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Investigating the dosimetric impact of seed location uncertainties in Collaborative Ocular Melanoma Study–based eye plaques

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ABSTRACT

PURPOSE: To quantify the dosimetric effects of random and systematic seed position uncertainties in Collaborative Ocular Melanoma Study–based eye plaques.

METHODS AND MATERIALS: An eye plaque dose calculation routine was created using Task Group 43 formalism. A variety of clinical configurations were simulated, including two seed models: ^{125}I and ^{103}Pd, three eye plaque sizes, and eight plaque/eye orientations. Dose was calculated at four ocular anatomic sites and three central axis plaque depths. Random seed positional uncertainty was modeled by adding Gaussian random displacements, in one of three seed-motion degrees of freedom, to each seed's nominal coordinate. Distributions of dosimetric outcomes were obtained and fitted after 10^6 randomizations. Similar analysis was performed for deterministic, systematic shifts of the plaque along the eye surface and radially from the globe center.

RESULTS: Random seed placement uncertainties of 0.2-mm root mean square (RMS) (amplitude) produce dose changes that are typically <4% for each degree of freedom (95% confidence interval). Systematic seed placement uncertainties are generally greater than random uncertainty 95% confidence intervals (factor of 0.72–2.15), with the relative magnitudes depending on plaque size and location of interest. Eye plaque dosimetry is most sensitive to seed movement toward the center of the eye. Dosimetric uncertainty also increases with increasing dose gradients, which are typically greatest near the inner sclera, with smaller plaques, and with lower energy radionuclides (e.g., ^{103}Pd).

CONCLUSIONS: Dosimetric uncertainties due to the random seed positional displacements anticipated in the clinic are expected to be <4% for each degree of freedom in most circumstances.

Keywords: Eye plaque; COMS; Brachytherapy; Uncertainties; Dosimetry; Ocular; Eye

Introduction

Eye plaque brachytherapy is a standard technique for the treatment of ocular malignancies (1, 2). Brachytherapy eye plaques are typically comprised of a metal alloy plaque, designed to shield extraocular structures from radiation dose, and a collection of radioactive seeds arranged in a prescribed pattern to generate a known dose distribution in the eye. In Collaborative Ocular Melanoma Study (COMS) plaques (3), the seed locations are determined by grooves in a silastic insert. The number and position of the seeds in the silastic insert are dependent on the size of the plaque. The concave gold alloy backing is concentric over the silastic insert to provide structural stability and shielding for nearby normal tissues lateral to and behind the plaque.

Patient survival metrics for eye plaque brachytherapy are comparable to alternative treatment methods, including enucleation and external beam radiotherapy (4, 5). Despite the average effectiveness of plaque brachytherapy, some patients are not cured of their disease. Potential explanations for localized treatment failures include an incorrectly defined clinical target volume, an insufficient prescribed dose to this volume, and/or a discrepancy in the planned vs. delivered doses. Considering the last, the accuracy of the prevailing Task Group 43 (TG-43) formalism used in eye plaque dose calculations, which assumes an isotropic, homogeneous water medium, is known to be limited. Monte Carlo simulations have demonstrated dosimetric differences on the order of ~10–20% when plaque heterogeneities are fully taken into account (6–10). These

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heterogeneity corrections, which are plaque size, radionuclide, and depth dependent, encompass effects such as scatter and attenuation by the gold alloy backing and silastic insert as well as related interseed effects (11). Furthermore, heterogeneous patient anatomy is not typically accounted for in commercially available treatment planning systems and adds additional uncertainty to the dose calculation. The magnitude of such anatomic heterogeneity effects is dependent on the location of the dose evaluation point (12–14).

Uncertainties in the position of the radioactive seeds which comprise the eye plaque also contribute to the dosimetric uncertainties associated with the aforementioned calculation techniques. Collective, systematic seed shifts are expected to produce significant dose deviations, particularly in the sharp dose gradient regions typical of eye plaques (15). The impact of random seed-to-seed positional variations, however, is less intuitive. These displacements could result from irregularities in the silastic insert manufacturing process, nonuniform distributions of radioactivity inside each seed, or from seeds which are smaller than the grooved slots in the silastic insert. In this latter case, improper seed centering in the groove or seed displacements due to motion are possible.

In this work, the dosimetric consequences of random eye plaque seed position variations are quantified. Various configurations of plaque size, plaque location, anatomic dose evaluation site, radionuclide, and seed displacement direction are considered. The dosimetric effects of systematic plaque shifts are also calculated and compared, where applicable, to the effects of random seed shifts. Through this analysis, dose uncertainties in realistic scenarios are tabulated, enabling case-specific determinations of clinical impact. Comparisons to other dosimetric uncertainties are also performed, allowing for the significance of seed position uncertainties to be judged against competing contributions.

Methods

To investigate the effects of seed position uncertainties in eye plaques, a dose calculation routine was developed in MATLAB (v8.0, The MathWorks, Inc., Natick, MA) using standard TG-43 line source formalism with consensus TG-43 data sets (16–22). The MATLAB routine was validated by comparison to a clinical treatment planning system (Brachyvision, Varian inc., Palo Alto, CA). The total dose to an arbitrary evaluation point in a water medium was calculated by summing over the individual dose contributions from each seed in the plaque collection. The nominal coordinates and orientations of the seeds in the plaque were determined according to standard COMS coordinates (3).

Seed position displacements from the nominal COMS coordinates were defined in the reference frame of the individual seeds using a Cartesian coordinate nomenclature (x, y, z) (Fig. 1a). Displacements in the $\hat{z}$ direction are given by seed displacements parallel to the plaque central axis, which runs from the radial center of the eye plaque to the globe center. A displacement in this direction represents the physical case of seeds not fully seated in their silastic insert grooves or silastic grooves which have incorrect depths. The $\hat{y}$ direction is parallel to the long axis of the seed. Seed displacements in this direction can occur when using seeds which are shorter than the groove length. Finally, $\hat{x}$ is in the direction of lateral displacements perpendicular to both $\hat{z}$ and $\hat{y}$. Seed displacements are expected to be minimal in this direction due to the narrow profile of the grooves which ensures a snug fit in the $\hat{x}$ direction.

The dosimetric effects of seed displacements in each degree of freedom were considered independently. This allows for greater generality because the relative amplitudes of displacements in each direction may be varied to suit a particular physical situation. Dosimetric uncertainties are expected to combine in quadrature for evaluation points sufficiently far away from the plaque (i.e., evaluation points in which the distance to the nearest seed is much greater than the seed displacement amplitude). First, each seed in the collection was shifted randomly from its nominal position along a single direction (e.g., $\hat{z}$). Each random shift was generated by sampling a normal distribution parameterized with a mean of zero and a standard deviation (SD) selected for the test. Even though the seed position is restricted to the groove, which potentially suggests a truncated distribution (i.e., box car), variance in the actual molded positions of the silastic grooves would be expected to obey a normal distribution. This choice thus preserves generality. Once all seeds in the given collection had been randomly permuted along a single direction (e.g., $\hat{z}$), the dose to the evaluation point was recalculated. This process was repeated many times to build up a smooth distribution of potential dose outcomes at the evaluation point due to random seed displacements. A sufficient number of randomizations were computed (10^6) such that the uncertainty in the SD of the dose outcome distributions was typically less than 1%. This full process was executed for seed displacement SDs ranging from 0 to 1 mm in steps of 0.1 mm.

This analysis of the dosimetric consequences of seed position uncertainties was performed for a variety of clinical scenarios, including differing radionuclides, plaque sizes, and plaque locations with respect to ocular critical structures. Two seeds of different radionuclides, Oncura 6711 I-125 (Oncura Inc., Arlington Heights, IL) and Theragenics 200 Pd-103 (Theragenics Corp., Buford, GA), were used for dose calculations (16, 17). The lower energy emissions of the ^{103}Pd source produce steeper dose gradients, which are expected to correlate with higher sensitivity to seed position uncertainties. These two radionuclides were simulated for small, medium, and large COMS-style plaque sizes (10 mm, 16 mm, and 22 mm). The plaque placement on the eye relative to critical ocular structures was also