DOSIMETRY MODEL FOR INTRAVASCULAR BRACHYTHERAPY TREATMENT PLANNING WITH RADIOISOTOPE EMITTING STENTS

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BACKGROUND

One of the major drawbacks of percutaneous transluminal coronary angioplasty (PTCA) is the high rate of restenosis, which occurs in approximately 30-50% of all patients undergoing the procedure [1-4]. Vascular irradiation, otherwise known as intravascular brachytherapy has emerged as an attractive candidate therapy for the treatment of restenosis. The three main components of restenosis, early recoil, remodeling and neointimal hyperplasia, can all potentially be successfully treated with a radioactive stent [2,3]. The stent serves as a scaffold, thus maintaining the lumen of the artery open, even after early recoil soon after the angioplasty procedure. The ionizing radiation emitted from the stent has been shown to have positive effects on the reduction of neointimal growth and vascular remodeling [3]. However, experimental results are inconsistent, and restenosis at stent edges, otherwise known as the "candy wrapper effect", has been identified as one of the main problems with this treatment modality [5].

Dosimetry plays a very important role in the success and safety of intravascular brachytherapy. While the overall benefits of this treatment are well documented, some uncertainties still remain with uniform radiation delivery, adverse effects, optimal radioisotope, radiation dose, dose rate, initial activity and target tissue [2-4]. The goal of a radioactive stent is to deliver an appropriate dose and dose rate to prevent restenosis with an acceptable level of toxicity. This is a crucial point in the planning of an intravascular brachytherapy treatment. So far, there is no adequate treatment planning system in intravascular brachytherapy specifically designed for radioactive stents.

OBJECTIVES

The aim of this study is to develop a general and versatile dosimetry and radiobiological model for the prediction of dose distribution and biological effects of stents with different radioisotopes, initial activities, dimensions and stent geometries. This model is also applied to demonstrate the radiobiological convenience of a dosing strategy based on the combination of different radioisotopes in the same stent, whether uniformly distributed or only on the stent edges for the treatment of edge restenosis. In addition, the 3D dose distribution of a novel ^{177}Lu stent is investigated and compared to the results obtained from a ^{32}P stent. This type of theoretical dose calculation can be useful for clinical decisions involving individualized treatment plans, clinical trials and animal experiments, as well as for the development of new stent designs. An effective planning system aims to improve the outcomes by modifying stent characteristics to optimize treatment.

METHODS

The algorithm for the dose calculation is written in Matlab and is based on the dose point kernel convolution technique described by Janicki et al [6]. A_0 is the stent's initial activity, λ is the decay constant

$$D(r,t) = \frac{A_0}{S\lambda} x[1 - \exp(-\lambda t)] x \int K(x) ds$$

of the radioisotope, S is the active stent area, and x is the distance between the source point on the stent surface and the field point where the dose is calculated. K(x) is the dose point kernel function. The dose point kernel (DPK) describes the distribution of absorbed dose around point-isotropic sources of electrons and beta particles in water [7]. This model uses information obtained from previously published dose point kernels for the radioisotopes of interest. In the case of ^{177}Lu, for which there is no previously published data, DPK values are calculated from monoenergetic electron kernels folded over the beta spectrum [7]. The first step in this dose calculation model is the projection of the 3D schematic of the stent into a 2D image from which the coordinate system of θ and Z is established (Fig.1). This coordinate system represents the source points from which the dose will be calculated at specific distances radially and axially from the surface of the stent.

The radiobiological impact on endothelial cells, smooth muscle cells and advenitital myofibroblasts is investigated by the generation

of dose-response or dose-survival curves according to the linear quadratic formalism [8]:

$$S = e^{-\alpha D - \beta D^2}$$

It expresses the surviving fraction (S) of cells as a function of dose (D). The constants α and β are characteristic of a given cell type and are 0.23 Gy^{-1} and 0.1 Gy^{-2} respectively for smooth muscle cells [9].

RESULTS

The following is an example of a simple stent geometry for which dose calculations are performed. It represents the area over which the numerical integration of the DPK convolution for the dose is calculated.

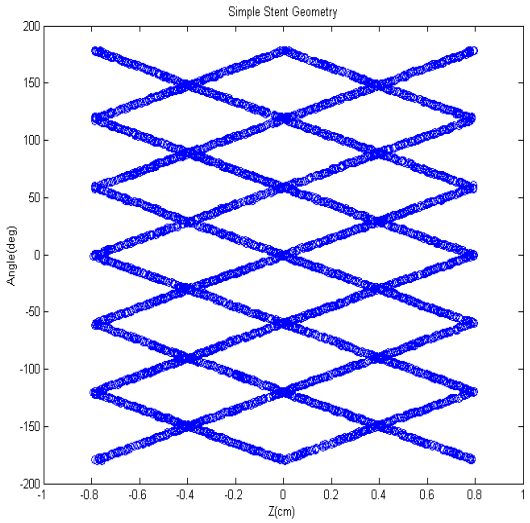

Figure 1. Simple stent geometry and coordinate system used for dose calculations

Preliminary dose calculations of the ^{177}Lu stent at a distance of 0.5 mm from the surface resulted in 3.1Gy/100μCi. The following table illustrates the effect of increasing dose on the survival fraction of a population of target cells, in this case taken as smooth muscle cells for a distance of 0.5 mm from the surface of the stent.

Activity (μCi)	Dose (Gy) at 0.5 mm	Surviving Fraction (%)
100	3.1	18.75
200	6.2	0.514
300	9.3	0.002065
500	15.5	1.042×10^{-10}

Table 1. Calculation of survival fraction of smooth muscle cells as a result of irradiation from a stent with different dose and initial activities

CONCLUSIONS

This dosimetry model is a practical and fast algorithm used for calculating the 3D dose distribution and biological effectiveness of radioactive stents with variations in geometry, radioisotope(s) and initial activity. The model's final result can be used to plan an intravascular brachytherapy treatment, aid in the development of an industrial design of a radioactive stent, and the planning of animal studies and clinical trials. This model will permit the assessment of the effectiveness of different radionuclides, or combinations of such, for addressing the problem of edge restenosis. In addition, the response of blood vessels to radiation treatment can be quite complex. Therefore, it is of great importance to study, model and understand the biological effects of radiation on vascular tissue to optimize the design of a specific brachytherapy treatment.

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