Leuco-crystal-violet micelle gel dosimeters: Component effects on dose-rate dependence

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Abstract. Designed experiments were performed to produce empirical models for the dose sensitivity, initial absorbance, and dose-rate dependence respectively for leuco-crystal violet (LCV) micelle gel dosimeters containing cetyltrimethylammonium bromide (CTAB) and 2,2,2-trichloroethanol (TCE). Previous gels of this type showed dose-rate dependent behaviour, producing an ~18% increase in dose sensitivity between dose rates of 100 and 600 cGy min\(^{-1}\).

Our models predict that the dose rate dependence can be reduced by increasing the concentration of TCE, CTAB and LCV. Increasing concentrations of LCV and CTAB produces a significant increase in dose sensitivity with a corresponding increase in initial absorbance. An optimization procedure was used to determine a nearly dose-rate independent gel which maintained high sensitivity and low initial absorbance. This gel which contains 33 mM CTAB, 1.25 mM LCV, and 96 mM TCE in 25 mM trichloroacetic acid and 4 wt% gelatin showed an increase in dose sensitivity of only 4% between dose rates of 100 and 600 cGy min\(^{-1}\), and provides an 80% greater dose sensitivity compared to Jordan’s standard gels with similar initial absorbance.

1. Introduction

Leucocrystal violet (LCV) micelle gel dosimeters developed by Babic et al [1] can be read optically and produce accurate 3-D dosimetry with excellent spatial stability, but have low dose sensitivity compared to alternatives such as Fricke gel dosimeters which use ferric ions as their reporter molecule [2]. LCV gels are preferable to leucomalachite green (LMG) gels, also developed by Jordan’s research group, because LCV is less soluble in water causing it to preferentially dissolve in micelles, thereby reducing diffusion [1,3,4]. Nasr et al. attempted to optimize Jordan’s LCV gel recipe by adjusting concentrations of LCV and Triton X-100 (Tx100) surfactant and adding 2,2,2-trichloroethanol (TCE) as a sensitizing agent [5, 6]. They found that increasing LCV concentration beyond ~1.25 mM leads to precipitation and formation of turbid gels [5, 6]. Increasing surfactant concentration can raise this limit at the cost of increased initial absorbance [5, 6] and viscosity during manufacture. More sensitive gels could not be produced using these ingredients without an undesirable increase in absorbance of the gel prior to irradiation. Because high initial absorbance was correlated with high Tx100 concentration, alternative surfactants were considered [5, 6]. Optimized gels using the surfactant cetyltrimethylammonium bromide (CTAB) showed higher dose sensitivity and excellent spatial stability while still maintaining low initial absorbance. But, unlike Jordan’s LCV gel, the proposed gel exhibited significant dose-rate dependence [6]. Dose-rate dependence has been observed in LMG micelle gels studied by Vandecasteele et al. who used sodium dodecyl sulfate as the surfactant. They reduced the undesirable dose-rate
dependence from 75% to 33% between dose rates of 50 and 400 cGy min\(^{-1}\) by manipulating concentrations of LMG, surfactant, and gelatin [7]. Høye et al. performed similar manipulations on silicone-based LMG dosimeter recipes, producing a dose-rate independent phantom by increasing the dye concentration at the cost of spatial stability [8].

2. Materials and Methods

2.1. Gel preparation

1- Add gelatin (Type A, 300 Bloom porcine skin) to 75 wt% of the total deionized water preheated to 60 °C (Mix A). Stir until gelatin dissolves and a final temperature of 45 °C is reached.
2- Add surfactant (CTAB or T\textsubscript{x}100), trichloroacetic acid (TCAA), and TCE (sensitizer) to the remaining deionized water (Mix B) and stir at room temperature until dissolved.
3- Add LCV into Mix B. Cover with a box and stir at room temperature for 5 minutes.
4- Pour Mix B into Mix A and stir for 5 minutes.
5- Pour this gel into 14 polystyrene cuvettes (4.5 mL, 10 mm path length) and cap. Record pH.
6- Refrigerate at 4 °C for 24 h, then place in a 22 °C water bath for 20 min. before irradiation.

2.2. Irradiation and scanning procedure

A Varian Clinac 6EX linear accelerator was used to irradiate the cuvettes to doses of 1, 2, 3, 5, 10, 15, and 20 Gy; half at 100 cGy min\(^{-1}\) and the rest at 600 cGy min\(^{-1}\), with 6 MV photons. Irradiation was conducted using an isocentric setup with a 100 cm source-to-axis distance, 1.5 cm plastic water build-up, 10 cm backscatter, and a 15x15 cm\(^2\) field size. Absorbance measurements were taken at 590 nm before \((A_0)\) and 10 mins. post-irradiation \((A_1)\) using a SpectoVis Plus spectrophotometer over the 380–900 nm wavelength range. Spectra were calibrated by subtracting the spectrum of a reference cuvette containing deionized water. The change in attenuation coefficient \((\Delta \mu)\) between the absorbances was calculated using:

\[
\Delta \mu = \ln(10) \cdot x^{-1}(A_1 - A_0)
\]

where \(x = 1\) cm is the cuvette path length.

2.3. Designed experiments to optimize LCV micelle gels made with CTAB and TCE

A two-level three-factor full factorial design (runs 1.1 to 1.8 in table 1) was conducted in random order along with 9 centre-point runs (averaged and displayed as run 1.9) and 3 replicates of the Jordan gel (displayed as run 1.0). Three replicates of Nasr’s gel optimized for high sensitivity (displayed as run 1.10) were also produced. Gelatin and TCAA concentrations were held at 4 wt% and 25 mM, respectively, in all gels. Linear regression (forced through the origin) was used to fit dose sensitivities (DS) for all gels at both dose rates (100 and 600 cGy min\(^{-1}\)). The sensitivity ratio (SR) was computed using:

\[
SR = \frac{DS(600)}{DS(100)}
\]

Models of the form:

\[
Y = \beta_0 + \beta_1[\text{CTAB}] + \beta_2[\text{LCV}] + \beta_3[\text{TCE}] + \beta_{12}[\text{CTAB}][\text{LCV}] + \beta_{13}[\text{CTAB}][\text{TCE}] + \beta_{23}[\text{LCV}][\text{TCE}]
\]

were fitted with JMP® statistical software using runs 1.1 to 1.10 in table 1 (where \(Y = A_0\), DS(100), DS(600), SR) and the resulting parameter estimates are reported in table 2. Replicate runs were used individually (not averaged) during the model fitting. Recipe optimization was performed in Matlab® using sequential quadratic programming.
3. Results and Discussion

3.1. Designed experiments to optimize LCV micelle gels made with CTAB and TCE

Dose sensitivities in table 1 are consistent with results of Nasr et al [6], with a similar variance observed at the centre points for dose sensitivity and initial absorbance. The initial absorbances in the current study are higher by ~0.01, potentially due to batch differences in chemicals and cuvettes used.

As apparent from the parameter estimates in table 2, increasing the concentration of CTAB and LCV has a significant influence on the dose sensitivity of the gels. This result was expected because increasing micelle and reporter molecule concentrations increases the probability that free radicals encounter LCV in micelles to produce the response. The concentration of the sensitizer (TCE) shows a significant influence on sensitivity at lower dose rates but may have less influence at higher dose rates.

In agreement with previous results from Nasr et al [6], increasing LCV concentration tends to increase the initial absorbance of the gel, as indicated by the positive value of 27.9 mM\(^{-1}\) in table 2 (significant at the 85% confidence level, but not at 95%). Note that, unlike gels manufactured with Tx100, increasing CTAB surfactant does not cause a significant increase in initial absorbance [6].

Estimated values of parameters \(\beta_1\), \(\beta_2\) and \(\beta_3\) in the SR model are all negative (except the CTAB-TCE interaction, and only \(\beta_3\) significant at the 95% confidence level), suggesting that recipes with more micelles, LCV and sensitizer tend to be less dose-rate dependent. This effect could be the result of a higher probability of free radicals encountering micelles and reacting with LCV to induce colour change.

The model equations of the form shown in equation 1 were used to search for an improved gel recipe, using the parameter values in table 2. The optimization process minimized the objective function:

\[
J = -DS(100) + \omega_1 A_0 + \omega_2 (SR - 1)^2
\]

where \(\omega_1\) and \(\omega_2\) are positive weighting factors (Gy\(^{-1}\) cm\(^{-1}\)) to set the relative importance of dose sensitivity, initial absorbance, and sensitivity ratio. Bounds on the species concentrations were set at 9 mM \(\leq [\text{CTAB}] \leq 33 \text{ mM}\), 0.75 mM \(\leq [\text{LCV}] \leq 1.25 \text{ mM}\), and 40 mM \(\leq [\text{TCE}] \leq 120 \text{ mM}\) to ensure reasonable gel recipes would be selected. Base values for \(\omega_1\) and \(\omega_2\) were set at 0.2 and 0.066, respectively, so that all three terms on the right-hand side of equation 2 are similar in magnitude. The resulting optimal gel is displayed as run 1.11 in table 1. Optimization was performed again with \(\omega_1 = 0\) and \(\omega_2 = 1\) to weigh heavily towards a dose-rate independent gel, resulting in the recipe for run 1.12. Run 1.11 produced a gel which maintained a reasonable sensitivity and initial colour compared to the other gels, however would still not be attractive for use in dosimetry with its 14% dose-rate dependence. Run 1.12 did produce a gel which had a more acceptable dose-rate dependence of 4% and a sensitivity similar to that of Nasr’s most sensitive gel (run 1.10) [6].

4. Conclusions

Radio-chromic LCV micelle gels manufactured with CTAB surfactant exhibit improved dose sensitivity and comparable initial absorbance when compared to the LCV gel proposed by Babic et al [1]. Unfortunately, these new gels can exhibit undesirable dose-rate dependence (as high as 32% between dose rates of 100 and 600 cGy min\(^{-1}\)). The degree of dose-rate dependence varies with the gel recipe. Linear regression results suggest that high concentrations of CTAB, LCV and TCE may ameliorate this effect. An optimized gel recipe was developed containing 33.0 mM CTAB, 1.25 mM LCV, 96.0 mM TCE, and 25.0 mM TCAA in 4 wt% gelatin. This gel showed only a small dose-rate dependence of 4% between the dose rates of 100 and 600 cGy min\(^{-1}\), which may be acceptable for practical 3-D dosimetry applications [9]. However, batches do show a large amount of variance and further work reproducing these results is necessary. The proposed gel has a dose sensitivity 80% higher than the original LCV micelle gel developed by Babic et al [1] while still at a similar initial absorbance. In future, we will explore the possibility to develop gels with lower dose-rate dependence and even higher dose sensitivity by expanding the bounds used for recipe optimization, and attempt to modify the preparation methods to produce more consistent results.
Table 1. Influences of CTAB, LCV, and TCE on the initial absorbance, dose sensitivities, and sensitivity ratio of LCV micelle gels. Gels shown use CTAB as their surfactant, except gel 1.0 which used Tx100. Errors shown are one standard deviation from the mean in runs where replicates were performed.

| Run | Surfactant [mM] | LCV [mM] | TCE [mM] | Initial Absorbance | Dose Sensitivity [x10^{-3} Gy^{-1} cm^{-1}] | Sensitivity Ratio | pH |
|-----|----------------|----------|----------|-------------------|---------------------------------------------|------------------|-----|
|     |                |          |          |                   | (100 cGy min^{-1}) | (600 cGy min^{-1}) |          |
| 1.0 | 4.0            | 1.0      | 0.0      | 0.041 ± 0.003     | 6.8 ± 0.6                      | 6.8 ± 0.5        | 0.99 ± 0.02 | 3.37|
| 1.1 | 9.0            | 0.75     | 40.0     | 0.034             | 6.31                          | 8.05             | 1.27       | 3.33|
| 1.2 | 9.0            | 0.75     | 80.0     | 0.033             | 7.83                          | 8.73             | 1.12       | 3.33|
| 1.3 | 9.0            | 1.25     | 40.0     | 0.056             | 7.21                          | 9.21             | 1.28       | 3.27|
| 1.4 | 9.0            | 1.25     | 80.0     | 0.046             | 7.51                          | 9.17             | 1.16       | 3.33|
| 1.5 | 25.0           | 0.75     | 40.0     | 0.035             | 7.44                          | 9.85             | 1.32       | 3.31|
| 1.6 | 25.0           | 0.75     | 80.0     | 0.044             | 9.83                          | 10.92            | 1.11       | 3.32|
| 1.7 | 25.0           | 1.25     | 40.0     | 0.047             | 9.30                          | 10.42            | 1.12       | 3.29|
| 1.8 | 25.0           | 1.25     | 80.0     | 0.054             | 12.37                         | 13.83            | 1.12       | 3.31|
| 1.9 | 17.0           | 1.0      | 60.0     | 0.042 ± 0.005     | 8.6 ± 0.5                     | 10.0 ± 0.5       | 1.16 ± 0.06 | 3.33|
| 1.10| 33.0           | 1.25     | 120.0    | 0.055 ± 0.005     | 12.6 ± 0.5                    | 12.8 ± 0.9       | 1.05 ± 0.08 | 3.32|
| 1.11| 9.0            | 0.90     | 120.0    | 0.040             | 9.80                          | 11.2             | 1.14       | 3.24|
| 1.12| 33.0           | 1.25     | 96.0     | 0.047             | 12.4                          | 12.9             | 1.04       | 3.22|

Table 2. Parameter estimates from regression analysis of the data in table 1 to model initial absorbance, dose sensitivity and sensitivity ratio; with units consistent with those provided in table 1. Bolded values are significant at a 95% confidence level.

| Parameter Coefficient | Parameter Estimates [x10^{-3}] |
|-----------------------|--------------------------------|
|                       | A {Initial Absorbance} | DS(100) {Sensitivity} | DS(600) {Sensitivity} | SR {Sensitivity Ratio} |
| β₀                   | 40.3                  | 0.246                  | 3.08                  | 1592                  |
| β₁                   | -2.45                 | 0.0940                 | 0.201                 | -10.3                 |
| β₂                   | 27.9                  | 3.41                   | 2.79                  | -238                  |
| β₃                   | -0.113                | 0.0727                 | 0.0277                | -7.74                 |
| β₁₂                  | 1.09                  | 0.0695                 | -0.0286               | -11.5                 |
| β₁₃                  | 0.0247                | -0.000516              | -0.000516             | -0.0320               |
| β₂₃                  | -0.336                | -0.029                 | 0.00478               | 5.64                  |

5. References
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