research article

Comparison of three film analysis softwares using EBT2 and EBT3 films in radiotherapy

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Introduction. The purpose of the study was to compare the results of gamma value based film analysis according to the used type of self-developer film and software product.

Material and methods. The films were irradiated with different treatment techniques such as 3D conformal and intensity modulated radiotherapy with static and rotational delivery. Stereotactic plans with conformal and intensity modulated arc techniques, using coplanar and non-coplanar beam setup were also evaluated. The data of irradiated film were compared with the planned planar dose distribution exported from the treatment planning system. Three film analysis software programs were evaluated: PTW Mephysto (PTW), FilmQA Pro (FQP) and radiohromic.com (RC). Both EBT2 and EBT3 types of films were examined. The comparisons of dose distributions were performed with gamma analysis using 10% cut-off level.

Results. The results of the gamma analysis for larger fields were between 78.3% and 98.3%, 75.7% and 100%, 80.2% and 98.8% with PTW, FQP and RC, respectively. The results of evaluation in case of stereotactic measurements were 76.8%–99.2% for PTW, 95.7%–100% for FQP and 91.2%–99.9% for RC.

Conclusions. All the three software programs are suitable for calibrating and evaluating films, performing gamma analysis, and can be used for patient specific quality assurance measurements. There is no direct connection between gamma passing rate and absolute accuracy or software quality, it is just a feature of the software. The interpretation of own results has to be defined on an institutional level according to given workflow and preliminary results.

Key words: radiochromic; IMRT; gamma analysis; film analysis software

Introduction

Over the years, film dosimetry has been developed into a powerful tool for radiotherapy treatment verification and quality assurance as a two-dimensional radiation detector system. Radiochromic film technology is based on diacetylene-dye radiation-sensitive monomers, which polymerize and change colour due to radiation. These types of films are self-developers, their colour changes directly after irradiation and they do not require chemical processing or film developing equipment. The dosimetric analysis can be applied by using a photo scanner and a special software.[1] The speed of polymerization depends on the environmental conditions, but it stabilizes after 24–48 h.[2] The darkening of the film is increasing with the exposed dose, and their relation is generally approximated by polynomial or rational functions. Radiochromic films are nearly tissue-equivalent, with low energy- and dose rate dependency.[3] For linear accelerators with more photon energies only one film calibration is necessary, but in kV photon energy range a new calibration is needed.[4,5] They have a high-spatial resolution suitable for dose distribution measurement in radiation fields with high dose gradients,

for example, in stereotactic irradiation or brachytherapy. Radiochromic films are water equivalent because the active layer is made up of low atomic number materials. The different types of films could have different layer arrangements, symmetric or asymmetric, and different material constructions containing C, H, O and Li. The contamination with high atomic number material (like Cl) is kept low, so the films are nearly water-equivalent.[6,7] The radiation sensitive monomers are located between an adhesive and a polyester protection layer. Since the introduction of the EBT2 film type, a yellow marker dye has been built in the active layer of the film to provide information about the subtle differences in the thickness of the active layer, thereby making the increment of the homogeneity possible, and reducing the sensitivity to artificial light.[6-8]

Materials and methods

Films

In this study we investigated the GafChromic EBT2 and EBT3 films (Ashland Inc., Wayne, New Jersey). The size of EBT2 film was 8″ x 10″. The layer arrangement of the EBT2 film is not symmetric; consequently, film orientation is important. The substrate of the film is clear polyester (175 μm) coated with an active layer (28μm) which is covered by a 25 μm pressure-sensitive adhesive wrap and the top of the film also has a polyester layer (50 μm).[9] The size of GafChromic EBT3 was 13″ x 17″. The single active layer of the film is nominally 28 μm thick and contains the active component, a marker dye. The active layer is between two 125 μm transparent matte polyester subtracts.[10] The film is symmetric, and an anti-Newton ring feature is added by the manufacturer.

Scanner

To digitize the film EPSON Expression 10000XL (Epson, Nagano, Japan) flatbed scanner was used with A3 scanning surface. The applied scanning parameters were as follows: transmission mode, positive film, no colour correction, landscape orientation, 48-bit RGB, 72 dpi resolution and TIFF file format.[10] Considerable warm up effect was not observed for our scanner, but before every scanning we waited at least fifteen minutes, and the first five scanned images were never used.[11] Every pixel in a colour image has three-channel (RGB) image signal. The scanned images can be evaluated by film analysis software.[12] The film-scanner response may depend on thickness variations in the active layer coated on the film, electronic noise, scanner instability, lateral artefact, local variations produced by systemic problems of the scanner, Newton rings, dust, scratches or other damage. The orientations of the films were noted during the irradiation, and they were positioned on the same way at the scanning, always at the same distance from the borders of the sensitive area of the scanner.[13] The uniformity of the scanner bed was defined by placing four, non-irradiated film pieces at the corners of the scanner to cover the whole scanning surface. The inhomogeneity map of our scanner was determined to find the quasi-homogeneous part of the scanner. According to this map, only the homogeneous middle part of the scanner was used for scanning. The films have also non-uniformity, but this effect was not examined or corrected. During the scanning, a glass layer was used as compressing media. The precision of the scanning method and the applied corrections affect the results of the gamma analysis, so the used methods always have to be reported.[14-17]

Calibration measurement

During the calibration a CIRS Plastic Water sheet phantom (CIRS Inc., Norfolk, VA, USA) was applied and the film was placed between the layers of the phantom (5 cm above and 10 cm under the film). The films were irradiated at the source surface distance (SSD) of 95 cm. The size of the calibration films was 2×5 cm, and the number of calibration points were 15 cGy, 30 cGy, 50 cGy, 100 cGy, 200 cGy, 300 cGy, 400 cGy, 550 cGy, 650 cGy, 750 cGy, 850 cGy, 950 cGy and the non-irradiated film (0 cGy). The waiting time between irradiation and scanning was always 24 hours. Always the same frame positions were used and lateral correction was not applied.

The scanning of one calibration series was repeated 18 and 60 months after the initial scan. The changes of the optical density values were evaluated for all three colour channels. The absolute and relative differences were also calculated.

Treatment planning and irradiation

The irradiation was performed with a Varian TrueBeam (Varian Medical Systems, Palo Alto, CA, USA) linear accelerator and Eclipse 13.6 (Varian Medical Systems, Palo Alto, CA, USA) treatment planning system with Analytical Anisotropic Algorithm (AAA) was used for dose calculation.

A pelvic case (prostate and nodal target) was planned with different treatment techniques, such as 3D conformal (3DCRT), intensity modulated radiation therapy with sliding-window (IMRT) and RapidArc (RA), and simultaneous integrated boost with arc therapy (RA-SIB). Small field, stereotactic radiotherapy plans were also created with conformal arc (CA) and RA techniques using coplanar and non-coplanar (NC) beam setup. For the pelvic plan 10 MV, for the stereotactic CA plan 6 MV, for the stereotactic RA plan 6 MV-FFF energy was used. The original patient treatment plan was copied to the CT scan of the CIRS solid water phantom. The same phantom was also used for the calibration. The depth of the film was 5 cm with 10 cm backscatter, the isocenter of the plan was positioned at the middle of the film. After the recalculation, the 2D dose distribution at the slice position of the film was exported, and the plan was delivered to the film with the given setup. The planned dose distribution was compared with the results of the film dose distribution using a film analysis software.

The gamma method

The gamma map comparison as introduced by Low *et al.* is widely used to judge agreement between treatment plan dose distribution and dose measurement.[18]

The gamma map function $\gamma(\mathbf{r}_{test})$ can be defined as minimum value of the following function, according to $\mathbf{r}_{reference}$:

$$\gamma(\mathbf{r}_{test}) = \sqrt{\left(\frac{\mathbf{r}_{test} - \mathbf{r}_{reference}}{\Delta_{distance}}\right)^2 + \left(\frac{d_{test}(\mathbf{r}_{test}) - d_{reference}(\mathbf{r}_{reference})}{\Delta_{dose}}\right)^2}$$

Where $d_{test}(\mathbf{r}_{test})$ is the dosemap of the test distribution and $d_{reference}(\mathbf{r}_{reference})$ is the reference distribution.

($\Delta_{dose,}$ $\Delta_{distance}$) also known as 'gamma criterion'. The tolerance Δ_{dose} is given in % and the distance $\Delta_{distance}$ in mm.

A point of the test distribution ($\mathbf{r}_{test}$) passes the test, if $\gamma \leq 1$. In our study the data were analysed using gamma evaluation with the following criteria: 2%, 2mm and 3%, 3mm, and normalization for local dose and global dose maximum with 10% threshold.[18-20]

During gamma comparison automatic matching with enabled rotation correction was used, and if it decided to be necessary, manual correction was applied. The planned distributions were the reference, and the film measurements were evaluated and compared to them.[21]

Statistics of gamma analysis and comparison was applied for the three different softwares. The results were calculated with GraphPad 8.0.1 (GraphPad Software, San Diego, CA) using ANOVA and post-hoc Dunn's test, based on all evaluated scans.

Software

Several different software programs can be applied for dosimetric the evaluation of radiochromic films. Three software products were analysed for film evaluation: PTW Mephysto (PTW), FilmQA Pro (FQP) and Radiochromic.com (RC). Each of them is dedicated for film scanning, calibration, dose map creation, gamma evaluation, and for image processing.[22-26]

PTW Mephysto (PTW)

The film analysis module of PTW Mephysto 3.0 software includes film scanning (FilmScan), calibration (FilmCal), film analysing (FilmAnalyse) options, and for gamma analysis PTW Mephysto VeriSoft 6.3 was used. This software works on the basis of single channel dosimetry which only takes into consideration the red channel from the RGB channels. One pixel value on the scanned film represents one dose value. In case of a single-channel dosimetry all response artefacts convert directly to dose artefacts. Applying this method, important data can be lost. Unfortunately, we could not find more information about the mathematical method of the software.

FilmQA Pro (FQP)

The FilmQA Pro 4.0 software is based on the Micke-Mayer method.[27] Different multichannel methods have been proposed in literature for film evaluation. This software is compact, tree structured with folders and files. Appropriate tutorials and training material on the handling of the software can be found on http://www.gafchromic.com.[28] In multichannel approach, three pixel values (RGB) on the scanned image represent one dose value.[27-29] Multichannel dosimetry makes it possible to reduce the artefacts, for example; the thickness of active layer, fingerprints or dust from the dose image. Radiochromic films provide a different response in each of the three colour channels, that way the signals can be separated into a dose-dependent

and a dose-independent part. The latter one can be corrected, so we can use the only dose-related data for the evaluation of films. Choosing wrong multichannel model, errors of the different colour channels can be combined, because their errors correlate with each other, and the overall error can be increased. Therefore, multichannel dosimetry is can be worse than single-channel dosimetry in case of wrong model selection.[30] As the dose range increases, the response of radiochromic film will be increasingly nonlinear. For this reason, the fitted polynomial function can oscillate between the data points at higher dose regions, therefore, if a polynomial calibration function is used, more calibration points are needed for fitting. The FilmQA Pro uses a special rational function for fitting the calibration curve on calibration data points because the rational function is monotonic, does not oscillate between data values and appropriate to the dosimetric properties of the radiochromic film. In clinical practice, four or five calibration points are enough for a correct calibration.

The calibration data have been fit using a function:

$$X(D) = (a + bD)/(c + D),$$

when the scanner response at dose D is $X(D)$ and, a,b,c are constants.

Radiochromic.com (RC)

This is a cloud computing web application for calibration and dosimetry of radiochromic films. The version number was 2.7. The user interface has a clear layout, available in a browser. In can be used as a free software with some limitations, and its extended version is commercially available. The software also applies multichannel dosimetry as FilmQA Pro but uses another channel independent perturbation model, the truncated normal distribution model. This model is considered as a metamodel which minimizes the uncertainty in the dose inherent in the method of channel independent perturbation**.** This model applies the first order Taylor expansion to the dose due to small perturbation.[31]

$$\begin{cases} D(r) = D_R(r) + \dot{D}_R(r)\Delta(r) + \epsilon_R(r) \\ D(r) = D_G(r) + \dot{D}_G(r)\Delta(r) + \epsilon_G(r) \\ D(r) = D_B(r) + \dot{D}_B(r)\Delta(r) + \epsilon_B(r) \end{cases}$$

$D(r)$ represents the dose absorbed by the film at point r. D_k is the absolute dose measured by the channel k (R,G,B), when no disturbance is present, and it is calculated directly from the calibration model

$\dot{D}_k(r)$ is the first derivative of the dose, with respect to the NOD (net optical density), at point r.

$\epsilon_k(r)$ is an error term accounting for the difference between the dose absorbed by the film and the dose measured in the channel k after correction by the perturbation.

The calculation algorithm of the program and the method of film analysis can be found on the website of the software: https://radiochromic.com. In order to perform calibration, dosimetry evaluation and gamma analysis, we uploaded the calibration films, the scanned film and the dose map exported from the treatment planning system to Radiochromic.com. It is also possible to make recalibration during the film evaluation.[32] From version 3.0 the application employs the Multigaussian model.[26]

Results

Auxiliary results

Scanner homogeneity

The homogeneity map of the scanner can be seen in Figure 1. Based on these results, it can be observed that the top 8 cm and the bottom 7 cm borders of the scanner's sensitive area are inhomogeneous. There are small inhomogeneities on the right and the left part of the scanner bed. For the film evaluation, we can use an approximately 15 cm wide homogeneous area in the centre of the scanner. Inside the homogeneous area the optical density has less than 4% deviation, outside the area it reaches 13%.

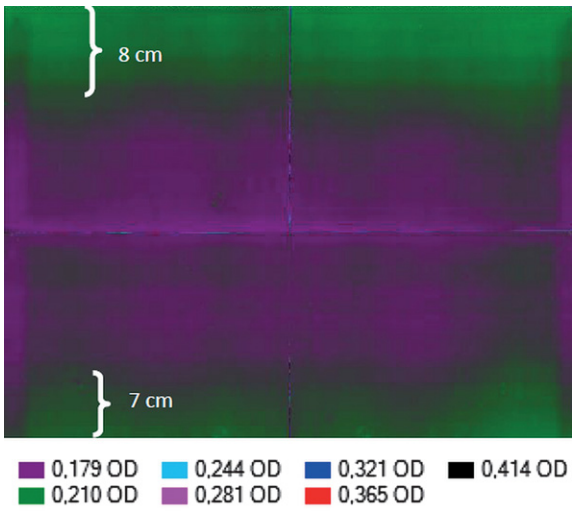


FIGURE 1. Inhomogeneity map of the full scanning surface **(A)** and the homogeneous area in the centre of the scanner glass **(B)**.

Long-time darkening

18 and 60 months after the first scanning of the calibrating films, we scanned the same EBT2 films again. For films that received lower dose the relative post-irradiation colouration was higher. The difference between the channels in terms of colouration is getting wider by time. In Figure 2 the relative change of the pixel values compared to the original scan at 18 months and 60 months can be observed, according to the exposure.

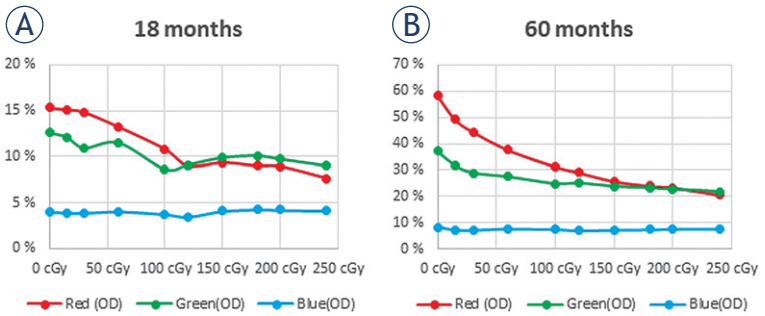


FIGURE 2. Change of optical density in % after 18 **(A)** and 60 **(B)** months of primary irradiation, in function of the primary irradiated dose (cGy).

Gamma analysis results

The results of the gamma analysis from the type of films and the three software products can be found in Table 1. The parameters of the gamma analysis were: 3%, 3 mm, and 2%, 2 mm, the negligible threshold dose was 10%, and the normalization of gamma analysis was performed on global dose maximum. A sample result - the evaluation of the RA-SIB plan with three software programs can be found in Figure 3.

The results of gamma analysis of stereotactic fields with EBT3 films can be found in Table 2. The negligible threshold dose was 10%. The gamma analysis was calculated in two ways; in the first case, the normalization was executed for global dose maximum and in the second case, we applied a harder limit, when the normalization was performed for local plan dose.

According to statistical analysis, the passing rates for FilmQA Pro were significantly higher than PTW Mephysto and Radiochromic.com.

TABLE 1. Pass rates of the gamma analysis using three software products; the negligible threshold dose was 10% and the normalization of gamma analysis was performed on global dose maximum. (RA: RapidArc, SIB: simultaneous integrated boost)

		3DCRT		IMRT		RA		RA – SIB	
		2%,2mm	3%,3mm	2%,2mm	3%,3mm	2%,2mm	3%,3mm	2%,2mm	3%,3mm
EBT2	PTW Mephysto	87.1 %	95.5 %	89.2 %	98.2 %	83.9 %	91.5 %	86.3 %	98.3 %
	FilmQA Pro	98.9 %	100.0 %	75.7 %	93.4 %	99.9 %	100.0 %	87.3 %	92.8 %
	radiochromic.com	87.2 %	98.1 %	80.2 %	93.1 %	90.4 %	98.5 %	84.2 %	95.3 %
EBT3	PTW Mephysto	86.6 %	94.4 %	78.3 %	93.8 %	92.0 %	97.8 %	86.8 %	93.4 %
	FilmQA Pro	99.0 %	99.9 %	82.6 %	95.0 %	98.3 %	99.4 %	87.9 %	91.9 %
	radiochromic.com	91.0 %	98.8 %	80.2 %	94.4 %	95.4 %	98.7 %	87.5 %	92.1 %

TABLE 2. Pass rates of gamma analysis of small stereotactic fields; the negligible threshold dose was 10% for EBT 3 films (CA: Conformal Arc, RA: RapidArc, NC: non-coplanar)

		CA		RA		NC - CA		NC – RA	
		2%,2mm	3%,3mm	2%,2mm	3% ,3mm	2%,2mm	3%,3mm	2%,2mm	3%,3mm
global	PTW Mephysto	97.0 %	99.2 %	87.9 %	90.2 %	95.1 %	98.6 %	89.2 %	93.5 %
	FilmQA Pro	100.0 %	100.0 %	98.5 %	100.0 %	99.8 %	100.0 %	99.2 %	100.0 %
	radiochromic.com	98.2 %	99.9 %	97.2 %	99.8 %	95.0 %	99.7 %	96.4 %	99.6 %
local	PTW Mephysto	95.2 %	97.2 %	87.4 %	89.9 %	93.1 %	97.9 %	76.8 %	83.1 %
	FilmQA Pro	99.9 %	99.9 %	95.7 %	99.9 %	99.5 %	100.0 %	98.7 %	99.5 %
	radiochromic.com	96.9 %	98.5 %	93.3 %	97.5 %	91.5 %	97.3 %	91.2 %	97.8 %

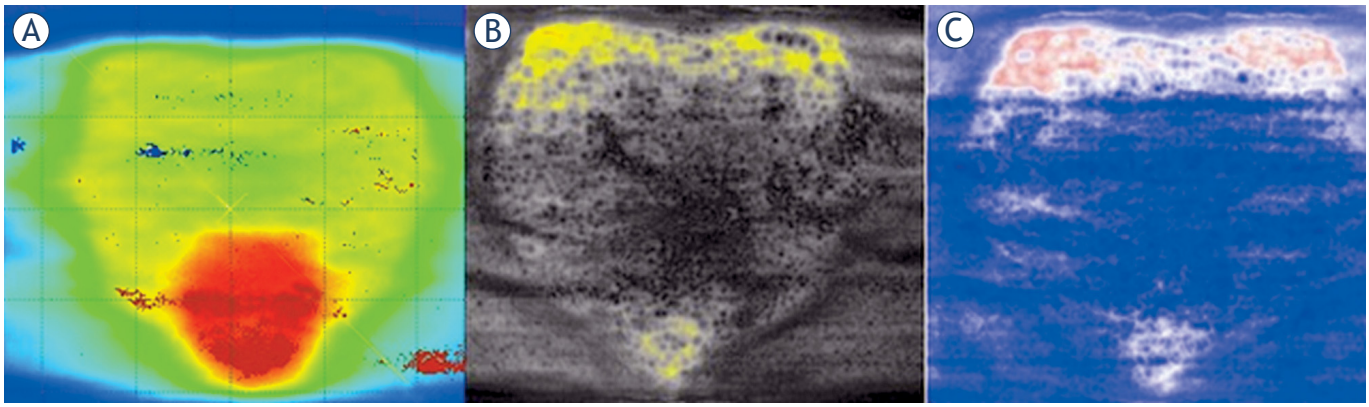
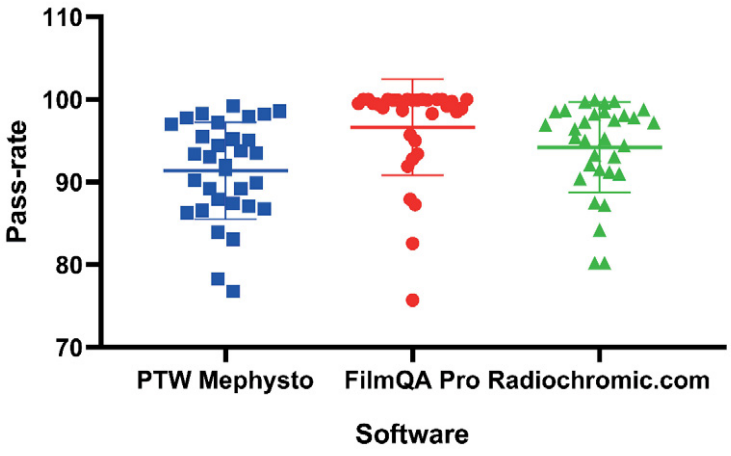


FIGURE 3. Evaluation of the simultaneous integrated boost (SIB) plan with PTW Mephysto **(A)**, FilmQAPro **(B)** and radiohromic.com **(C)**.

TABLE 3. Statistical evaluation and visualisation of the gamma passing rates for the three different softwares, according to all analysed cases

Gamma passing rate statistics (%)			
	PTW Mephysto	FilmQA Pro	Radiochromic.com
Minimum	76.8	75.7	80.2
Maximum	99.2	100.0	99.9
Median	92.6	99.5	95.9
Mean	91.4	96.6	94.2
Std. Deviation	5.9	5.8	5.5
Lower 95% CI	89.3	94.5	92.3
Upper 95% CI	93.5	98.8	96.2

Dunn's multiple comparisons test	Adjusted P Value	Significant?
PTW Mephysto vs. FilmQA Pro	<0,0001	Yes
PTW Mephysto vs. Radiochromic.com	0.1824	No
FilmQA Pro vs. Radiochromic.com	0.0005	Yes



Discussion

During the preparation of the film data, the calibration and the scanning process have to be handled very carefully. Based on the results showed in Figure 1, it is recommended to limit the scanner area to the homogeneous part, or corrections need to be applied at the border of film scanner. In case of large PTVs which cover the whole film surface, the gamma analysis showed higher deviations which were caused by the edge effects during our IMRT treatment plan evaluation.

The quality of calibration curves and the time passed since the preparation of the calibration curve can also influence the results of dosimetry analysis. More accurate results can be received with a larger number of calibration points and shorter intervals between the calibration and the film evaluation. According to our results seen in Figure 2, in case of re-evaluation of older film scans the recalibration is crucial.[33,34] The presented changes are summation of the film ageing and the scanner characteristics changes, and both effect have to be taken into consideration during long-time usage.

Our gamma analysis results are in accordance with those found in the literature. The fact that in many cases the threshold dose and the normalization method (local dose or global maximum dose) are not published makes the comparison more difficult. Agnew *et al.* showed, that the selection and the settings of the software has a crucial effect on the gamma passing rates.[35] Cosumano *et al.* examined stereotactic irradiation plans (small field, large fraction dose) with EBT3 films. For the gamma criteria of 5%, 1 mm they received 94.3%.[36] For the stereotactic plan, Wen *et al.* applied a different criteria, for 3%, 1 mm and they found a 95±4.2% agreement during the evaluation of plans.[37] Hanusová *et al.*

using PTW VeriSoft v3.1 found in average 97.03% for EBT3 and 85.81% for EBT2 films agreement with for static IMRT fields with 3%, 3 mm and 5% threshold level.[38] Lewis *et al.* applied FQP software and achieved a correspondence ranged between 95% and 99% for all the treatment fields studied using the gamma test criterion of 2%, 2 mm to evaluate the measurements.[39] Also with FQP Marrazzo *et al.* found with single- and multichannel analysis for linac measurements the passing rates in average with 2%, 2mm criteria are 91% and 80%, with 3%, 3mm criteria are 98% and 94%, respectively.[40] According to Calvo-Ortega *et al.* with RC software the agreement is between 87.6% and 99.8% using fast protocol for IMRT plans with 3%, 3 mm criteria and 10% threshold.[41]

The software products have possibilities for automatic dose map and film fusion, but these do not always work perfectly. Manual matching is possible for all three software programs; in this case, results highly depend on the user's skills and experience. During the evaluation with FilmQA Pro and RC there is an opportunity for recalibration of sensitometric curves with the actual zero and dose maximum points. This option has a significant impact on the workflow of gamma analysis, it makes easier and faster the usage of the films from the same badge. Table 3 summarizes the statistical evaluation of our measurements. The FQP has significantly higher passing rate, than the other two softwares. As Table 1 shows, for EBT3 films the difference between the software programs is lower than for EBT2 films. In case of stereotactic plans, the agreement for the CA plans were better than for the RA plans, and for the coplanar cases were better than for the non-coplanars, as can be seen on Table 2. Using local instead of global normalization the number of passing points were decreased, but the differences between the plans were the same, independently from the used software. The advantage of self-developing film as compared to the semi-conductor or ionchamber based detector matrix is that it has a better spatial resolution, which allows us to handle the high dose-gradients in case of state-of-art ultra-conformal (stereotactic) plans. The disadvantage of films as compared to other detectors is that the usage of film is time-consuming. The film has to be prepared before the measurement and they have to be handled very carefully. The results cannot be executed immediately after the measurement, the irradiated films have to be scanned and calibrated according to strictly defined methods after the irradiation.

Based on our measurements, the EBT2 and EBT3 films are suitable for dose plan verification of 3DCRT and IMRT treatments combined with any of the 3 analysed software programs. All three evaluation programs are suitable for calibrating and evaluating films, and performing the gamma analysis. The deficiency of this paper is that some applications have been improved in the last few years, new models like Multigaussian are implemented. By using different softwares in the gamma analysis, the authors cannot exclude the influence of the implementation of the gamma calculation in the final result. Therefore, this paper is not testing which software provides more accurate film dose distributions, neither which dose distributions are more similar to the ones calculated with the treatment planning system. Based on the results, it is recommended to always use a new calibration curve during the film evaluation and the homogeneous area of the scanner should be used for scanning. Both types of films and the three software products are very sensitive to calibration, the users must pay close attention to preparation, film handling and timing. We recommend using 2%, 2 mm agreement criteria with 10% threshold for evaluating with gamma analysis. This way the results will be slightly lower, but it will be easier to identify the problematic points during the evaluation. Every institute has to define their own limit of acceptance level according to their own workflow and experience.

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