The Multigaussian method: a new approach to mitigating spatial heterogeneities with multichannel radiochromic film dosimetry

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Abstract
The main objective of multichannel radiochromic film dosimetry methods is to correct, or at least mitigate, spatial heterogeneities in the film-scanner response, especially variations in the active layer thickness. To this end, films can also be scanned prior to irradiation. In this study, the abilities of various single channel and multichannel methods to reduce spatial heterogeneities, with and without scanning before irradiation, were tested. Red, green and blue single channel models, two additive channel independent perturbation (CHIP) models and two multiplicative CHIP models were compared with the Multigaussian method. The Multigaussian method is a new approach to multichannel dosimetry, based on experimental findings. It assumes that the probability density function of the response vector formed by the pixel values of the different color channels, including irradiated and non-irradiated scans, follows a multivariate Gaussian distribution. The Multigaussian method provided more accurate doses than the other models under comparison, especially when incorporating the information of the film prior to irradiation. The relative dose differences between reference doses measured with MatriXX and film doses were examined. After applying inter-scan and lateral corrections, the lowest mean absolute errors were 0.8% and 1.0% for the Multigaussian method with and without the information of the scan before irradiation, respectively. Followed by the uniform multiplicative CHIP and red single channel models, using pixel values and net optical density, respectively, both with 1.1%.

1. Introduction
Small fields, steep dose gradients or regions without electronic equilibrium are some of the many situations in which radiation doses can be measured using radiochromic films. Particular strengths of radiochromic films are weak energy dependence (Rink et al. 2007, Richter et al. 2009, Arjomandy et al. 2010, Lindsay et al. 2010, Massillon-JL et al. 2012, Bekerat et al. 2014), near water-equivalence (Niroomand-Rad et al. 1998, Crijns et al. 2013), and high spatial resolution. On the other hand, the dosimetry system composed of radiochromic films and a flatbed scanner suffers from several sources of uncertainty, which can affect the film (e.g. differences in the active layer thickness (Hartmann et al. 2010), evolution of film darkening with post-irradiation time (Andrés et al. 2010, Chang et al. 2014), dependency on humidity and temperature (Rink et al. 2008), noncatalytic and ultraviolet-catalyzed polymerization (Girard et al. 2012), scratches), the scanner (e.g. the warming-up of the lamp (Paelinck et al. 2007, Ferreira et al. 2009), inter-scan variations (Lewis and Devic 2015, Méndez et al. 2016), noise (Bouchard et al. 2009, van Hoof et al. 2012), dust), or the interaction between film and scanner (e.g. the lateral artifact (Schoenfeld et al. 2014, van Battum et al. 2015, Schoenfeld et al. 2016), the dependency on the orientation of the film on the scanner bed (Butson et al. 2009), the dependency on film-to-light source distance (Lewis and Devic 2015, Palmer et al. 2015), Newton rings (Dreindl et al. 2014), the cross talk effect (van Battum et al. 2015)). Film handling and scanning protocols (Niroomand-Rad et al. 1998, Bouchard et al. 2009), corrections (Lewis et al. 2012, Méndez et al. 2013, Lewis and Chan 2015, Lewis and Devic 2015, Méndez et al. 2016, Ruiz-Morales et al. 2017) and multichannel dosimetry methods (Micke et al. 2011, Mayer et al. 2012, Azorín et al. 2014, Méndez et al. 2014) have
been developed to reduce uncertainties and deliver precise and accurate doses (Palmer et al 2013, Vera-Sánchez et al 2018).

Multichannel radiochromic film dosimetry methods combine the information provided by all three color channels (R, G and B) of the scanner. In order to do so, the perturbation of the film-scanner response caused by different sources of uncertainty must be (explicitly or implicitly) modeled. Current multichannel methods assume that changes in the response for the different channels are positively correlated. Moreover, perturbations should be small. For example, even though the lateral artifact produces positively correlated perturbations (i.e. pixel values decrease with the distance from the center of the scan for all three channels, given a constant dose), these perturbations increase with the dose and the distance from the center, eventually becoming excessive for multichannel models (Schoenfeld et al 2016). The primary targets of multichannel film dosimetry are the spatial heterogeneities of the response and, in particular, differences in the active layer thickness. These differences can also be addressed by incorporating the information of the film prior to irradiation employing net optical density (NOD) as the film-scanner response.

The purpose of this study was to select the most accurate method from among the methods under comparison for mitigating spatial heterogeneities in the response. The effectiveness of NOD and various multichannel models was compared with a novel approach to multichannel radiochromic film dosimetry which we have called the Multigaussian method.

2. Methods and materials

2.1. Measurements

Commonly, multichannel models are evaluated using the gamma index: a sample of clinical plans are calculated with the treatment planning system (TPS) and posteriorly irradiated, dose distributions are computed with each multichannel model and the multichannel model that produces dose distributions which are most similar to the TPS doses according to the gamma index is deemed to be the most accurate model (Azorín et al 2014, Méndez et al 2015, Menegotti et al 2008, Palmer et al 2015). This procedure has several drawbacks (Clasie et al 2012): apart from the accuracy of the multichannel model, the gamma index depends on the shape of the dose distribution in the individual plans, the noise in the distributions, the tolerance criteria, the interpolation method implemented for the gamma index computation, the choice of reference and evaluation dose distributions, the accuracy of the TPS, etc.

In this work, the measurement protocol was designed with the aim of minimizing the influence of any source of uncertainty other than the spatial heterogeneity of the response. Two lots of Gafchromic EBT3 films (lots 06061401 and 04071601) and one lot of EBT-XD films (lot 12101501) were employed. They were identified as lots A, B and C, respectively. The dosimetry system was completed with an Epson Expression 10000XL flatbed scanner (Seiko Epson Corporation, Nagano, Japan) and the scanning software Epson Scan v3.49a. Five films per lot were scanned prior to and 24 h following irradiation. Irradiation was delivered with a 6 MV beam from a Novalis Tx accelerator (Varian, Palo Alto, CA, USA). Films were positioned at source-axis distance (SAD) on top of the IBA MatriXX detector (IBA Dosimetry GmbH, Germany) inside the IBA MULTICube phantom. Doses were simultaneously measured with the MatriXX detector. Field dimensions were 20 × 20 cm² for lot A and 25 × 25 cm² for lots B and C. Films were irradiated with 1, 2, 4, 8 and 16 Gy for lots A and B, and 2, 4, 8, 16 and 32 Gy for lot C. In this setup, 1 Gy corresponded to 109 MU.

Before use, the scanner was warmed up for at least 30 min. Films were centered on the scanner bed with a transparent frame. In order to correct inter-scan variations, a 20.32 × 4.50 cm² unexposed fragment was kept in a constant position and scanned together with the films. Films were scanned in portrait orientation (i.e. the scanner lamp was parallel to the short side of the film). The distance between film and lamp was kept constant by placing a 3 mm thick glass sheet on top of the film (Lewis and Devic 2015, Palmer et al 2015). Scans were acquired in transmission mode with a resolution of 50 dpi. Processing tools were disabled. Ten scans were taken for each film, the first five were discarded and the resulting image was the median of the remaining five scans. Images were saved as 48-bit RGB format (16 bit per channel) TIFF files.

2.2. Data set

From the measurements, each pixel of each film was associated with a position \((x, y)\), three (R, G and B) pixel values (PVs) prior to irradiation, three PVs after irradiation, and the dose measured with MatriXX at that position. MatriXX dose arrays, which have a resolution of 7.62 mm px⁻¹, were bicubically interpolated to the resolution of the films. MatriXX was chosen as the reference detector for acquiring accurate reference doses. However, the difference in resolution between film and MatriXX can be a problem when steep dose gradients are present. In order to avoid large dose gradients, which are also associated with higher uncertainties, points with a measured dose lower than 95% of the nominal dose were excluded from the set. Data analysis was implemented in the R environment (R Core Team 2012).
Inter-scan and lateral corrections were applied on irradiated and non-irradiated PVs. Inter-scan variations were corrected using the unexposed fragment, following the column correction method (Méndez et al 2016). Lateral corrections were applied according to the model

$$v(x) = \alpha_1(x - x_c) + \alpha_2(x - x_c)^2 + \hat{v}(x)(1 + \beta_1(x - x_c) + \beta_2(x - x_c)^2)$$  

(1)

where $\hat{v}$ represents the PV before the lateral correction, $x$ is the coordinate on the axis parallel to the lamp, $x_c$ is the position of the center of the scanner, and $\nu$ are corrected PVs (Méndez et al 2013, Lewis and Chan 2015). The images of unexposed films can facilitate the determination of the parameters in this equation. If we symbolize with $\nu_0(x)$ and $\nu_1$ the PV as a function of $x$ of unexposed films before and after applying lateral corrections, we can rewrite the model as

$$v(x) = \nu_0 + (\hat{v}(x) - \nu_0(x))(1 + \beta_1(x - x_c) + \beta_2(x - x_c)^2).$$  

(2)

Apart from being trivially obtained, another advantage of using $\nu_0(x)$ and $\nu_1$ is that they are robust against variations in the active layer, since they can be calculated from the average (or median) of several films. For each color channel, $\nu_0(x)$ and $\nu_1$ in equation (2) were fitted from the median of the film scans prior to irradiation, and the $\beta$ parameters were derived from the irradiated films. The corrected PVs are necessary for computing the $\beta$ parameters. Corrected PVs were derived from measured doses. The relationship between PVs and measured doses (i.e. the calibration) was calculated using regions of interest (ROIs) with dimensions $3 \times 3 \ cm^2$ centered on the fields. Sensitometric and inverse sensitometric curves for all three color channels were modeled with natural cubic splines.

Therefore, apart from the positions, measured irradiated PVs, measured non-irradiated PVs, and measured doses, the data set included PVs after applying inter-scan corrections and PVs after applying inter-scan and lateral corrections.

2.3. The Multigaussian method

Recently, Vera-Sánchez et al (2018) found that the probability density functions (PDFs) of film-scanner responses are well described by multivariate Gaussian distributions for each dose level. This behavior was identified for PVs after irradiation. We confirmed this result and discovered that it also holds for PVs prior to irradiation: every possible combination of two channels (whether irradiated or non-irradiated) can be approximated by a bivariate Gaussian distribution. This property points to a novel approach to radiochromic film dosimetry: the Multigaussian method.

The Multigaussian method considers that, given a dose $D$, the probability of the response vector $z$ (i.e. the vector with the responses $z_k$ for each channel) obeys a multivariate Gaussian distribution

$$P(z \mid D) \sim \mathcal{N}_k(\mu(D), \Sigma(D)).$$  

(3)

Here, $k$ is the number of different channels (i.e. irradiated channels and optionally non-irradiated channels), $\mu$ is the vector of expected values of the response and $\Sigma$ is the covariance matrix

$$\Sigma_{ij} = \text{cov}[z_i, z_j] = E[(z_i - \mu_i)(z_j - \mu_j)].$$  

(4)

During the calibration, $\mu(D)$ and $\Sigma(D)$ can be measured for a set of doses. For the remaining doses, they should be interpolated. In this study, we interpolated $\mu_i(D)$ and $\Sigma_{ij}(D)$ with natural cubic splines.

Following a Bayesian approach, the probability of each dose $D$ given a response vector $z$ can be computed as

$$P(D \mid z) = \frac{P(z \mid D)P(D)}{P(z)} \propto P(z \mid D)$$  

(5)

where the prior probabilities of $D$ are considered to be equiprobable.

Therefore, given a response $z$, the dose (or more precisely the PDF of the dose) can be obtained by

$$P(D \mid z) \propto \exp \left( -\frac{1}{2}(z - \mu(D))^\top \Sigma(D)^{-1}(z - \mu(D)) \right).$$  

(6)

Knowing the PDF of the dose, both the expected dose and its type B uncertainty can be derived. The dose absorbed by the film was considered to be the value $D$ with the highest probability. The uncertainty ($\sigma_D$) was derived from the dose interval defined by the values with half of the maximum probability (i.e. the full width at half maximum, or FWHM, of equation (6)), since $\text{FWHM} = 2\sigma_D\sqrt{2\ln 2}$.

2.4. Model selection

The Multigaussian method was compared with red (R), green (G) and blue (B) single channel models, two additive channel independent perturbation (CHIP) models and two multiplicative CHIP models.

The relevance of scanning before irradiation was also evaluated. The Multigaussian method can integrate information from the film prior to irradiation as additional dimensions of the response vector ($z_k$) in terms of
PVs. In this work, the Multigaussian method was applied with and without non-irradiated channels, while the other models were calculated with PVs and NODs as the response. The additional use of optical density (OD) was discarded since there is only a change of coordinates between PV and OD. NOD was computed as

\[ z := \log_{10} \frac{\nu_{\text{non}}}{\nu_{\text{irr}}} \]  

(7)

where \( \nu_{\text{irr}} \) indicates the PVs of the irradiated film, and \( \nu_{\text{non}} \) indicates the PVs of the film prior to irradiation.

Model parameters were fitted from the calibration ROIs. Doses were calculated for the whole data set and compared with the doses measured with MatriXX.

2.4.1. Single channel models

In single channel models, film doses are defined as

\[ D(r) = D_k(z_k(r)) + \epsilon_k(r) \]  

(8)

where \( D_k \) denotes the calibration function for color channel \( k \), \( z_k(r) \) is the film-scanner response at point \( r \), and \( \epsilon_k \) is an error term. Single channel models cannot mitigate spatial heterogeneities unless NODs are used as the response.

2.4.2. Additive CHIP models

Additive CHIP models consider that there exists a perturbation (\( \Delta \)) of the response, which is additive and approximately equal for all channels:

\[ D(r) = D_k(z_k(r)) + \Delta(r) + \delta_k(r) \]  

(9)

where \( \delta_k \) symbolizes the error term. The perturbation is presumed to be small. Thus, a first-order Taylor expansion of the dose in terms of the channel independent perturbation yields

\[ D(r) = D_k(z_k(r)) + \dot{D}_k(z_k(r))\Delta(r) + \epsilon_k(r) \]  

(10)

where \( \dot{D}_k \) is the first derivative of \( D_k \) with respect to \( z_k \) and \( \epsilon_k \) is an error term. Different assumptions about the PDFs of the perturbations and the error term lead to different estimations of the dose (Méndez et al 2014). In this work, two additive models were studied. Both of these considered that all \( \epsilon_k \) were normally distributed with equal variance (\( \sigma^2_\epsilon \)). One of the models, (i.e. the uniform multiplicative CHIP, or Mayer model) employed a uniform distribution for the PDF of the perturbation \( \Delta \), and the other model, (i.e. the normal multiplicative CHIP) employed a normal distribution with variance \( \sigma^2_\Delta \). For both models, the dose is computed as

\[ d = \frac{\left( \sum_{k=1}^{n} \dot{D}_k \right) \left( \sum_{k=1}^{n} D_k \dot{D}_k \right) - \left( \sum_{k=1}^{n} D_k \right)^2 - n \left( \gamma + \sum_{k=1}^{n} \Delta_k \right) \Delta_k^2}{\left( \sum_{k=1}^{n} D_k \right)^2 - n \left( \gamma + \sum_{k=1}^{n} \Delta_k \right)^2} \]  

(11)

where \( \gamma \) is the ratio \( \sigma^2_\epsilon / \sigma^2_\Delta \), which is zero for the Mayer model.

2.4.3. Multiplicative CHIP models

Multiplicative CHIP models assume a multiplicative perturbation, which is approximately equal for all channels:

\[ D(r) = D_k(\Delta(r)z_k(r) + \delta_k(r)) \]  

(12)

Again, different PDFs for \( \Delta \) or \( \delta_k \) give rise to different dose distributions. As in the case of additive models, two multiplicative models were analyzed. All \( \delta_k \) followed the same normal distribution (i.e. \( \delta_k \sim N(0, \sigma^2_\delta) \)). In the first model, (i.e. the uniform multiplicative CHIP) the PDF of \( \Delta \) was uniformly distributed, while it was normally distributed (i.e. \( \Delta \sim N(1, \sigma^2_\Delta) \)) in the second model (i.e. the normal multiplicative CHIP). For both models, the most likely value of the dose is

\[ d = \arg \max_D P(D) = \arg \min_D \left( \frac{\left( \Delta - 1 \right)^2}{\sigma^2_\delta} + \sum_k \frac{\delta^2_k}{\sigma^2_\delta} \right) = \arg \min_D \left( \frac{\left( \Delta - 1 \right)^2 + \frac{1}{\gamma} \sum_k \delta^2_k}{\sigma^2_\delta} \right) \]  

(13)

where \( \gamma \) is the ratio \( \sigma^2_\epsilon / \sigma^2_\Delta \). This ratio is zero for the uniform multiplicative CHIP.

In order to calculate the dose \( d \), given \( D \), it can be deduced from equation (13) that

\[ \Delta = \gamma + \sum_k z_k \mu_k \]  

(14)

and

\[ \delta_k = \mu_k - \Delta z_k \]  

(15)

where \( \mu_k \) is obtained from the calibration \( D = D_k(\mu_k) \).
The best results for the normal multiplicative CHIP model were obtained with $\gamma = 5 \times 10^8$, which is roughly the square of the mean PV, meaning that both $\Delta$ and $\delta_k$ contributed to the perturbation with similar weight. This same $\gamma$ value was employed with the normal additive CHIP model.

**Figure 1.** Three of the dose distributions employed during the validation.

**Figure 2.** Joint PDF of perturbations in PVs for different combinations of color channels (X and Y axes) and different doses (in Gy, represented in the columns).
2.5. Dose interpolation

Apart from mitigating spatial heterogeneities, a multichannel film dosimetry method should accurately interpolate doses not covered by the calibration. EBT3 films from lot 05011702 were irradiated with an Elekta Synergy (Elekta AB, Sweden) linac using a 6 MV photon beam. The calibration comprised seven $20.32 \times 3.50$ cm$^2$ strips exposed with 0, 1, 2, 4, 6, 8 and 10 Gy, respectively. Seven films were irradiated with doses within the calibration range and different complex geometries formed by combinations of $6 \times 6$ cm$^2$ squares. As an example, three of the geometries can be found in figure 1. Since the shape of the dose distribution was regarded as not relevant, we employed these configurations instead of clinical plans with the purpose of avoiding steep dose gradients as much as possible in order to compare films with MatriXX. MatriXX dose arrays were bicubically interpolated to the resolution of the films. Inter-scan and lateral corrections were applied. According to equation (2), lateral corrections were derived from the film scans prior to irradiation and the calibration. The unexposed fragment from the calibration was kept in each scan to apply inter-scan corrections.

Table 1. Errors, defined as relative dose differences (%), of film doses compared to doses measured with MatriXX. For each lot, mean and standard deviations ($k = 1$) are shown, and for all three lots combined, root mean square errors (RMSE) and mean absolute errors (MAE).

| Film dosimetry method | Lot A       | Lot B       | Lot C       | RMSE | MAE |
|-----------------------|-------------|-------------|-------------|------|-----|
| R channel (PV)        | 0.0 ± 1.7   | −1.0 ± 2.3  | −0.3 ± 2.0  | 2.0  | 1.5 |
| G channel (PV)        | 0.0 ± 2.0   | −1.0 ± 3.1  | −0.5 ± 2.8  | 2.6  | 1.9 |
| B channel (PV)        | −0.1 ± 3.8  | −3.7 ± 9.2  | −2.0 ± 9.5  | 7.2  | 4.9 |
| Uniform additive CHIP (PV) | −0.1 ± 1.6 | −0.4 ± 2.4  | −0.1 ± 1.3  | 1.7  | 1.3 |
| Normal additive CHIP (PV) | 0.0 ± 2.4 | −1.9 ± 4.7  | −0.9 ± 4.5  | 3.8  | 2.7 |
| Uniform multiplicative CHIP (PV) | −0.1 ± 1.6 | −0.5 ± 1.5  | −0.1 ± 1.3  | 1.5  | 1.1 |
| Normal multiplicative CHIP (PV) | −0.1 ± 1.6 | −0.9 ± 1.7  | −0.2 ± 1.3  | 1.6  | 1.3 |
| Multigaussian (irr)   | −0.1 ± 1.4  | −0.4 ± 1.4  | −0.3 ± 1.1  | 1.3  | 1.0 |
| R channel (NOD)       | −0.2 ± 1.2  | 0.0 ± 1.7   | 0.3 ± 1.6   | 1.5  | 1.1 |
| G channel (NOD)       | 0.0 ± 1.6   | 0.4 ± 2.6   | 0.6 ± 2.5   | 2.2  | 1.6 |
| B channel (NOD)       | 0.5 ± 2.9   | 0.8 ± 3.8   | 1.2 ± 4.9   | 3.9  | 2.5 |
| Uniform additive CHIP (NOD) | −0.6 ± 1.6 | −0.3 ± 2.0  | 0.1 ± 1.8   | 1.8  | 1.4 |
| Normal additive CHIP (NOD) | 0.1 ± 1.7 | 0.4 ± 2.3   | 0.7 ± 2.6   | 2.2  | 1.6 |
| Uniform multiplicative CHIP (NOD) | 3.5 ± 13.0 | 5.0 ± 13.6  | 7.6 ± 23.3  | 16.9 | 9.8 |
| Normal multiplicative CHIP (NOD) | −0.1 ± 1.3 | 0.2 ± 1.8   | 0.4 ± 1.6   | 1.6  | 1.2 |
| Multigaussian (irr, non) | −0.1 ± 1.1 | 0.0 ± 1.2   | −0.1 ± 1.0  | 1.1  | 0.8 |

Table 2. Errors, defined as relative dose differences (%), of film doses without applying lateral corrections compared to doses measured with MatriXX. For each lot, mean and standard deviations ($k = 1$) are shown, and for all three lots combined, root mean square errors (RMSE) and mean absolute errors (MAE).

| Film dosimetry method | Lot A       | Lot B       | Lot C       | RMSE | MAE |
|-----------------------|-------------|-------------|-------------|------|-----|
| R channel (PV)        | 3.7 ± 4.0   | 2.2 ± 4.4   | 2.3 ± 3.2   | 4.7  | 3.5 |
| G channel (PV)        | 1.6 ± 2.9   | 1.3 ± 4.8   | 1.8 ± 4.4   | 4.3  | 3.0 |
| B channel (PV)        | 4.7 ± 7.6   | 2.1 ± 12.7  | 4.9 ± 13.5  | 11.8 | 7.6 |
| Uniform additive CHIP (PV) | 0.2 ± 2.0 | 0.7 ± 2.1   | 0.8 ± 1.9   | 2.1  | 1.6 |
| Normal additive CHIP (PV) | 3.3 ± 4.4 | 1.9 ± 6.9   | 3.0 ± 6.8   | 6.6  | 4.6 |
| Uniform multiplicative CHIP (PV) | 1.1 ± 1.8 | 1.4 ± 2.7   | 1.1 ± 2.1   | 2.5  | 1.9 |
| Normal multiplicative CHIP (PV) | 2.1 ± 2.5 | 1.2 ± 2.9   | 1.5 ± 2.1   | 3.0  | 2.3 |
| Multigaussian (irr)   | 1.5 ± 2.0   | 1.5 ± 2.6   | 0.9 ± 1.5   | 2.4  | 1.8 |
| R channel (NOD)       | 2.8 ± 3.5   | 2.3 ± 3.5   | 1.7 ± 2.5   | 3.9  | 2.8 |
| G channel (NOD)       | 0.8 ± 1.7   | 1.3 ± 2.8   | 1.3 ± 2.7   | 2.6  | 1.9 |
| B channel (NOD)       | 1.2 ± 3.0   | 0.1 ± 3.7   | 0.9 ± 5.0   | 4.0  | 2.6 |
| Uniform additive CHIP (NOD) | 2.4 ± 3.6 | 3.1 ± 4.2   | 2.0 ± 2.9   | 4.3  | 3.1 |
| Normal additive CHIP (NOD) | 1.6 ± 2.2 | 1.2 ± 2.7   | 1.3 ± 2.8   | 2.9  | 2.1 |
| Uniform multiplicative CHIP (NOD) | −4.0 ± 12.4 | 0.7 ± 12.7 | 3.3 ± 22.4 | 15.6 | 10.4 |
| Normal multiplicative CHIP (NOD) | 1.5 ± 1.9 | 1.4 ± 2.4   | 1.4 ± 2.1   | 2.6  | 2.0 |
| Multigaussian (irr, non) | 1.1 ± 1.5 | 1.3 ± 2.0   | 0.6 ± 1.3   | 1.9  | 1.4 |
3. Results

3.1. Multivariate Gaussian distributions

Figure 2 shows the plots of the joint probabilities of perturbations (i.e. $P(\Delta_i, \Delta_j)$) for different combinations of color channels and different doses. The perturbations were calculated as the differences between the mean PV and the PV of each point in the ROIs used for the calibration. Measured PVs were analyzed prior to irradiation (channels R non, G non and B non) and after irradiation (channels R, G and B). For illustration purposes, only four combinations of channels using the films from lot A are shown. A similar behavior was observed irrespective of channel combination, lot and film. It can be observed that the perturbations are small (in general, lower than 2% of the response) and positively correlated, and that the joint probabilities might be approximated with bivariate Gaussian distributions.

3.2. Model selection

We calculated the errors, defined as the relative dose differences between doses measured with MatriXX and film doses, obtained with each dosimetry model. Table 1 condenses this information for each lot and for the combination of all three lots. For each lot, the mean relative dose differences and their standard deviations are shown. In order to select the most accurate model, root mean square errors (RMSE) and mean absolute errors (MAE) were computed for the combination of lots. All three lots were given the same weight; thus, the combined RMSE was the geometric mean of the RMSE of each lot (Méndez 2015), and the MAE was the mean of the MAEs. Table 2 shows how errors increase when lateral corrections were not applied. The model with the lowest RMSE is the most likely model whenever the errors are normally distributed. However, it can be seen from figure 3 that this is not always the case. Figure 3 plots densities of relative dose differences between doses measured with MatriXX and film doses, with films combined or segregated. Two models from lot B are shown as an example. Even though relative dose differences were approximately normally distributed in many cases, this was not general, especially when lateral corrections were not applied. In addition, RMSE is sensitive to outliers. MAE has a direct physical interpretation and is robust to outliers. Both RMSE and MAE were analyzed, and both led to the same conclusions.

Figures 4 and 5 show the relative dose differences between doses measured with MatriXX and doses calculated with different dosimetry models. For the sake of clarity, only the R channel, the uniform additive CHIP, the normal multiplicative CHIP and the Multigaussian models are included. In figure 4, irradiated PVs were employed as the response. In figure 5, the Multigaussian model used both irradiated and non-irradiated PVs and the rest of the models employed NODs. In both figures, inter-scan and lateral corrections were applied. Although only films from lot C are shown, all three lots produced similar outcomes.

Figure 3. Density of relative dose differences between doses measured with MatriXX and film doses: (a) combining all the films, (b) segregated by film (in rows, labeled with film nominal doses in Gy). Black solid lines represent Multigaussian (irr, non) data, and red dotted lines G channel (PV) data. Lot B films are shown.
Figure 4. Dose differences between measured doses and doses calculated with each film dosimetry model. Irradiated PVs after applying inter-scan and lateral corrections were employed as response. Films from lot C are showed. Each column plots one film designated by its nominal dose (in Gy).
3.3. Dose interpolation

Table 3 presents the MAEs between doses measured with MatriXX and film doses. The MAEs combine all seven films employed for validating dose interpolations.

4. Discussion

4.1. Dose uncertainties

MatriXX and film doses were compared employing the most probable values of the dose from both dosimeters. Alternatively, dose uncertainties could be taken into account and the probability of both doses being equal could...
be computed by integrating over the distribution of possible doses. This approach was regarded as excessively complex given the present accuracy of film dosimetry models. Figure 6 plots the dose distribution and relative uncertainty of one of the films used for validating dose interpolations calculated with the Multigaussian (irr, non) model. Uncertainties were calculated according to the FWHM of equation (6). Dose uncertainty estimations should be regarded with caution, because the model is an approximation and other important sources of uncertainty, (e.g. intra-lot differences) were not included.

4.2. Model selection
It can be observed that the Multigaussian model delivered more accurate doses. However, no method corrects for spatial heterogeneities completely. Low frequency heterogeneities, presumably due to active layer variations, are still visible (González-López et al 2017).

Whether using only the scans of irradiated films, or including the scans prior to irradiation, the Multigaussian model gave lower dose differences than the other models in the comparison.

Scanning prior to and after irradiation improved the results of the Multigaussian, single channel and normal (additive or multiplicative) CHIP models, but this was not true for the uniform CHIP models. There are several possible reasons for this behavior. One possible reason is that NOD responses have more uncertainty than PVs since they combine two PV measures. Furthermore, multichannel models are (largely heuristic) approximations, which may be more or less accurate depending on the type of response, on the actual deviation of the response from the calibration, on the shape of the sensitometric curves (Méndez et al 2014) and even on the particular algorithmic implementation of the model. The uniform multiplicative CHIP model was found to be particularly sensitive to NOD values at least in our implementation, which explains its performance as shown in tables 1 and 2.

Even though multichannel models partially mitigate the lateral artifact, lateral corrections are necessary in order to obtain the most accurate doses with each model. This is especially important for single channel models.

4.3. Dose interpolation
A film lot calibration relates the response of the dosimetry system with the dose absorbed by the film. When a given dose produces a different response, the response is regarded as perturbed. The response was perturbed in table 1 by spatial heterogeneities, in table 2 by spatial heterogeneities and the lateral artifact, and in table 3 by spatial heterogeneities and intra-lot differences. Even though Multigaussian models were still more accurate than the other models under comparison, the MAEs were substantially larger in table 3, which points to the importance of also applying re-calibration corrections for accurate film dose calculations (Ruiz-Morales et al 2017).

Table 3. Errors, defined as relative dose differences (%), of film doses compared to doses measured with MatriXX. Mean absolute errors (MAE) combining all films are shown.

| Film dosimetry method                          | MAE  |
|-----------------------------------------------|------|
| R channel (PV)                                | 4.8  |
| G channel (PV)                                | 4.5  |
| B channel (PV)                                | 5.2  |
| Uniform additive CHIP (PV)                    | 5.1  |
| Normal additive CHIP (PV)                     | 4.7  |
| Uniform multiplicative CHIP (PV)              | 4.1  |
| Normal multiplicative CHIP (PV)               | 4.8  |
| Multigaussian (irr)                           | 2.6  |
| R channel (NOD)                               | 3.2  |
| G channel (NOD)                               | 3.0  |
| B channel (NOD)                               | 3.3  |
| Uniform additive CHIP (NOD)                   | 3.7  |
| Normal additive CHIP (NOD)                    | 3.0  |
| Uniform multiplicative CHIP (NOD)             | 5.3  |
| Normal multiplicative CHIP (NOD)              | 2.8  |
| Multigaussian (irr, non)                      | 2.5  |
5. Conclusions

The purpose of this work was to analyze how well different radiochromic film dosimetry models reduce spatial heterogeneities. The design of the experiment aimed to minimize any other sources of uncertainty. Single channel and multichannel methods, including a novel multichannel approach to film dosimetry called the Multigaussian method, were compared. The convenience of scanning both prior to and after irradiation was examined too.

The Multigaussian method provided more accurate doses than the other models. The best results were obtained with the Multigaussian method integrating the information from the film before irradiation. This information is not integrated as net optical density but as additional elements in the response vector, which is composed of the pixel values of the different color channels including irradiated and non-irradiated scans. The assumption of the Multigaussian method is that the probability density function of the response vector follows a multivariate Gaussian distribution. This assumption is based on empirical findings.

Although the Multigaussian method obtained the best agreement between doses measured with film and MatriXX, spatial heterogeneities, presumably caused by variations in the active layer thickness, are still present. Therefore, new and more accurate multichannel radiochromic film dosimetry methods are necessary. This research demonstrates a new way of tackling the problem.

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Figure 6. Dose (a) and relative uncertainty (b) of a film calculated with the Multigaussian (irr, non) model.
