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Measurement of gold nanofilm dose enhancement using unlaminated radiochromic film

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Purpose: Bombarding high-\(Z\) material with x-ray radiation releases Auger electrons and Coster–Kronig electrons, along with deeper penetrating fluorescent x-rays and photoelectrons. The Auger and Coster–Kronig electron penetration distance is on the order of nanometers to micrometers in water or tissue, creating a large dose enhancement accompanied by a RBE greater than 1 at the cellular level. The authors’ aim is to measure the gold nanofilm dose enhancement factor (DEF) at the cellular level with unlaminated radiochromic film via primary 50 kVp tungsten x-ray spectrum interaction, similar to an electronic brachytherapy spectrum.

Methods: Unlaminated Gafchromic® EBT2 film and Monte Carlo modeling were combined to derive DEF models. Gold film of thickness 23.1 ± 4.3 nm and surface roughness of 1.2 ± 0.2 nm was placed in contact with unlaminated radiochromic film in a downstream orientation and exposed to a 50 kVp tungsten bremsstrahlung, mean energy 19.2 keV. Film response correction factors were derived by Monte Carlo modeling of electron energy deposition in the film’s active layer, and by measuring film energy dependence from 4.5 keV to 50 kVp.

Results: The measured DEF within a 13.6 μm thick water layer was 0.29 with a mean dose of 94 ± 9.4 cGy from Au emissions and 324 ± 32.4 cGy from the 50 kVp primary beam. Monte Carlo derived correction factors allowed determination of Au contributed dose in shallower depths at 0.25 μm intervals. Maximum DEF of 18.31 was found in the first 0.25 μm water depth.

Conclusions: Dose enhancement from Au nanofilm can be measured at the cellular level using unlaminated radiochromic film. Complementing the measured dose value with Monte Carlo calculations allows estimation of dose enhancement at depth increments within the cellular range.

1. INTRODUCTION

Radiation dose enhancement occurs in low-Z material at low-Z/high-Z interfaces when exposed to ionizing radiation. This is primarily due to the photoelectric interactions in the high-Z material. Some of the photoelectrons and Auger electrons released in the high-Z material escape the material and penetrate into the surrounding low-Z medium (i.e., tissue) where an abrupt increase in dose occurs. Targeting cancer cells with this dose enhancement through high-Z nanoparticles in the cell may have positive consequences on cell kill, especially as the Auger relative biological effectiveness (RBE) is reported to be...
greater than 1. The higher RBE is a function of the high LET values for these low-energy electrons, for example, 28 keV/µm at 0.1 keV.6

The dose enhancement factor (DEF) is defined as the ratio of dose to water with high-Z material present to the dose to water in the absence of high-Z material. Published Monte Carlo simulation DEF results for similar spectra often times do not agree and, for many cases, simulated DEF values are much higher than the experimental RBE values.2–4,7–9 This necessitates more experimental and computational studies into the causes of these discrepancies. Investigations into Au foil-based dose enhancement measured DEFs ranging from 55 to 114 in the energy range 40–120 kVp using a 150 µm thick Au foil, with measured human lymphocyte RBE values ranging from 1.7 to 2.2 at 60 kVp, and 50 at 80 kVp.2–4 Monte Carlo simulations of intracellular Au nanoparticles (AuNPs) DEF and RBE found DEFs from 1.4 to 1384 at energies ranging from Pd-103 to 6 MV with the maximum DEF around 50 kVp, while simulated RBEs varied from 1.1 to 2.1.7–9 Investigators also found dependencies on AuNP diameter, AuNP concentration, and incident energy. Findings of high DEF and RBE values using AuNPs at photon spectrums from 40 to 60 kVp suggest that good radiation therapy AuNP dose enhancement would occur with electronic brachytherapy devices such as the Xoft, Inc., Axxent™ system (Xoft, Inc., San Jose, CA), Zeiss Intrabeam system (Carl Zeiss Meditec©, Gosewitzcher Strasse 51-52, 07745 Jena, Germany), or Elekta Esteya skin brachytherapy system (Elekta, Inc., Atlanta, GA).

Radiographic film in unlaminated form is a potential dosimeter for measuring the nanoparticle DEF in a method similar to thermally stimulated exoelectron (TSEE) dosimetry primarily because the film’s unprotected active layer can be placed in direct contact with high-Z material for direct absorption of Auger and photoelectrons.2 Other advantages of a radiographic film include its near tissue-equivalence, adequate low-energy sensitivity, thin active layer, and relatively low cost.10

There have been recent investigations into short range dose measurement and the effects of high-Z materials or interface effects on dose. Devic et al. used laminated Gafchromic® EBT2 film along with an Attix parallel plate chamber and extrapolation chamber to perform shallow-depth skin dosimetry at 6 MV without nanoparticles present.11 Guidelli and Baffa studied the effects of nanoparticle concentration and primary radiation energy on the DEF using alanine dosimeters and electron spin resonance spectroscopy finding an increase in DEF greater than 1 with increased nanoparticle concentration and reduced primary beam energy, but without attention to changes in dose with depth.12 Rahman et al. measured Au nanoparticle DEF values ranging from 1.64 to 1.76 using synchrotron and super-ficial kilovoltage x-rays and normoxic type polyacrylamide gel analyzed by MRI with a voxel dimension of 700 × 700 × 1000 µm.13 Das et al. performed Monte Carlo studies of dose perturbation at the micron level for 60–300 kVp x-rays and Cs-137 beams upon Pb.14,15

A challenge in the use of unlaminated Gafchromic film in Auger and photoelectron dosimetry at these low energies is presented by the penetration of the electrons to a depth in the film sensitive layer that is far short of the full thickness of 30 µm. Furthermore, calibration of the film is performed using radiation energies that produce uniform energy deposition throughout the entire thickness of the active layer. This study attempts to address these problems by combining calibration of unlaminated film with Monte Carlo modeling of electron and x-ray emissions induced in Au by 50 kVp x-rays. Monte Carlo determination of the depth dose properties of the induced Au emissions in the Gafchromic film provides a model that allows extrapolation of a single uniform equivalent dose (UED) measurement in the film to dose at varying depths, out to the maximum depth of energy deposition of the Auger and photoelectrons, which is less than 30 µm. This also allows the use of film calibrations derived from uniform energy deposition throughout the film active layer using x-ray fluorescent energy of approximately 4.5 keV and tungsten bremsstrahlung energy of 50 kVp.

2. MATERIALS AND METHODS
2.A. Experimental setup

Unlaminated Ashland Gafchromic® EBT2 film was used as the dosimeter.16,17 The 30 µm thick film active layer was pressed against the 23.1 ± 4.3 nm thick, surface roughness 1.2 ± 0.2 nm gold film on plastic substrate, sandwiched between solid water layers of thickness 3 mm on the x-ray source side and 5 mm on the beam exit side as shown in Fig. 1. The same arrangement was used for film calibration at 50 kVp without Au. The tungsten bremsstrahlung dose contribution was determined with the same arrangement but without Au on the plastic substrate. Photoelectron and Auger electron presence was tested by repeating the exposures and film analysis with 2.5 µm of Mylar between the gold and film, the assumption being that the Mylar would absorb the low-energy electrons with the result of no measurable difference in optical density (OD) between the films exposed with and without gold.

2.B. Monte Carlo geant4 simulation

A geant4 simulation was performed to determine the energy deposition of the gold film layer on the EBT2 film and in water.18 Geometry of the simulation consisted of homogeneous layers of bulk material stacked in the order in which they were used in the measurements. No attempt was made to model individual nanoparticles within the enhancing layer. With the exception of the EBT2 emulsion layer, the material and associated physical properties for each layer were assigned using NIST data built into the geant4 package. The nanoparticle layer was modeled as bulk gold, the plastic layer onto which the nanoparticle layer was sputtered was modeled as bulk polycarbonate, and the back material of the EBT2 film was modeled as bulk Mylar. The material assigned to the emulsion layer was constructed as a density-appropriate homogeneous bulk material consisting of the eight individual elemental components weighted to reproduce the chemical composition of the film.
The X-ray source was constructed using an implementation of the `G4GeneralParticleSource` class with a spectrum binned into 1 keV intervals for sampling. The source was modeled as a simple 1×1 cm plane parallel beam. To model the physical interactions of the geometry with the source, the built-in physics list `G4EmPenelopePhysics` was used. This physics list is a GEANT4 implementation of the physics processes included in the standard PENELOPE Monte Carlo code. A `G4EmProcessOptions` object was used to activate fluorescence, de-excitation, and Auger processes. Production cuts for both photons and electrons were set to 0.05 \( \mu \text{m} \).

Total energy deposition in the film emulsion layer was scored at each step by filling an AIDA-formatted histogram. A separate histogram was used to score the energy deposited in the emulsion layer due to any particle whose existence was a result of an interaction in the nanoparticle layer. To distinguish between secondaries created in the nanoparticle layer and in the other layers of the geometry, a `G4TtrackingInformation` object was attached preferentially to those tracks originating in the nanoparticle layer. The tracking information was successively copied to all daughters created from any track that originated in the nanoparticle layer, and this information was queried at each energy deposition event to determine how the event should be scored.

GEANT4 Monte Carlo generated depth-energy curves in the radiographic film active layer and in water are presented in Sec. 3, Figs. 4(a) and 4(b) for the 20 nm Au layer, showing separate contributions from the gold and primary bremsstrahlung as well as their totals. Each data set was produced using \( 2 \times 10^9 \) runs. Energy was sampled at 0.25 \( \mu \text{m} \) depth increments.

We define the quantity uniform equivalent DEF (UEDEF) as the ratio of energy deposition from nanoparticle contributions to the energy deposition from the primary 50 kVp bremsstrahlung alone, summed to a given depth. Uniform equivalent is an appropriate terminology as it will be shown that the Au nanoparticle contribution to dose occurs mostly just beneath the surface. Uniform equivalent DEF values to given depths in EBT2 film and water were calculated from Monte Carlo energy deposition data by the following method:

\[
(\text{UEDEF}_{\text{MC}})_N = \frac{\sum_{i=1}^{N} E(d_i)}{\sum_{i=1}^{N} E(d_i)} \frac{\text{Au}}{50\text{kVp}},
\]

where \( E(d_i) \) is the energy deposited at depth \( d_i \) in the EBT2 active layer or in water, where depths are increments of 0.25 \( \mu \text{m} \) such that

\[
d_i = i \times 0.25 \mu \text{m};
\]

subscripts Au and 50 kVp refer to the nanoparticle contribution and the primary bremsstrahlung contribution, respectively; and \( N \) is the total number of 0.25 \( \mu \text{m} \) depth increments determining the depth of summation.

### 2.C. Nanoparticle film samples preparation and analysis

The gold films were prepared using an Ernest F. Fullam sputter coater. The plastic substrates were sputtered with gold for about 60 s with 50 mA current and under 200 mTorr
pressure. Atomic force microscopy (AFM) imaging was conducted using the Dimension 3100 AFM from VEECO. In order to measure the film thickness and surface morphology, AFM tapping mode in air was used. The AFM tips were silicon probes from VEECO with a nominal frequency at 150 kHz. Software NANOSCOPE version 5.12 was used to analyze the data. Before each thickness measurement, the film was scratched with a razor blade to expose the substrate. All thickness data were obtained by measuring the step height between the film surface and the exposed substrate, using the sectional height analysis command on AFM height images.

2.D. Film dosimetry models

Auger and photoelectron dose measurement with film is based on the principle that the combined OD of multiple layers of overlaid film is equal to the sum of the individual OD values of each layer. Our methodology was developed to deal with two difficulties inherent in trying to measure Auger and photoelectron dose using un laminated radiochromic film. The first problem is the penetration depth of the Auger and photoelectrons being less than the thickness of the radiochromic sensitive layer. Energy deposition is not uniform throughout the entire thickness. If it were possible to peel away radiochromic layers of equal thickness, one would find the greatest OD near the irradiated surface, decreasing rapidly in successive layers. Monte Carlo calculations show 99.9% of the energy deposited in the first 6.5 μm in a 30 μm thick radiochromic layer. Isolating the electron contribution to the overall OD in the radiochromic layer was done by subtracting the OD of 50 kVp irradiation without gold (OD_{50kVp}) from the OD of irradiation with gold (OD_{Au}). These are defined as

\[
OD_{Au} = \log_{10} \left( \frac{I_U}{I_{Au}} \right),
\]

\[
OD_{50kVp} = \log_{10} \left( \frac{I_U}{I_{50kVp}} \right).
\]

\[ I_U \] is the mean pixel intensity for an unexposed film, \( I_{Au} \) is the mean pixel value for the exposed film with gold film interaction, and \( I_{50kVp} \) is the mean pixel value for the film exposed to the 50 kVp x-ray spectrum without gold.

The second problem is the energy dependence of the film. We accounted for the energy dependence by performing film OD versus dose calibrations at multiple energies using fluorescent x-rays from various metals, and the primary beam lightly filtered 50 kVp tungsten bremsstrahlung. The multiple energies were used to examine the trend in response with energy. We measured OD to dose calibration relations for the 50 kVp spectrum and the lowest energy x-ray in our group of metals, the Ti Kα of 4.51 keV. As will be seen in Sec. 3, the response curves grow closer together as energy decreases with what could be considered a nonexistent gap between Cr at 5.41 keV and Ti at 4.51 keV, the gap increasing with increasing fluorescent x-ray energy. This supports the use of the Ti fluorescent energy, as the electron energies from the gold increasing fluorescent x-ray energy. This supports the use of Cr at 5.41 keV and Ti at 4.51 keV, the gap increasing with what could be considered a nonexistent gap between the response curves grow closer together as energy decreases.

K energy. We measured OD to dose calibration relations for the lightly filtered 50 kVp tungsten bremsstrahlung. The multiple OD versus dose calibrations at multiple energies using fluorescent layers of each layer. Our methodology was developed to deal with two difficulties inherent in trying to measure Auger and photoelectrons being less than the thickness of the radiochromic sensitive layer. Energy deposition is not uniform throughout the entire thickness. If it were possible to peel away radiochromic layers of equal thickness, one would find the greatest OD near the irradiated surface, decreasing rapidly in successive layers. Monte Carlo calculations show 99.9% of the energy deposited in the first 6.5 μm in a 30 μm thick radiochromic layer. Isolating the electron contribution to the overall OD in the radiochromic layer was done by subtracting the OD of 50 kVp irradiation without gold (OD_{50kVp}) from the OD of irradiation with gold (OD_{Au}). These are defined as

\[
OD_{Au} = \log_{10} \left( \frac{I_U}{I_{Au}} \right),
\]

\[
OD_{50kVp} = \log_{10} \left( \frac{I_U}{I_{50kVp}} \right).
\]

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In the following descriptions, UED is defined as the total Au nanofilm dose within a layer of water extending from the surface to a given depth. The UEDEF at a given depth is the Au nanofilm uniform equivalent dose within a layer of water extending from the surface to a given depth, divided by the 50 kVp dose in that same layer in the absence of Au nanofilm. The Au nanofilm dose per 0.25 μm layer is computed as the weighted subtraction of uniform equivalent doses at neighboring incremental depths.

The first model determines the UED and UEDEF out to the maximum range of electron penetration discernible in the EBT2 film. The measured dose from the Au nanofilm contribution, represented as \( D_{Au} \), is computed as

\[
D_{Au} = F_{cal,Ti}(\text{net OD}_{Au}).
\]

\( F_{cal,Ti} \) is a third order polynomial describing dose to water as a function of net OD from Ti fluorescent x-ray, presented in Sec. 3, Fig. 3. The net OD used in the \( F_{cal,Ti} \) function was determined as

\[
\text{net OD}_{Au} = (\text{OD}_{Au} - \text{OD}_{50kVp}).
\]

Equation (6) reduces to

\[
\text{net OD}_{Au} = \log_{10} \left( \frac{I_{50kVp}}{I_{Au}} \right).
\]

Film-based 50 kVp x-ray dose to water was determined as

\[
D_{50kVp} = F_{cal,50kVp}(\text{OD}_{50kVp}).
\]

\( F_{cal,50kVp} \) is a third order polynomial describing dose to water as a function of net OD from the 50 kVp x-ray, presented in Sec. 3, Fig. 3.

The measured UEDEF is computed as

\[
\text{UEDEF}_{Meas} = \frac{D_{Au}}{D_{50kVp}}.
\]

This method determines a dose to water value from energy deposition in the EBT2 active layer, within a range that extends to approximately the end of the Au nanofilm contribution range. The measured range is limited by the farthest depth at which energy deposition causes polymerization in the EBT2. Matching the measured UEDEF with Monte Carlo UEDEF allows determination of the effective depth of polymerization on the plot of Monte Carlo UEDEF versus depth in water, presented in Sec. 3, Fig. 5.

Given that the 50 kVp dose contribution is effectively constant throughout the entire depth, the Au-produced UED within a given depth of \( N \) quantity of 0.25 μm increments can be computed by

\[
(\text{UED}_{Au})_N = (\bar{D}_{Au}) \times \left( \frac{\text{UEDEF}_{Meas}}{(\text{UED}_{MC})_N} \right),
\]

where \((\text{UED}_{MC})_N\) is determined by Eq. (1), \( D_{Au} \) is determined by Eq. (5), and \( \text{UEDEF}_{Meas} \) is determined by Eq. (9). The \((\text{UED}_{Au})_N\) are presented in Sec. 3, Fig. 6(a).

Dose per 0.25 μm at depth section \( i + 1 \) represented by \((\Delta D_{Au})_{i+1}\) is found by

\[
(\Delta D_{Au})_{i+1} = (i + 1) \times (\text{UED}_{Au})_{i+1} - i \times (\text{UED}_{Au})_i.
\]

The \((\Delta D_{Au})_{i+1}\) are presented in Sec. 3, Fig. 6(b).
The second model combines Monte Carlo generated energy deposition data with film OD measurements to determine a correction variable to be applied to the net OD of the Au layer such that 

\[(UED_{\text{Au}})_{N} = F_{\text{cal}, Ti}(\text{EDC}_{N} \times \text{net OD}_{\text{Au}}), \] (12)

where EDC \(i\) is the energy depth correction, determined by matching the ratio of Eqs. (12) and (8) to Eq. (1), i.e.,

\[\frac{\text{UEDEF}_{\text{MC}}}{\text{UEDEF}_{\text{MC}}_{50kVp}}_{i} = \frac{F_{\text{cal}, Ti}(\text{EDC}_{i} \times \text{net OD}_{\text{Au}})}{F_{\text{cal}, 50kVp}(\text{OD}_{50kVp})} = \frac{\left(\sum_{i=1}^{N} E(d_{i})\right)_{\text{Au}}}{\left(\sum_{i=1}^{N} E(d_{i})\right)_{50kVp}}. \] (13)

Polynomial relations are generated between EDC and UED \(i\) as well as EDC and depth. These are presented in Sec. 3, Figs. 7(a) and 7(b). The EDC is dependent on Au film thickness, as Monte Carlo generated energy deposition and DEF vary with Au film thickness.

2.E. Film calibration

Film was calibrated with the 50 kVp tungsten x-ray spectrum, and with the low-energy fluorescent x-ray energies listed in Table I along with transition ratios. Film was scanned into TIFF format at 72 ppi and 48 bits RGB using a Microtek Scanmaker i800 transmission scanner with consistent scan orientation for all samples. Film analysis was performed using the green component, recommended for the maximum dose range of the EBT2 film. Film response calibration curves and polynomial fits are given in Sec. 3. The calibration curves for titanium, 50 kVp x-rays, and intermediate fluorescent energies are included to demonstrate the trend in film response with energy.

2.F. Samples irradiation

Six trials of sample irradiations, with and without gold, were performed on a Pantak HF 300 adjustable output x-ray generator and tungsten anode tube operating at 50 kVp, 10 mA tube current, with a 3 mm beryllium window and no added filtration. The circular field diameter was 24 cm. The mean energy of the beam was 19.2 keV. The x-ray spectrum was calculated using the software SpekCalc version 1.1 for Windows.

2.G. Dose rate measurement

Primary beam dose rates at 50 kVp were calibrated with an NIST-traceable Radcal 10X5-6M ion chamber (Radcal Corporation, Monrovia, CA). Average 50 kVp dose rate at the level of the samples was 232 cGy/min. Fluorescent x-ray dose rates used in film calibration and ERC determination were measured with an extrapolation ion chamber model EIC-1 manufactured by Far West Technology, Inc. (Goleta, CA). Dose rate to water (cGy/min) was calculated as in

\[D_{\text{med}} = \left(\frac{W}{e} \cdot \bar{N} \cdot C_{TP} \left(\frac{\mu_{\text{en}}}{\rho}\right)_{\text{med}}\right)_{\text{air}} \times \text{Air mass}, \] (14)

where \((W/e)\) is the energy per charge separation in air, 33.97 eV/ion pair, \(\bar{N}\) is the rate of charge collection in C/min for a zero thickness window, and \((\mu_{\text{en}}/\rho)_{\text{med}}\) is the mass energy absorption coefficient ratio of water to air weighted by the radiative transition probabilities (Table I). The point of measurement is at the inner surface of the ion chamber entrance window. Charge collection rates were averaged over plate separations of 1, 2, 3, and 4 mm. Charge readings at zero polyethylene window thickness were extrapolated from charge readings at eight window thicknesses ranging from 6.90 to 16.56 mg/cm² in progressive thicknesses of 1.38 mg/cm² each.

Fluorescent x-rays were generated using a silver anode 55 kVp x-ray spectrum incident upon high purity metal. The x-ray tube was a Seifert broad focus silver anode DX-Ag12x2-S with 300 μm beryllium window (Seifert X-Ray Corporation, Fairview Village, PA). The generator was a Spellman model DF60N3 operated at 55 kVp and 45 mA (Spellman High Voltage Electronics Corp., Hauppauge, NY).

| Table I. Metals and their fluorescent x-ray energies used to determine the film ERC. |
|-----------------|---------------|-----------------|-----------------|
| Metal | \(K_{\alpha}\) energy (keV) | \(K_{\beta}\) energy (keV) | Transition probability ratios of \(K_{\beta}/K_{\alpha}\) |
| Ti | 4.51 | 4.93 | 0.133 |
| Cr | 5.41 | 5.95 | 0.133 |
| Fe | 6.40 | 7.06 | 0.134 |
| Co | 6.93 | 7.65 | 0.135 |
| Zn | 8.64 | 9.37 | 0.136 |
| Mo | 17.48 | 19.61 | 0.197 |

![Fig. 2. AFM 3D height image of the gold film. The scan size is 2x2 μm² and the z range is 20 nm.](image-url)
3. RESULTS

The AFM measurement results are presented in Fig. 2. Film thickness of 23.1 ± 4.3 nm was obtained via sectional height analysis based on randomly picked 20 positions across the surface of the nanoparticle film. By performing 3D height imaging of a 2 × 2 µm² square, a surface roughness of 1.2 ± 0.2 nm was measured. The film surface roughness is the root-mean-squared roughness \( \text{RMS} = \left[ \frac{\sum (z_i^2)}{N} \right]^{1/2} \) where \( z_i \) is the height value of each measurement point and \( N \) is the number of measurement points in AFM height images.

Film calibration curves are given in Fig. 3. The general OD trend with energy agrees with that found by Cai et al. for 14.8 versus 1.5 keV x-rays.23 Spacing between curves progressively decreases with energy, which supports the use of the lowest fluorescence energy of the group as the calibration energy for Au emissions.

Monte Carlo generated energy depositions are presented in Figs. 4(a) and 4(b) for water and EBT2 film layer with 20 nm Au film. As seen in Figs. 4(a) and 4(b), electron energy deposition in the EBT2 film drops to 50% of the peak surface value at approximately 0.6 µm, and to 5% of the peak surface value at a depth of approximately 2.9 µm. In water, 50% occurs at approximately 0.6 µm while 5% falls at approximately 3.2 µm. The maximum Auger electron energy from gold is 2.1 keV.19 Fluorescent x-ray and Auger yields from Au are 35% and 65%, respectively. The fluorescent X-rays, therefore, make a minor contribution to the energy deposition in the film relative to the Auger and photoelectrons, since the minimum energy L series fluorescent x-ray from gold is 8.494 keV at 10.46% intensity with 98% transmission through the 30 µm thick film sensitive layer.

Monte Carlo calculated \( \text{UEDEF}_{\text{MC}} \) values in water and EBT2 per Eq. (1) are presented in Fig. 5. The water DEF in the first 0.25 µm is 18.31.

The \( \text{UEDEF}_{\text{MC}} \) from Gafchromic film was 0.29 corresponding to a depth of 12.8 µm in EBT2 and 13.6 µm in water. This suggests that the effective depth of measurement of OD in the Gafchromic active layer for these experimental conditions was approximately 12.8 µm. The uniform equivalent dose at a given depth per Eq. (10) \( (\text{UED}_{\text{Au}}) \), and the dose per 0.25 µm increment per Eq. (11) \( (\Delta D_{\text{Au}}) \), is given in Figs. 6(a) and 6(b), respectively.

Film OD values produced with the 2.5 µm Mylar attenuator, with and without gold, differed by one OD standard error, evidence of absorption of the low-energy electrons in the Mylar. The film OD standard error was derived from the standard error in the scanned film pixel values.
The relations between EDC, UEDEF, and depth in water from model 2, Eqs. (12) and (13), are given in Figs. 7(a) and 7(b). The EDC was adjusted at each depth interval to achieve agreement with the Monte Carlo generated UEDEF to two decimal places.

4. CONCLUSIONS AND DISCUSSION

Two Monte Carlo based models were developed for relating a Gafchromic film measurement of Au nanofilm photoelectric-induced emissions to uniform equivalent dose to given depths, dose per 0.25 µm layer at given depths, and uniform equivalent DEF to given depths. Uniform equivalent dose is defined as the total Au nanofilm dose within a layer of water extending from the surface to a given depth. Uniform equivalent DEF at a given depth is the Au nanofilm uniform equivalent dose within a layer of water extending from the surface to a given depth, divided by the 50 kVp dose in that same layer in the absence of Au nanofilm. The Au nanofilm dose per 0.25 µm layer is computed as the weighted difference between uniform equivalent doses at neighboring incremental depths.

A tungsten 50 kVp spectrum (mean 19.2 keV) was chosen as the primary beam, as our intent was to investigate AuNP dose enhancing properties at electronic brachytherapy energies. The DEF dropped to zero with 2.5 µm Mylar filtration interposed between gold and film, zero meaning an OD change within one standard deviation of uncertainty as measured by interpixel variation in the OD in an area of uniform density.

Complete attenuation by the 2.5 µm thick Mylar supports the hypothesis that the DEF in this case is the result of absorption of low-energy Auger electrons and photoelectrons in the film.

The Au nanofilm layer thickness was verified by AFM as 23.1 ± 4.3 nm. The surface roughness was determined by AFM as 1.2 ± 0.2 nm.

The measured Au emission integral DEF in water was 0.29 ± 0.03 out to a depth of 13.6 µm. Maximum DEF was 18.3 in the first 0.25 µm. Our DEF result depended on estimates concerning electron penetration depth in the Gafchromic film and film energy dependence. We also investigated 10 and 30 nm thick Au films using Monte Carlo and found that energy deposition and DEF are proportional to thickness. Therefore, parameters of models 1 and 2 will depend on Au thickness. We did not investigate other Gafchromic film formulations as EBT2 was the only formulation available unlaminated.

There are several caveats to consider. The Gafchromic film is limited in depth resolution. As described by Soares when discussing the 2D planar resolution of Gafchromic film, the absolute limit, in principle, should be governed by the 0.75 µm physical size of the chromophores in the film active layer.24 The same should apply to the depth resolution. Energy deposited at depths less than 0.74 µm cannot be discriminated and will contribute dose to a larger volume defined by the resolution limit. A further limitation of the film and our Monte Carlo model is the assumption of a homogeneous structure in the film active layer, while the true physical structure comprises rodlike structures in the monomer crystals with gaps between.25,26 Modeling the true structure of the film might shift the energy...
deposition curve deeper and thereby decrease the EDC and measured dose, with a second Monte Carlo depth-energy curve still required for water.

The question arises as to how dosimetric measurements with a continuous sheet of Au relate to individual nanoparticle dosimetry. If we regard the Au film as a close-packed planar arrangement of AuNPs, the absolute radiation dose at a point in water near the Au-water interface from our Au film would probably be greater than that from an isolated AuNP due to contributions from neighboring nanoparticles. Zygmanski et al. studied the effects of simulation geometry on gold nanoparticle microdosimetry. They found that the relation between dose enhancement ratio (DER) for a cluster of Au nanoparticles and a single nanoparticle is nonlinear. Where as a single particle can have a DER range of 100–200 nm, a cluster may have a DER range of 1–2 μm. This suggests that great caution is recommended if our results are to be related or scaled to individual particles.

We attempted to develop a novel technique of measuring the nanofilm contributed component of dose associated with a primary x-ray fluence. Dosimetry measurement on the micrometer scale is challenging and accompanied by great uncertainty. This method is constrained by the limited depth resolution of the film, and assumptions regarding the energy-depth relation of Auger and photoelectrons in the film active layer, albeit Monte Carlo-based.

In summary, dose enhancement from Au nanofilm can be estimated at the cellular level using un laminated radiochromic film. Complementing the measured dose value with Monte Carlo calculations allows estimation of dose enhancement at depth increments within the cellular range.

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