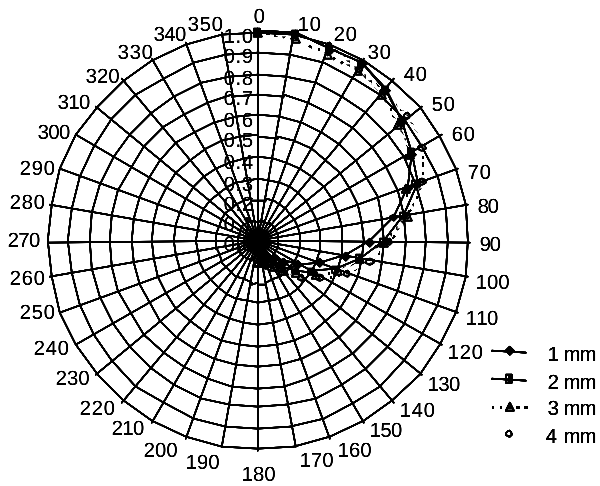

Fig. 5. Relative azimuthal dose distribution at bisector plane in polar coordinate by distances from the center of the source: π source with tungsten shield.

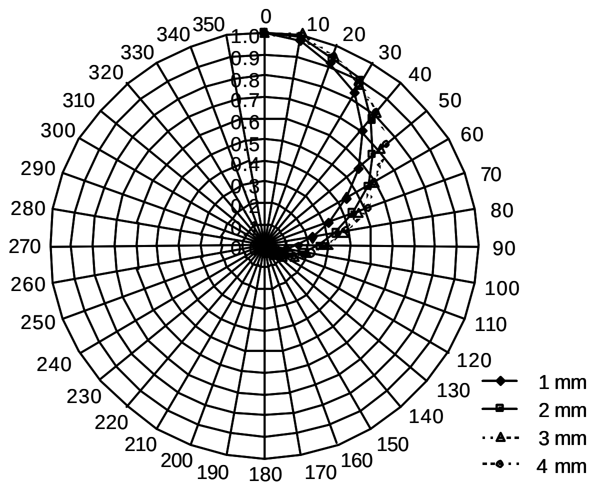

Fig. 7. Relative azimuthaldosedistribution at bisectorplane in polar coordinate bydistancesfrom thecenter of the source: 1/2 π source with tungsten shield.

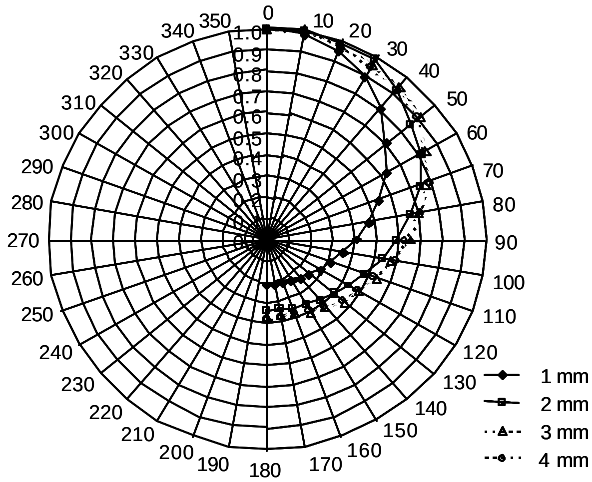

Fig. 6. Relative azimuthal dose distribution at bisectorplane in polar coordinate bydistancesfromthecenterofthesource: 1/2 π source with stainless steel shield.

Table 2. Intensity Modulability and Angular Length: values are at radius of 1 mm

	IM	A_{80}	A_{50}	A_{20}
1/2 Source SS Shield	3.2	74	114	NA
1/2 Source W Shield	19.4	64	93	123
1/4 Source SS Shield	4.7	40	75	NA
1/4 Source W Shield	65.8	32	56	84

SS: stainless steel, W: tungsten

with a stainlesssteel shield and a tungstenshield,respectively. Relativedosevaluesare normalizedtothedosevalueat 0°, where the doserateismaximalateachradius. The degree of intensity modulationisdependent of the asymmetry of the azimuthal dose distribution for each shielded source. Therefore, itisusefulto define a quantity,intensity modulability (*IM*), thatistheratio ofthemaximumandminimumdoserates. Itisclearthatahigher resolutionofintensity modulation can beobtainedwith a higher *IM*. With an ideal shielding material, the minimumreaches to zero, thusresulting in a *IM* of infinity. We also define angular index (A_X), which is anangle where doserate is *X* percent of themaximum. Apparently, we canuse angularindextoindicate a range of angles for which the dose rate iseither significant or insignificant. For example, A_{80}=40° means dose distribution is equal toorhigherthan80%of maximum between-40° (320) and 40°. It isexpectedthat A_X canbecorrelatedwithan optimum number ofdwellpositions. On the other hand, A_{20}=150° indicates dose is equal to orlowerthan20%intherangeof150° to 210°. Itisintuitive that an 1/2 π sourcegives a higher *IM* than a π source does (refertoFig.4 ~ 7). It is also obviousthat tungsten is a better shielding material compared withstainlesssteel because it provides better *IM*s. Table 2 summarizes *IM*, A_{80}, A_{50}, and A_{20} obtained at radius of 1 mmforeachsourcedesign. Relative radial dosedistributions are similar to each other for all four different sourcedesignswithslightlyfaster dosefalloffforthe1/2 πsource. Fig. 8 and 9 show relative radial dose distributions for the π and 1/2 π sourcewithtungsten shields, respectively. Polynomial equations were fittedtothecalculateddosedistributions and were

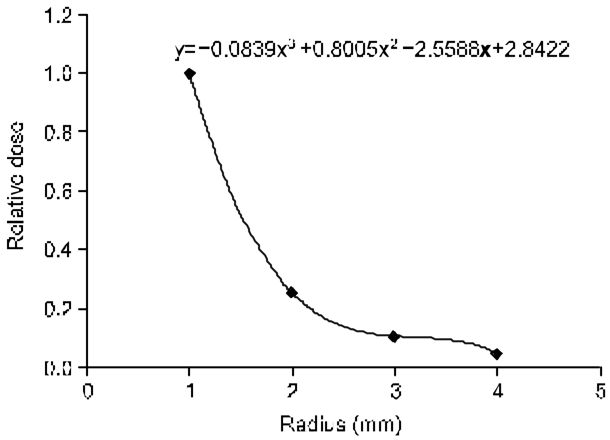

Fig. 8. Relative radial dosedistributionatbisectorplane: π source with tungsten shield. A polynomial-fittingequation is obtained for dose optimization with x=radial distance from the center and y=relative dose (dotted line).

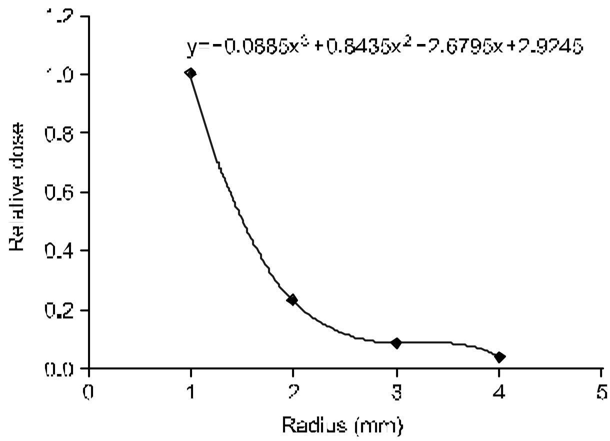

Fig. 9. Relative radial dose distribution at bisector plane: 1/2π source with tungsten shield. A polynomial-fitting equation is obtained for dose optimization with x=radial distance from the center and y=relative dose (dotted line).

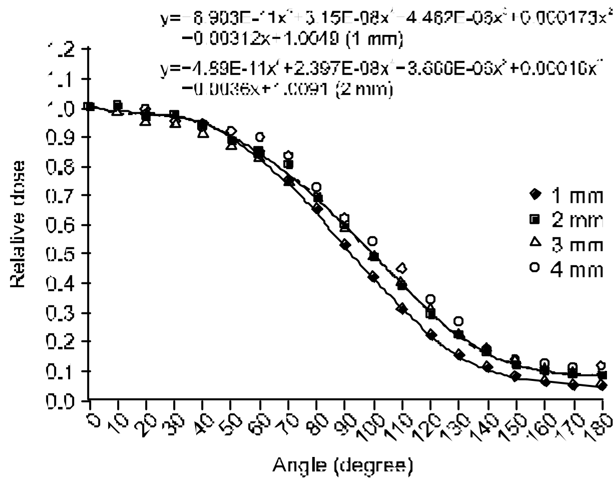

Fig.10. Relative azimuthal dose distribution at bisector plane: π source with tungsten shield. Polynomial-fitting equations are obtained for dose optimization with x=azimuthal angle and y=relative dose (dotted lines).

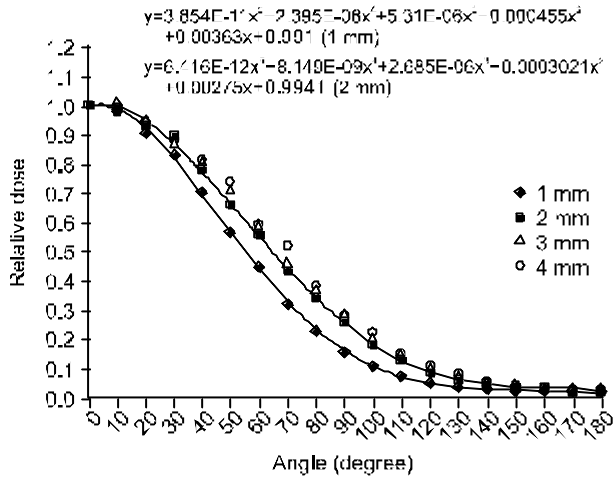

Fig. 11. Relative azimuthal dose distribution at bisectorplane:1/2π source with tungsten shield. Polynomial-fitting equations are obtained for dose optimization with x=azimuthal angle and y=relative dose (dotted lines).

used for dose optimization calculations. For dose optimization, azimuthal dosedistributions also werefitted for the π and 1/2π source with tungsten shields (Fig. 10 and 11, respectively). Although the difference in the azimuthal dose distributionsfor the 1 mm and 2 mm radii is significant, the differences among 2, 3, and 4 mmradii are insignificant. Therefore, we obtained a single fitting equation for the dose optimization calculation that isrepresentativeofazimuthal dosedistributionsatradii 2 mmand greater from the center of the source.

2. Dose optimization

Optimized relative azimuthal dosedistributions areshown in Fig. 12 and 13, respectively, for the π and 1/2π source with tungstenshields. Doses arecalculated at 15° intervals using dwell times obtained through optimization. Values are normalized to the maximum. For comparison, dose distributions from a conventional source designthat has uniform dose intensity in the azimuthal direction are also shown. It is very clear that IMBS

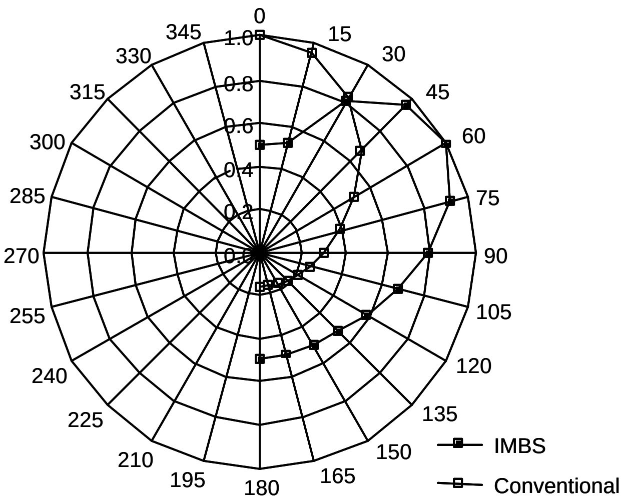

Fig. 12. Relative optimized azimuthal dose distribution at bisector plane in polar coordinate: π source with tungsten shield. Dose distribution with conventional source is also shown for comparison.

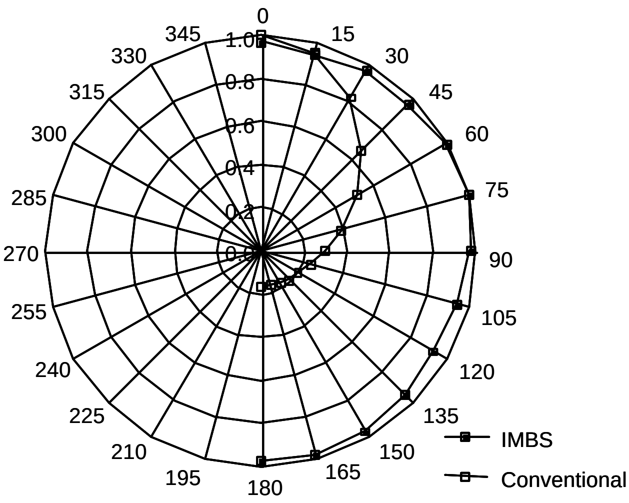

Fig. 13. Relative optimized azimuthal dose distribution at bisector plane in polar coordinate: $1/2\pi$ source with tungsten shield. Dose distribution with conventional source is also shown for comparison.

provides a much improved dose distribution, especially the $1/2\pi$

Table 3. Relative Optimized Dwell Times: normalized to t_1

	t_1	t_2	t_3	t_4
1/2 Source W Shield	1	0	11.57	0
1/4 Source W Shield	1	0.55	9.63	0.55

W: tungsten

source design. Compared with the minimum dose of 13% in conventional source design, IMBS gives 48% in the π source design and 93% in the $1/2\pi$ source design. Table 3 summarizes optimized relative dwell times. Whereas direct matrix inversion was achieved for the $1/2\pi$ source, a forward optimization was performed with the π source because a negative dwell time was obtained by the direct inverse method. As shown in Table 3, only two dwell positions, t_1 and t_2 have dwell times for the π source.

Discussion

We have considered only a two-dimensional geometry for this feasibility test. In a clinical situation, dose optimizations should be performed in three-dimensional geometry. Dose contribution from axial direction is rather close to 1/r fall off than $1/r^2$, which makes dose heterogeneity less severe in general. This, therefore, will make dose homogeneity slightly better. Three-dimensional optimization must also take into account the axial inhomogeneity in vessel cross-section, vessel curvature, dosimetric perturbation by plaque, and relative motion between the vessel and the source. Therefore, it is critically important to utilize IVUS images to obtain more accurate spatial information of clinical geometry. IVUS images can potentially provide data on source off-centering, geometry of vessel, plaque composition and thickness, and vessel motion. Three-dimensional dose optimization will be possible by stepping (axial direction) and rotation (radial direction) of the source. Treatment time can be a disadvantage of this method compared to current practice with beta source. However, when we consider the typical delivery time needed with ^{192}Ir source, it could be within a range reasonably acceptable. It can be reduced by optimal isotope, source length, and operating mechanisms.

Fabrication of IMB delivery system is a real challenge. We are considering mechanical approach currently. There are wires that can be rotated to certain degree without cranking even when it is located in a curved catheter. A test is ongoing to find how much and accurately control the angular rotation with several different wires. If that kind of wire is found, the source can be connected to the end of the wire and rotated clockwise 180^o and counterclockwise 180^o. Another possible approach is to use electrical control system. There are already a lot of electrical devices that require rotation within blood vessel (e.g., IVUS). Therefore, we believe, it will be possible to make an electrical device that can control the angular rotation of source. Electrical device will give higher precision but be more expensive.

The concept of IMB will not be restricted to intravascular therapy. This technique can be utilized for conventional brachytherapy as the image-guided brachytherapy becomes more important and popular. When itiscombinedwithcurrentremote after-loading technique like HDR (High Dose Rate) brachytherapy, IMB may berealizedwithrelative ease.Uniformityof azimuthal dose distribution in intravascular brachytherapy can be improved enormously by intensity modulated brachytherapy (IMB). IMB can be performed with the shielded source design proposed inthis paper and a delivery system (yettobedesigned) that permits controlled angular rotation of this source around itsown long axis. With sucha system, optimizeddosedistribution can bedeliveredbyacombinationofdwellpositions and dwell times in azimuthal coordinates. In a simple off-centering case, a conventional intravascular brachytherapy source delivers azimuthal dose distribution with an 87%difference between the maximum and the minimum dose to thelumen surface. Thistype ofdosenon-uniformity can be easily reduced to less than 7% with an intensity modulated brachytherapy source. The assumptionismadehere thattheangularrotationofthe source can be controlled.

This paper describesa novel brachytherapysourcedesign and a conceptual source delivery system that has the potential to significantly improve dose uniformity in intravascular brachytherapy. Further development of thisconcept hingesonbuilding a delivery system that preciselycontrols the angular motion of a radiation source in a small-diameter catheter. This is not completely out of the realm of reality as there are several electromechanical devices routinely used in microsurgery that have precision motion requirements much more stringent than those of the proposed intravascular brachytherapy delivery system. We have started some preliminary discussions with our electrical/biomedical engineering departments to build such a device. Other significant challenges include theinterpretationof IVUS imagesforsourceoff-centering, geometry ofvessel,plaque composition and thickness, and vessel motion.

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혈관내 방사선치료를 위한 이론적 선원 설계 및 선량적 관점에서의 적합성 연구: 출력변조를 이용한 근접치료에 대한 제안

Florida 대학교 방사선종양학과*, 방사선원자력공학과[†],
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목 적: 본 연구는 새로운 근접치료선원의 이론적 설계를 통해 출력변조를 이용한 혈관내 방사선치료를 제안한다.
대상 및 방법: 제시된 이론적 선원은 기존의 선원과는 달리 선원물질과 차폐물질(스테인리스 스틸, 또는 텅스텐) 둘 다로 구성되며 이는 방위방향으로 비대칭적 방사선량을 제공할 수 있게 한다. 따라서, 방위방향으로 선원의 방향과 체류시간을 조절함으로써 출력변조를 통한 근접치료가 가능해진다. Novoste Beta-Cath system에서 사용하는 Sr-90/Y 전자방출 선원과 유사한 모양의 두 가지 단순화한 선원을 연구의 대상으로 고려하였다. 첫 번째 선원은 선원물질과 차폐물질이 각각 반씩 차지하며, 두 번째 선원은 1/4은 선원물질로, 나머지 3/4은 차폐물질로 구성된다. 두 선원에 대해 방위 및 방사방향으로의 선량분포를 MCNP 몬테 카를로 코드를 이용하여 계산하였다.
결 과: 선원이 혈관내의 중심에 위치하지 않게 되는 가상조건에서의 선량최적화 계산을 시도한 결과, 혈관내벽에 미치는 선량의 최고치와 최저치의 차이가 87%에서 7%까지 줄어들 수 있음을 보였다.
결 론: 본 연구에서 제시된 이론적 선원은 선량적 관점에서의 적합성 여부에 관해 매우 고무적인 결과를 보여줌으로써 출력변조를 통한 혈관내 근접방사선치료의 가능성을 나타내었다. 본 과제의 다음 단계는 굵기가 가는 맥관내에서 선원의 위치를 파악하여 그를 방위방향으로 정확하게 회전시킬 수 있는 방사선 전달 체계의 개발이라 할 수 있다.

핵심용어: 출력변조, 혈관내 근접치료, MCNP