On the use of VIP Gel dosimetry in HDR brachytherapy

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Abstract An experimental procedure is discussed with regard to its potential in \textsuperscript{192}Ir HDR brachytherapy dosimetry. Two samples of VIP normoxic gel formulation are used; one for gel response calibration and the other for acquiring experimental data. Using the same irradiation method for both calibration and experimental purposes (an \textsuperscript{192}Ir HDR brachytherapy source) and treating the two samples identically (i.e. the two samples are prepared, irradiated and scanned at the same time and stored together at all times) leads to total dose uncertainties comparable to those of other well established dosimetry methods over a significant dose range (~7Gy-40Gy). In this dose range, the described procedure can be used to either acquire absolute dosimetry results for the characterisation of new \textsuperscript{192}Ir HDR brachytherapy sources, or to facilitate the planning of relative dosimetry experiments for the verification of calculations by new generation treatment planning systems that are currently phasing in, in complex 3D dose distributions involving inhomogeneities and finite medium geometries.

1. Introduction
Polymer gel dosimetry, the only inherently three dimensional (3D) dosimetry method currently available, has proved effective for the verification of complex dose distributions, especially in the case where steep dose gradients are involved such as those encountered in brachytherapy or stereotactic radiosurgery. In the majority of polymer gel dosimetry studies, however, results are reported in the form of relative dose distributions, i.e. normalized to a point in the dosimeter’s volume where dose is
known by means of calculation or the use of an “absolute” dosimeter. Polymer gels are not inherently absolute dosimeters in the sense that measurements (irrespective of the imaging modality employed) are not directly translated to dose based on fundamental physical processes and constants, but rather using a calibration procedure. Nonetheless, polymer gel dosimetry could be employed to report absolute dosimetric data as well as relative dosimetry results, with an uncertainty comparable to other well established dosimetric methods. This is discussed in this work for 192Ir High Dose Rate (HDR) brachytherapy dosimetry using a normoxic gel with appropriate calibration and experimental procedures, and Magnetic Resonance Imaging (MRI) as the readout method.

2. Materials and methods

2.1. Gel preparation and irradiation

A recently introduced normoxic polymer gel formulation referred to as VIP [1, 2, 3], was used for the purpose of this work. This formulation is based on VIPAR gel formulation [4 and aims at retaining the wide dose range of VIPAR response [5] while extending it in the low dose region [2, 3], and eliminating the deoxygenation procedure to achieve speed, ease of manufacture and increased reproducibility of the dosimetric’s characteristics.

N,N’-methylenebisacrylamide (4%), N-Vinylpyrrolidone (8%), gelatin (7.5%), Copper Sulfate (0.0008%) and Ascorbic Acid (0.007%) were diluted in hyperpure water (resistivity > 18 MΩ cm) as described elsewhere [2, 3]. Two 100 ml borosilicate glass bottles were used as gel containers with a closed end glass catheter fitted through the cap to ensure impermeability to oxygen through the irradiation catheter. The gel filled bottles were tightly sealed and left overnight in a cool, dark place for the gel to solidify before irradiation.

The brachytherapy irradiation was carried out using a VariSource 192Ir (5 mm active core length) HDR remote afterloader (Varian Oncology Systems, Palo Alto, USA) programmed for each bottle to irradiate in a single dwell position for 283.5 s, with a source kerma strength (S_k) at the time of irradiation of 12861.42 cGy cm²/h (with a 3% uncertainty). Taking into account that 11.15 Gy was delivered at 1 cm distance along the transversal source axis.

The irradiated gel samples were scanned after 2 days, providing ample time for the polymerization and crosslinking procedures to evolve and for achieving thermal equilibrium of the gel substance.

2.2. Magnetic Resonance readout and data acquisition

The irradiated gel samples were scanned in the same session using a 1.5 T whole body Philips Gyroscan NT MR imager (Philips Medical Systems, Best, The Netherlands) and a quadrature RF receiver coil. Both bottles were placed in the center of the receiver coil and as close as possible to one another to ensure minimal RF field inhomogeneities. A 3D Carr-Purcell-Meiboom-Gill (CPMG) imaging pulse sequence (20 equidistant echoes, TE=40 ms, TR=2000 ms) was employed. Axial slices were reconstructed with an in-plane imaging pixel of (0.73864 x 0.73864) mm² and 0.75 mm slice thickness to enhance spatial resolution and minimize averaging effects in the steep dose gradient regions close to the HDR source.

The echo base images were exported in DICOM format and a 3D relaxation time (T_2) matrix was reconstructed through the application of a least squares mono-exponential fitting routine of pixel signal intensity versus echo time for each pixel in all echo base images. The relaxation rate (R_2=1/T_2) 3D matrix was used to calibrate the dosimeter’s response over dose, by matching gel response data to corresponding doses at various distances along the source’s transverse axis.

2.3. Calibration procedure and associated uncertainty

The reference dosimetric data used for calibration were Monte Carlo (MC) calculated relative dosimetry results for the HDR source along its transverse axis [6] coupled with the source S_k at the time of irradiation. The MC data set presents an uncertainty of less than 1%, while S_k uncertainty is
3%. Thus, the reference dose data set presents an overall uncertainty of 3% since Sk uncertainty is the dominant factor.

The spatial matching of the delivered dose distribution to the gel response distribution is crucial to an accurate calibration procedure. This is accomplished with excellent accuracy (<0.05 mm) by taking advantage of the source’s cylindrical symmetry. Due to this symmetry the registered signal around the source’s center presents a point and an axis of symmetry which can be pinpointed in a reference coordinates system by the use of image processing algorithms in the three dimensional dataset. The source center is calculated to be the center of mass of the signal distribution in the irradiated gel volume, and its central axis as the line connecting the centers of the ellipsoidal distributions in sequential axial slices.

For distances ($r_i$) spanning from 3 mm from the source’s center up to 22 mm along its transverse axis, with a step of 0.74 mm, the signal residing on a circle of radius $r_i$ around the source was averaged ($R_{2i} = \overline{R_2}(r_i)$) and its standard deviation ($\overline{\sigma_{R_2}} = \overline{\sigma}(r_i)$) was calculated to be used as a meaningful measure of the uncertainty of the mean due to random effects associated with the measuring procedure and the determination of the source’s center. In the implementation of the above procedure the spacing of data points on each circle’s circumference was chosen to be comparable to the pixel size.

The dosimeter’s response values ($R_{2i}$) to different dose levels (reference dose values, $D_i$) were matched to form a dose-response curve (figure 1). The VIP response is linear from 2.5 Gy up to 33 Gy, with sublinearity gradually setting in at higher doses. For brachytherapy dosimetry purposes a wide range of doses is necessitated. Thus a second degree polynomial function ($R = a_1D^2+a_2D+a_3$) was fitted to the response data ($R_{2i}=f(D_i)$) to make use of a larger dose range of VIP gel response. The coefficients of the fitting function were determined by weighted least squares regression, since each point in the dose-response data-set is known with different uncertainty, as clearly seen in figure 1. The weights used were equal to the inverse squared standard deviation for each point ($w_i=1/\overline{\sigma_{R_2}^2}$).

The constants of the fitting function were found to be: $a_1=-(0.00028\pm0.00004) \, \text{Gy}^{-2} \cdot \text{s}^{-1}$, $a_2=(0.0792\pm0.0018) \, (\text{Gy} \cdot \text{s})^{-1}$ and $a_3=1.341\pm0.011 \, \text{s}^{-1}$.

The above described calibration function is used to obtain doses ($D_{exp}$) in an experiment which produces gel response measurements ($R_{2meas}$). The sources of uncertainty to be considered in experimental dosimetry using this calibration procedure are the uncertainties of the fitting coefficients and the uncertainty of the reference doses ($u_{Dref}$). Thus the calibration uncertainty of a measured dose would be:

$$u_{cal} = \sqrt{\sum \left( \frac{\delta_{cal}}{\overline{\delta a_i}} \cdot \delta a_i \right)^2 + (0.03 \cdot D)^2}$$

(1)

$$u_{Dref} = (D/Sk)u_{Sk}=0.03D$$

(2).

2.4. Experimental dosimetry uncertainty
Besides calibration uncertainty, experimental dosimetry results are subject to the uncertainty induced by the use of the polymer gel – MRI method to register the signal distribution to be translated to the corresponding dose distribution around the HDR source. Thus the uncertainty of the measured dose shall include the uncertainty of the measured $R_2$ values ($u_{meas}$) which incorporates all uncertainty factors related to noise and discrepancies induced to the final measurement due to MR scanning, radiation and chemical factors [7]. The cumulative effect of all these factors, which end up affecting
the final measurement in a statistical way, can be quantified by the standard deviation of the measured $R^2$ values which is easily calculated due to the cylindrical symmetry in single source dwell position irradiations as described above. Moreover, the use of normoxic gel of the same preparation batch for both calibration and measurement bottles, combined with an experimental procedure that secures the same thermal history and the same irradiation and scanning conditions for both samples, cancels out the effect of the majority of potential systematic uncertainties and ensures that the effect of those remaining is kept minimal and relatively smaller than the uncertainty already accounted for by the combination of $u_{cal}$ and $u_{meas}$.

3. Results & discussion

Figure 2 presents the relative percent uncertainties induced in experimental brachytherapy dosimetry by (a) the calibration procedure and (b) the measurement process. The effect of the reference dose uncertainty is constant while the coefficients' effect is comparable to that of $u_{Dref}$ for a range of doses spanning from 5 Gy up to about 35 Gy, summing up to a total dose uncertainty due to the calibration procedure below 5% in this range (figure 2a). The uncertainty in the measured dose due to the measurement solely (i.e. apart from the calibration procedure) spans in a much wider range of dose percentages (figure 2b), whereas the general trend is similar to that shown in figure 2a: a region of more or less low uncertainty (below 4%) outside of which the uncertainty increases rapidly.

The total uncertainty of measured dose is presented in figure 3. In the range from 7 Gy up to 37 Gy (which corresponds to a distance range
from 13 mm down to 5.4 mm along the source’s transversal axis) the uncertainty is lower than 6%, the suggested limit of uncertainty for an experimental dosimetry method used to characterize a new HDR source [8]. Thus the VIP polymer gel-based method proposed herein can be used for the dosimetric characterization of an $^{192}$Ir HDR source, preferably using two different experimental gel bottles irradiated so as to cover the distance range of interest around the source with acceptable accuracy.

In order to demonstrate this potential the polymer gel measured dose along a line parallel to the source long axis at 5 mm distance is compared to the corresponding MC-based, reference dose distribution in figure 4. The gel measured values emanate from the second gel bottle, with the experimental dose values being computed using the calibration data of the first gel bottle. In this figure it can be seen that although significant uncertainties occur in a few, relatively high dose points, the experimental dose distribution is in excellent agreement with the reference dose distribution since this distribution is deduced by experimental dose results averaged according to cylindrical symmetry, and most important, concurrent measurement of a dose distribution (an inherent advantage of the polymer gel method) constricts the effect of individual point uncertainties.

An experimental procedure similar to that proposed herein has been successfully employed with a different gel formulation for the dosimetry of low energy/low dose rate brachytherapy sources [9, 10]. In such applications however not only inter-batch but also intra-batch variability is an issue due to the low source $S_k$ that leads to prolonged irradiation times. In HDR brachytherapy dosimetry, the small irradiation times determine a time frame that allows for the response of a polymer gel dosimeter, especially a normoxic one, to be accurately evaluated. It should also be noted that the optimum experimental dose range, in terms of dose uncertainty, could be extended if the calibration source $S_k$ was known with improved accuracy.

4. Conclusions
Irradiation of a gel sample with a single HDR source dwell position allows for a meaningful estimation of precision through repeatability (i.e. the agreement of concurrent measurements carried out under the same conditions of measurement) by exploiting the cylindrical symmetry of delivered dose and corresponding measured response. An experimental procedure that treats normoxic gel filled bottles for calibration and experimental purposes identically, in terms of storage, irradiation and scanning conditions, ensures minimal effect of systematic uncertainties. The total dose uncertainties of the method were calculated and found comparable to those related to other well established dosimetry methods, with the added advantage of concurrent measurements in three dimensions in a single experiment and for an adequate dose range. This dose range can be used for the dosimetric characterization of new HDR source designs that have been recently proposed, as well as for the verification of complex three dimensional dose distributions in brachytherapy.

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Figure 4: MC and experimental dose profiles along a line parallel to the source axis at a 5 mm distance
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