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Dosimetric comparison of DEFGEL and PAGAT formulae paired with an MRI acquisition

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Abstract. Normoxic Polyacrylamide Gels, or nPAGs, are 3D gel dosimeters that measure dose through the process of radiation-induced polymerization. Two nPAG formulae are DEFGEL and PAGAT, which are very similar, but differ mainly due to different weight fractions of monomers. The dosimetric resolutions of the two formulae when paired with a Spin-Echo (SE) MRI sequence and a monoexponential fit were compared over a range of 0-15 Gy. It was found that in the dose range 0-6 Gy the PAGAT formula generally showed a much finer dose resolution, while the DEFGEL formula showed a finer resolution from 8-15 Gy.

1. Introduction

Gel dosimeters such as polyacrylamide gels (PAGs) and normoxic polyacrylamide gels (nPAGs) can measure 3D dose distributions, while maintaining tissue equivalence, dose rate independence, and angular independence [1-4]. This family of gel dosimeters operates through the radiation-induced polymerization of the monomer acrylamide and the cross linking monomer N,N'-methylenebis-acrylamide (Bis) [5]. This polymerization changes the optical density (OD) and transverse nuclear magnetic relaxation rate (R_2) as a function of dose, which allows the dose to the gel to be characterized through optical readout or MRI acquisition [6, 7]. Two types of nPAGs are the DEFGEL formula [8] and the PAGAT formula [9], which differ only by the amount of monomers present in each gel type and the form of the antioxidant. Specifically, the DEFGEL formula has a 6% monomer fraction by weight, while the PAGAT formula has 9%. This difference in monomers concentration causes each dosimeter to result in different dose responses and dose response calibrations [10]. The goal of this investigation is to compare the dose response of both gel formulae through an analysis of the dose resolutions of the gels over a range of 0-15 Gy.

2. Method

2.1. Gel Fabrication & Irradiation

Twelve gel dosimeters were fabricated in-house, six using the DEFGEL formula described by Yeo *et al* and six using the PAGAT formula described by Venning *et al* [9, 10]. Both batches of gel were prepared using the methods described by Yeo *et al* [8], but in the case of PAGAT, THPC, the chloride form of the antioxidant THP, was used as opposed to the sulfate form used in DEFGEL. All gel dosimeters were

fabricated in 7.0 mL BD Vacutainer® Serum (Becton, Dickinson and Company, Franklin Lakes, NJ) glass vials.

To ensure accurate and precise gel doses, gel irradiations were performed by placing the dosimeters in a Sun Nuclear 1D Scanner™ (Sun Nuclear Corporation, Melbourne, FL). All irradiations were performed using a Varian Clinac 21EX at the University of Wisconsin Medical Radiation Research Center (UWMRRC) with a 6MV beam and a repetition rate of 600 MU per minute. The irradiations were performed at a depth of 5.5 cm in liquid water with a source-to-surface distance (SSD) of 100 cm and a 10 cm x 10 cm field size. The centers of the vials were positioned on the central axis (CAX).

2.2. MR Scanning

Gel R_2 data were acquired using a 3T MRI scanner (SIGNA PET/MR, GE Healthcare, Waukesha, WI) and an 8-channel receive-only head coil. All scans were acquired using a spin-echo (SE) pulse sequence using the parameters shown in Table 1. The TE values used for the scans were based on the optimal SE parameters described in the parameter optimization of De Deene and Baldock [7] The echoes from each scan session were used to create R_2 maps by performing a linear fit of the natural logarithm of the echo signals at each echo time on a voxel-by-voxel basis. Mean R_2 values and their standard deviations were gathered for a central, rectangular, region of interest (ROI) in each of the gels for dose response fits.

Table 1. Spin-Echo scan parameters used to gather the R2 data.

DEFGEL Scan Parameters		**PAGAT Scan Parameters**	
Repetition Time (TR)	5000 ms	Repetition Time (TR)	5000 ms
Echo Time (TE)	20 ms, 512 ms	Echo Time (TE)	20 ms, 330 ms
Echoes (NE)	2	Echoes (NE)	2
Averages (NEX)	1	Averages (NEX)	1
Acquisition Matrix	128 x 128	Acquisition Matrix	128 x128
Field of View (FOV)	128 x 128 mm^2	Field of View (FOV)	128 x 128 mm^2
Spatial Resolution	1 mm^2	Spatial Resolution	1 mm^2
Number of Slices (NS)	1 - Coronal	Number of Slices (NS)	1 - Coronal
Slice Thickness	3 mm	Slice Thickness	3 mm
Scan Time	11.66 min/echo	Scan Time	11.66 min/echo

2.3. Dose Response and Dose Resolution

In order to characterize the dose response of each gel formula the mean R_2 versus dose relationship was fit to the following monoexponential function [7] using MATLAB,

$$R_2(s^{-1}) = R_{2,sat} - \Delta R_2 \cdot \exp(-\alpha * D(Gy)). \qquad (1)$$

In this equation, the fitting parameter $R_{2,sat}$ represents the saturated R_2 value of the gel, the fitting parameter ΔR_2 represents the range of R_2 values possible for the gel, and α is an exponential fitting parameter.

To evaluate the intrinsic dosimetric precision of each of the gels paired with an MRI acquisition, the metric of dose resolution was used. Dose resolution takes into account both the inherent dose sensitivity of the gel, along with the SNR of the MR acquisitions. Dose resolution was calculated using the formalism of Baldock *et al* [11, 12]. In this formalism, the dose resolution of two dose peaks measured from a gel dosimetry system with a confidence level of *p* is defined as:

$$D_{\Delta}^{p} = k_p \sqrt{2} \sigma_D \qquad (2)$$

where k_p is a coverage factor, which is 1.96 for a 95% confidence level, and σ_D is estimated to be the combined dosimetric uncertainty. Given that the Type B uncertainties of the dose are negligible when

compared to the Type A uncertainty due to the standard deviation of the R_2 measurements [8], the combined uncertainty simplifies to:

$$u_C^2(D) = \left[\frac{\delta D}{\delta R_2}\right]^2 u^2(R_2), \quad (3)$$

where $u(R_2)$ is the standard uncertainty of the R_2 measurements, which was estimated to be the standard deviations of the mean R_2 values.

Equation 1 can be rearranged to calculate dose as a function of R_2:

$$D(Gy) = \frac{1}{\alpha}\ln\left(\frac{\Delta R_2}{R_{2,sat} - R_2(s^{-1})}\right). \quad (4)$$

Combining equations 3 and 4, the final equation for dose resolution becomes:

$$D_\Delta^p = k_p\sqrt{2}\sqrt{\left(\frac{1}{\alpha(R_{2,sat} - R_2(s^{-1}))}\right)^2 \left(\sigma(R_2)\right)^2}. \quad (5)$$

The value of 1.96 was used for the coverage factor k_p in the following dose resolution calculations to represent a 95% confidence level.

3. Results and Discussion

3.1. Dose Response

The measured mean R_2 values and their standard deviations are shown in Table 2 and the resultant monoexponential fits are shown in Figure 1 and Table 3. Both dose responses showed excellent fits to the monoexponential equation, with R^2 values of 0.9999 and 0.9994 for DEFGEL and PAGAT, respectively. Over the 0-15 Gy dose range investigated, the PAGAT gel resulted in a much larger range of R_2 values due to a much steeper initial slope. The values of $R_{2,sat}$ and ΔR_2 for both gels were quite similar, suggesting that the PAGAT gel response saturated at a much faster rate than the DEFGEL.

Table 2. Mean R_2 values measured within a central ROI of each dosimeter, the standard deviation of each mean, the dose uncertainties calculated from these values, and the resultant dose resolutions with a 95% confidence level.

	DEFGEL					PAGAT				
Dose (Gy)	**R2 (s^{-1})**	**Σ (s^{-1})**	**Σ (%)**	**u_c(D) (Gy)**	**Dose Resolution 95% (Gy)**	**R2 (s^{-1})**	**Σ (s^{-1})**	**σ (%)**	**u_c(D) (Gy)**	**Dose Resolution 95% (Gy)**
15	3.0643	0.0358	1.17	0.48	1.33	5.3044	0.0675	1.27	1.29	3.57
10	2.6567	0.0367	1.38	0.42	1.17	5.0154	0.0718	1.43	0.70	1.95
8	2.4872	0.0321	1.29	0.35	0.96	4.6636	0.0682	1.46	0.42	1.16
6	2.2867	0.0338	1.48	0.34	0.95	4.3060	0.0606	1.41	0.27	0.75
2	1.8791	0.0252	1.34	0.23	0.63	3.0047	0.0382	1.27	0.09	0.24
0	1.6408	0.0232	1.41	0.20	0.54	1.9720	0.0387	1.96	0.06	0.17

Table 3. Fitting parameters for the monoexponential fits of the dose response data.

	$R_{2,sat}$ (s^{-1})	**ΔR_2 (s^{-1})**	**A (Gy^{-1})**
DEFGEL	5.475	3.831	0.0309
PAGAT	5.609	3.648	0.1718

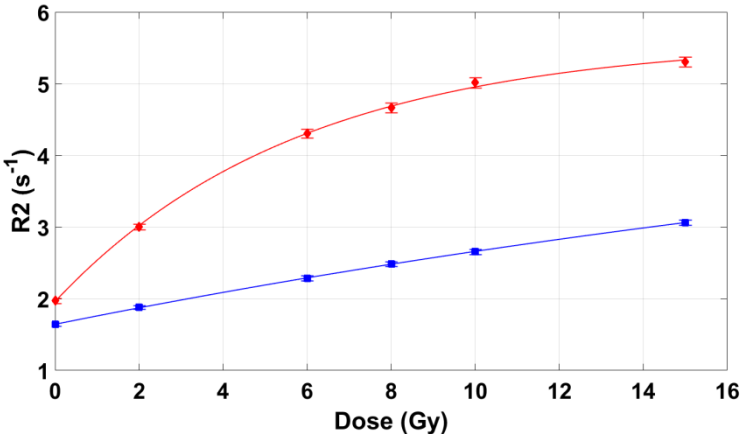

Figure 1. The dose response fits of DEFGEL (blue squares) and PAGAT (red diamonds).

3.2 Dose Resolution

The resulting dose resolution values are provided in Table 2. Over a range from 0-6 Gy, the PAGAT formula showed a much finer resolution than the DEFGEL formula. This is likely due to the larger amount of monomers in PAGAT, which increases the dose sensitivity of the gel. As the dose response of the PAGAT began to saturate, the dose resolution of the DEFGEL formula was improved relative to the PAGAT formula (as seen in the range of 8-15 Gy). This was due to the more linear nature of the DEFGEL formula's dose response, allowing for it to better distinguish higher doses due to no polymerization saturation. The dose resolutions found in this study are generally larger than those found in the literature, except for the values for PAGAT at low doses [9-13]. This is likely because a monoexponential fit, as opposed to a linear fit, was used to calculate dose resolution to account for saturation effects, causing coarser dose resolutions at high doses. Also, the larger Type A uncertainties caused by the small vials and their MRI acquisition may have also worsened dose resolution.

4. Conclusion

In this study the dose responses of the DEFGEL and PAGAT formulae were evaluated and compared using the metric of dose resolution. It can be concluded that the DEFGEL formula showed a better dose resolution at doses ranging from 8-15 Gy, while the PAGAT formula had superior dose resolution at lower doses ranging from 0-6 Gy. This conclusion suggests that when paired with MRI, each gel could be more effective in different applications. For example, the DEFGEL formula would be much more appropriate for a 3D dosimeter to be used as a dose target in cases with high dose fractions, like in phantoms used to measure doses from SBRT, SRS, and other hypofractionated treatment modalities. In contrast, PAGAT would an appropriate dosimeter for measuring the doses from treatment modalities with more standard dose fractions.

5. Acknowledgements

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