BRACHYTHERAPY DOSE MEASUREMENTS IN HETEROGENEOUS TISSUES

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Abstract

Recently, Beaulieu et al. published an article providing guidance for Model-Based Dose Calculation Algorithms (MBDCAs), where tissue heterogeneity considerations are addressed. It is well-known that TG-43 formalism which considers only water medium is limited and significant dose differences have been found comparing both methodologies. The aim of the present work is to experimentally quantify dose values in heterogeneous medium using different dose measurement methods and techniques and compare them with those obtained with Monte Carlo simulations. Experiments have been performed using a Nucletron microSelectron-HDR Ir-192 brachytherapy source and a heterogeneous phantom composed by PMMA and different tissue equivalent cylinders like bone, lungs and muscle. Several dose measurements were obtained using tissue equivalent materials with height 1.8 cm and 4.3 cm positioned between the radiation source and the detectors. Radiochromic films, TLDs and MOSFETS have been used for the dose measurements. Film dosimetry has been performed using two methodologies: a) linearization for dose-response curve based on calibration curves to create a functional form that linearizes the dose response and b)

multichannel analysis dosimetry where the multiple color channels are analyzed allowing to address not only disturbances in the measurements caused by thickness variation in the film layer, but also, separate other external influences in the filme response. All experiments have been simulated using the MCNP5 Monte Carlo radiation transport code. Comparison of experimental results are in good agreement with calculated dose values with differences less than 6% for almost all cases.

Keywords: brachytherapy; dosimetry; Monte Carlo; HDR; MOSFETS; radiochromic films; TLD, MCNP5.

1.- INTRODUCTION

Brachytherapy is a cancer treatment modality which uses radioactive source inside the patient´s body in contrast to external beam high-energy radiation. Currently, this treatment follows the guidance of the AAPM Radiation Therapy Committee Task Group (TG-43) which considers that the tumor and the surrounding tissues are composed by homogeneous water media [Rivard *et al.*, 2004]. More recently, several issues of dosimetric concerns have been raised by this simplistic TG-43 formalism and were published by another AAPM Task Group - TG-186 [Beaulieu *et al.*, 2012]. Some of those dosimetric issues are the necessity of a more accurate patient tissue composition and density data, which was demonstrated to be one of the sources in dose calculation errors. For example, mass density values extracted from CT images based on Hounsfield numbers depends on the CT x-ray spectra which average energy varies as long as it crosses the media and tissue composition data is subject to an even more greater source of errors.

The quantification of differences in dose estimates caused by the above mentioned concerns were published in several works through the estimate of $D_{m,m}$, $D_{w,m}$ and D_{TG43} relationship using the cavity theory, where $D_{m,m}$ is the dose value with the dose-specification in the medium with medium composition assignment; $D_{w,m}$ is the dose value with the dose-specification in water with medium composition assignment and D_{TG43} is the

dose value calculated using the TG-43 formalism [Beaulieu *et al.*, 2012; Landry et al., 2010; Yang and Rivard, 2011]. For example, [Landry *et al.*, 2011] presented considerable differences between $D_{m,m}$ and $D_{w,m}$ in prostate and breast tissues for different low energy brachytherapy sources like ^{125}I, ^{103}Pd and a 50 keV x-ray source. However, even for higher energy sources as ^{192}Ir considerable differences have been found depending on the target tissue as cortical bone and lungs.

Knowing that dosimetry formalism in brachytherapy is moving forward from TG-43 to model-based dose calculation algorithms (MBDCAs), experimental dose measurements in heterogeneous media takes a very important role in the process of propping MBCDAs for brachytherapy dosimetry.

Some characteristic aspects in brachytherapy sources as short range and small dimensions require special radiation detection procedures to provide adequate and accurate dose values. The most common detectors used for dose measurements in brachytherapy are thermoluminescent dosimeters (TLDs) and radiochromic films. MOSFETs are also a good candidate due to its small dimension and on-line response to radiation for *in vivo* measurements.

The objective of this work was to perform several dose measurements using radiochromic films, TLDs and MOSFETS detectors in a heterogeneous phantom composed by different tissue-equivalent materials with an HDR ^{192}Ir brachytherapy source. Measured dose values have been compared with the results obtained by Monte Carlo simulation using the MCNP5 radiation transport code [Briesmeister 2008].

2.- MATERIALS AND METHODS

2.1.- Experimental setup

The dose measurements were performed in a phantom composed by PMMA plates (Figure 1) with different thickness. Some of those plates have a 3 cm diameter central hole where

different types of tissue-equivalent cylinders can be inserted. All disc plates have 3 cm of diameter and height of 1.8 cm or 4.3 cm. Nine different types of material have been considered: PMMA, two types of lung tissues (inhale and exhale), adipose, muscle, breast and three types of bone with different densities. Figure 1 illustrates the PMMA plates and tissue-equivalent cylinders (CIRS tissue-equivalent materials) used in the experiments and Table 1 presents the density of each material used. Lung (inhale) and bone-2 have height 1.8 cm while the others cylinders have height 4.3 cm.

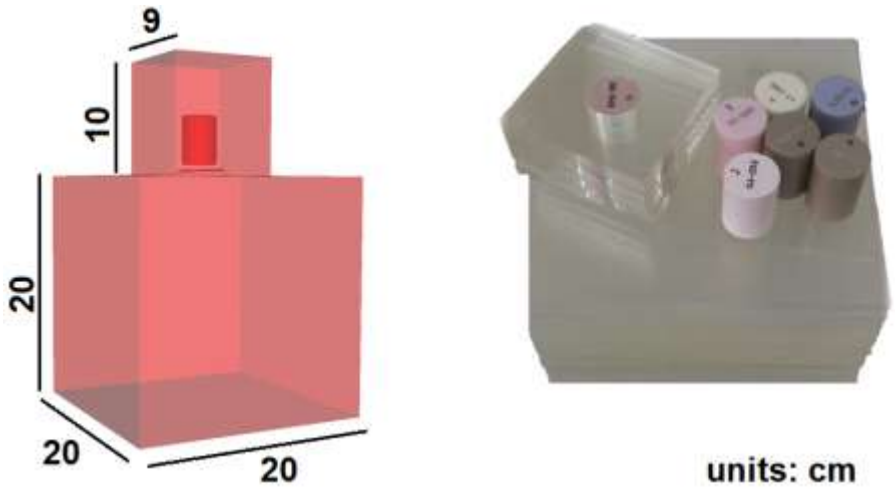

Figure 1.- PMMA plates and CIRS tissue-equivalent cylinders inserted in the center with the catheter (blue) for the Ir-192 source positioning.

Table 1.- Tissue-equivalent material densities.

Materials	Density g/cm^3
PMMA	1.19
Lung(inhale)	0.20
Lung(exhale)	0.51
Adipose	0.96
Breast	0.99
Muscle	1.06
Bone-1	1.16
Bone-2	1.66
Bone-3	2.15

The heterogeneous materials were inserted between the source and the detectors, which were aligned with the center of the phantom and fixed at a distance of 2.0 cm and 4.5 cm from the source for the cylinders with height 1.8 cm and 4.3 cm, respectively. Three irradiations were performed for each dosimeter (MOSFET, film and TLD) totaling nine irradiations for the 4.3 cm height material and six irradiations for the 1.8 cm height material since TLDs were not used for the latest case.

2.2.- MOSFETS

MOSFET detectors are a good alternative for brachytherapy dosimetry due to its small sensitive volume and the possibility for *in vivo* on-line dose monitoring. The MOSFET response to radiation is observed measuring the threshold voltage change which can be related to dose through correction factor, CF, which basically takes into account the variation of sensitivity with the threshold voltage and the energy dependency, according to the expression given by [Zilio *et al.*, 2006]:

$$CF = \frac{\dot{D}_{ref}}{\Delta\dot{V}_{ref} \cdot f_S(\dot{V}_{ref}) \cdot f_E(d_{ref})} \quad (1)$$

where $\dot{D}_{ref}$ is the dose rate value at a reference position, d_{ref}; $f_S(\dot{V}_{ref})$ and $f_E(d_{ref})$ are the sensitivity and energy dependence correction factors and $\dot{V}_{ref}$ is the voltage variation.

The sensitivity variation with the threshold voltage, V_{th}, presents a linear dependence according to equation 2:

$$f_s(V) = 1 + L.(V - V_I) \quad (2)$$

where L accounts for the linear sensitivity reduction with the voltage V and V_I is the initial threshold voltage in volts.

The energy dependency adopted here was also proposed by [Zilio *et al.*, 2006] and is described by equation 3:

$$W(E) = \left\{1 - e^{[-a_1(E-E_1)]}\right\}.\left(1 + \frac{a_2}{(E-E_2)^3}\right) \quad (3)$$

where a_1, a_2, E_1 and E_2 are given fitting parameters. For this work, these parameters were taken from [Zilio *et al.*, 2006]. As can be seen from the equation 3, the photon energy, E, at the point of measurement should be known, so that, in this work, it was obtained by Monte Carlo simulation using the MCNP5 code. This equation also shows that the MOSFET response is inversely proportional to the energy, so that, the softening of the photon energy spectra at longer distances, increases the MOSFET response. Therefore, the energy correction factor, $f_E(d)$, is defined as the inverse of energy response W(E). In the present work we utilized the microMOSFETs from Best Medical Canada LTD model TN-502RDM-H.

2.3.- Radiochromic films

Two methodologies have been applied for film dosimetry in the present work. The first methodology was first proposed by [Devic *et al.*, 2012] were a functional form is obtained from the calibration curve to linearize the nonlinear dose-response of the radiochromic films. The second methodology was proposed by [Micke *et al.*, 2011] where the film are scanned using RGB channels allowing to separate the nondose-dependent part of the film image from the dependent part of the absorbed dose. In this work we have utilized the GAFCHROMIC™ EBT2 film models (Lot #A0515201).

2.3.1.- Dose-response linearization

The function form that linearizes the dose response can be expressed by the following equation [Devic *et al.*, 2012]:

$$D = a.(-1).\frac{netOD^{2/3}}{\ln(netOD)} = a.\zeta \quad (4)$$

where netOD is the net optical density and ***a*** is a parameter which depends on at least one calibration value, but for relative dose measurements it is not required. The net optical densities were obtained from the subtraction of the film image data scanned before and after the irradiation which gives the pixel values before and after the irradiation, respectively. The relationship of the optical density and pixel values, *pv*, is given by:

$$netOD = OD_{after} - OD_{before} = \log\left(\frac{pv_{before}}{pv_{after}}\right) \quad (5)$$

Knowing the relationship between the dose and net optical density and using equation 5, it is possible to obtain dose values in each voxel of the scanned film. This methodology eliminates the calibration process reducing the experimental uncertainty.

2.3.2.- Multichannel dosimetry

The multichannel film dosimetry utilizes the information from the dose-related color channels values, (R,G,B) and has the advantage of taking into account any disturbance, Δ, that might be present in the radiochromic film and is not related to the energy deposition as variations in the film active layer. Assuming that the measured optical density due to dose D can be expressed by the product of the optical density without perturbation and the disturbance Δ, the optical density formulation for each color channel C is given by [Micke *et al.*, 2011]:

$$OD_C(D) = OD_C^D(D).\Delta \quad (6)$$

where $OD_C(D)$ is the measured optical density and $OD_C^D(D)$ is the component of the optical density which does not depend on the perturbation, but only of dose D. Averaging $OD_c(D)$ in a homogeneous region we have:

$$\overline{OD_C(D)} = OD_C^D(D).\bar{\Delta} \quad (7)$$

$$\overline{OD_C(D)} = OD_C(D).\frac{\Delta}{\bar{\Delta}} \quad (8)$$

where $\bar{\Delta}=\frac{1}{N}\sum_{ij}\Delta$ and N is the number of pixels (i,j) in the region.

From the calibration curve of each channel C, or table, the optical density, $\{\overline{OD}(D_i);\ D_i\}_C$ is known for each dose D_i, therefore, the dose can be obtained by:

$$D = [\overline{OD_C}]^{-1}(OD_C.\frac{\Delta}{\bar{\Delta}}) \quad (9)$$

However, considering that the dose is independent on the color channel C, and knowing that it carries the perturbation term, Δ, from a sequence of multiple channels values we can utilized the least square function as function of Δ, L(Δ), to minimize the differences between the dose values obtained from different channels R, G and B using the following equations:

$$L(\Delta) = \sum_{C_i \neq C_j}\left(D_{C_i} - D_{C_j}\right)^2 \quad (10)$$

$$\frac{dL(\Delta)}{d\Delta} = 0 \quad (11)$$

2.4.- TLD

Thermoluminescent dosimeters (LiF:Mg:Ti – TLD100) with radius 1.5 mm and thickness less than 0.4 mm were calibrate through 5 irradiations with following procedure: a) thermal treatment where the TLDs were kept under 400º C for one hour and, then under 100ºC for two hours; b) irradiation procedure using a PMMA phantom; c) acquisition process performed with an automatic reader (Harshaw 5500).

2.5.- MCNP5 Simulations

The experiment setup as described in section 2.1 has been modeled into the MCNP5 Monte Carlo code for dose calculation. The Ir-192 source energy spectrum was taken from the

National Nuclear Data Center and the cross-section data from MCPLIB84 photon cross-section library [Briesmeister 2008].

The composition of materials that compose the heterogeneous phantom were those provided by the manufacturer. Considering charge particle equilibrium, CPE, the energy deposition in the target volumes was obtained by the track length estimator, tally F6, where secondary electron transport is not considered but its energy is locally deposited in the media. Simulation were performed for 10^9 particles with energy cutoff of 1 keV.

3.- RESULTS

3.1.- MOSFETS calibration

MOSFETS are high energy-dependent with $f_E(d)$ corresponding to approximately 40% of the dosimeter response. The sensitivity variation with the threshold voltage (V_{th}) obtained with 50 consecutive irradiations of 15s each, is much less significant and follows the equation:

$$f_s = 1 - 0.0006 * (V_f - V_i) \quad (12)$$

The uncertainty of the angular coefficient is around 100% and is a reasonable indicative of the system stabilization since during the stabilization time wider differences were observed including even positive coefficients.

3.2.- Film calibration

Although the linearization methodology requires only one calibration point a calibration curves with 8 points (Figure 2.a) was obtained to verify the linear behavior within the dose range adopted that runs from 0.5 Gy up to 15 Gy. Table 2 shows the uncertainty components adopted. The mean of the experimental points standard deviation corresponds

to the highest standard deviation observed for three films irradiated under the same conditions.

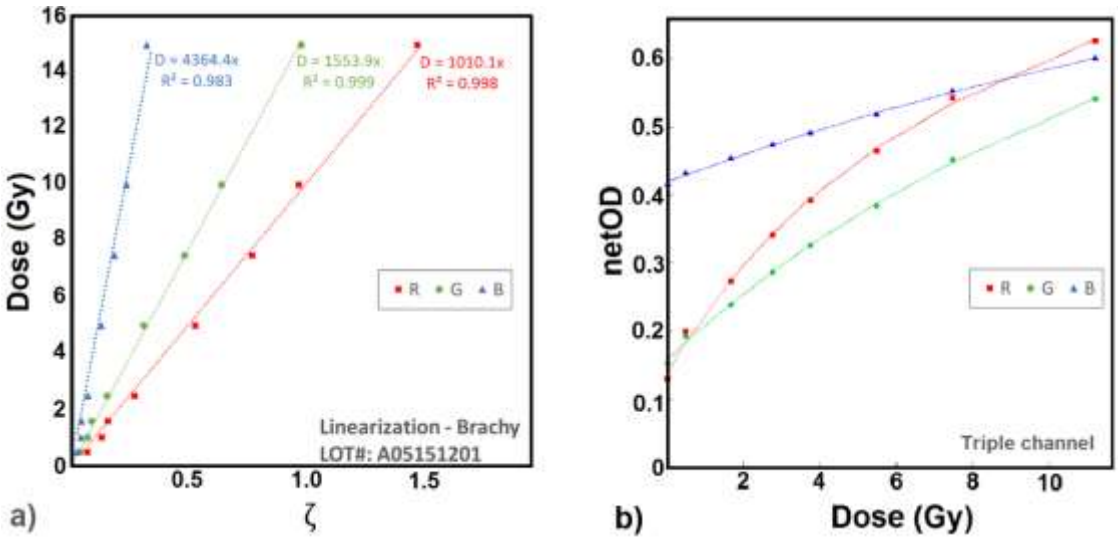

Figure 2. Calibration curves obtained using the linearization **(a)** and the triple channel **(b)** approaches.

Table 2 - Uncertainty components obtained from experimental results and from Aldelaijan *et al.* [2011]. The methodology proposed by Devic et al. eliminates calibration curve fits, reducing the experimental uncertainty.

Uncertainty components	**Type A**	**Type B**
Source-to-film positioning	0.5%	
Scanner homogeneity		0.2%
Scanner reproducibility	0.1%	
Net OD measurement reproducibility	1.1%	
Calibration curve fit – only for triple channel		2.3%
Reference dose		2.5%
Mean of the experimental values standard deviation – worst case	4.0%	
Total uncertainty (k=1) - linearization	4.8%	
Total uncertainty (k=1) - triple channel	5.4%	

3.3.- Experimental results

Experimental and calculated dose values using different procedures are presented in Table 3 for different materials and thickness. The calculated dose values uncertainties are less than 1% (k=1).

Table 3.- Experimental and calculated dose values in cGy for different materials. Values inside the brackets correspond to the difference (%) between the experimental and the calculated (MCNP5) values. Uncertainties are less than 4.5% for all measurements performed with TLDs.

Material	Height (cm)	MCNP5	TLD	MOSFET	FILM (linear)	FILM (triple channel)
Bone-2	1.8	35.5	-	31.5(-11.3)	34.5(-2.8)	34.7-(2.3)
Lung ex.	1.8	39.0	-	37.2(-4.6)	38.4(-1.5)	38.0(-2.6)
Lung in.	4.3	113.1	113.2(0.1)	109.0(-3.7)	-	-
Adipose	4.3	95.3	91.1(-4.4)	92.9(-2.5)	99.7(4.6)	-
Breast	4.3	94.4	95.6(1.3)	95.4(1.1)	-	-
Muscle	4.3	92.3	95.6(3.5)	86.7(-6.1)	92.1(-0.3)	-
PMMA	4.3	90.5	90.2(-0.3)	88.7(-1.9)	88.8(-1.9)	
Bone-1	4.3	90.8	91.8(1.1)	90.3(-0.6)	-	-
Bone-3	4.3	72.4	74.1(2.3)	71.2(-1.6)	-	-

4.- DISCUSSION

Experiments using brachytherapy sources are particularly complex due to the high dose gradient, which may lead to high experimental differences. The highest difference observed between experimental and calculate results is 11.3%, which was traced to miss alignments that also happened for other, suppressed, cases. The significance of positioning uncertainties is inversely proportional to the distance source-detector resulting in a better agreement for all cases performed with distance source-detector of 4.5 cm.

All but one result presented good agreement with differences less than 6% for almost all materials and dosimeters, which showed similar accuracy. The linearization and the triple channel approach produced similar results, although, they have differences that should be taken into account. The linearization method is simpler, has lower uncertainty and does not request a calibration curve while the triple channel methodology can reduce the effect of non-dose related components as variation on the thickness of the active layer and even dust.

The MOSFET sensitivity variation with threshold voltage is represented by a linear equation and although the angular coefficient uncertainty is around 100% it is influence in the dose value correction has shown to be negligible.

5.- CONCLUSIONS

This work presented measured and calculated dose values in heterogeneous media using three measuring methods: MOSFETS, TLDSs and radiochromic films. MOSFETS are particularly interesting due to the possibility of *in vivo* measurements but present greater uncertainties and energy dependency. TLD are very small making it interesting for accurate dose values for small regions of interest brachytherapy and radiochromic films provide with a high spatial resolution dose distribution which is important for high gradient brachytherapy doses. The Monte Carlo code MCNP5 has been used not only for dose values estimate but also to determine the photon mean energy for MOSFET energy dependency factor calculation. The calculated/experimental dose comparison demonstrated good agreement and indicates the adequacy of the experimental methodologies applied and also the dose estimate approach via MCNP5 code to be used in MBDCAs procedures.

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