

CONSIDERATIONS ON TWO TYPES OF SOLID-STATE DOSIMETERS FOR
IONIZING RADIATION

BY

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Dedication

My dissertation is in memory of my father who raised me with lots of unwavering love, taught me about life more than anybody else and led me to the righteous path. This work is also dedicated to my mom for her ongoing support and love. Her encouragement always gives me strength and courage.

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Portions of the dissertation have been finished during the COVID-19 pandemic. I would like to pay tribute to front-line healthcare and essential workers, researchers, volunteers and those who sacrificed and struggled to save lives and help the community. Sincere condolences are offered to those who suffered from family, mental, emotional and financial losses during this difficult time.

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List of Abbreviations

Abbreviation	Meaning
AAPM	American Association of Physicists in Medicine
ADCL	Accredited Dosimetry Calibration Laboratory
CCD	Charge-Coupled Device
CRT	Conformal Radiation Therapy
CT	Computed Tomography
CTV	Clinical Target Volume
DMLC	Dynamic Multileaf Collimator
EBT	External Beam Therapy
FFF	Flattening Filter Free
GK	Gamma Knife
GTV	Gross Tumour Target Volume
HDR	High Dose Rate
IMRT	Intensity Modulated Radiation Therapy
kV	Kilovoltage
LA	Lateral Artifact
LDR	Low Dose Rate
LiPCDA	Lithium Pentacosanoate
MLC	Multileaf Collimator
MOSFET	Metal-Oxide-Semiconductor Field-Effect Transistor
MRI	Magnetic Resonance Imaging

List of Abbreviations Cont.

Abbreviation	Meaning
MV	Megavoltage
NOD	Net Optical Density
OAF	Off-Axis Factor
OD	Optical Density
OFET	Organic Field-Effect Transistor
PET	Positron Emission Tomography
PV	Pixel Value
QA	Quality Assurance
RCF	Radiochromic Film
RGB	Red-Green-Blue
ROI	Region of Interest
SBRT	Stereotactic Body Radiation Therapy
SNR	Signal-to-Noise Ratio
SRS	Stereotactic Radiosurgery
SRT	Stereotactic Radiation Therapy
SSD	Source-to-Surface Distance
TG	Task Group
TPS	Treatment Planning System
VMAT	Volumetric-Modulated Arc Therapy
XD	Extended Dose

Abstract

Radiation therapy is a common type of treatment for cancer. Being able to measure the ionization radiation dose distribution with high resolution is of great importance for characterizing radiation devices and for quality assurance of patient radiation procedures. Two solid-state devices have been studied for their radiation dosimetric properties, to bring potential improvements for their use as dosimeters.

First, radiochromic film is a robust two-dimensional dosimeter with high resolution measurement capability. When digitized on a flatbed photo scanner, the fidelity of radiochromic film dosimetry is primarily affected by film active layer non-uniformity and the lateral artifact. At lower doses the low signal-to-noise ratio makes film active layer non-uniformity the primary source of error for accurate dosimetry. The error from the lateral artifact gradually increases with increasing dose. The first focus of this work is to develop a novel and efficient lateral artifact correction method as well as a channel weighted analytical method for film active layer non-uniformity correction. This channel weighted analytical approach accounts for the physical phenomenon that red, green and blue light with the same intensity are attenuated differently by the same attenuator. This phenomenon is characterized by the channel specific Napierian attenuation coefficient. For certain dose ranges and lateral positions on the scanner window, the new channel weighted analysis demonstrates better agreement with the plans calculated by the treatment planning system than the channel-independent analytical algorithm. The channel weighted approach does not require pre-irradiation film scans and is compatible with the existing, efficient one-scan protocol. The novel lateral artifact correction method is based on the one-scan protocol. The method utilizes fully exposed radiochromic film strips and corrects the lateral artifact in the dose domain of multichannel dosimetry. And it compensates for non-uniform off-axis output from open fields of a linear accelerator and the film active layer non-uniformity. This unique layout is symmetric about the scanner central-axis and covers the sufficient lateral space of a flatbed scanner. Radiation treatment plans validated with the new channel weighted and lateral artifact correction methods show improvements in passing rates, when quantitatively analyzed using gamma criteria for the agreement of dose and distance parameters.

Second, the metal-oxide-semiconductor field-effect transistor dosimeter can be used for in-vivo dose monitoring in external beam dosimetry for radiation therapy and radiosurgery. In this study, the response of an organic thin-film device to megavoltage X-rays is characterized. The device is based on organic field-effect transistor.

Chapter 1

Introduction

Absorbed dose is the amount of energy deposited per unit mass by ionizing radiation. Radiochromic film is a robust 2-dimensional dosimeter with high spatial resolution for measuring the dose distribution of ionizing radiation. Radiochromic film dosimetry is the application of spectroscopy. The absorption spectra change of radiochromic film scales with the absorbed dose of ionizing radiation. One of the applications of the metal-oxide-semiconductor field-effect transistor is for dose measurement of ionizing radiation. The threshold voltage shift of a metal-oxide-semiconductor field-effect transistor is proportional to the radiation dose.

1.1 Ionizing radiation and absorbed dose

Photons (X-rays, gamma rays, high energy ultraviolet rays) and particles (such as alpha particles, electrons, neutrons, protons) with sufficient energy are forms of ionizing radiation. Ionizing radiation frees electrons from atoms. Absorbed dose is the quantity of energy deposited in matter per unit mass by ionizing radiation. The SI unit of the dose is gray ($1 \text{ Gy} = 1 \text{ J/kg}$).

1.2 Principles of radiochromic film (RCF) dosimetry

RCF in this work refers to GAFChromicTM (Ashland, Bridgewater, NJ) EBT 3, EBT-XD, HD-V2, MD-V3 and XR-QA as radiochromic films suitable for different dose

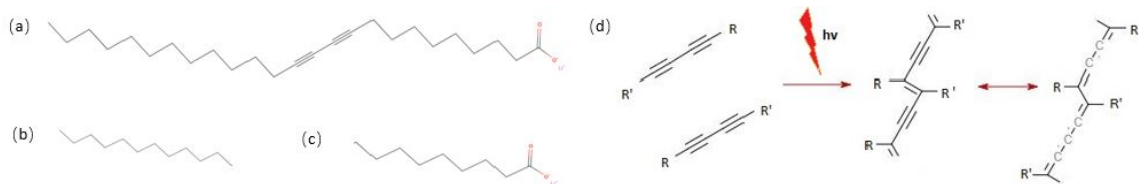


Figure 1.1: (a) The skeletal structure of LiPCDA. (b)skeletal structure of -R (c) skeletal structure of -R' (d)1,4 polymerization of LiPCDA catalyzed by radiation.

ranges for dosimetry purposes relevant to diagnostic imaging procedures and radiation treatment. The active component of radiochromic film such as GAFChromicTM EBT3 film is Lithium-10,12-pentacosadiynoate (LiPCDA) whose skeletal structure is displayed in Fig. 1.1. Ionizing radiation catalyzes the the 1,4 polymerization of LiPCDA molecules that changes the absorption spectra of RCF as shown in Figs. 1.2 and 1.3. The 1,4 polymerization continues after the irradiation causing the post-irradiation OD growth, the rate of which decreases significantly 24 hours after the irradiation.^{1,2} This requires the consistent waiting time window between the irradiation and scanning for both calibration and application RCF.³ The RCF used in this work is EBT3 film which is ideally suitable for dose range 0.2-10 Gy. RCF is a robust 2-D ionizing radiation dosimeter with high resolution and flexibility.⁴ RCF provides advantages such as near tissue-equivalence, water immersibility, weak energy dependence, incident radiation beam angular independence, near dose rate independence,⁵ room light insensitivity and wide dynamic range. Temperature during the irradiation period showed negligible effect on optical density (OD) or transmitted intensity of RCF readout.⁷ Girard *et al.*⁸ studied temperature effect during the post-exposure storage period, the temperature effect of the flatbed scanner window during scanning and the impact from humidity. Thus, RCF is usually stored and scanned at room temperatures. Though RCF is largely light insensitive, RCF should be stored in a dark environment and handled efficiently while in the presence of light. RCF can be cut to any size and is free of post-exposure chemical and physical processing. Schematic view of the symmetric structures of EBT3 and EBT-XD can be found in

Fig. 1.4. Compared to the past generations of EBT3 film, the current generation, EBT3 and EBT-XD film is surfaced by silica particles to distance the film itself to the scanner window to eliminate Newton's rings from thin-film interference.

Applications of RCF include patient specific quality assurance (QA) in stereotactic radiosurgery (SRS), stereotactic body radiation therapy (SBRT),^{9,10} intensity modulated radiation therapy (IMRT),^{11,12} Volumetric-modulated arc therapy (VMAT) (Fig. 1.6), high dose rate (HDR) /low dose rate (LDR) brachytherapy,¹³⁻¹⁹ kilovoltage(kV) imaging dose measurement,²⁰ SRS/SBRT radiosurgery unit commissioning,^{9,21} *in-vivo* dosimetry,^{22,23} superficial region dosimetry²⁴ and dose calculation algorithm validation and comparison.²⁵ Another important aspect is its application for small field dosimetry²⁶ of clinical photon, proton and electron beams, such as relative

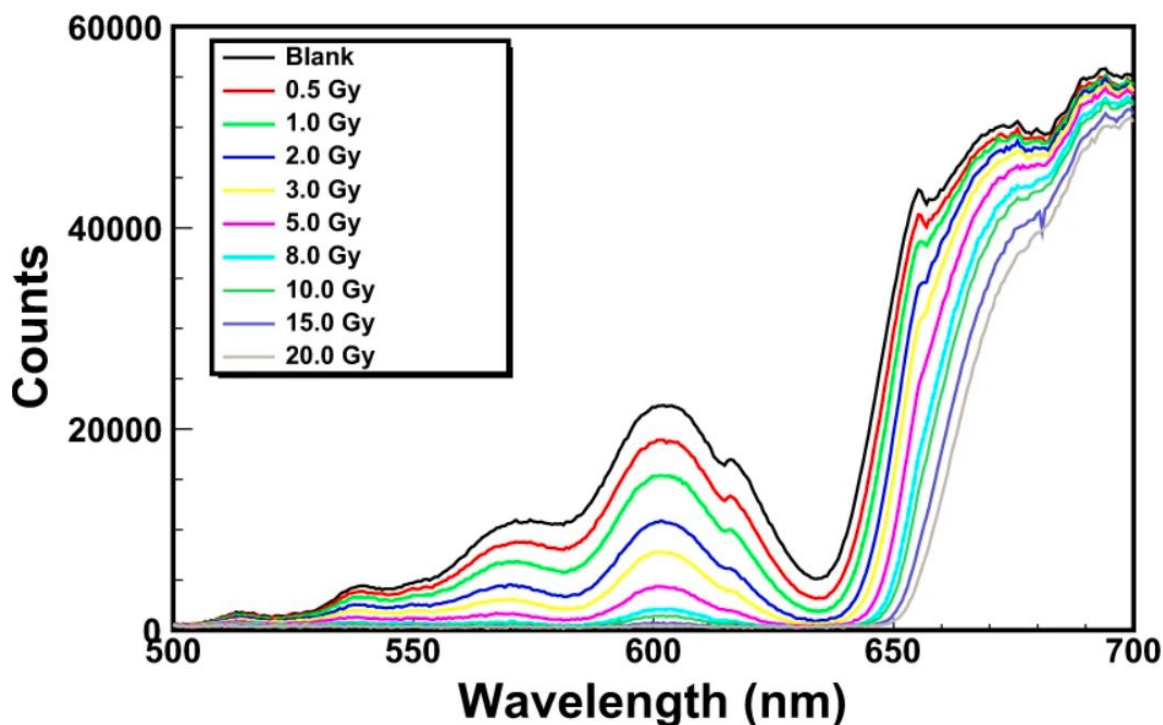


Figure 1.2: Visible absorption spectra for GAFChromic[™] EBT 3 when exposed to Cobalt-60 gamma rays for different dose levels up to 20 Gy. Of interest are the peaks located around 610 nm. [Reprinted from Casolaro *et al.*⁶ with permission from Creative Commons Attribution 4.0 International License-<http://creativecommons.org/licenses/by/4.0/>.]

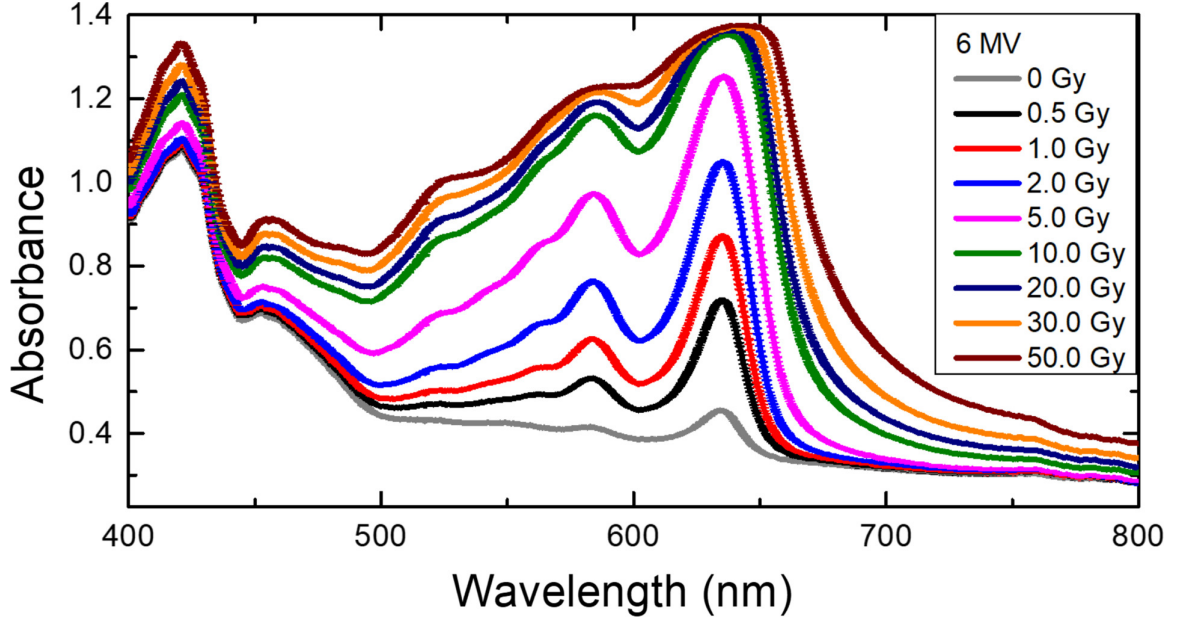


Figure 1.3: Net absorption spectra for GAFChromic[™] EBT3 when exposed to 6 MV X-rays up to 50 Gy. Of interest are the peaks located around 630 nm. [Reprinted from León-Marroquín *et al.*,⁵ with permission from the Wiley Materials. ©WILEY All rights reserved]

output factor measurements.^{27–29} In addition, EBT-3 film can also be used for geometry applications such as pinpoint test of radiation focus point and patient positioning system,^{30,31} end-to-end tests of Leksell Gamma Knife (GK) and its dosimetric validation^{32,33} and CyberKnife.³⁴ RCF dosimetry is the application of spectroscopy.^{5,6,35–39} León-Marroquín *et al.*⁵ proved that the spectra of EBT3 is independent of dose rate and beam quality for megavoltage photon and electron beams including delivered under flattening filter-free (FFF) mode. But it has film batch (lot number) and spectrometer dependence (as shown in Fig. 1.2 and Fig. 1.3). This indicates that for RCF dosimetry, dose calibration needs to be performed for every lot/batch of film for a specific densitometer system.^{5,39} The readout of RCF is typically performed with a densitometer, such as a 3-color (RGB) flatbed color scanner.⁴⁰ For instance, an Epson[®] 10000XL-12000XL photo scanner is recommended by the RCF vendor, Ashland (Bridgewater, NJ) due to its high performance. Dose calibration for RCF usually involves assigning known dose numbers to optical density (OD) values or

equivalent and then fitting pairs to a calibration function which often takes the form of reciprocal function or high-order polynomials. In terms of calibration utilizing OD values, the curve fittings often take the form:⁴¹

$$\bar{d}_i = \log_{10} \frac{a_i + b_i D}{c_i + D}, \quad (1.1)$$

where a_i , b_i and c_i are channel specific fitting coefficients to be determined by the curve fittings (e.g. Fig. 1.5) for each color channel i , $\bar{d}_i$ are the mean OD values of each selected region of interest (ROI). Note that during the dose calibration process,

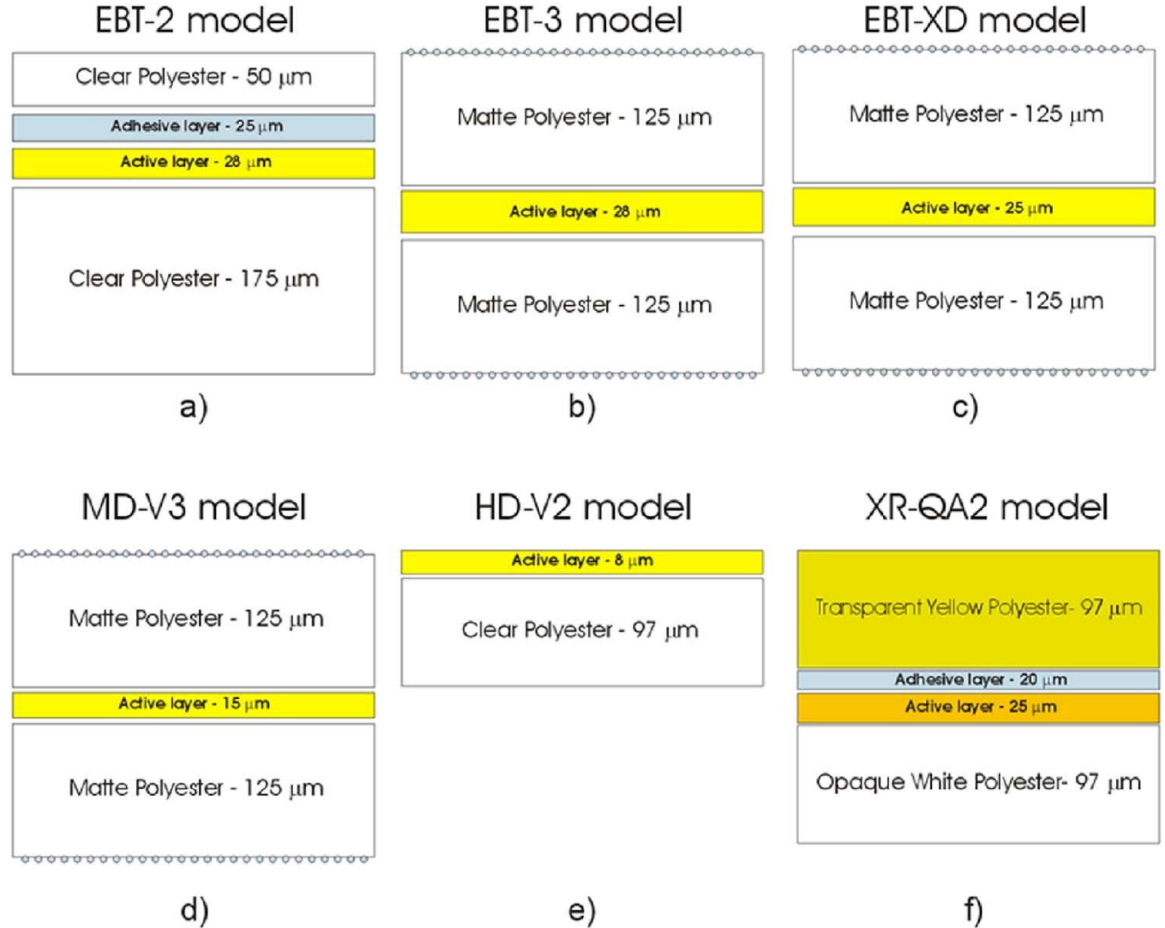


Figure 1.4: Diagram of GAFChromicTM EBT2, EBT3 and EBT-XD cross-section structure: an active layer is sandwiched by clear matte polyester surfaced by silica particles to eliminate Newton's ring artifact for new generation radiotherapy films such as EBT3, EBT-XD and MD-V3 film. Reprinted from Devic *et al.*¹ with permission from Elsevier. All rights reserved.

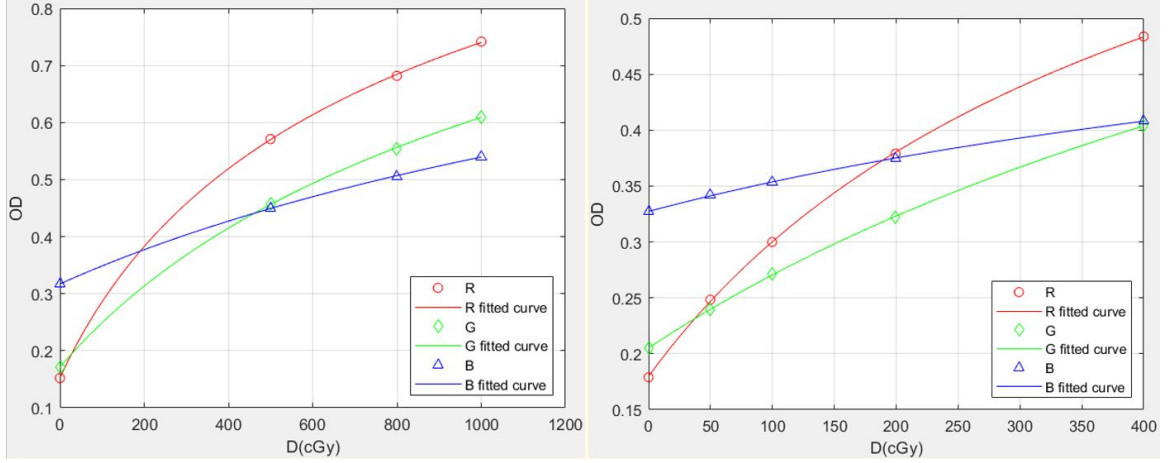


Figure 1.5: Red, green and blue channel dose calibration curves for GAFChromicTM EBT3 film for lower dose range (right) and higher dose range (left).

Table 1.1: RCF type and its suitable dose range.

RCF type	EBT3	EBT-XD	MD-V3	HD-V2	XR-QA2	XR-RV3
Dose range	0.2-10 Gy	0.4-40 Gy	1-100 Gy	10-1000 Gy	0.1-20 cGy	0.1-20 cGy

the same absorbed dose values (D) are assigned to OD values from all three channels. The curve fitting is independently performed for each color channel as shown in Fig. 1.5. Curve fittings can also be performed using raw pixel value (PV) intensity.² The quality of such curve fittings such as the goodness of fit is an important aspect for accurate film dosimetry. The quantitative use of RCF involves challenges such as thickness non-uniformities of the active layer, scan-to-scan variability artifact and the lateral artifact (LA). Accurate dosimetry depends on three major aspects: proper handling and scanning, dose calibration, dosimetry model and artifact countermeasures and corrections. The widely accepted one-scan protocol³ corrects the scan-to-scan variability artifact.

This dissertation proposes a channel weighted triple-channel dosimetry method and a novel and efficient correction method for the LA of radiochromic film dosimetry.

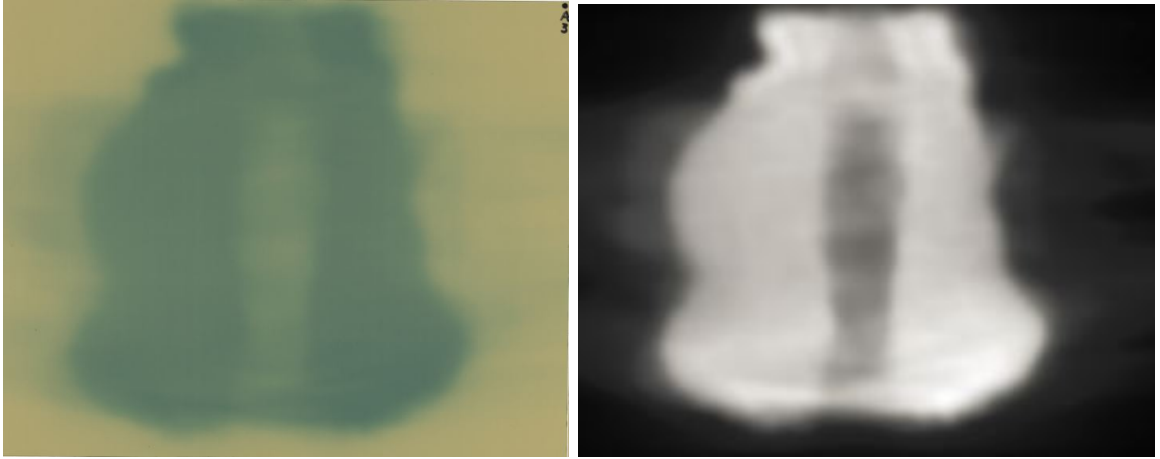


Figure 1.6: Left: A sheet of GAFChromic[™] EBT3 film inside a solid water phantom exposed to a clinical bilateral neck VMAT plan from 6 MV x-rays; right: Gray-level dose map of the coronal plane in which the film sits calculated by RaySearch Laboratories RayStation6 TPS.

1.3 Patient specific IMRT/VMAT quality assurance with RCF

Using IMRT QA dose plans made by a treatment planning system (TPS) for testing and evaluation of RCF measurements provides a robust platform to compare different film dosimetry methods including single and triple dosimetry methods. The treatment planning system utilizing a well-known collapsed cone convolution superposition dose computing^{43,44} algorithm provides a theoretical dose calculation for a spatially distributed 3-dimensional (3D) dose profile. RCF measures 2-dimensional (2D), or planar, dose or plane distribution with high resolution. The external beam therapy (EBT) typically involves radiation delivery technique such as 3D-conformal radiation therapy (3D-CRT), IMRT or VMAT. A 2D plane can be extracted to the plane where the film sits.

Before the initiation of the treatment planning for a patient, imaging modalities such as computed tomography (CT), positron emission tomography (PET) and magnetic resonance imaging (MRI) usually provide simulation for patient modelings which include image registration and computer-aided contours. CT provides relative elec-

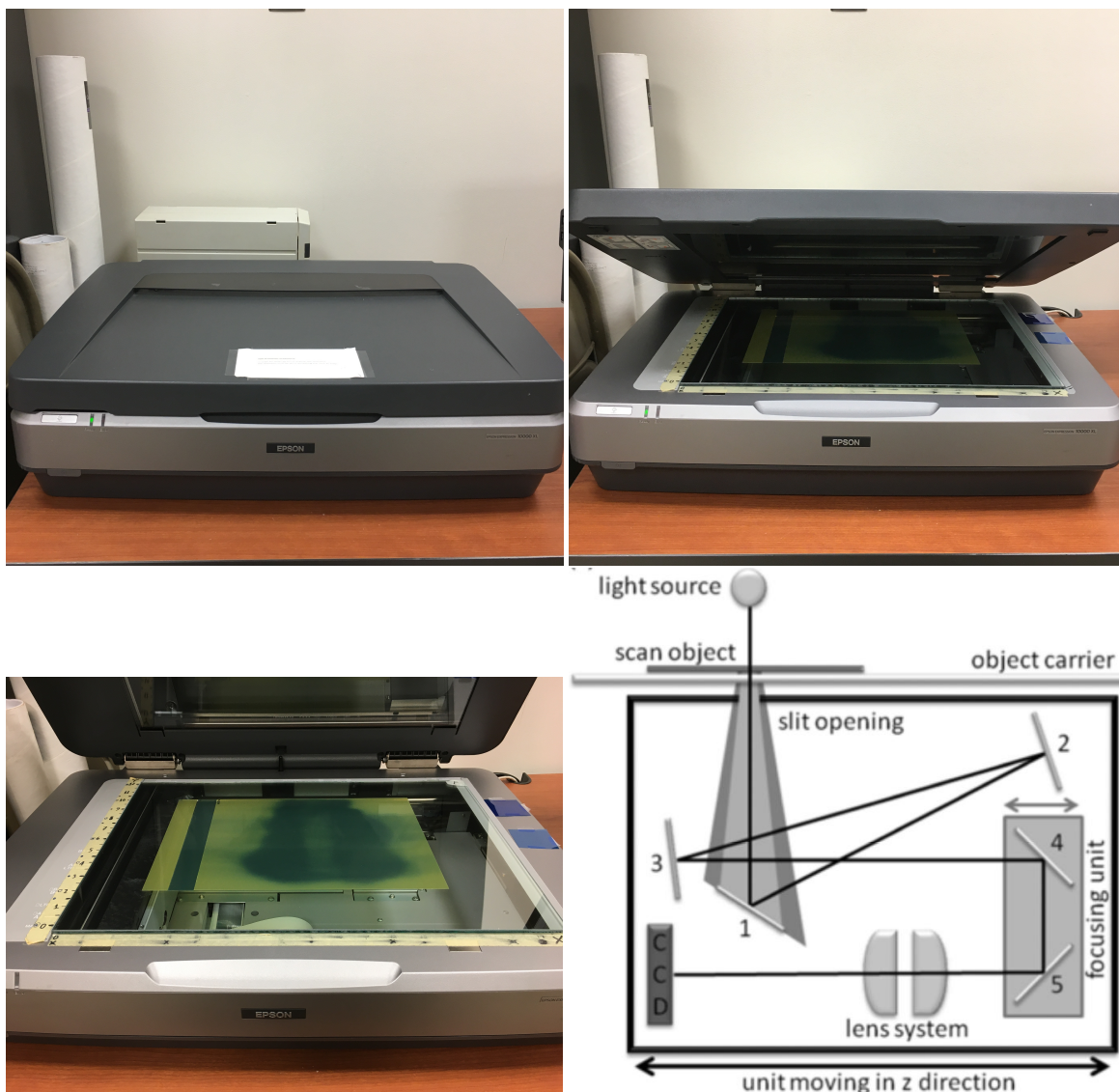


Figure 1.7: Upper left: An Epson Expression 10000XL photo scanner with the transparency unit closed. Upper Right: the scanner with the transparency unit open. Lower left: Exposed application EBT3 film centered on the scanner window with an unexposed strip for scan-to-scan variability correction and a full exposed reference film strip. Lower right: Schematic shows the optical path under the transmission scanning mode within an Epson Expression 10000XL photo scanner: Light transmitted through RCF is reflected by the mirrors inside the optical system and detected by CCD camera arrays⁴² ©Institute of Physics and Engineering in Medicine. Reproduced by permission of IOP Publishing. All rights reserved.

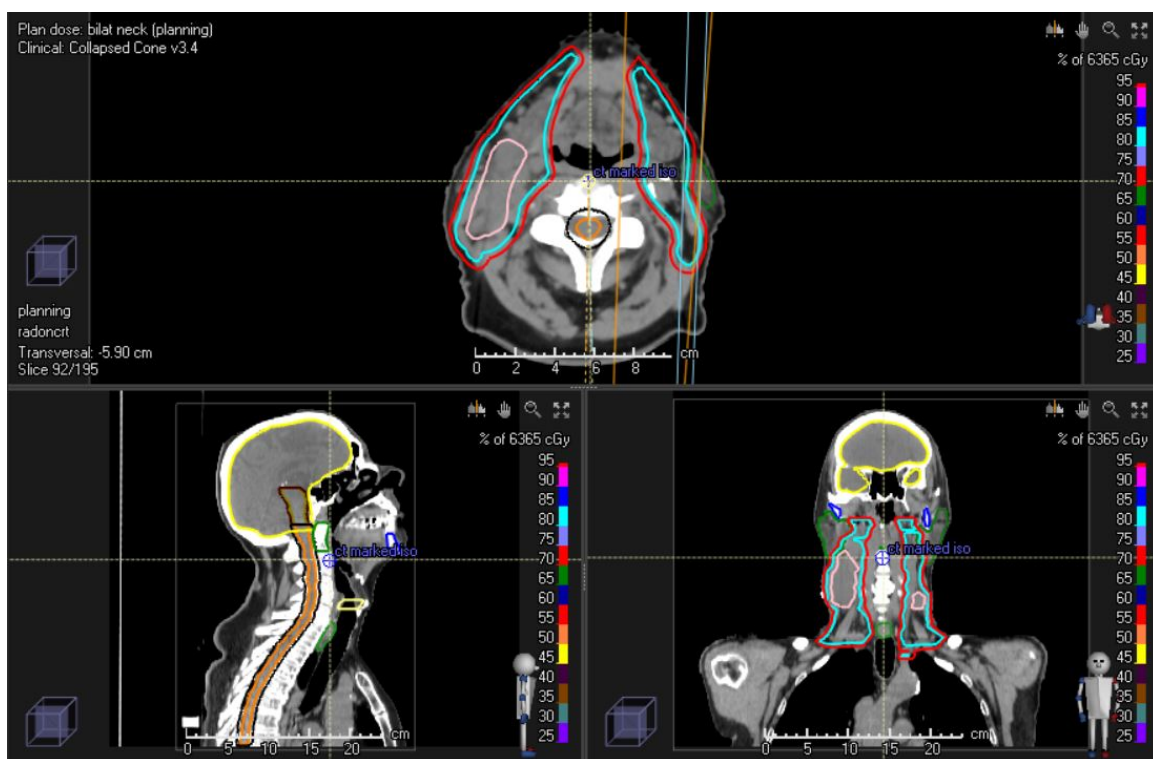


Figure 1.8: Patient Modelings: The contours of critical structures such as brain, spinal cord, brain stem, parotid gland and mandible bone from the primary CT scan. The gross tumour target volume (GTV), the clinical target volume (CTV) and the planning target volume (PTV) of the bilateral neck are shown with three distinct contours.(Courtesy of Wake Forest Baptist Health)

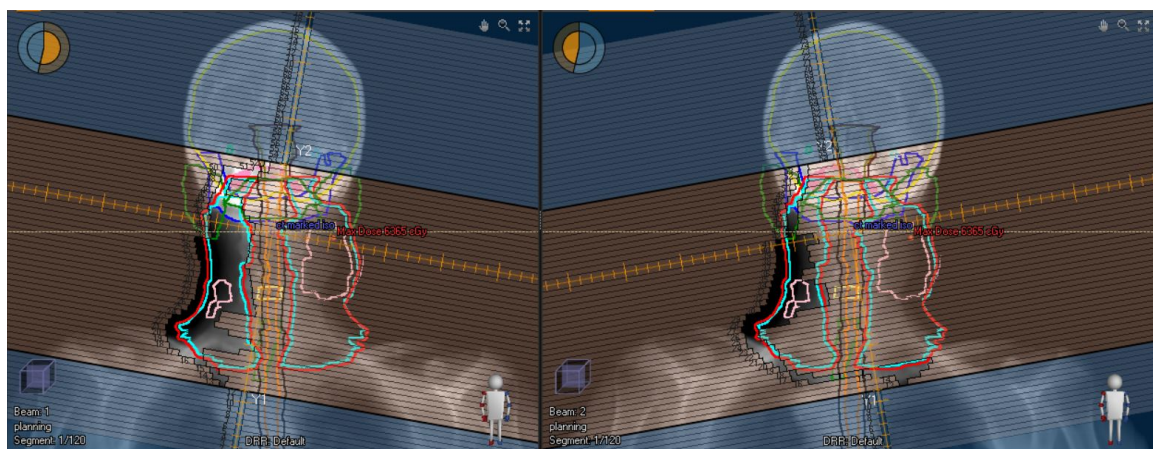


Figure 1.9: The beam's eye view (BEV) generated by a digitally reconstructed radiography from CT shows the shape of MLC of 2 partial VMAT arcs personalized to the targeted volume of the bilateral neck. (Courtesy of Wake Forest Baptist Health)

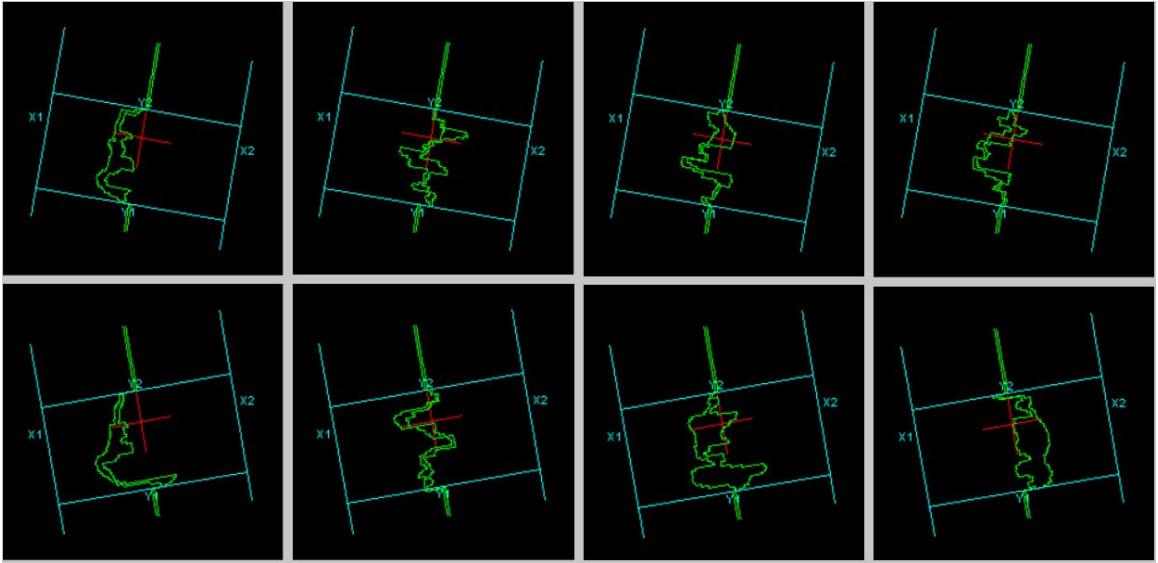


Figure 1.10: The VMAT DMLC display at 4 moments in MOSAIQ[®] record and verify system. Upper row: clockwise first arc; Lower row: counter clockwise second arc. The rotation of gantry shown in Fig. 1.16 in combination of the simultaneous DMLC enables the fast delivery of radiation to complex target volume. (Courtesy of Wake Forest Baptist Health)

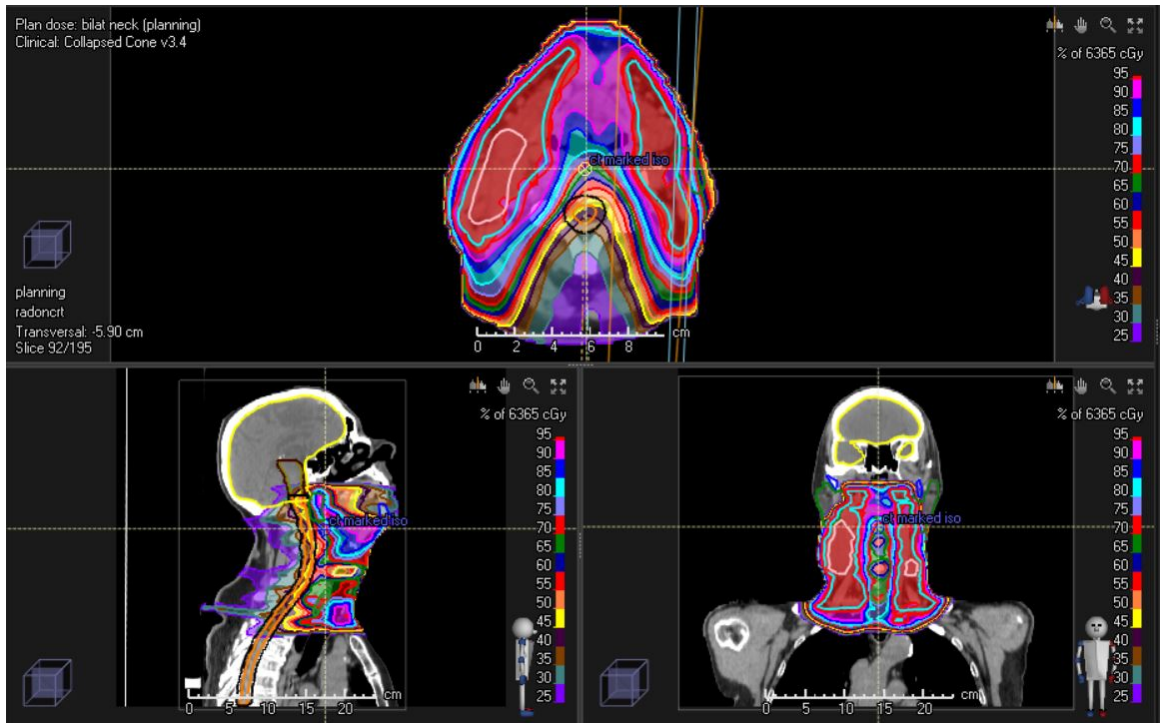


Figure 1.11: 3D dose painting of the resulting treatment planning for the bilateral neck case. (Courtesy of Wake Forest Baptist Health)

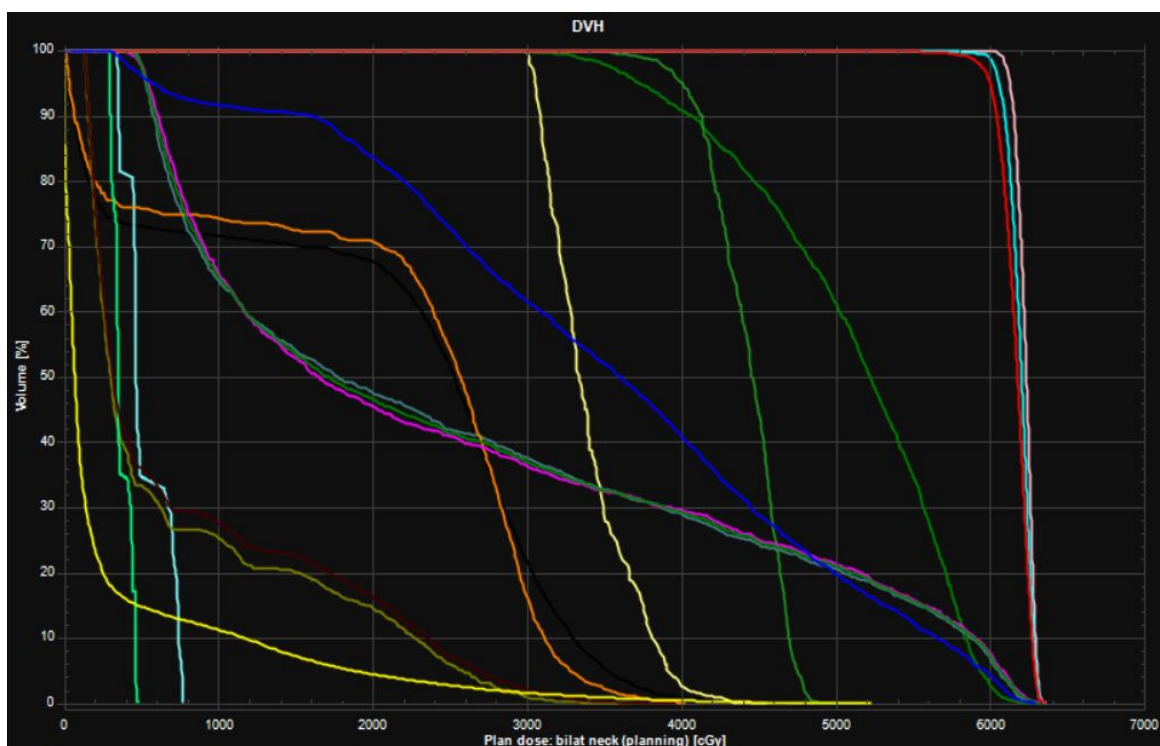


Figure 1.12: The dose volume histogram of the clinical bilateral neck VMAT plan. (Courtesy of Wake Forest Baptist Health)

Dose	ROI	ROI vol. [cm ³]	Dose [cGy]							% outside grid
			D99	D98	D95	Average	D50	D2	D1	
Plan dose: bilat neck (...)	bone	36.75	3322	3489	3722	5083	5221	6032	6079	0 %
Plan dose: bilat neck (...)	Bone_Mandible	50.92	361	406	561	3523	3604	6091	6147	0 %
Plan dose: bilat neck (...)	Brain	1422.85	0	0	0	321	69	2785	3398	0 %
Plan dose: bilat neck (...)	Brainstem	19.87	136	138	146	734	303	2869	2995	0 %
Plan dose: bilat neck (...)	Brainstem_PRV3	30.69	134	138	148	798	316	2998	3228	0 %
Plan dose: bilat neck (...)	Cochlea_L	0.2	294	295	297	373	353	467	468	0 %
Plan dose: bilat neck (...)	Cochlea_R	0.2	343	346	349	533	466	772	772	0 %
Plan dose: bilat neck (...)	CTV_6000	395	5994	6023	6061	6195	6205	6313	6320	0 %
Plan dose: bilat neck (...)	Esophagus	7.37	3733	3867	4003	4425	4455	4798	4822	0 %
Plan dose: bilat neck (...)	GTVn	71.34	6080	6096	6127	6229	6236	6318	6323	0 %
Plan dose: bilat neck (...)	Larynx	4.29	3013	3017	3053	3399	3337	4047	4213	0 %
Plan dose: bilat neck (...)	Parotid_L	39.6	459	494	546	2591	1647	6178	6226	0 %
Plan dose: bilat neck (...)	Parotid_R	37.25	481	496	530	2593	1770	6157	6192	0 %
Plan dose: bilat neck (...)	Parotids	76.85	475	496	536	2594	1711	6167	6210	0 %
Plan dose: bilat neck (...)	PTV6000_Eval	584.39	5859	5933	6000	6164	6178	6308	6317	0 %
Plan dose: bilat neck (...)	SpinalCord_Cerv	23.69	18	21	33	2050	2564	3533	3703	0 %
Plan dose: bilat neck (...)	SpinalCord_PRV5	88.53	16	18	28	2020	2528	3780	3964	0 %

Figure 1.13: Dose charts of the targeted volumes and critical structures for the bilateral neck VMAT plan. (Courtesy of Wake Forest Baptist Health)

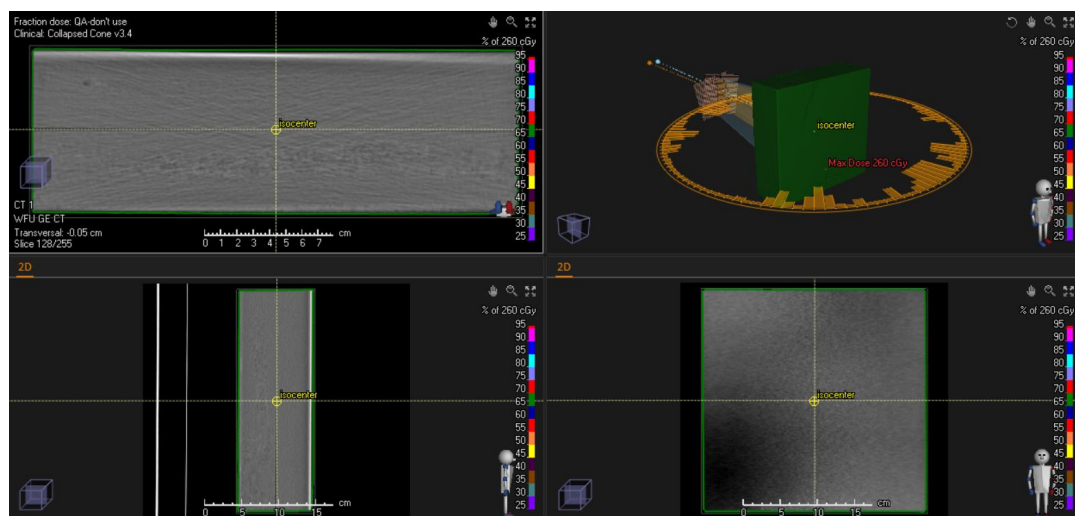


Figure 1.14: Axial, sagittal and coronal view of Solid Water[®] phantom for receiving IMRT/VMAT treatment delivery. The geometry center of the phantom was set to coincide with the radiation focal point, i.e. isocenter of a linear accelerator

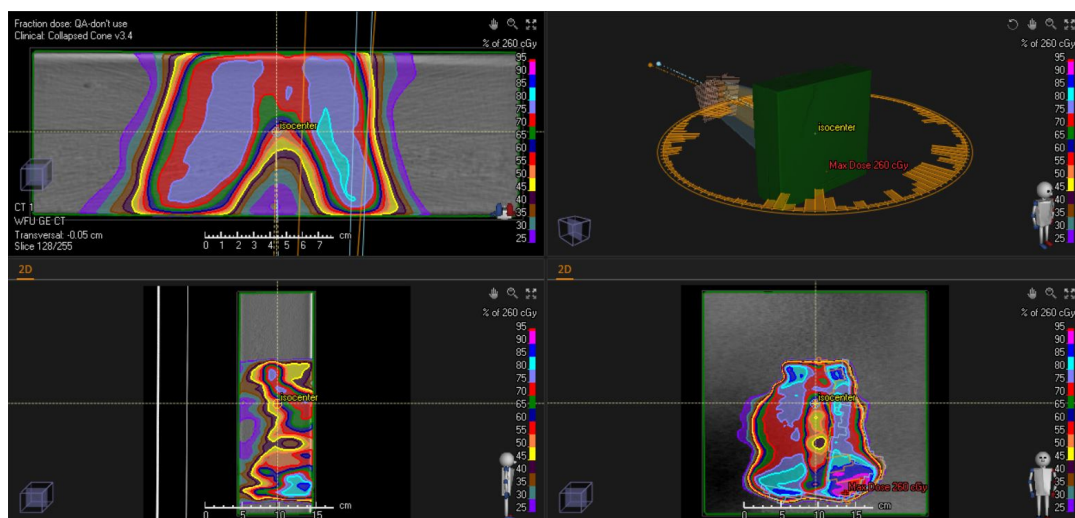


Figure 1.15: 3D dose painting of the resulting VMAT QA plan.

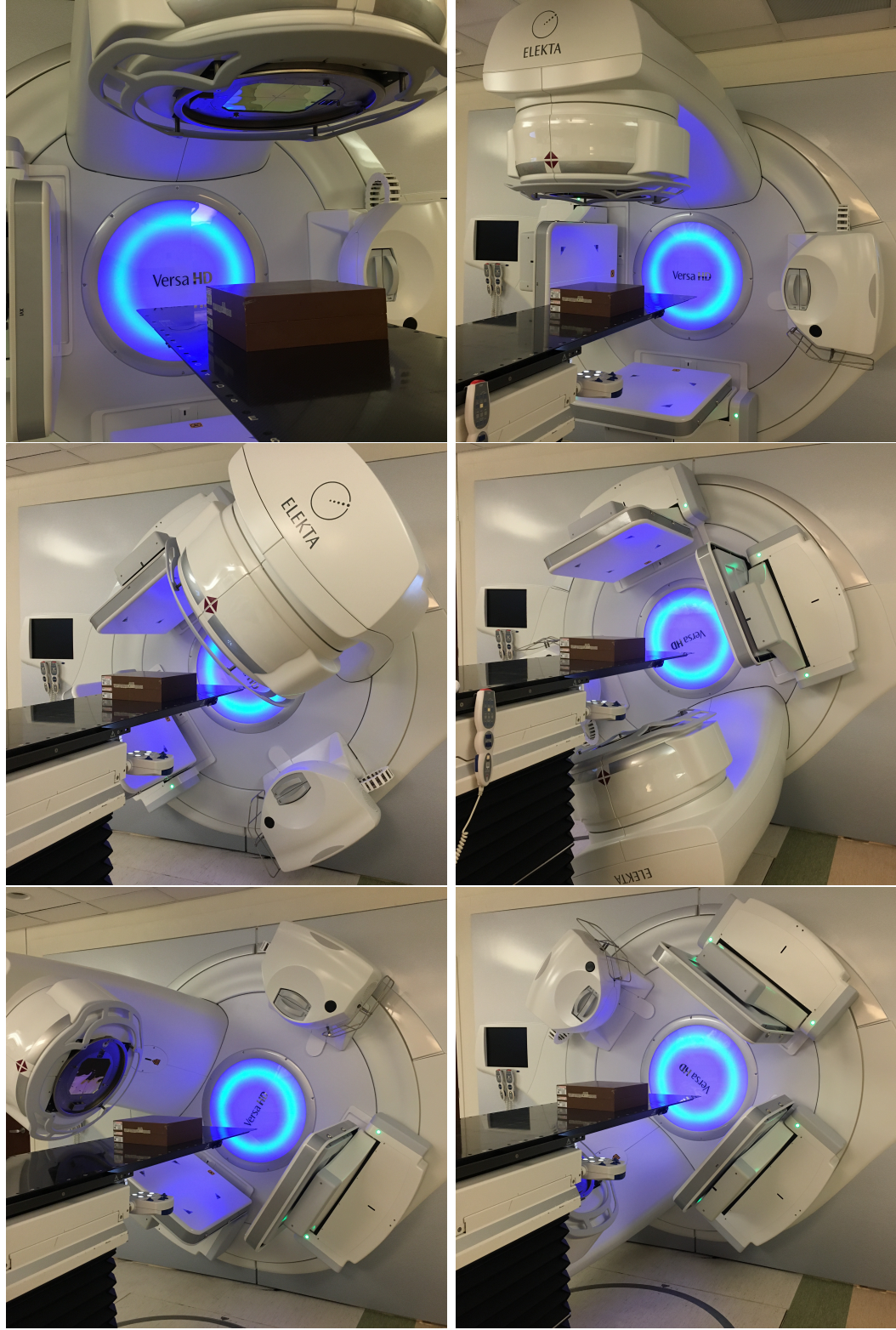


Figure 1.16: GAFChromic[™] EBT3 RCF sandwiched between 2 slabs of $10 \times 10 \times 5$ Solid Water[®] phantoms on the treatment couch of an Elekta Versa HD[™] linear accelerator with a rotating gantry. The phantom was laterally set up by beams at gantry angle 90° and 270° with SSD=85 cm. For gantry angle 0° , the SSD for set-up beam was 95 cm.

tron density information for dose calculation during the treatment planning process. MRI scans provides excellent soft-tissue contrast. Functional images from PET scan contain metabolism information from radioactive tracker intake. The use of hybrid imaging modalities such as PET/CT and PET/MRI allows more accurate diagnosis and higher quality treatment planning. After delineation of the target, maximum reduction of the normal tissue and critical organ toxicity is always of great importance, because different structures have specific tolerance on dose, i.e., the amount of ionizing radiation. A treatment planning system (TPS) is a platform for computing dose distributions, including automated dose computation based on enforced constraints and multi-criteria optimization. The computer algorithm of a TPS allows the modeling of the interaction between the adjustable incident radiation beam and patient anatomy. The commonly used radiation types for therapeutic purposes are X-rays, gamma-rays, electrons and protons. The treatment planning process aims to deliver certain amount of dose to the intended target which is usually at depth inside a patient's body at the same time maximumly sparing normal tissue including critical structures. IMRT and VMAT are two delivery techniques using external beam therapy, such as a medical linear accelerator. IMRT usually refers to the step-and-shoot technique with mostly static multileaf collimator (MLC). VMAT typically refers to the rapid arc delivering technique with mostly dynamic MLC and continuous rotating gantry. Dose volume histogram (DVH)⁴⁵ is commonly used to evaluate clinical plans for radiotherapy. It can be used to compare different plans or to evaluate different structures such as the target volume and organs at risk (Fig. 1.12). Patient specific QA is required before a patient gets treated by an IMRT or VMAT plan created specifically for the patients' anatomy and target shape and biology. It is a type of personalized medicine. The QA process is dedicated to ensure the planned dose distribution can be delivered and independently verified via experimental measurements. The patient specific QA aims to compare the measured and planned dose distribution and to further evaluate

the difference, potential errors and its implication for patient safety and treatment. Uncertainties involved during the beam delivery process included and are not limited to errors from beam modeling, gantry angle, MLC positions and leakage, collimator angle and machine output. Various IMRT/VMAT QA tools have been developed to measure the dose distribution, such as ArcCHECK and MapCHECK (Sun Nuclear, Melbourne, FL) or electronic portal imaging device (EPID) based dosimetry system. RCF is a robust 2D dosimeter with high measurement resolution and low uncertainties. Combined with slab phantoms, it has been developed and widely used as an IMRT QA tool. The patient specific IMRT/VMAT QA plan can be delivered to a phantom within which RCF is located (Fig. 1.16). The irradiated RCF from the resulting setup captured the dose distribution of the bilateral neck as shown in Fig. 1.6 (left). This enables testing film dosimetry method for compensating spatial non-uniformity of film active layer as well as the lateral artifact from the joint effect of RCF-flatbed scanner system.

1.4 Metal-oxide-semiconductor field-effect transistor dosimeter

One of the applications of metal-oxide-semiconductor field-effect transistor (MOSFET) is for radiation dose measurement. The MOSFET dosimeter has been used for *in-vivo* dose monitoring and verification for radiation therapy such as external beam therapy^{46–49} and brachytherapy,^{50–53} diagnostic⁵⁴ and image-guided procedures⁵⁵ that involve ionizing radiation. When a MOSFET dosimeter is exposed to ionizing radiation, pairs of electron-holes are generated within the dielectric layer by the incident radiation. Electrons are with higher mobility than holes and quickly escape from the gate electrode contact. While holes move towards the interface of dielectric and semiconductor where they become trapped forming a positively charged thin layer. The

difference in voltage shift before and after exposure can be measured, and is proportional to radiation dose. MOSFET dosimeter can be operated in a biased mode with the real-time dose readout. It can also be operated in an un-biased mode providing passive dose readings after the irradiation. The organic field-effect transistor (OFET) based thin-film device has inherent advantages over its inorganic counterpart such as low cost, high physical flexibility which enables large area, biocompatible applications. Recently, there have been efforts^{56,57} on characterizing the response, (threshold voltage shift in particular) of OFET based thin-film transistors to ionizing radiation.

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Chapter 2

A Novel and Efficient Lateral Artifact Correction Method Combined with Dose Calibration For Radiochromic Film Dosimetry

This work presents an efficient method that combines calibration and the lateral artifact (LA) correction in a single scan for radiochromic film (RCF) dosimetry with a commonly used flatbed scanner. Instead of addressing the artifact in the domain of optical density (OD) or equivalent, this method presents a dose-domain LA correction model designed for multichannel dosimetry that incorporates a built-in RCF strip as an object of reference to coordinate the LA correction. The algorithm corrects LA in the dose domain after separating the LA from the mingling of the off-axis non-uniform dose profile of an open field and RCF active layer non-uniform thickness across the RCF strips. The lateral multichannel dose values are directly corrected in the multichannel dose domain via lateral position dependent coefficients of the second order polynomials. The LA correction coefficients are obtained at lateral positions using a unique layout of RCF calibration strips correlating the multichannel dose value at a lateral position to a known dose value projected by a color channel specified off-axis factor (OAF). The OAFs were obtained from a film strip that stands out orthogonally to the remaining strips, namely, the outstanding strip. The layout is laterally centered and composed of one outstanding film strip, five parallel strips fully exposed by a $25 \times 25 \text{ cm}^2$ standard open field, and one unexposed film strip, also parallel to the irradiated strips. A clinical (left lung) IMRT, a (right lung) VMAT plan and two $20 \times 20 \text{ cm}^2$ simple geometry plans irradiated with different monitor units (MUs) were delivered for the validation of the LA correction method. Gamma index analysis showed increased gamma passing rates after the LA correction for the evaluation treatment planning system (TPS) plans, with 3%/3mm gamma passing rate of the VMAT plan scored 100% for all three color channels after the LA correction. The film strip layout covered sufficient lateral space and only a single scan was needed for both RCF calibration and the LA correction. The method requires

neither measurements from a different spare dosimeter (such as a 1-D profiler or a 2-D matrix) for the off-axis beam profile nor a separate multi-scan process exclusive for the LA correction.

2.1 Introduction

Radiochromic film (RCF) is a robust 2-dimensional (2-D) ionizing radiation dosimeter with near-tissue equivalence, high spatial resolution and physical flexibility.¹ RCF also has advantages such as weak energy,^{2,3} dose rate,³ temperature^{4,5} and humidity⁶ dependence within commonly encountered clinical environments and a range of therapeutic beams. One of the major applications of RCF is patient specific quality assurance (QA) for intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT). RCF is normally digitized by a flatbed color scanner, and its calibration is usually performed by irradiating over a range of known doses in a standard geometry.

LA is the scanner charge-coupled device (CCD) array output inhomogeneity artifact for lateral positions off the scanner central axis relative to the scanning direction along which the scanner lamp moves. LA is a joint optical effect between the flatbed scanner and RCF, evident by the fact that the CCD array captures uniform intensity without RCF positioned on the scanner window. The LA arises from RCF scanning and is increasingly prominent for larger radiation doses and increased perpendicular distance from the scanner central axis,⁷⁻¹¹ which is perpendicular to the lamp length and divides the lamp length into symmetrical halves geometrically. LA remains a potential acute source of error for RCF dosimetry especially for high doses and large exposed areas.

Multichannel dosimetry utilizes all three color channels, red (R), green (G), and blue (B) to compensate for RCF active layer non-uniformity, instead of using the three channels separately and independently. The robustness of multichannel dosimetry compared to single and dual channel dosimetry methods has been confirmed.¹¹⁻²¹

The single channel dosimetry method, with either the red or green channel alone, results in more acute LA. The multichannel dosimetry method often mitigates the LA partially.^{11–13,18,22} Further correction of LA may increase dose map fidelity.^{11,18,21,23} A benefit of attempting to correct the LA via directly correcting multichannel dose values, i.e., correcting LA in the dose domain, is that the dose independent part, primarily RCF active layer non-uniformity has been corrected within such a domain already transformed by multichannel dosimetry.

Various LA correction methods have been proposed^{7–11,23,24} either in the domain of optical density (OD), or transmission intensity pixel value (PV) of a scanner (or netOD, netPV). These methods generally involve using small RCF pieces irradiated at various dose levels and positioned at different lateral sites of a scanning window,^{7,8,10,11,23,24} with multiple scans and often with gaps between selected lateral positions. The OD (PV) values from the same exposed RCF piece positioned along the lateral direction show a roughly open-up (open-down) parabola in shape and can thus be corrected by curve fitting to correlate the vertex value to the lateral values on parabolas.^{8–10,18} However, the goodness and symmetry of parabolic fits may not be satisfactory depending on absorbed doses, lateral positions and the color channel of interest. These methods were mostly designed only for single channel dosimetry, typically the red channel in either the OD or PV domain. Lewis and Chan^{11,23} presented a method using a two-point rescaling in the PV domain to correct the LA for all three color channels.

For contemporary RCF dosimetry, without correcting the LA in practice, users are merely cautioned about the LA by the RCF protocol or user’s guide. Various factors possibly limit the LA correction from being widely adopted even though it can be a one-time flatbed scanner commissioning process exclusive for the LA for a particular scanner. RCF pieces with different dose levels are needed and positioned on the scanner window with the corresponding number of scans for each of a number

of selected lateral positions. Scan-to-scan variability is another known factor⁴ that needs to be scaled properly such that preferably an unexposed piece of RCF is present every time at the same spot to eliminate the scan-to-scan variability between different scans for the LA. After each scan, the RCF pieces need to be removed and repositioned at another one of multiple selected lateral positions. Accurate positioning of RCF pieces and correlating RCF coordinates used for LA characterization to future RCF applications is challenging especially in regards of efficiency as there are no reference positioning marks on a scanning window for RCFs of various sizes. Namely, one cannot tell from a scanned image of RCF its definite lateral location in respect to the scanner central axis without doing extra work on marking and aligning. Lateral positions are unlimited but in reality one can only put RCF pieces on selected lateral positions. There are often gaps left between the selected lateral coordinates (or selected dose levels depending on the particular method), usually a few centimeters between the marked lateral positions. One may have to carefully balance between the number of selected lateral positions and the size of gaps so that the process is not too onerous, closing down the gaps to a acceptable level that allows proper and meaningful interpolations. This paper describes a novel and efficient LA correction method that can be potentially integrated into the existing, one-scan RCF calibration protocol, utilizing RCF strips for detailed lateral profile, and providing a built-in object of reference included in each scan as a whole, capable of knowing the lateral position of any scanned RCF.

EBT stands for external beam therapy. EBT type RCF has also been used for high dose rate^{17,25} and low dose rate²⁶ brachytherapy dosimetry. The contemporary EBT film generation, EBT3, had undergone systematic structure changes for performance enhancement including the incorporation of the new crystal form, marker dye, single active layer, symmetric structure and silica microparticles.^{27,28} Another LA correction method with the parabola fit, implemented in the PV domain for the first generation

of EBT film (bluish in color), used a slit field with the jaws of the linac partially closed to irradiate an entire RCF sheet and at the same time incorporated a 2-D chamber array that captured the field flatness information⁹ for its LA correction. It was validated with an IMRT plan and a specially designed dose pattern via the same 2-D ion-chamber array for the (red) single channel dosimetry only and for dose levels up to 2.5 Gy.

There are two primary concerns for using exposed RCF strips stretching across the full or majority width of the scanner to perform LA correction. First is the off-axis, non-uniform beam profile from standard open fields of a linear accelerator, which cannot expose the RCF strip uniformly across a wide distance, e.g., the flatness of a standard 30×30 cm² open field is typically around 2-3% at a depth of 5 cm in water with source-to-surface distance (SSD) at 95 cm. Second is the non-uniformity of RCF active layer thickness which results in various sensitivities at different RCF regions. Thus, any pixel of a RCF strip is simultaneously affected by three factors, the LA, the off-axis output factor and the RCF active layer thickness at that particular coordinate. Unlike the existing OD or PV based correction models, this work instead presents a LA correction method in the multichannel dose domain addressing, overcoming the mingling of several effects: the LA, inhomogeneous exposure from a standard open field and RCF active layer non-uniformity.

2.2 Materials and methods

2.2.1 Irradiation and scanning

Six RCF strips (Fig. 2.1, blue rectangles) were taken from one single sheet of GAFChromicTM EBT3 film (Ashland, Bridgewater, NJ). The leftmost outstanding strip in Fig. 2.2 was cut from another sheet of RCF from the same lot, as shown in Fig. 2.1 (red rectangle) to keep the same scanning orientation (portrait, in this

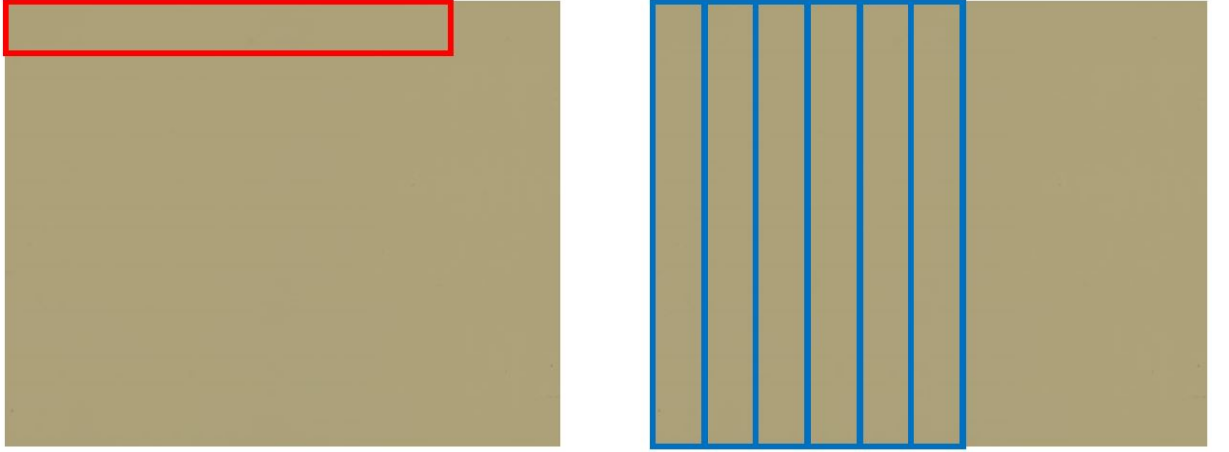


Figure 2.1: Two ordinary sheets of unexposed GAFChromic™ EBT3 film has size 203.2 mm×254.0 mm(8"×10"). Left: A first film sheet provides a reference film strip (8"×1" or 203.2 mm×25.4 mm), cut lengthwise from the sheet outlined by the red rectangle and corresponding to the leftmost outstanding strip in Fig. 2.2. Right: a second film sheet provides six film strips (also 8" or 203.2 mm long), cut orthogonally with length perpendicular to the scanning direction (blue rectangles). These strips correspond to the group of six strips on the right side of Fig. 2.2

case) with the parallel strips. All seven strips have approximately the same length which can be read from the axes in Fig. 2.2. The RCF strips were irradiated by a 25×25 cm² open field at depth=5 cm and SSD=95 cm with 6 different doses inside a 30×30×10 cm³ Solid Water® phantom (Gammex, Middleton, WI), one at a time. These strips were irradiated at the exact same position, centered in the crosshairs of a 25×25 cm² light field with gantry parked at angle 0°. All irradiations were done by 6 MV photon beams from a Versa HD™ linear accelerator (Elekta, Stockholm, Sweden). A farmer type ionization chamber (PTW, Freiburg im Breisgau, Germany) calibrated by an accredited dosimetry calibration laboratory was used to acquire dose values for the RCF calibration. The unique layout of six exposed strips and one unexposed film strip is shown in Fig. 2.2. The entire layout of the film strips was centered on the scanning window in the lateral direction. The layout was symmetrical about the scanner central axis along which the lamp moves, as the arrow points in Fig. 2.2, with **C** denoting the scanner central axis (**C**-axis). All the exposed areas of RCFs fell

into the lateral positions covered by the strips as shown in Fig. 2.2. RCF scans were performed on an Epson[®] Expression 10000 XL photo scanner (Epson America, Long Beach, CA) with transmission scanning mode at least 72 hours after exposure to minimize the effect from post-irradiation OD growth. The flatbed scanner was warmed up for 15 minutes by performing about 10 empty scans prior to the RCF scans. The scanning settings were 48-bit (16-bit per channel) RGB, uncompressed TIFF image with all color correction features turned off. The portrait scanning orientation was deployed throughout the study. RCF was handled per American Association of Physicists in Medicine Task Group No.55.²⁹ An unexposed RCF strip, the rightmost in Fig. 2.2 was included for calibration (along with the remaining strips) and also to eliminate scan-to-scan variabilities²² between calibration and application scans. It also served as an object of reference for each scan assuring that all the exposed areas of application RCFs were within its range in the lateral direction on the scanner window. A 3.5 mm thin clear glass plate was used to compress RCF avoiding the Callier effect^{4,11,17,30} arising from the RCF curvature during the scanning process.

2.2.2 Data analysis

The data analysis throughout the study was programmed in MATLAB edition R2018b which in turn produced all the figures. Nonlinear least squares was deployed for all operations that involved fitting functions to data points, which included dose calibration and the LA correction coefficient acquisitions. A Cartesian coordinate system was used for spatial specification as displayed in Fig. 2.2. The coordinates of a point are (i, j) with the physical unit of length, millimeter (mm). The i axis is on top and j axis is on the left side. The i and j axes cross at the origin point $(0, 0)$. Note that this is a global coordinate system not only for the unique layout of the strips displayed in Fig. 2.2, but also for all the digitized RCFs.

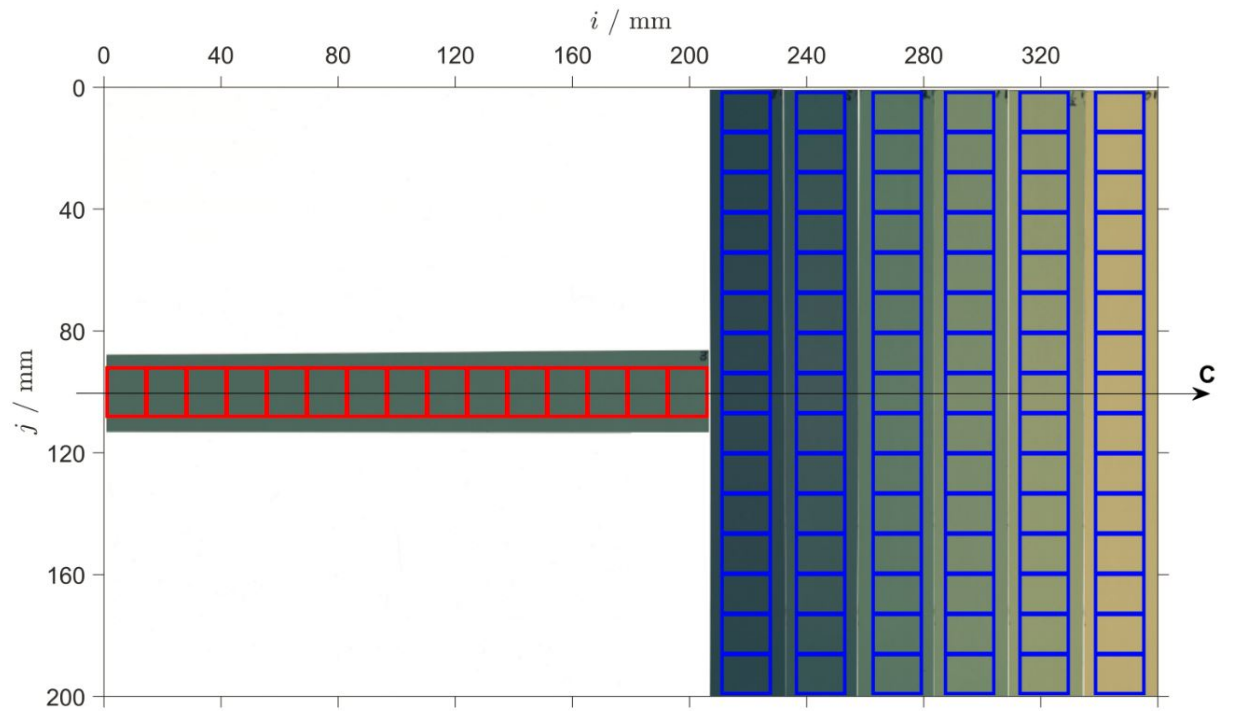


Figure 2.2: The unique layout of six full exposed strips along with an unexposed strip(rightmost), the leftmost strip was cut from the area outlined by the solid red rectangle as shown in Fig. 2.1 to maintain the portrait scanning orientation with the rest of calibration strips. 'C' stands for the scanner central axis (C-axis) along which the scanner lamp moves.

2.2.3 The novel LA correction method

The unprocessed grayscale intensity I_k with range $[0 \ 65535]$ is converted to OD value d_k for each color channel k at each point with coordinate (i, j) :

$$d_k(i, j) = -\log_{10} \left(\frac{I_k(i, j)}{I_0} \right). \quad (2.1)$$

For a 48-bit(16-bit per channel) RGB TIFF image, the maximum, unattenuated intensity I_0 of all three color channels from a RGB flatbed scanner shares the same value, $2^{16} - 1$. Along the scanner central axis denoted by **C** in Fig. 2.2, the individual mean OD value of seven midmost $16 \times 14 \text{ mm}^2$ patch areas on each of the seven strips is obtained for the RCF dose calibration. The corresponding calibration dose values for these seven midmost patches across the scanner central axis including the one on the outstanding strip in Fig. 2.2 from the left to right were 300.1 (the outstanding strip), 799.7, 499.6 200.4, 99.7, 49.4 and 0 cGy (six parallel strips). These dose values were assigned to the midmost patch on each film strip including the outstanding strip. The densitometric calibration function which correlates OD values to doses for a color channel k , i.e., $\{d_k, D_k(d_k)\}$ is

$$D_k(d_k) = \frac{c_k - b_k 10^{d_k}}{a_k 10^{d_k} - 1}, \quad (2.2)$$

where a_k, b_k and c_k are color channel specific fitting parameters and d_k stands for an OD value of the k th color channel. A look-up dose value $D_k(i, j)$ of the color channel k , i.e., the dose value from the single channel dosimetry method, can be acquired through the calibration function above given an OD value $d_k(i, j)$ at any point (i, j) on RCF.

Micke *et al.*¹² introduced the loss function $\Omega(i, j)$ that uses the least squares to minimize the squared dose difference between any two color channels k and m after

RCF active layer thickness non-uniformity compensation,

$$\Omega(i, j) = \sum_{k \neq m}^3 (\hat{D}_k(i, j) - \hat{D}_m(i, j))^2 \quad (2.3)$$

wherein Mayer *et al.*¹³ provided an analytical approximation which the optimized dose values are given in all three color channels at each location (i, j) . The optimized multichannel dose value of the k th color channel is $\hat{D}_k(i, j)$ which is expressed in forms of $D_k(i, j)$ and its derivative term $\dot{D}_k(i, j)$, per the algorithm by Mayer *et al.*. $D_k(i, j)$ and $\dot{D}_k(i, j)$ are computed at each position (i, j) for color channel k per the dose calibration function Eq. (3.7) and its derivative $\dot{D}_k$. $\hat{D}_k(i, j)$ generates channel specific dose values for all RCFs including the calibration scan (Fig. 2.2) and any following RCF scans for applications such as IMRT/VMAT patient QA, flatness and symmetry check, machine commissioning, etc. $\hat{D}_k$ is the dose domain of interest, within which the RCF active layer non-uniformity has been corrected already via Eq.(2.3).

The red and blue grid, i.e., the fifteen equally divided rectangles on each film strip in Fig. 2.2 were matched exactly in size and dimension to apply the off-axis factors (OAFs) from the leftmost outstanding strip to the irradiated, parallel strips by Eq.(2.4). The OAF is defined as the ratio of an off-axis point dose at a specific depth to the dose value at the cross point of the beam central axis. For the RGB dose maps of Fig. 2.2 computed by $\hat{D}_k(i, j)$, one can state that the known dose values $\hat{D}_k^c(i, j)$ for the k th channel at any lateral coordinate j can be calculated by applying OAF_k obtained from the leftmost outstanding strip to the known **C**-axis dose values $\bar{D}(i, \mathbf{C})$ of the parallel strips:

$$\hat{D}_k^c(i, j) = \bar{D}(i, \mathbf{C}) \cdot \text{OAF}_k \quad (2.4)$$

wherein

$$\bar{\mathcal{D}}(i, \mathbf{C}) = \{799.7, 499.6, 200.4, 99.7, 49.4\}, \quad (2.5)$$

the set of doses delivered for RCF calibration. Evidently, Eq.2.4 applies for all the parallel strips irradiated except the rightmost unexposed film strip, that is, "0" was excluded in Eq.(2.5). The centered 14 mm/40-pixel narrow belt of the leftmost outstanding strip was equally divided into fifteen rectangular regions(outlined by red rectangles of Fig. 2.2) along the $\mathbf{C}$ -axis for OAF acquisitions. These dose values were perfectly centered, not lateral and were thus more trusted because they received the least impact from the LA induced distortion. This is the same reason that the midmost rectangles across the $\mathbf{C}$ -axis in Fig. 2.2 are used for densitometric calibration. For color channel k , OAF_k was obtained via the leftmost outstanding strip by normalizing the dose values of the belt regions to the mean dose value of the midmost patch in Fig. 2.2 of the same strip. The fifteen red rectangles used for OAF generations were matched to all the parallel strips with blue rectangles in Fig. 2.2 for the LA correction coefficient acquisitions. Unlike the other parallel strips which were exposed, the known dose value at the lateral coordinate j of the rightmost unexposed film strip is bound to share the same value as its $\mathbf{C}$ -axis counterpart($j = 101.7$) which is 0 cGy. For each color channel k , the multichannel dose value $\hat{D}_k(i, j)$ at a position (i, j) can be corrected by the following expression, a second-degree polynomial:

$$\hat{D}_k^c(i, j) = \sum_{n=1}^3 p_{n,k}(j) \hat{D}_k^{3-n}(i, j) \quad (2.6)$$

where $\hat{D}_k^c(i, j)$ is the multichannel dose value after the LA correction at a point (i, j) for the k th color channel and $\hat{D}_k(i, j)$ is the corresponding raw dose value. From Fig. 2.2, the LA correction coefficients $p_{1,k}(j)$, $p_{2,k}(j)$ and $p_{3,k}(j)$ were determined by correlating the known dose value, $\hat{D}_k^c$ of Eq.(2.4) and its corresponding raw value $\hat{D}_k$, that is, $\{\hat{D}_k, \hat{D}_k^c\}$ for the color channel k at a lateral position j . For each lateral

position j and color channel k , it had six pairs of $\{\hat{D}_k, \hat{D}_k^c\}$ for the generation of three LA correction coefficients, $p_{n,k}$ of Eq.(2.6), as the case of six parallel film strips in Fig. 2.2. These coefficients were obtained solely from a single-scan as shown in Fig. 2.2 and then applied to any digitized RCF converting a raw multichannel dose distribution $(\hat{D}_k(i, j))$ into the corrected one $(\hat{D}_k^c(i, j))$ through Eq.(2.6).

2.2.4 Validation of the LA correction method

A clinical right lung VMAT plan, a left lung IMRT plan and two 20×20 cm² simple geometry plans were selected from RayStation6 TPS(RaySearch Laboratories, Stockholm, Sweden). A stack of two slabs of Solid Water[®] phantom, each with a dimension of $30 \times 30 \times 5$ cm³, were scanned by a Discovery ST hybrid PET/CT scanner(GE Healthcare, Chicago, IL). The CT image set of the Solid Water[®] phantom was exported to TPS to calculate the plans for comparison. The application RCFs were placed at the same coronal plane as the calibration strips inside the $30 \times 30 \times 10$ cm³ Solid Water[®] phantom for irradiation, which is at 5 cm depth with SSD = 95 cm (gantry angle 0°). On the left-right dimension, the phantom was positioned on the treatment couch by the set-up beams of SSD = 85 cm with gantry angles at 90° and 270°. The IMRT plan had large an exposed area and the VMAT plan was with high doses. The plane maximum dose was 315 cGy for the IMRT plan, 825 cGy for the VMAT. For the 20×20 cm² simple geometry plans, 598 and 797 MUs were delivered for each. The exposed areas of the IMRT and simple geometry RCFs were centered on the scanning window. The VMAT film was laterally positioned away from the scanner central axis and within the lateral range covered by the calibration strips on the scanning window to stress any LA. The 2-D gamma index analysis³¹ was used for dose map comparison with RCF measurement as reference and TPS plan as evaluation.³² Gamma index passing rates were calculated with the threshold (TH)

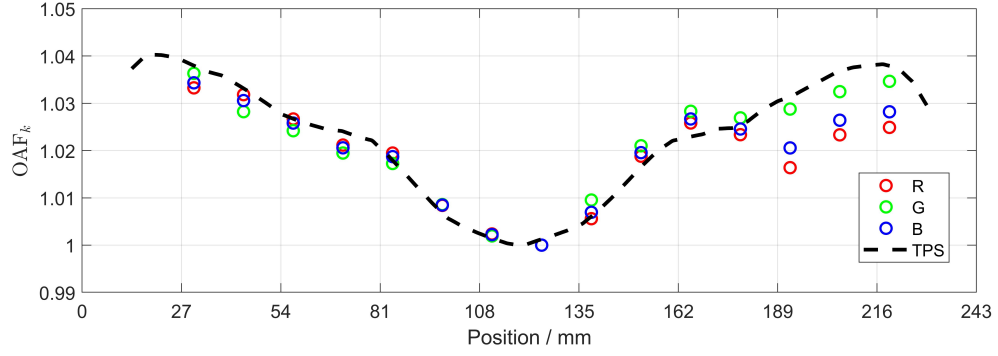


Figure 2.3: OAFs from the outstanding strip were compared to TPS showing roughly 4% flatness of a $25 \times 25 \text{ cm}^2$ open field at 5cm depth with SSD=95 cm.

of 10% of the maximum dose of each TPS generated 2-D evaluation plan. The TPS plans were resized to match the dose spacing of RCF. The gamma index maps were compared before and after the LA correction for each plan. The TPS in this study only served the purpose of comparison and validation rather than inputting any info for the LA correction.

2.3 Results

The OAFs generated from the outstanding strip are shown in Fig. 2.3. In Fig. 2.4, the curve fittings of Eq.(2.6) are displayed at two lateral positions $j=20 \text{ mm}$ and $j=169 \text{ mm}$. The resulting coefficients for the LA correction, $p_{n,k}$ are summarized in Table 2.1. Likewise, Eq.(2.6) were fitted to data points from each of fifteen rows of blue rectangles on the parallel strips in Figs. 2.2. Fig. 2.5 shows the resulting LA correction coefficients for the lateral positions within the lateral range covered by the unique layout of the film strips. With all the LA correction coefficients in place (Fig. 2.5), and the multichannel RGB dose maps of any application RCF ready, the LA correction was directly applied in the multichannel dose domain of $\hat{D}_k(i, j)$. Figs. 2.6, 2.7, 2.8 and 2.9 are the gamma index maps with the side-by-

Table 2.1: The resulting coefficients from curve fittings in Fig. 2.4 for $j = 20$ mm and $j = 169$ mm corresponding to the lateral locations of the 2nd and 13th row of rectangles on the parallel strips in Fig. 2.2.

	$j = 20$ mm			$j = 169$ mm		
Correction coefficients	R	G	B	R	G	B
$p_{1,k}(j)[\times 10^{-4}]$	-1.749	-0.788	-0.896	-1.715	-0.960	-1.118
$p_{2,k}(j)$	0.983	0.985	0.960	0.999	1.002	0.987
$p_{3,k}(j)$	1.046	5.154	3.480	-2.719	0.094	-1.171

side comparison before and after the LA correction for the IMRT, VMAT and each of two 20×20 cm² simple geometry plans respectively. On the left hand side is the 2-D gamma index distribution before the LA correction and on the right hand is its after-correction counterpart. The resulting gamma index passing rates ($\gamma < 1$) of the IMRT plan before and after the LA correction are summarized in Table 2.2 with the dose difference and the distance to agreement (DTA) tolerance as 1%/1 mm and 2%/2mm respectively. Table 2.3 is a summary of the passing rates of gamma index analysis with a commonly used evaluation criteria, dose difference 3% and DTA 3 mm, i.e., 3%/3mm for all three color channels. After the LA correction, the VMAT plan gamma index passing rates were promoted to 100% for all three channels under the same 3%/3 mm criteria, compared to 87.1% before the LA correction, as mapped in Fig. 2.7.

2.4 Discussion

The unattenuated response of the flatbed scanner is near-uniform along the lateral direction without laying RCF on the scanning window. However, the CCD array

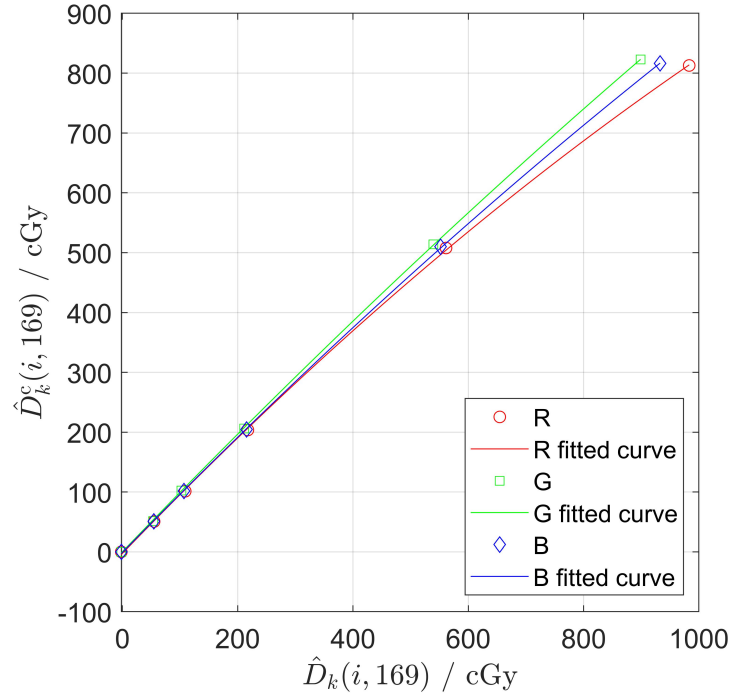
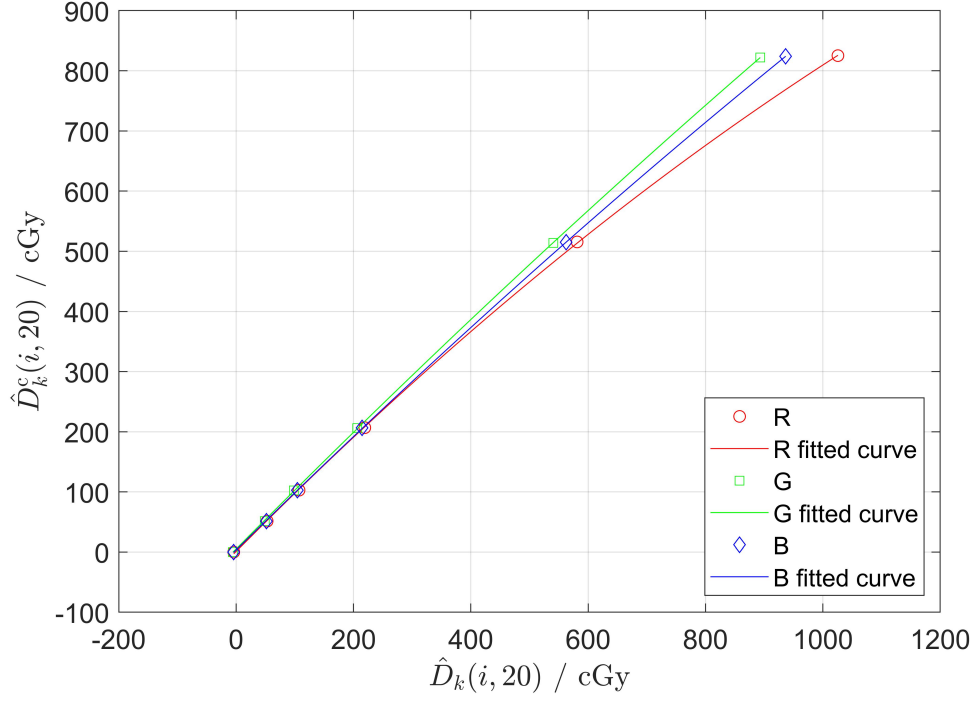


Figure 2.4: Curve fitting for Eq.(2.6) at two lateral positions $j = 20$ and $j = 169$ corresponding to the rectangles of the 2nd and 13th row (from top to bottom) on parallel film strips in Fig. 2.2 for each color channel k , i.e., R, G and B respectively.

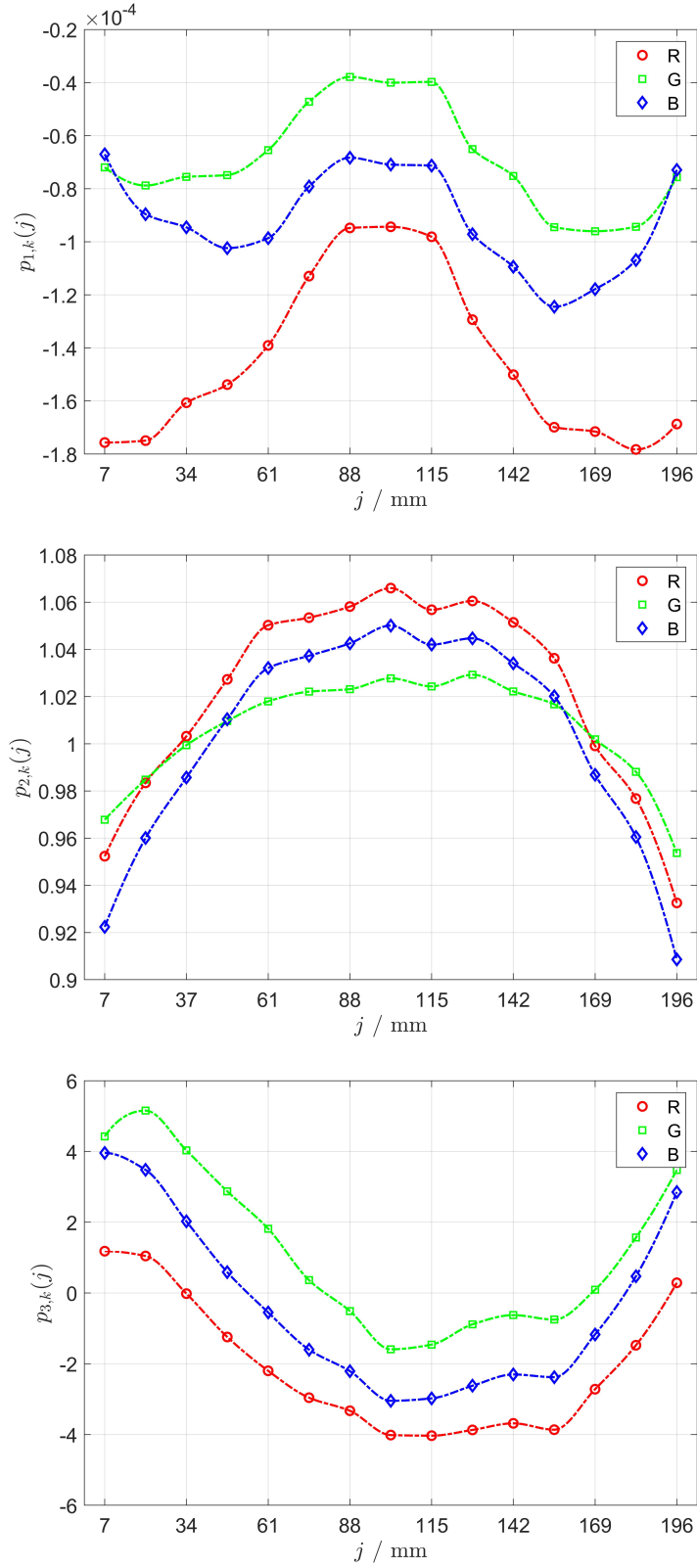


Figure 2.5: The LA correction coefficients $p_{1,k}$, $p_{2,k}$ and $p_{3,k}$ along the lateral direction (j axis) for each color channel k , i.e., R, G and B respectively.

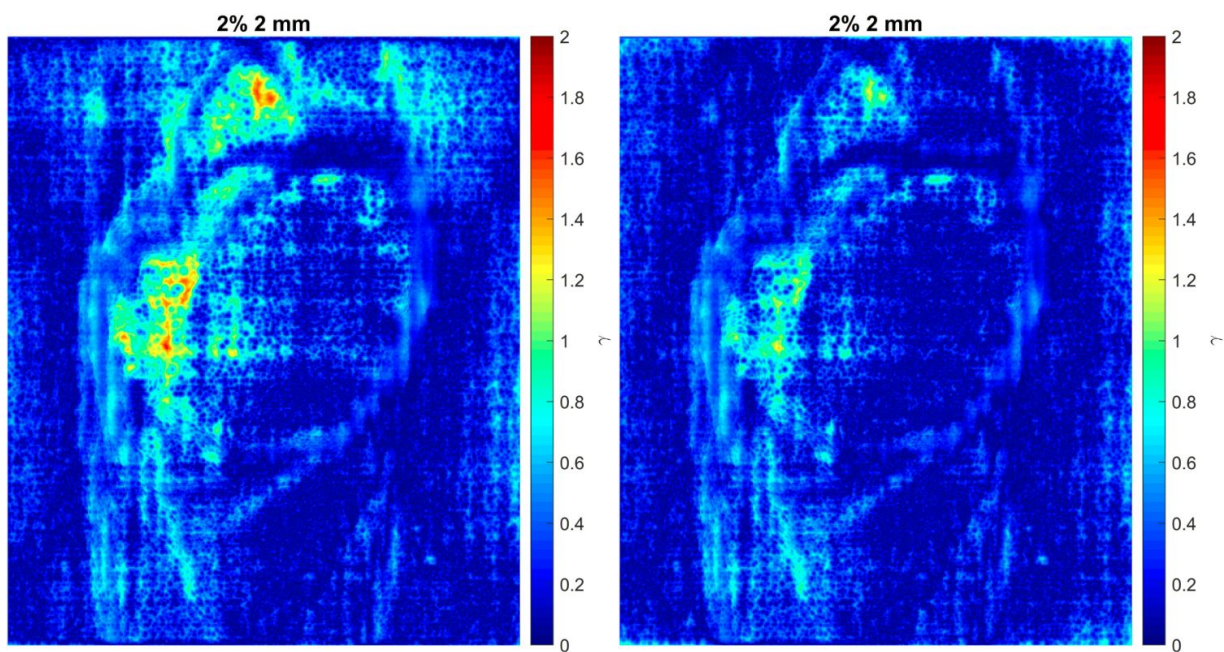


Figure 2.6: The side by side comparison of 2%/2 mm gamma index mapping of the IMRT distribution with the film measurement as the reference and the corresponding 2-D TPS plan as the evaluation.

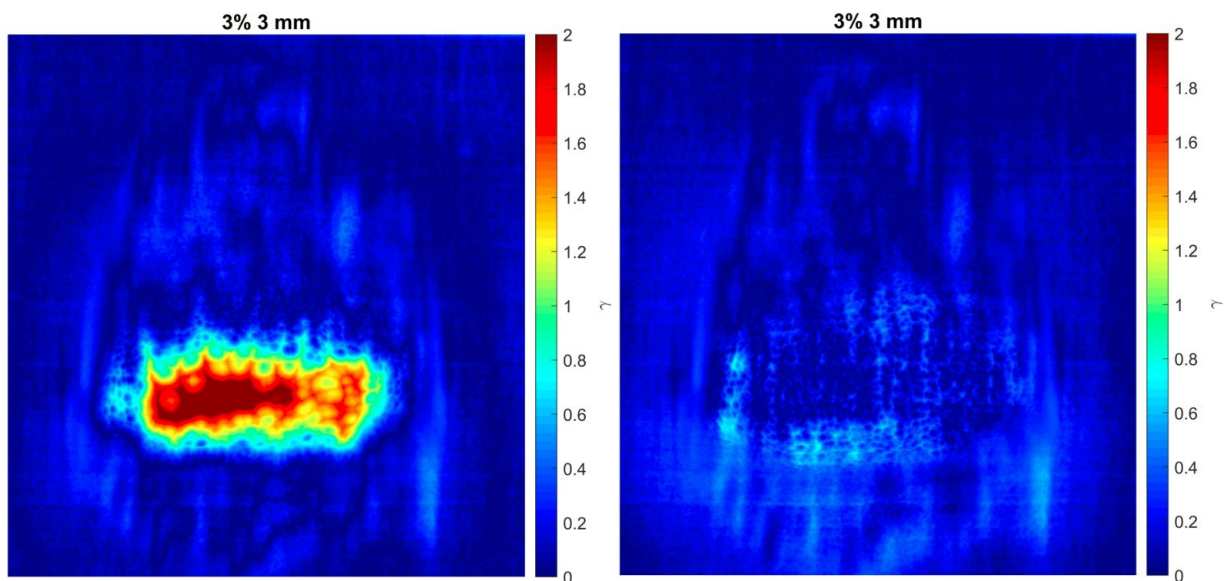


Figure 2.7: The side by side comparison of 3%/3 mm gamma index map of the VMAT plan: the exposed area of the RCF was laterally displaced away from the scanner central axis to stress any LA yet within the lateral range covered by the unique layout.

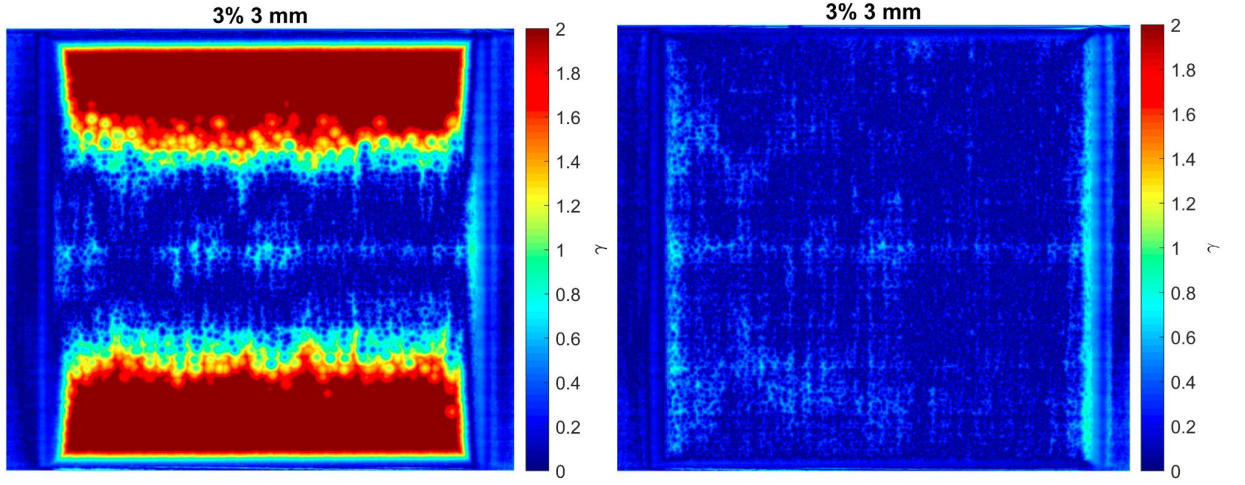


Figure 2.8: The side by side comparison of 3%/3 mm gamma index map of the 598 MUs 20×20 cm² simple geometry plan.

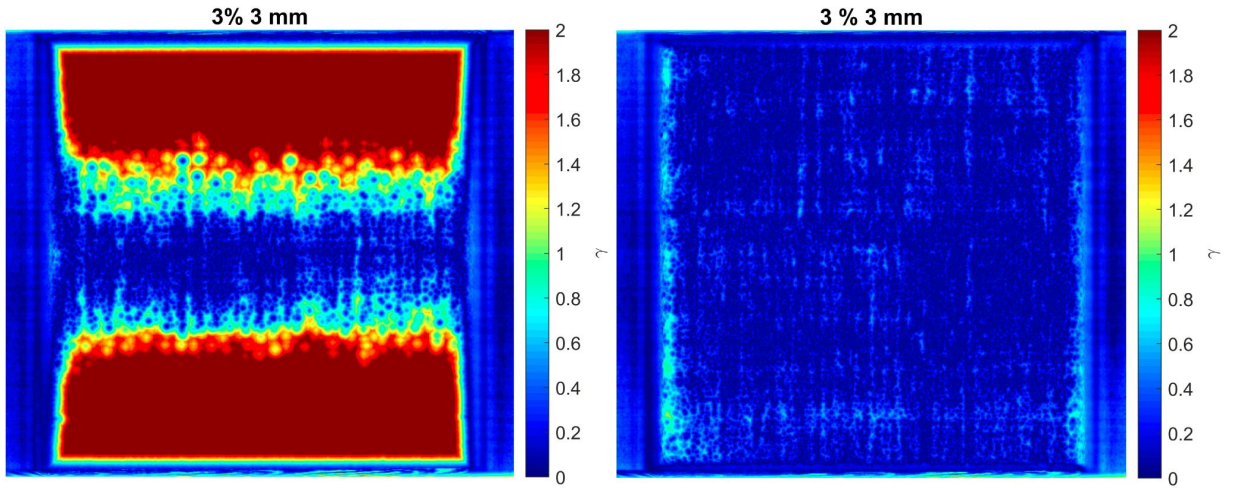


Figure 2.9: The side by side comparison of 3%/3 mm gamma index map of the 797 MUs 20×20 cm² simple geometry plan.

Table 2.2: Passing rates of gamma index analysis with the TH of 10% of the maximum dose of the evaluation IMRT plan.

Color channel	R		G		B	
Passing rates($\gamma < 1$)	1%/1 mm	2%/2 mm	1%/1 mm	2%/2 mm	1%/1 mm	2%/2 mm
Before LA correction	75.9%	96.9%	71.4 %	97.3 %	81.3 %	97.5 %
After LA correction	90.2%	99.9%	88.2%	99.7 %	89.6 %	99.9 %

Table 2.3: The passing rates of gamma index analysis for 3%/3 mm tolerance with the TH 10% (598 and 797 MUs from a 20×20 cm² standard open field).

	598 MUs		797 MUs	
Color Channel	Before($\gamma < 1$)	After($\gamma < 1$)	Before($\gamma < 1$)	After($\gamma < 1$)
R	59.8%	100%	50.5%	99.9%
G	86.0%	99.9 %	82.0%	99.9%
B	67.2%	100 %	60.4%	99.9%

responds differently to the exact same piece of RCF scanned at different lateral positions known as the LA. The lateral artifact is noteworthy as it's not caused by either the scanner or RCF alone, rather an interplay of both. GAFChromicTM EBT3 and EBT-XD film are known to have scan orientation dependence. Thus, all RCFs including calibration and application films have to be kept in the same orientation in respect to the original RCF sheet. This is the reason why the leftmost outstanding strip in Fig. 2.2 was cut from a RCF sheet as shown in Fig. 2.1, outlined in red rather than blue, in order to keep the same scanning orientation with the other parallel strips. If all the strips were indifferently cut from a single sheet outlined in blue for this study, the outstanding strip would have the landscape scanning orientation

instead of the portrait scanning orientation of the parallel strips, which would have invalidated the dose calibration and the resulting dose maps generated and their artifact correction. RCF is a polarizer due to the preferential crystal alignment direction during the chemical spray process of RCF production. The active layer of RCF is made of crystals of a lithium salt which is paramagnetic below its Curie temperature, caused by the spin of the unpaired 2s electrons of lithium ions. These likely explain the reason why RCF has the orientation dependence and the phenomenon that the presence of magnetic field³³ has an impact on RCF read-out including its LA, e.g. RCF irradiated by an MR-linac.³⁴

The unpolarized light from scanner lamp becomes polarized after passing through RCF. The cause of LA is the scanner optical path effect of RCF polarized transmission light.^{35–37} Pérez Azorin *et al.*³⁸ used the polarized light with the polarization direction aligned with RCF coating direction for RCF scans resulting in great reduction of the LA. It is possible that both the active layer crystal preferential orientation and the effective coating direction contribute to the polarization effect. The transmission mode is less noisy and recommended by the GAFChromicTM vendor for scanning transparent RCF types like EBT2, EBT3 and EBT-XD. Méndez *et al.*^{18,39} applied multichannel dosimetry to fourteen application RCFs scanned with both reflection and transmission scanning mode and observed no statistical difference³⁹ between the two in regards to dose map fidelity. Unlike in transmission mode, when a thin glass sheet is needed to compress RCF curvature^{4,30} during the scanning process, the white reflection mat mounted on a transparency unit effectively compresses RCF when using the reflection scanning mode. An Epson[®] Expression 10000XL flatbed scanner has two mobile lamps. One is above the scanner window and located within the scanner cover. This lamp gets activated when using the transmission mode. The other light source/lamp is located below the scanner window for the use of the reflection mode only. We once explored the LA with two fully exposed RCF strips scanned with

the reflection mode and found that the LA in the PV domain appeared to be the severest in channel B and the mildest in channel R, which is opposite to that of the transmission mode. This observation is in line with the phenomenon that transmission and reflection images often complement each other. From the perspective of the optical path, the final intensity collected by the CCD array were the sum of light reflected by the RCF active layer and light reflected by the matte finish of the white reflection mat. Whereas in transmission mode, the light coming from above travels through RCF and directly enters the scanner mirror system before being captured by the CCD in the end.

The method presented in this study does not require any input from either TPS or a different 2-D dosimeter such as a 2-D diode/chamber matrix, or an EPID dosimeter for off-axis output factors involved for this work. It instead only needs to fully expose the RCF calibration strips by a standard open field and with a unique layout during the RCF scanning process as demonstrated in Fig. 2.2. The OAFs were from the leftmost outstanding strip, without any help from a 1-D profiler or alike. All the information including color channel specified OAFs needed for the LA correction was directly from the single-scan RCF layout. This enables RCF to function as an independent high resolution 2-D dosimeter. The 2-D ion-chamber or diode array/matrix is another type of popular 2-D dosimeter with lower resolution but not every clinic has one in operation. In our clinic, patient specific IMRT/VMAT QA is performed by an ArcCHECK[®] CavityPlug[™](Sun Nuclear, Melbourne, FL) system, not by RCF, a 2-D matrix or an electronic portal imaging device(EPID). Unlike the common RCF calibration process, the dose calibration process of the HeliGrid[™] diode array of the ArcCHECK[®] requires the TPS plan of a standard open field, as well as an inserted ion-chamber for the absolute dose scaling.

Other RCF calibration methods exist such as using RCF irradiated by a percentage depth dose(PDD),^{40,41} a wedge^{18,42} and other specially designed dose patterns.

These unique methods have advantages on efficiency as they only require a single exposure of a single RCF sheet as well as a single scan, instead of successive exposures of multiple RCF fragments and they usually involve using a TPS generated plan^{18,42} or a water phantom PDD scan^{40,43} for RCF calibration. The GAFChromicTM vendor instead recommends using 10×10 cm² standard open field to partially irradiate film strips, one at a time. This recommendation is more widely followed possibly due to two reasons. First, performance of the TPS may vary depending on multiple variables, e.g., commercial developer, field size, dose calculation algorithm, beam modeling method, users' commissioning inputs and the specific linear accelerator, either similar or dissimilar. Thus RCF calibration by TPS may be prone to inadvertent bias. Similarly, specially designed dose patterns using a wedge or multileaf collimator (MLC) may bring in more uncertainties aside from the TPS itself. Second, from the reference dosimetry standpoint, readings from an ion-chamber are more directly traceable to a standard calibration laboratory than those of TPS plans which usually have a large number of dose values over a dynamic range. The PDD scan in a water tank is desired but the process is not frequently performed. In this study, film strips were fully exposed successively by a 25×25 cm² standard open field with different MUs and calibrated by an ion-chamber.

Physics intuition is to correct LA in the OD or PV domain. However, RCF thickness non-uniformity, non-uniform open field dose profile and the LA are mixed across the full exposed strips. This work instead made LA corrections in the dose-domain of multichannel dosimetry which compensated non-uniformity of RCF active layer thickness ahead of making corrections on LA. Together with off-axis non-uniform field output measured and fully taken into account by Eq.(2.4), the LA was left solely as the subject of correction.^{11,23} found that the LA and its correction have major dependence on scanners and minor dependence on film lots. Upon the arrival of the new film lot for an end user, calibration is always needed regardless and thus this

study offers an option to characterize and correct LA with no extra work except a unique layout for a single scan. Said differently, the method provides a simple way that uniquely blends RCF calibration and the LA correction into a single-scan. This process is instead of a separate flatbed scanner commissioning process with the measurements exclusively for the correction of LA. EBT3 film is suitable for the dose range from 0.2 Gy to 10 Gy which covers the dose range of this study. The per-fraction maximum dose value of a step-and-shoot IMRT plan usually ranges between 1 and 4 Gy. The plan maximum dose of a rapid-arc VMAT often exceeds 4 Gy. The multichannel dosimetry method requires the slopes of calibration curves of three color channels, i.e., $\dot{D}_k$ to be sufficiently different among the channels, at a given dose number. The slopes of RGB calibration curves increasingly approach each other when dose approaching 10 Gy. To continue the use of multichannel dosimetry for doses near 10 Gy or higher, EBT-XD is the film of choice for doses ranging from 10 Gy to 40 Gy, ideal for stereotactic body radiation therapy (SBRT), stereotactic radiosurgery (SRS) and other higher dose applications. EBT-XD film has the active layer made of a different crystal form²³ of the same chemical as EBT3 to adjust sensitivities for higher dose applications. However, the LA did not vanish for EBT-XD.^{23,44,45} Lewis and Chan²³ also discovered that the LA characterization and correction method for EBT3 can be used in EBT-XD film. They also found that for the RCFs scanned on a particular flatbed scanner, the LA correction coefficients obtained from one film lot can be applied to another lot without negatively affecting the gamma index passing rates.¹¹ The coefficients of the k th color channel, $p_{n,k}$ of Eq.(2.6) only depend on the lateral position, j . For any lateral coordinate, the correction coefficients are the same across all dose levels of interest, as evidenced by Fig. 2.4, and are independent of the OD/PV.

Fig. 2.1 is an illustration of how film strips in Fig. 2.2 were cut and orientated. It is not meant to be that a scan of any unexposed, intact RCF sheet is needed to

implement this method. The single-scan in Fig. 2.2 was all it took for both calibration and the LA correction for any application RCF, such as patient IMRT/VMAT films, flatness symmetry check films. The remaining RCF sheet after cropping the outstanding strip needed in Fig. 2.2 was used as the application RCF for the VMAT plan measurement instead of being wasted. OAFs from all three channels as shown in Fig. 2.3 bore the resemblance to OAFs from the TPS. Those values were then applied to the exposed parallel strips. In Table 2.2, the robustness of the LA correction on the IMRT plan was reflected in the promotion of the gamma passing rates with the tighter criteria 1%/1 mm and 2%/2 mm. The IMRT film was with lower doses and thus less impacted by the LA. For this reason the tighter criteria were used to validate this LA correction method for the IMRT plan. Unlike that of the IMRT film, the profound LA resulted in a number of pixels with gamma index values above the display maximum value, 2, in the dark red area as shown in Figs. 2.7, 2.8 and Fig. 2.9. The display does not mean that those gamma values were all the same and equal to 2. Instead, those regions were with gamma index values well over 2 before the LA correction and below 1 after applying the LA correction.

The method has an advantage on the ease of RCF positioning and the LA correction coordinating. Due to the physical size of RCF, the exposed area of an application RCF always fell into the range covered by the layout in Fig. 2.2 with the portrait scanning orientation. The unexposed, rightmost strip used for scan-to-scan variability correction was also used as a spatial reference for the scans of application RCFs. And in principle there is no need for attention on positioning application RCF as long as the exposed region of RCF is placed within the lateral range covered by the rightmost unexposed film strip. This is regardless of the exact location of application RCF on the scanner window as the LA does not have a dependence on coordinate i . And the rightmost unexposed presents as an object of reference for each application scan, and by referring to it, the lateral positions of interest (j) can always

be correlated to the the global coordinate system (i, j) of the single-scan layout as shown in Fig. 2.2. In practice, one can tape this laterally centered, rightmost unexposed film strip indefinitely up with the scanner window so that any digitized scan would include the application RCF and this entire unexposed strip. In this way, one would tell the definite lateral location of any point of interest on a RCF, in respect to the scanner central axis. Once this rightmost unexposed film strip is fixed on the scanner window for positioning reference, it no longer serves as zero dose film due to the repeated light exposure from the scanner lamp. Thus, one needs another piece of unexposed film as the zero dose. However, this LA correction method does not work for RCF or any part of the RCF positioned beyond the reach of the parallel strips in the lateral direction on a scanner window. LA persists on occasion even with multichannel dosimetry capable of partially mitigating the LA. Cautions and further corrections are advised especially for RCF with high dose and large exposed areas. The LA within the lateral range of interest is often negligible in the blue channel with multichannel dosimetry for low doses of a typical step-and-shoot IMRT distribution. For an end user using the portrait scanning orientation as in this study, we also recommend assessing the expected 2-D dose distribution and adjusting RCF orientation accordingly ahead of dose delivery to assure that the longer span of an exposed area does not stretch along the RCF width. In other words, one should let the longer span of the exposed area expand along the RCF length and then center the exposed area about the scanner central axis to minimize the LA when possible, given that not all planar dose distributions are round-like or square-like.

Epson[®] Expression 10000-12000XL photo flatbed scanners are recommended by the GAFChromic[™] vendor for RCF scanning. The single-scan only refers to the layout in Fig. 2.2, not including application RCF scans such as IMRT/VMAT films, machine commissioning films, etc. For flatbed scanners with a smaller sized scanner window, such as Epson[®] Expression 1680 and Perfection V800 scanners, the unique

layout in Fig. 2.2 would not be able to fit in because the entire layout would be oversized at i direction. An obvious solution is to break the single-scan layout into a double one while keeping the rightmost unexposed film strip for scan-to-scan variability correction and as the object of reference during each scan. This can be done by scanning the outstanding strip together with one or two parallel film strips including the rightmost unexposed strip as the first scan. Then the second scan would include the remaining parallel strips, again with the rightmost unexposed film strip undisplaced.

2.5 Conclusions

An efficient dose-domain LA correction method for multichannel dosimetry is presented. The novel method with a built-in spatial reference strip can be integrated into the one-scan RCF calibration protocol. Also, OAF measurements from a 1-D profiler or a different 2-D dosimeter like a 2-D ion-chamber/diode matrix are not needed with this unique layout. The method corrects the LA in the dose domain of multichannel dosimetry after compensating non-uniform off-axis output from open fields of a linear accelerator and the RCF active layer non-uniformity. It is designed for multichannel dosimetry providing improved gamma passing rates when compared to the TPS calculated plans.

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Chapter 3

A Channel Weighted Analytical Method for Radiochromic Film Dosimetry

This chapter aims to develop and evaluate a channel weighted (CW) analytical method for triple-channel radiochromic film (RCF) dosimetry. Red, green and blue light intensity are attenuated and absorbed differently by the same chemical species contained in the active layer of a RCF. This physical phenomenon is characterized by the color channel-dependent Napierian attenuation coefficients. The CW method uses channel-specific attenuation, correlated by its relative weighting factors specific to each color channel. After weighting the channel-specific attenuation the sum of squared remainder difference between any two color channels is then minimized, providing a triple color channel-weighted method. Four simple geometry plans, two step-and-shoot intensity-modulated radiation therapy (IMRT) plans and a multi-arc volumetric modulated arc therapy (VMAT) plan were used to evaluate the new method, with quantitative comparison to the conventional triple-channel and single-channel RCF dosimetry methods. The plane maximum doses of the treatment planning system (TPS) plans ranged between 25.9 and 826 cGy. All RCFs were irradiated by 6 MV photon beams and scanned per a one-scan protocol using the transmission scanning mode on a flatbed photo scanner. The dose difference maps between RCF measurement and TPS plans were normalized to the plane maximum dose of each TPS calculated plan. For the IMRT and VMAT plans, two-dimensional (2-D) global gamma index analysis was used to compare RCF measured and TPS calculated dose distributions. The mean gamma value was calculated for each IMRT/VMAT plan. For both the simple geometry and IMRT/VMAT plans, the percentage dose difference was averaged across all regions. A 10% threshold (TH) of the plane maximum of each plan was used for all evaluations. Compared to the existing RCF dosimetry methods, the new CW triple channel dosimetry method achieves one of the lowest mean gamma values and mean dose differences across four simple geometry plans and the IMRT/VMAT plans. Better agreement with the TPS calculated plans was found at the lower dose range (0-1 Gy) and higher dose range (5-9 Gy).

3.1 Introduction

Radiochromic film (RCF) is a robust ionization radiation dosimeter with high two-dimensional (2-D) spatial resolution, near-tissue equivalence and physical flexibility. Triple-channel dosimetry simultaneously uses all three (red, green and blue) color channels to optimize dose values instead of using the channels separately and independently. An advantage of the original triple-channel dosimetry method^{1,2} is that it does not require scanning RCF *prior* to irradiation. Triple-channel dosimetry mainly serves two purposes:¹⁻⁴ 1) compensating for film active layer non-uniformities and 2) mitigating/reducing the lateral artifact/parabola effect³⁻¹⁰ (an acute source of error for RCF dosimetry). This work aims to better compensate for such non-uniformities and further reduce the lateral artifact/parabola effect, while maintaining the benefit of the original triple-channel dosimetry method^{1,2} and the popular one-scan protocol¹¹ which eliminate the need to scan RCF *prior* to irradiation. The original triple-channel dosimetry method outdated the double-exposure technique¹² and demonstrated superiority in regards to efficiency and accuracy especially in combination with the widely adopted one-scan RCF protocol,¹¹ which minimizes the number of scans: one scan to digitize all the calibration strips/fragments and another single scan combining an application RCF and the reference strips to eliminate the environmental and inter-scan variability issues.¹¹ The need to scan only irradiated RCF has been one of the advantages of original triple channel dosimetry.^{1,2} This technique enables users to scan each RCF only once^{1,2,11} and to avoid scanning the same RCF twice, both *prior* to irradiation and subsequent to irradiation for both calibration and application RCFs. Van Hoof *et al.*¹³ evaluated the original triple-channel dosimetry method with RCFs irradiated by a 5×5 cm² field and found it performs at least as well as single-channel dosimetry with scanning RCF *prior* to irradiation. This is especially true for RCF with a large exposed area, due to the parabola effect/lateral artifact reduction achieved by triple-channel dosimetry. Various publications in the litera-

tures^{1,2,6,11,13,14} also evaluated triple-channel dosimetry and found it performs better than single-channel dosimetry without scanning RCF *prior* to irradiation. The one-scan protocol in conjunction with triple-channel dosimetry has a dose measurement uncertainty of 1-2%.^{6,11,13} Micke *et al.*¹ outlined, Mayer *et al.*² further developed a channel-independent perturbation¹⁵ with the first-order Taylor expansion. Méndez *et al.*¹⁶ and Pérez Azorín *et al.*¹⁴ followed suit and found that original triple channel dosimetry can be further improved by scanning every RCF *prior* to irradiation and incorporating the information from pre-irradiated RCF scan. However, there are potential issues in scanning RCF before and after irradiation. These include increased uncertainties from different scans^{11,15} and decreased efficiency caused by the doubled workload for scanning and the need for co-registering pre-irradiated and irradiated RCF. Ideally, RCF should be positioned at the exact lateral position on the scanner window before and after the exposure to ensure proper pixel-by-pixel spatial subtraction since the RCF transmission intensity has a lateral coordinate dependence^{3-5,7-9} caused by the lateral artifact or parabola effect. Inter-scan variability¹¹ is another consideration since pre-irradiation and post-irradiation RCF are not digitized in a single-scan.

RCF active layer thickness inhomogeneity^{17,18} caused by the chemical spraying and coating during manufacturing has been a major concern for high fidelity dosimetry, as intensity differences of 3.7% caused by thickness non-uniformities result in a dose determination uncertainty of $\pm 8.7\%$ at 1 Gy¹⁸ using the single red-channel dosimetry method. The intensity of RCF transmitted light is a mixture of multiple factors within which the dominant factor is the dose: the higher the dose, the darker the RCF appears and thus more light is absorbed resulting in less transmission intensity. The lateral artifact, or parabola effect³⁻¹⁰ has color channel dependence and is proportional to dose levels and the perpendicular distance from the scanner central axis (along which the scanner lamp moves). The causes^{4,10,19} of the artifact were theoretic-

cally explained and experimentally verified by Schoenfeld *et al.*^{7,9} and Van Battum *et al.*⁸ Over the low dose range, the accuracy of RCF dosimetry is primarily affected by the active layer inhomogeneity due to the low signal-to-noise ratio (signal from the absorbed dose is relatively weak when compared to RCF active layer non-uniformity).¹ As the dose level increases resulting in an increased signal-to-noise ratio, lateral artifact/parabola effect gradually replaces the active layer non-uniformity as the primary source of error for high fidelity dosimetry. Triple-channel dosimetry greatly mitigates the lateral artifact for the common dose range of step-and-shoot IMRT plans.^{1-4,11} However, the artifact remains an acute source of error for RCFs with higher doses and large exposed area. Therefore, it is crucial to properly compensate for dose independent factors and optimize the dose value at any point of interest from the combined effect of thickness non-uniformity, the lateral artifact/parabola effect and radiation induced polymerization.

EBT3 film is a 2-D dosimeter for the optimum dose range 0.2-10 Gy (specified by the manufacturer) and is recommended to be digitized on a high-quality flatbed color scanner. In scanner operation, the red (R), green (G) and blue (B) wavelength components from a scanner lamp are filtered by an optical system and then captured by a CCD camera, forming three intensity channels. The flatbed scanner light source emits light containing continuous wavelengths in the visible light spectrum between infrared and ultraviolet. Particular color channels, i , are attenuated differently by the same material, denoted by different Napierian attenuation coefficients μ_i across the electromagnetic spectrum. This work is based on the physical observation that visible light of red, green and blue intensity are attenuated differently by the same chemical species, in this case, the active layer of RCF, and, therefore, need to be weighted accordingly.

3.2 Materials and methods

3.2.1 The channel weighted (CW) approach

Although a planar dosimeter, RCF is a thin three-dimensional (3-D) sheet with coordinates x, y, z , where x and y are the planar coordinates and the z coordinate represents the film thickness. The attenuation of light during RCF scanning can be characterized by the Beer-Lambert law:

$$\frac{I_i(x, y)}{I_0} = \exp \sum_{k=1}^M \left(-\sigma_k \int_0^l n_k(z) dz \right), \quad (3.1)$$

where I_0 and $I_i(x, y)$ are the pixel value (PV) intensity of incident and transmitted light respectively at a location (x, y) for color channel i ($i = R, G$ or B), $n_k(z)$ is the number density of the k th attenuator, and l is the path length of the light through the k th attenuator at the specific attenuation cross section σ_k . σ_k has the dimension of an infinitely small area; it expresses the likelihood of interaction between the photons of the beam and the molecules of the attenuator species and thus has a dependence on photon energy spectrum, or wavelength bandwidth of visible light, in this case, color channel i ,

$$\sigma_k = \sigma_k^i. \quad (3.2)$$

The size of pixels from a scanner generated image is a constant and can be adjusted from the scanner driver via CCD detector arrays. The active layer of RCF is sandwiched by two layers of clear polyester¹⁵ which is known to have near-zero attenuation ($\mu_i = 0$) for the visible light spectrum, such that the exponential term is very close to 1. For wavelengths within the visible bandwidth, the items such as the clear glass sheet used for RCF compression and the scanner window are clear and allow nearly total transmission with very little attenuation. The only remaining attenuator is the RCF active layer which is a mixture of marker dye and lithium pentacosa-10,12-

diynoate (LiPCDA). Thus, the number of attenuators in Eq. (3.1) reduces to $M = 1$. It is natural to assume uniform $n(z)$ across the thickness of RCF because the active layer is made of material of the same mixture, meaning

$$n(z) = n_D. \quad (3.3)$$

It has been noted that the number density of active layer, n_D has a dose (D) dependence: how densely the chain polymerization packs LiPCDA crystal (determines how transparent the active layer of RCF appears) is proportional to the absorbed dose.¹⁵ However, the thickness varies at different locations of cross sections. The thickness of the active layer of RCF is nominally $27 \mu m$ which facilitates uniform attenuation along the optical path. The Napierian attenuation coefficient then becomes

$$\mu_i^D(z) = \sigma_k^i n_D \quad (3.4)$$

which is assumed to be uniform at z direction within the range of RCF thickness. This allows the Beer-Lambert law for the attenuation of light by RCF during the scanning process to be written as

$$\frac{I_i(x, y)}{I_0} = \exp \left(- \int_0^{\tau(x, y)} \mu_i^D(z) dz \right) \quad (3.5)$$

where $\tau(x, y)$ is the local thickness of the RCF active layer at position (x, y) . The underlying mechanism of RCF is radiation induced polymerization. The transmission of RCF relates largely to the amount of polymerization, which depends on the amount of ionizing radiation exposure. The higher the dose, the less transparent RCF appears to be because the amount of polymerization scales with the amount of radiation dose within certain range (Dose dependence passed from n_D to μ_i^D per Eq.(3.4), from subscript to superscript). Note that the other dependence of μ_i^D is the R, G or B

color channel i . For an RGB flatbed color scanner with the setting of 16 bits per channel, the maximum, unattenuated signal value, i.e. PV intensity I_0 of all three color channels are assigned to approximately the same value, crosswise and lengthwise, of $2^{16} - 1$ or 65535. If there is no observed signal, the PV intensity is 0. The possible range of PV intensity has to be between 0 and 65535 per the scanner operation. This can be confirmed by reading an empty scan without any RCF or attenuator positioned on the scanner window. Slight variations of this uniform background PV intensity, 65535, exist due to the electronic noise from the scanner circuit. Given the amount of attenuation varies with thickness, from Eq. (3.5), the optical density (OD) value, $d_i(\tau(x, y))$ of a given dose D at each point (x, y) for color channel i can be expressed as a function of its local thickness $\tau(x, y)$,

$$d_i(\tau(x, y)) = -\log_{10} \left(\frac{I_i(x, y)}{I_0} \right) = \log_{10} e \cdot \mu_i^D \tau(x, y). \quad (3.6)$$

The densitometric function correlates mean OD values, of a just sufficient number of pixels N from uniform exposed ROIs, to dose values, i.e. $\{\bar{d}_i, \mathcal{D}\}$ via the densitometry curve for each color channel i .

$$D_i(\bar{d}_i) = \frac{c_i - b_i 10^{\bar{d}_i}}{a_i 10^{\bar{d}_i} - 1} \quad (3.7)$$

Mean thickness $\bar{\tau}$ of a ROI containing N pixels,

$$\bar{\tau} = \frac{1}{N} \sum_{xy} \tau(x, y) \quad (3.8)$$

yields a mean OD, $\bar{d}_i$ of the ROI

$$\bar{d}_i = \frac{1}{N} \sum_{xy} d_i(x, y) = \log_{10} e \cdot \mu_i^D \bar{\tau} \quad (3.9)$$

One can find the straightforward relationship between $\bar{d}_i$ and $\bar{\tau}$ from Eq.(3.9). Thus, the dose calibration function, Eq.(3.7) at any given dose can be expressed as a composite function ($\mathbf{D}_i(\bar{\tau})$) of a single variable, $\bar{\tau}$,

$$\mathbf{D}_i(\bar{\tau}) = D_i(\bar{d}_i(\bar{\tau})) = \frac{c_i - b_i 10^{\bar{d}_i(\bar{\tau})}}{a_i 10^{\bar{d}_i(\bar{\tau})} - 1}. \quad (3.10)$$

The chain rule is needed to express the derivative of the composite function above, Eq.(3.10),

$$\mathbf{D}'_i(\bar{\tau}) = D'_i(\bar{d}_i(\bar{\tau}))\bar{d}'_i(\bar{\tau}) = \log_{10} e \cdot D'_i(\bar{d}_i(\bar{\tau}))\mu_i^D \quad (3.11)$$

wherein $D'_i(\bar{d}_i(\bar{\tau}))$ is the first derivative of the calibration function, Eq.(3.7) with respect to the variable $\bar{d}_i(\bar{\tau})$:

$$D'_i(\bar{d}_i(\bar{\tau})) = \frac{b_i 10^{\bar{d}_i(\bar{\tau})} \ln 10}{a_i 10^{\bar{d}_i(\bar{\tau})} - 1} - \frac{(a_i 10^{\bar{d}_i(\bar{\tau})} \ln 10)(c_i - b_i 10^{\bar{d}_i(\bar{\tau})})}{(a_i 10^{\bar{d}_i(\bar{\tau})} - 1)^2}. \quad (3.12)$$

The dosimetric goal of RCF is to project a dose map with uniform sensitivity, i.e. the same uniform thickness, $\bar{\tau}$ assumed for dose calibration. However, with variable thickness $\tau(x, y)$ of the active layer, compared to an effective mean thickness $\bar{\tau}$ during RCF dose calibration, there can be deviations when evaluating Eq.(3.7) directly at the local OD value, $d(\tau(x, y))$ at position (x, y) whose thickness is $\tau(x, y)$. For smooth functions, Eq.(3.7) are differentiable within the domain of interest: Eq.(3.12). The composite function Eq.(3.10) of the i th color channel can be evaluated about a local

thickness $\tau(x, y)$ per Taylor's theorem at position (x, y) as

$$\begin{aligned}
\mathbf{D}_i(\bar{\tau}; x, y) &= \mathbf{D}_i(\tau(x, y)) + \frac{\mathbf{D}'_i(\tau(x, y))}{1!}(\bar{\tau} - \tau(x, y)) + \sum_{n=2}^{\infty} \frac{\mathbf{D}_i^{(n)}(\tau(x, y))}{n!}(\bar{\tau} - \tau(x, y))^n \\
&= D_i(d_i(\tau(x, y))) + \log_{10} e \cdot \mu_i^D \frac{D'_i(d_i(\tau(x, y)))}{1!}(\bar{\tau} - \tau(x, y)) + \\
&\quad \sum_{n=2}^{\infty} (\log_{10} e)^n \cdot (\mu_i^D)^n \frac{D_i^{(n)}(d_i(\tau(x, y)))}{n!}(\bar{\tau} - \tau(x, y))^n
\end{aligned} \tag{3.13}$$

wherein $D'_i(d_i(\tau(x, y)))$ and $D_i^{(n)}(d_i(\tau(x, y)))$ are the first and the n th derivative of the calibration function (Eq.(3.7)) evaluated at the local OD value $(d_i(\tau(x, y)))$ at location (x, y) with its local thickness $\tau(x, y)$ respectively. From Eq.(3.6), one can choose one color channel X as a base to generate weighting factors w_i for all three channels. This selection can be any channel, i.e. $X = \text{R, G or B}$.

$$w_i(x, y) = \frac{d_i(\tau(x, y))}{d_X(\tau(x, y))} = \frac{\mu_i^D}{\mu_X^D} = \frac{\mu_i^D(\bar{\tau} - \tau(x, y))}{\mu_X^D(\bar{\tau} - \tau(x, y))} \tag{3.14}$$

For example, if one chooses color channel G, the resulting w_G for color channel G is 1 across all locations (x, y) . Recall that during the dose calibration, three color channels are interchangeable and assigned to the same dose value at a ROI with mean thickness $\bar{\tau}$, that is,

$$\mathbf{D}_i(\bar{\tau}) = \mathcal{D} = \bar{\mathbf{D}}_i(\bar{\tau}). \tag{3.15}$$

Such is the goal of triple-channel dosimetry, to evaluate the dose value at any point of interest with coordinate (x, y) on an application RCF at the uniform thickness $\bar{\tau}$ instead of its actual local thickness $\tau(x, y)$,

$$D(\bar{\tau}; x, y) = \mathbf{D}_i(\bar{\tau}; x, y) = \bar{\mathbf{D}}_i(\bar{\tau}; x, y) \tag{3.16}$$

Note that the three channels are interchangeable and treated equally since the unattenuated PV intensity, I_0 is mapped to the same, maximumly allowed value 65535

for each color channel at each point (x, y) . It is the Napierian attenuation coefficient that is weighted according to Eq.(3.14). Given that $\mu_i^D(\bar{\tau} - \tau(x, y))$ is a small term and from Eqs.(3.13) and (3.14), the remainder term of the linear approximation for the color channel i is:

$$\sum_{n=2}^{\infty} (\log_{10} e)^n \cdot \frac{D_i^{(n)}(d_i(\tau(x, y)))}{n!} (w_i(x, y) \mu_X^D(\bar{\tau} - \tau(x, y)))^n = D(\bar{\tau}; x, y) - D_i(d_i(\tau(x, y))) - \log_{10} e \cdot \frac{D_i'(d_i(\tau(x, y)))}{1!} w_i(x, y) \mu_X^D(\bar{\tau} - \tau(x, y)). \quad (3.17)$$

The error of single-channel dosimetry differs from one color channel to another. Ideally, after the triple-channel optimization, the error term represented by the remainder should be equal or very close among all three channels. To minimize the remainder differences between any two color channels i and j , the sum of the squared differences can be expressed as:

$$S(\mu_X^D(\bar{\tau} - \tau(x, y))) = \sum_{i \neq j} \left(\sum_{n=2}^{\infty} (\log_{10} e)^n \cdot \left(\frac{D_i^{(n)}(d_i(\tau(x, y)))}{n!} (w_i(x, y) \mu_X^D(\bar{\tau} - \tau(x, y)))^n - \frac{D_j^{(n)}(d_j(\tau(x, y)))}{n!} (w_j(x, y) \mu_X^D(\bar{\tau} - \tau(x, y)))^n \right) \right)^2 \quad (3.18)$$

This sum of squared difference is a function of one unknown variable, $\mu_X^D(\bar{\tau} - \tau(x, y))$. This is instead of three variables, $\mu_i^D(\bar{\tau} - \tau(x, y))$ since the remaining two variables can be determined by the weighting factors in Eq.(3.14). By inserting Eq.(3.17) into Eq.(3.18), the order of $\mu_X^D(\bar{\tau} - \tau(x, y))$ is reduced to 1. The derivative of the sum function in respect to $\mu_X^D(\bar{\tau} - \tau(x, y))$ is needed to minimize Eq.(3.18):

$$S'(\mu_X^D(\bar{\tau} - \tau(x, y))) = 0. \quad (3.19)$$

This $\mu_X^D(\bar{\tau} - \tau(x, y))$ can be solved from the equation above. From the weighting factor as expressed in Eq.(3.14), one can get this channel specific term

$$\begin{aligned} \mu_i^D(\bar{\tau} - \tau(x, y)) &= w_i(x, y) \mu_X^D(\bar{\tau} - \tau(x, y)) = -w_i(x, y) \cdot \\ &\frac{\sum_{i \neq j} (D_i(d_i(\tau(x, y))) - D_j(d_j(\tau(x, y))))((w_i(x, y)D'_i(d_i(\tau(x, y)))) - w_j(x, y)D'_j(d_j(\tau(x, y))))}{\log_{10} e \cdot \sum_{i \neq j} (w_i(x, y)D'_i(d_i(\tau(x, y)))) - w_j(x, y)D'_j(d_j(\tau(x, y))))^2} \end{aligned} \quad (3.20)$$

Combining Eqs.(3.13), (3.16) and (3.20), one can find the final dose value from this channel weighted triple-channel dosimetry as

$$\begin{aligned} D(\bar{\tau}; x, y) &= \bar{\mathbf{D}}_i(\bar{\tau}; x, y) = \bar{D}_i(d_i(\tau(x, y))) - \left(\sum_i w_i(x, y) D'_i(d_i(\tau(x, y))) \right) \cdot \\ &\frac{\sum_{i \neq j} (D_i(d_i(\tau(x, y))) - D_j(d_j(\tau(x, y))))((w_i(x, y)D'_i(d_i(\tau(x, y)))) - w_j(x, y)D'_j(d_j(\tau(x, y))))}{m \sum_{i \neq j} (w_i(x, y)D'_i(d_i(\tau(x, y)))) - w_j(x, y)D'_j(d_j(\tau(x, y))))^2} \end{aligned} \quad (3.21)$$

wherein $\bar{\mathbf{D}}_i(\bar{\tau}; x, y)$ and $\bar{D}_i(d_i(\tau(x, y)))$ are arithmetic means of all the color channels, and m is the total number of color channels, $m = 3$ in this case.

3.2.2 Original triple-channel dosimetry

Micke *et al.*¹ outlined the multichannel method using a channel-independent disturbance map¹⁵ and the least squares for non-uniformity correction. Mayer *et al.*² further developed the channel-independent perturbation/disturbance method and also provided a solution to the method by Micke *et al.*¹ For comparison with the new, channel-weighted method, we have implemented both the method by Mayer *et al.* and Mayer *et al.*'s enhanced solution to the method of Micke *et al.*¹ The two methods generate identical dose distributions, combined as Micke-Mayer method (MM), i.e., the subtraction of one from the other yields zero across all regions. This equivalence has also been validated in this work. The MM method performs better than

single-channel dosimetry.^{1,2,6,13,14,16} It has also been reported² that the arithmetic mean value (MN) of all three channels, $\bar{D}_i(d_i(\tau(x, y)))$ can closely approximate the optimized dose value by Mayer *et al.* if certain mathematical conditions are met. The MN approach has been tested² and demonstrated comparable accuracy compared to the optimized approach of Mayer *et al.* The underlying assumption of MN approach is that $\mu_i^D(\bar{\tau} - \tau(x, y)) = 0$, also neglecting any connection between channels, like in Eq.(3.14). None of the original methods require scanning RCF films *prior* to irradiation which has been an advantage of triple-channel dosimetry aside from the improved dose map fidelity. In addition, Mayer *et al.*² also found that both MM and MN approach performed better than other RCF dosimetry methods at the time including the dual and hybrid channel dosimetry methods.

Micke *et al.*¹ suggested that the multichannel method is symmetric with respect to all the color channels and that dose values are given in three color channels and are very close between channels after the triple-channel optimization. Micke *et al.*¹ did not specify which one of the three channel provides the most probable dose after the triple-channel optimization. Mayer *et al.*² instead gave one optimized or most probable value per location^{2,14,16} which is equivalent to the average of the three optimized dose values put forth by Micke *et al.*¹

In this work the lateral artifact/parabola effect also was not corrected separately, consistent for appropriate comparison with the original triple-channel dosimetry and the widely adopted one-scan protocol.^{1,2,6,10,11,14}

3.2.3 Single-channel dosimetry

RCF dose calibration is often accomplished by pairing the averaged OD values of film regions to known dose values $\mathcal{D}$, i.e., $\{\bar{d}_i, \mathcal{D}\}$. The calibration functions essentially stabilize at an effective mean thickness $\bar{\tau}$, which is usually different from a local or

point thickness $\tau(x, y)$ at coordinates (x, y) on an application film. Single-channel dosimetry gives dose maps (R, G and B) from the following equation,

$$D_i(d_i(x, y)) = \frac{c_i - b_i 10^{d_i(x, y)}}{a_i 10^{d_i(x, y)} - 1} \quad (3.22)$$

wherein $d_i(x, y)$ or $d_i(\tau(x, y))$ is the local OD value at (x, y) on RCF with its local thickness $\tau(x, y)$, a_i, b_i and c_i are channel specific coefficients determined by curve fittings to Eq.(3.7). The R, G and B channels are not symmetric or interchangeable for single-channel dosimetry. The red channel is used^{1, 5, 6, 10, 11, 14, 16} for single-channel dosimetry because the absorption spectral changes have been found to be more sensitive to dose for the wavelength bandwidth of red light, known as the primary peak.²⁰ There is notable difference between Eq.(3.7) and (3.22) and one should not confuse the mean OD used for dose calibration $\{\bar{d}_i, \mathcal{D}\}$ with $\{d_i, D_i(d_i)\}$. $\{d_i, D_i(d_i)\}$ is used to estimate dose values via single-channel dosimetry in Eq.(3.22). Single-channel dosimetry does not correlate different Napierian attenuation coefficients (μ_i^D) among the three channels. It also ignores the thickness variation between a local thickness $\tau(x, y)$ and the effective mean thickness $\bar{\tau}$ of the dose calibration process as mentioned in the previous section.

3.2.4 Data analysis

All the RCF dosimetry approaches along with the quantitative comparison methods in this study were programmed in MATLAB R2018b, as were the data analysis and generation of figures. Non-linear least squares was used for fitting data points to dose calibration functions.

3.2.5 The evaluation method

Four $20 \times 20 \text{ cm}^2$ simple-geometry plans, noted as S1, S2, S3 and S4 along with two step-and-shoot IMRT plans and a multi-arc VMAT plan (abbreviated as N1, N2 and A1 respectively) were selected from RayStation6 (RaySearch Laboratories, Stockholm, Sweden) treatment planning system (TPS). A $30 \times 30 \times 10 \text{ cm}^3$ Solid Water[®] phantom (Gammex, Middletown, WI) was CT-scanned on a Discovery ST hybrid PET/CT scanner (GE Healthcare, Chicago, IL). The CT image set of the phantom was exported to TPS as a QA phantom to calculate the plans for comparison. The plane maximum dose was 259, 314 and 826 cGy for N1, N2 and A1 respectively. For $20 \times 20 \text{ cm}^2$ simple-geometry plans, 25, 50, 598 and 797 MUs were delivered for the plan S1, S2, S3 and S4 respectively. The dose difference map is calculated by subtracting TPS plan from RCF measurement. Two-dimensional gamma index analysis²¹ was used for IMRT/VMAT dose map comparison with RCF measurement as reference and TPS plan as evaluation.^{22,23} A 10% threshold (TH) of the plane maximum of each plan was used for all evaluations. The TPS plans were resized to match the pixel spacing of scanned RCF images. The RCF dosimetry methods compared include three triple-channel dosimetry methods (CW, MM and MN) and the single red-channel (R) dosimetry method.

3.2.6 Irradiation and scanning

All GAFChromic[™] EBT3 (Ashland, Bridgewater, NJ) films including the calibration strips were irradiated in the coronal plane at 5 cm depth of a $30 \times 30 \times 10 \text{ cm}^3$ Solid Water[™] phantom with SSD=95 cm using 6 MV photon beam from a Versa[™] HD linear accelerator (Elekta, Stockholm, Sweden). The calibration strips were irradiated one at a time¹¹ with dose levels between 0 and 10 Gy. The RCF scans were performed at least 72 hours after irradiation on an Expression 10000 XL photo

scanner (Epson America, Los Alamitos, CA) with the transmission scanning mode and the portrait scanning orientation. The flatbed scanner was warmed up for 10 minutes by performing empty scans prior to the film scans. The scan settings were 48-bit (16-bit per channel) RGB at 72 dpi resolution,¹¹ uncompressed TIFF image with all color correction features turned off. RCFs were handled per recommendations of AAPM TG-55¹² and the one-scan protocol.¹¹ The exposed areas of the RCFs were laterally centered on the scanning window to minimize the impact from any lateral artifact/parabola effect. In order to test the lateral artifact mitigation/reduction capability of this channel-weighted approach, the exposed area of the VMAT film was displaced laterally approximately 3 inches away from the scanner central axis on the scanning window to stress any lateral artifact/parabola effect. An unexposed film strip was used to eliminate scan-to-scan variabilities between the calibration scan and application scans.¹¹ A thin clear glass plate was used to compress RCF during the scanning process to avoid the Callier effect arising from the RCF curvature.²⁴ The entire process including the irradiation and scanning are performed per the one-scan protocol,¹¹ following the GAFChromicTM EBT3 film user guide.

3.3 Results

Figs. 3.1)-3.5 are the dose difference maps configured in the order of the plane maximum dose (S1, N1, N2, S3, A1), from the lowest 25.9 cGy of the 20×20 cm² simple geometry plan to the highest 826 cGy of the VMAT plan. EBT3 RCF is capable of high resolution measurement. For each RCF measurement, there are several hundred thousand pixels with TH 10% with the recommended 72 dpi used in this work. The average dose differences are therefore statistically meaningful and are summarized in Table 3.3 for the seven evaluation plans. For the IMRT plans, N1 and N2, the mean gamma values are summarized in Table 3.1 and 3.2. The triple-channel RCF dosime-

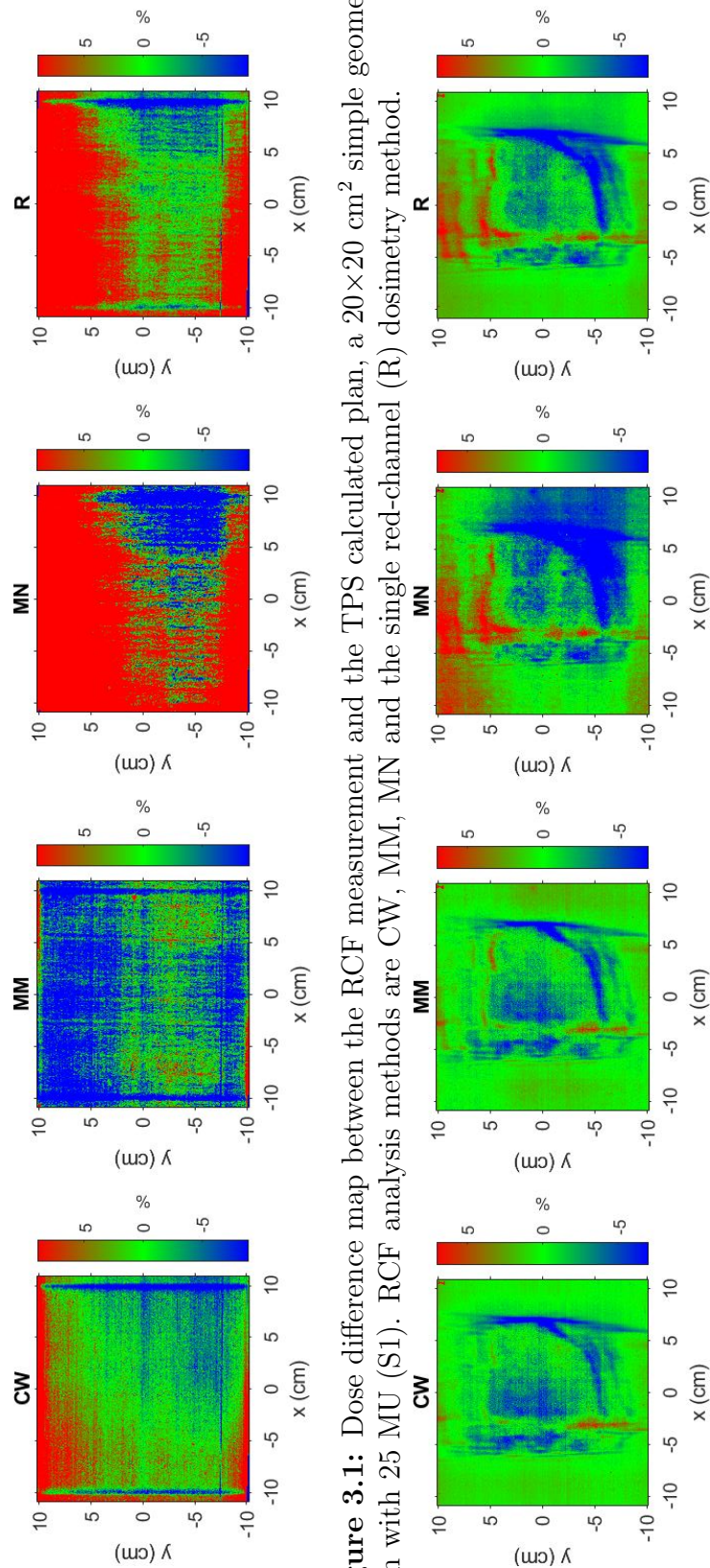


Figure 3.1: Dose difference map between the RCF measurement and the TPS calculated plan, a 20×20 cm² simple geometry plan with 25 MU (S1). RCF analysis methods are CW, MM, MN and the single red-channel (R) dosimetry method.

Figure 3.2: Dose difference maps of a step-and-shoot IMRT plan: N1

try methods compared are CW, MM and MN. For the VMAT plan, N1, the gamma passing rates (the mean gamma values) of 2%/2 mm criteria are 100% (0.203) for CW, 92.1% (0.335) for MM, 94.7% (0.390) for MN and 83.2% (0.569) for the single red-channel (R) dosimetry method.

For the CW method, the color channel chosen (X) for Eq.(3.14) does not affect the outcome of the dose maps since R, G and B color channels were treated equally and mathematically interchangeable.

Table 3.1: Passing rates ($\gamma < 1$) of gamma index analysis and mean gamma value for 2%/2 mm and 2%/3 mm criteria with the TH 10% of the IMRT plan, N1.

	CW		MM		MN		R	
Criteria	$\gamma < 1$	$\bar{\gamma}$	$\gamma < 1$	$\bar{\gamma}$	$\gamma < 1$	$\bar{\gamma}$	$\gamma < 1$	$\bar{\gamma}$
2%/2 mm	94.5%	0.370	93.9 %	0.370	73.6%	0.693	84.3 %	0.571
2%/3 mm	96.9%	0.286	96.9 %	0.286	85.1%	0.521	95.6 %	0.438

Table 3.2: Passing rates of gamma index analysis and mean gamma value for 2%/3 mm and 2%/2 mm tolerance with the TH 10% of the IMRT plan, N2.

	CW		MM		MN		R	
Criteria	$\gamma < 1$	$\bar{\gamma}$	$\gamma < 1$	$\bar{\gamma}$	$\gamma < 1$	$\bar{\gamma}$	$\gamma < 1$	$\bar{\gamma}$
2%/2 mm	99.1%	0.271	99.4 %	0.276	65.0%	0.852	82.2 %	0.617
2%/3 mm	99.8%	0.206	99.8 %	0.210	75.6%	0.682	87.9 %	0.500

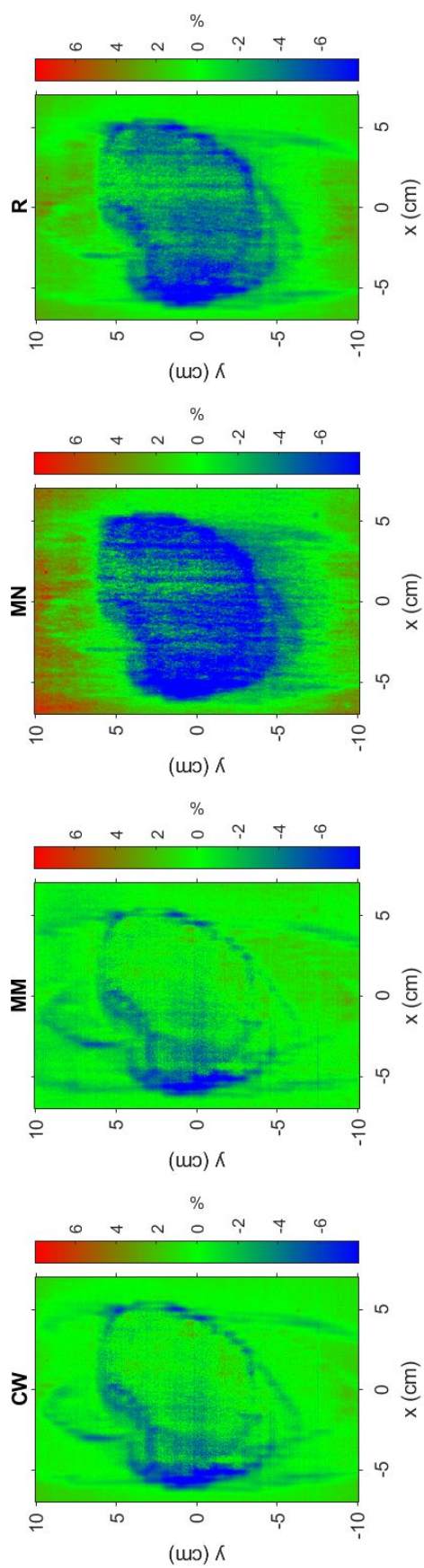


Figure 3.3: Dose difference map of a step-and-shoot IMRT plan: N2

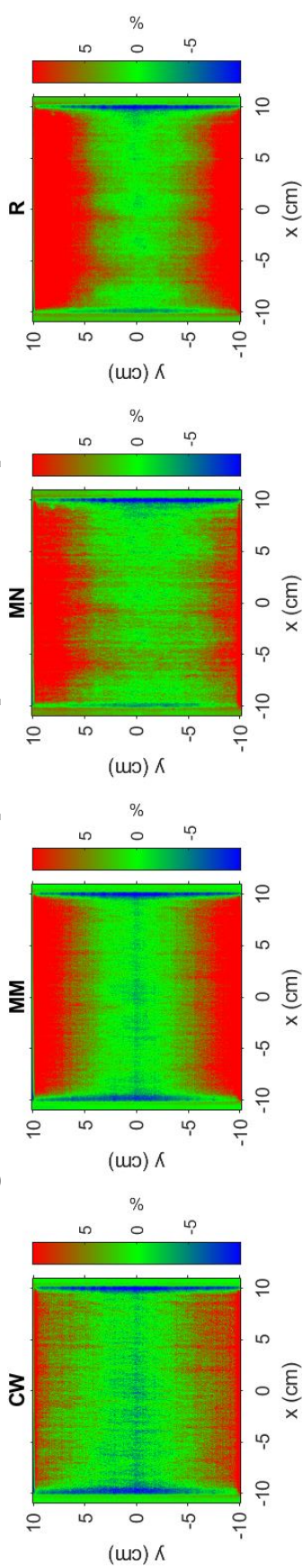


Figure 3.4: Dose difference map of the 20x20 cm² simple geometry plan with 598MU (S3).

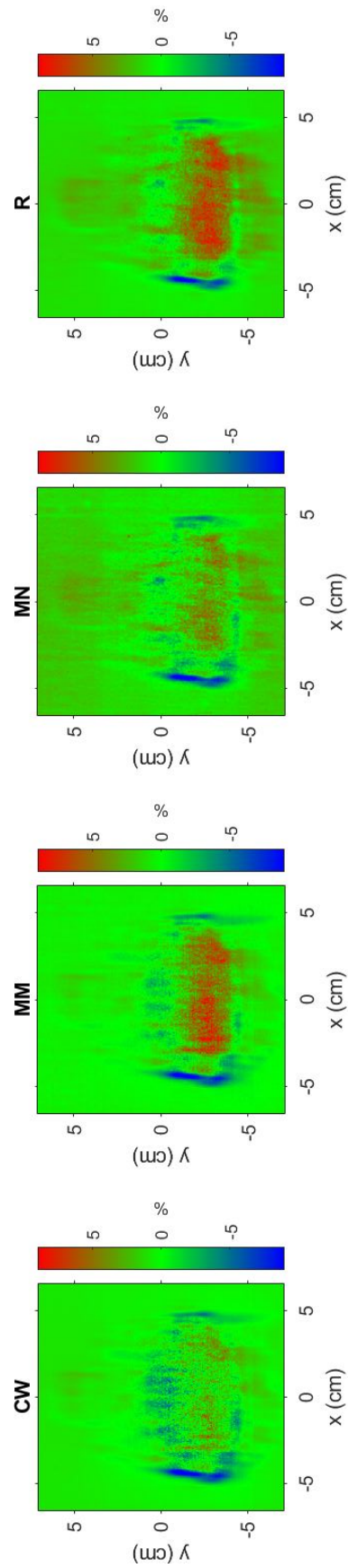


Figure 3.5: Dose difference map of the multi-arc VMAT plan (A1). Note that the exposed area of the VMAT film was laterally positioned about 3 inches away from the scanner central axis on the scanner window to stress any lateral artifact/parabola effect.

Table 3.3: Passing rates for 5% dose difference (dd) tolerance and mean dose difference ($\overline{dd}$) with the TH 10% for each of the seven evaluation plans. RCF dosimetry methods compared are CW, MM, MN and the single red-channel (R) dosimetry method.

Plan	CW		MM		MN		R	
	dd<5%	$\overline{dd}$	dd<5%	$\overline{dd}$	dd<5%	$\overline{dd}$	dd<5%	$\overline{dd}$
S1 (25 MU)	72.0%	3.9%	47.4 %	6.0%	31.0%	8.8%	46.4 %	6.9%
S2 (50 MU)	87.8%	2.9%	79.3 %	3.3%	36.0%	8.1%	59.4%	5.0%
N1	94.4%	2.0%	93.5 %	2.1%	73.8%	3.8%	88.2%	2.9%
N2	96.4%	1.4%	96.7 %	1.4%	68.3%	3.9%	89.0%	2.6%
S3 (598 MU)	75.0%	3.4%	58.6 %	4.9%	63.8%	4.6%	52.8%	6.1%
S4 (797 MU)	87.1%	2.6%	53.4 %	6.0%	61.9%	4.5%	41.6%	8.1%
A1	98.0%	1.3%	91.4 %	1.8%	98.0%	1.8%	88.8%	2.4%

3.4 Discussion

CW and MM show comparable agreement with the TPS for the step-and-shoot IMRT plans, N1 and N2. Better agreement with the TPS are found using CW than MM and MN for dose ranges between 0.2-0.6 Gy and 5-9 Gy. CW reduces the lateral artifact/parabola effect more effectively than MM and MN as shown in Figs.3.4 and 3.5. Note that in Fig.3.1, the plane maximum dose is 25.9 cGy and, therefore, a 5% dose difference represents an absolute dose difference of only 1.3 cGy. In this work, it was observed that MN delivers better agreement with TPS than MM only at the high dose range, 5-9 Gy. At the lower dose range (Figs. 3.1-3.3), MM shows better agreement with TPS than MN.

The dose map fidelity at very low dose levels has a strong dependence on the

RCF active layer inhomogeneity due to the low signal-to-noise ratio.¹ The lateral artifact/parabola effect is known to have minimal presence at this dose level especially when using triple-channel dosimetry. Thus, the large open field simple geometry plans with 25 and 50 MU were selected to evaluate the new CW method. Using simple geometry plans can avoid uncertainties from wedge, MLC, gantry, collimator angles and other beam modifiers. The main purpose of this study is to evaluate and compare the RCF dosimetry methods in the context of IMRT/VMAT QA. This approach is different from the purpose of routine IMRT/VMAT QA. Comparing RCF measurement to the TPS calculated plans alone might not be sufficient given the existence of other 2-D dosimeters, such as 2-D chamber/diode matrix devices and EPID dosimeter. But not every clinic has such 2-D dosimeters in operation. In our clinic, the IMRT/VMAT QA is performed with the ArcCHECK CavityPlugTM system not with RCF or MatriXX.

Dose difference is the most straightforward way to compare two dose distributions.^{22,23} However, IMRT/VMAT dose distributions usually have gradients. A relatively small misalignment between the two steep dose gradients can show large dose differences,^{21,22} i.e., the dose difference is oversensitive to the small spatial offsets.^{22,23} The gamma index was invented to mitigate this effect^{22,23} by having two axes, dose difference and distance contribute equally to the gamma index. For example, in Figs. 3.2, 3.3 and 3.5, large dose differences (>4%) in CW and MM are observed at some high gradient areas as shown in blue. The resulting gamma index values of those areas were smaller than 1.0 in the corresponding gamma maps with criteria 2%/ 2 mm. This is because the final gamma index value of a particular reference point is the minimum gamma value after evaluating all the points within the acceptance ellipse area. Those evaluation points have a relative large dose range within a small distance due to the steep dose gradient. Low *et al.*²³ summarized the limitations^{22,23} of the gamma index as discussed by other authors. For simple geometry plans (S1-S4),

gamma index analysis was not used since the plans were irradiated by the large open field with little dose gradient.

3.4.1 Dose calibration with PV, netPV, OD and netOD

Dose calibration can be done by linking the known dose numbers to PV, netPV, OD or netOD values for each color channel i . However, using netPV or netOD requires scanning all RCFs (including both calibration and application RCFs) *prior* to irradiation. The definitions and its physical implications are summarized as the following expressions:

$$\text{PV}_i = [I_i(x, y)]_{irr} = I_0 e^{-\mu_i^D \tau(x, y)}, \quad (3.23)$$

$$\text{netPV}_i = [I_i(x, y)]_{non} - [I_i(x, y)]_{irr} = I_0 \left(e^{-\mu_i^{D=0} \tau(x, y)} - e^{-\mu_i^D \tau(x, y)} \right) \quad (3.24)$$

wherein $[I_i(x, y)]_{irr}$ is the transmitted PV intensity pixel value at (x, y) on the irradiated RCF, and $[I_i(x, y)]_{non}$ is the corresponding transmitted PV intensity value *prior* to irradiation. $\mu_i^{D=0}$ is the Napierian attenuation coefficient for the i th color channel at dose level 0 cGy, i.e. unexposed RCF.

$$\text{OD}_i = [d(x, y)]_{irr} = -\log_{10} \frac{[I_i(x, y)]_{irr}}{I_0} = -\log_{10} \frac{\text{PV}_i}{I_0} = \log_{10} e \cdot \mu_i^D \tau(x, y), \quad (3.25)$$

$$\text{netOD}_i = [d(x, y)]_{irr} - [d(x, y)]_{non} = -\log_{10} \frac{[I_i(x, y)]_{irr}}{[I_i(x, y)]_{non}} = \log_{10} e \cdot (\mu_i^D - \mu_i^{D=0}) \tau(x, y) \quad (3.26)$$

wherein $[d_i(x, y)]_{irr}$ is the OD value at (x, y) on the irradiated RCF, and $[d_i(x, y)]_{non}$ is its corresponding OD value *prior* to irradiation. The equations above are applicable to both the less noisy transmission scanning mode recommended by the RCF vendor and the reflective scanning mode (used with the white matte finish mounted on the scanner

transparency unit). However, the underlying optical path for the reflective scanning mode is a combination of reflectance and transmittance which would double the local thickness $\tau(x, y)$ in the expressions above. Note that OD is just PV in logarithmic scale instead of the linear scale demonstrated by Eq.(3.25), so there is no actual difference between OD and PV. The dose calibration in this work was performed without scanning RCF *prior* to irradiation (as was done in the original triple-channel dosimetry method). The fidelity of a dose map, Eq.(3.21) relies on the goodness of fit of the dose calibration functions (Eq.(3.7)) and the derivatives (Eq.(3.12)) of the dose calibration. During the dose calibration process, careful attention must be paid to center the exposed areas of calibration strips around the scanner central axis, selecting ROIs across and about the scanner central axis with just sufficient pixels to minimize any impact from the lateral artifact/parabola effect and to ensure that no apparent outliers are included when fitting data points to the calibration functions.

This work demonstrates an algorithm that maintains the high efficiency and low uncertainty aspect of the original triple-channel dosimetry^{1,2} and is compatible with the widely adopted one-scan protocol,¹¹ that is, without using netOD, netPV or equivalent for dose calibration and dose map generation. Also Eqs.(3.8)-(3.10) are in context of the widely adopted one-scan protocol,¹¹ as recommended by the GAFChromicTM vendor, which includes selecting uniformly exposed, laterally centered ROIs in a single-scan and assigning known dose values accordingly. Other RCF calibration methods exist including using percentage depth dose (PDD),²⁵ wedge¹⁶ and other specially designed dose patterns. The analytical modeling including Eqs.(3.8)-(3.10) may not be suitable to these alternative dose calibration methods which often involve dose gradients.

3.4.2 Napierian attenuation coefficient

Similar to the linear attenuation coefficient, $\mu\Delta x$ (Δx is the unit voxel) used during the reconstruction process of computed tomography (CT), $\mu_i^D\delta t$ in this work has been analytically "reconstructed" by Eq.(3.20), given that $\delta t = \bar{\tau} - \tau(x, y)$. The goal of CT reconstruction is to demonstrate contrast through Hounsfield scale. There is no need to visualize $\mu_i^D\delta t$ for RCF dosimetry, rather it's used to optimize the projected dose at each location by solving channel specific $\mu_i^D\delta t$ and to compensate accordingly. A typical CT scanner has an x-ray energy range of 80-140 kV. Whereas, the photon energy of visible light ranges between 1.63 and 3.26 eV, given that the wavelength bandwidth is 380-760 nm. A dual energy CT generates two sets of $\mu\Delta x$ resulting in two sets of Hounsfield unit of each voxel for each energy spectrum. Similarly, the three channels (R, G, B) of flatbed scanners give three sets of $\mu_i^D\delta t$ as noted by the subscript i in Eq.(3.20). This work was inspired by this similarity. We found that the transform of domain from the PV to OD (Eq.(3.25)). i.e. using OD instead of PV makes it drastically easier to weigh the distinct Napierian attenuation coefficients μ_i^D for each color channel i . This is reflected by the simple correlation in Eq.(3.6) which makes the straightforward weighting factors in Eq.(3.14) possible.

Note that the number of attenuators is down to 1 (only RCF active layer) in Eq.(3.5) from M in Eq.(3.1). Attenuations from other dose-independent attenuators like annotations by permanent pen and dust are theoretically not accounted for. During the CT reconstruction process, different types of attenuators are accounted for because the x-ray generator rotates around the object which provides the abundant data sets composed of thousands of projection views over at least 180°. This is not the case during the RCF scanning process: the lamp is located in the scanner cover (transparency unit) and only does the translational motion to deliver parallel beams. There is simply not enough data to reconstruct Napierian attenuation coefficients for certain dose-independent parts such as different attenuators on the film surface

(pen annotations, dust, etc.). With these artifacts impacting according to the sum of squares, Eq.(3.18) has these additional unknowns, besides $\mu_i^D(\bar{\tau} - \tau(x, y))$. Reconstruction of the linear attenuation coefficient at each voxel for a CT-scan, $\mu\Delta x$ is more complex and more capable in terms of taking into account different attenuating species than the case of RCF. Based on the authors' experience, the impact of annotations from a permanent pen on a dose map cannot be removed and are often visible in the optimized dose domain as experienced by end users. Because the ink of a permanent pen annotation is from a different chemical species than the lithium salt of RCF active layer and thus has a different attenuation coefficient from that in Eq.(3.4). Several common dose-independent attenuators such as dust and marker drawings cannot be completely removed by triple-channel dosimetry alone. However, the impact from these factors can be reduced by triple-channel dosimetry.

The unattenuated PV intensity of all three color channels is assigned to approximately the same value 65535 by the flatbed scanner. If the Napierian attenuation coefficients were the same μ_i^D for all three color channels, the OD and PV values for all three channels would be the same per Eq.(3.6). This is not the case as end users have experienced that PV or OD have major differences at the same spot between color channels. The model in this work includes the color channel specified μ_i^D which is the reflection of the phenomenon that R, G and B lights are attenuated differently by the same chemical species. Quantum mechanically, light fields will act to couple quantum states of the matter determined by the atomic and molecular composition of the material and determine the absorption spectrum. The energy difference between the two quantum states determines the likelihood of the light absorption frequencies. This likelihood or probability is classically denoted as σ_i in Eq.(3.2) which should also have a channel/wavelength spectrum dependence as noted in the subscript i instead of being channel-independent.

Micke *et al.*¹ and Mayer *et al.*² proposed a channel-independent^{2,15,16} disturbance

factor, assuming the disturbance/perturbation term, Δ is the same for all three channels:^{2, 15, 16}

$$\Delta = \Delta_R = \Delta_G = \Delta_B. \quad (3.27)$$

Mendez *et al.*¹⁶ continued with the assumption on the channel-independent perturbation, Δ and found that empirically using a truncated normal distribution as the probability density function of Δ statistically performs better than the uniform distribution models. In contrast to the one-scan protocol,¹¹ in the study of Mendez *et al.*,¹⁶ RCF was calibrated with netOD and the fourth order polynomials using a TPS calculated plan of a 60° wedge plan. We found that Δ_i is associated with the channel specific μ_i^D and in theory have a color channel i dependence (Δ_i). However, such correlation (g) between Δ_i and μ_i^D , varies in forms across the domain used for dose calibration, i.e., PV, netPV, OD and netOD each results in a unique g , which is itself channel-dependent regardless of the domain selected for dose calibration, though this dependence is also traditionally ignored. In theory, using netOD and netPV would have smaller Δ_i than its OD and PV counterpart for each color channel i . Regardless, the perturbation/disturbance Δ term should have a channel dependence resulting from the channel-dependent Napierian attenuation coefficient μ_i^D . This is reflected by the phenomenon that red, green and blue light with the same intensity are attenuated differently by the same chemical species, i.e. the attenuation is dependent on the energy spectrum of the incident photons.

3.5 Conclusions

A channel weighted analytical method has been developed for triple-channel radiochromic film dosimetry. The method accounts for the physical phenomenon that red, green and blue light with the same intensity are attenuated differently by the same attenuator, characterized by the channel specific Napierian attenuation coeffi-

cient. Better agreement with the TPS calculated plans was found at the lower dose range (0-1 Gy) and higher dose range (5-9 Gy) with more lateral coordinates. The channel weighted approach for RCF dosimetry does not require pre-irradiation RCF scans and is compatible with the existing, efficient one-scan protocol.

More measurements using RCFs from different lots (with different lot numbers) are needed to comprehensively evaluate the performance of this new channel-weighted analytical method regarding its ability to correct film active layer non-uniformity and mitigate the lateral artifact.

Appendix

Alternatively to the sum of squares used in Eq.(3.18), one can minimize the sum of the squared remainder term,

$$Z(\mu_X^D(\bar{\tau}-\tau(x,y)), D(\bar{\tau};x,y)) = \sum_i \left(\sum_{n=2}^{\infty} (\log_{10} e)^n \cdot \frac{D_i^{(n)}(d_i(\tau(x,y)))}{n!} (w_i(x,y) \mu_X^D(\bar{\tau}-\tau(x,y)))^n \right)^2 \quad (3.28)$$

After inserting Eq.(3.17) into the equation above, one can find that the expression above has two variables, $\mu_X^D(\bar{\tau}-\tau(x,y))$ and $D(\bar{\tau};x,y)$. To minimize this sum of squares, $Z'_{\mu_X^D(\bar{\tau}-\tau(x,y))} = 0$ and $Z'_{D(\bar{\tau};x,y)} = 0$ gives

$$\begin{aligned} \sum_i \begin{pmatrix} D'_i(d_i(\tau(x,y)))w_i(x,y) & D_i^2(d_i(\tau(x,y)))w_i^2(x,y) \\ -1 & D'_i(d_i(\tau(x,y)))w_i(x,y) \end{pmatrix} \begin{pmatrix} D(\bar{\tau};x,y) \\ \mu_X^D(\bar{\tau}-\tau(x,y)) \end{pmatrix} \\ = - \sum_i \begin{pmatrix} D'_i(d_i(\tau(x,y)))D_i(d_i(\tau(x,y)))w_i(x,y) \\ D_i(d_i(\tau(x,y))) \end{pmatrix}. \end{aligned}$$

The channel weighted method accounts for the attenuation variance among different channels as to electromagnetic wave radiation interactions with matter. One can

evaluate the absorbed dose $D(\bar{\tau}; x, y)$ at a uniform thickness $\bar{\tau}$ (instead of its local thickness $\tau(x, y)$ across all locations (x, y) with this new method

$$D(\bar{\tau}; x, y) = \frac{p\phi - q\psi}{mp - q^2} \quad (3.29)$$

where p , q , ϕ and ψ are expressed as follows:

$$p = \sum_i D_i^2(d_i(\tau(x, y)))w_i^2(x, y), \quad (3.30)$$

$$q = \sum_i D'_i(d_i(\tau(x, y)))w_i(x, y), \quad (3.31)$$

$$\phi = \sum_i D_i(d_i(\tau(x, y))), \quad (3.32)$$

$$\psi = \sum_i D'_i(d_i(\tau(x, y)))w_i(x, y)D_i(d_i(\tau(x, y))). \quad (3.33)$$

And m is the total number of channels involved, as the case of R, G and B, $m = 3$ for triple-channel dosimetry. The dose map from Eq.(3.29) is identical to that of Eq (3.21).

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Chapter 4

Characterization of Dosimetric Response of Organic Field Effect Transistor to Megavoltage X-ray Irradiation

This study aims to develop and characterize the dosimetry response of an organic field-effect transistor (OFET). 2,8-Difluoro-5,11-bis (triethylsilylethynyl) (diF-TES-ADT) semiconductor film was deposited by spin coating to fabricate OFETs. The OFET-RAD samples were placed at depth 1.5cm inside a 30×30×11.5 cm custom Solid-WaterTMphantom. The samples were irradiated at SSD=100 cm by a standard 10×10 cm² field from an Elekta Versa HDTM linear accelerator with accumulated dose levels between 0 and 100cGy with a 20cGy increment, between 100cGy to 1100 cGy with a 200cGy increment. The threshold voltages were extracted from the square root of the drain current with respect to the gate-source voltage. The threshold voltage shift of the FETs was observed as a function of cumulative dose. Confirmed by capacitance measurements, the dielectric is unaffected by megavoltage x-ray irradiation. The charge carrier mobility remains unchanged as a function of dose. No significant chemical changes in the organic semiconductor film were observed from nuclear magnetic resonance, gas chromatography, UV-Vis, and thin-layer chromatography. OFET-RAD are fabricated and evaluated upon the irradiation. In the 0 to 100 cGy range, positive shifts of the threshold voltage were recorded indicating the electron trapping.

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Author contributions: A.M.Z., T.R., J.D.B. and O.D.J designed the project. A.M.Z., H.F.I., and O.D.J. analyzed the results. A.M.Z. and D.S.F. fabricated and characterized the OFET devices. A.M.Z., D.S.F, T.R., and J.D.B. performed X-ray irradiation of OFET devices. E.H. and J.E.A. synthesized the organic semiconductors and performed chemical analysis of irradiated diF-TES-ADT. A.M.Z. and O.D.J. wrote the manuscript.

In the 100 cGy to 1000 cGy range, negative shifts are recorded as a potential result of spatial disorder introduced in the organic semiconductor layer. OFET-RAD can be fabricated over a large area, is flexible, and can be conformal to any surface over a large area. Additionally, polymer-based devices are mechanically robust, and can withstand bending radii of up to 9 mm.

Organic Field-Effect Transistors as Flexible, Tissue-Equivalent Radiation Dosimeters in Medical Applications

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Radiation therapy is one of the most prevalent procedures for cancer treatment, but the risks of malignancies induced by peripheral beam in healthy tissues surrounding the target is high. Therefore, being able to accurately measure the exposure dose is a critical aspect of patient care. Here a radiation detector based on an organic field-effect transistor (RAD-OFET) is introduced, an in vivo dosimeter that can be placed directly on a patient's skin to validate in real time the dose being delivered and ensure that for nearby regions an acceptable level of low dose is being received. This device reduces the errors faced by current technologies in approximating the dose profile in a patient's body, is sensitive for doses relevant to radiation treatment procedures, and robust when incorporated into conformal large-area electronics. A model is proposed to describe the operation of RAD-OFETs, based on the interplay between charge photogeneration and trapping.

Cancer is one of the most common causes of death, with alarming growth rates worldwide, but fortunately can be treated with early diagnosis and care. Over the past decades, heroic research efforts focused on elucidating the causes and developing effective treatments for this disease, with chemotherapy, radiation therapy and surgery emerging as the leading approaches for treating

cancer patients. In radiation therapy, one of the most common procedures, high-energy ionizing photon and electron radiation is used to destroy or reduce the growth of cancer cells. Most modern treatment systems utilize linear accelerators to generate beams of electrons or X-rays in the megavolt (MV) range, radioisotopes that produce gamma rays, or, more recently, cyclotrons to produce high energy protons.^[1] One of the biggest challenges in radiation oncology is to deliver the radiation only to the regions where the malignant cells are located, since the ionizing radiation can injure healthy tissues surrounding the target volumes.^[2] Many techniques have been implemented for maximizing the target dose, while minimizing normal tissue dose—this balance is always considered when planning a

patient's radiation regimen. Radiation treatment regimens include high-dose single fraction (e.g., stereotactic radiosurgery (SRS)), hypofractionated (stereotactic body radiation treatment (SBRT)), conventional fractionated (3D conformal radiation treatment (3D-CRT)), and intensity modulated radiation treatment (IMRT) techniques that encompass considerations for physical and biological optimization criteria. Being able to measure the absorbed dose with high accuracy and sensitivity is therefore critical to successful patient treatment and long-term survival. In contemporary clinical routines, first the beam is shaped, and the dose distribution is measured using a cylindrical diode array inside a poly(methyl methacrylate), (PMMA), phantom and then compared to the calculated dose distribution from a planning system, a quality assurance process that takes place a priori, during a treatment planning phase. Modern computers and machine learning techniques aid technicians in estimating the dose distribution within the patient by accounting for differences in geometry and composition between the patient and the detector, but unfortunately uncertainties persist.^[3,4] In addition, positioning of the patient and even minor movements (e.g., breathing), can alter the received dose and targeted volume, and thus affect the outcome of the procedure. During the therapy session, electronic portal imaging devices (EPIDs) are used to ensure accurate beam placement, but the large number of variables involved in the post-processing of the data can result in significant errors in the approximated dose profile in a patient's body due to inhomogeneities in the target (muscles/bones/adipose tissue), and

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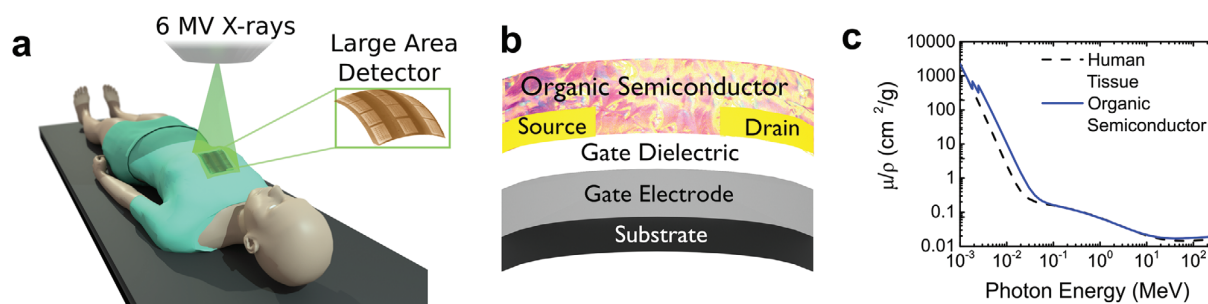


Figure 1. Flexible, large-area radiation dosimeters based on organic transistors—RAD-OFETs. a) Illustration of the placement of the RAD-OFET on patients during radiation therapy, b) architecture of an individual RAD-OFET sensing element, and c) comparison of the mass attenuation coefficient for human tissue and organic semiconductor over the large range of photon energies used for imaging and cancer treatment.

person-to-person variations in the patient's anatomic structures. Alternative in vivo dosimeters were developed to validate the dose being delivered and ensure that for nearby regions an acceptable level of low dose is being received. Metal-oxide semiconductor field-effect transistors (MOSFETs) and photodiodes based on inorganic semiconductors (e.g., Silicon) can approximate the dose at the site of irradiation, however these devices can be invasive since they often rely on implantation into patient. The solution to these problems is placing the detector directly at the point where the radiation interacts with the human body, similar to a smart bandage (Figure 1a). This approach can greatly enhance the accuracy of the measurements by eliminating the need for extensive data processing. At the same time, it will reduce the complexity and cost of the instruments and, therefore, the treatment. Here, we report on such radiation dosimeters based on organic field-effect transistors (OFETs), called "RAD-OFETs" (Radiation Detectors based on Organic Field-Effect Transistors). These detectors take advantage of the key properties of organic semiconductors (OSCs): they are lightweight, conformal to the curvature of the human skin surface (Figure 1b), and thin enough to be placed at the site of irradiation without disturbing the delivered dose. The similarity in the density of organic compounds and human tissue, given by the comparable atomic numbers (Z) (Figure 1c), minimizes the correction factor for estimating the dose applied to the patient. We focus on energies ranging between 0 to 6 MeV and obtain sensitivities as high as $(5.2 \times 10^7 \pm 0.3 \times 10^7) \mu\text{C Gy}^{-1} \text{cm}^{-3}$ in RAD-OFETs fabricated on flexible substrates, with an exceptional robustness upon bending. The RAD-OFET dosimeters function by monitoring the shift in the threshold voltage of the OFETs and we propose a model that describes the physical mechanism responsible for the observed changes. The model is based on photo-generation of charges upon X-ray exposure, followed by a distinct response to interaction with radiation of the electrons and holes, respectively. We find that the electron trapping at the semiconductor/dielectric interface occurs regardless of the absorbed dose. On the contrary, the dynamics of hole transport is given by the accumulation due to photoelectric effect and trapping by defects generated in the organic semiconductor film, a process which is dependent on the radiation dose. Our medical-grade X-ray dosimeters offer high sensitivity and ease of operation, while also taking advantage of the simple processing of organic materials, where large-area arrays can be easily fabricated on flexi-

ble substrates using solution-coating manufacturing techniques. These results provide a simple, yet effective and cost-efficient solution for detection of ionizing radiation, which may yield new products for medical diagnostics and treatment dose measurement using low-cost large-area portable or wearable detectors. The versatile chemistry of organic compounds allows for fine tuning of the atomic number Z by modifications in the molecular structure to match the Z of any target material, whether it be bone, fat (adipose) tissue, or muscle tissue, therefore making this technique suitable for dose monitoring during imaging and treatment of a wide variety of medical radiation procedures.^[5] These results uncover new opportunities for organic circuits that will not only improve the quality of healthcare through better, lower cost in vivo dose monitoring during radiation therapy, but can also have applications into portable and wearable detectors or high energy radiation detectors for defense and space applications.

Organic semiconductors have drawn considerable attention in the medical field due to their inherent versatility in molecular design, their ease of processing, and biocompatibility. Devices made from OSCs can withstand temperatures used in sterilization,^[6] are stable in aqueous environments,^[7] and have been included in applications like heart rate monitors,^[8] and large area imaging arrays,^[9–11] placed on biocompatible substrates.^[12,13] The use of biocompatible substrates has enabled ultra-lightweight sensors for bio-interfacing, from sensors thin enough to be attached directly to heart tissues to act as an electrocardiogram,^[14,15] to neural probes capable of controlling neurotransmitter delivery.^[16] Novel device design has also opened up pathways to electrochemical devices, which can be used to sense metabolites produced in the body and act as bio-powered sensors operating off electrochemical reactions with human skin to sense glucose and peptides.^[17,18] Radiation detection using organic materials is a developing area, with applications ranging from hazardous material identification and homeland security, to imaging, personnel safety or space applications.^[5,11,19–22] Much of this work, however, has focused on high radiation doses, or charged particle detection. Here we focus on radiation doses between 0.1 and 10 Gy ($1 \text{ Gy} = 1 \text{ J kg}^{-1}$), which are typical values for medical imaging and therapy: for example doses of 0.0005 cGy account for dental and limb X-ray imaging, 0.01 to 0.2 cGy are used for torso imaging, 0.4 to 2 cGy for body CT scans, 2.5 cGy for positron emission tomography (PET) scans, while radiation treatment of

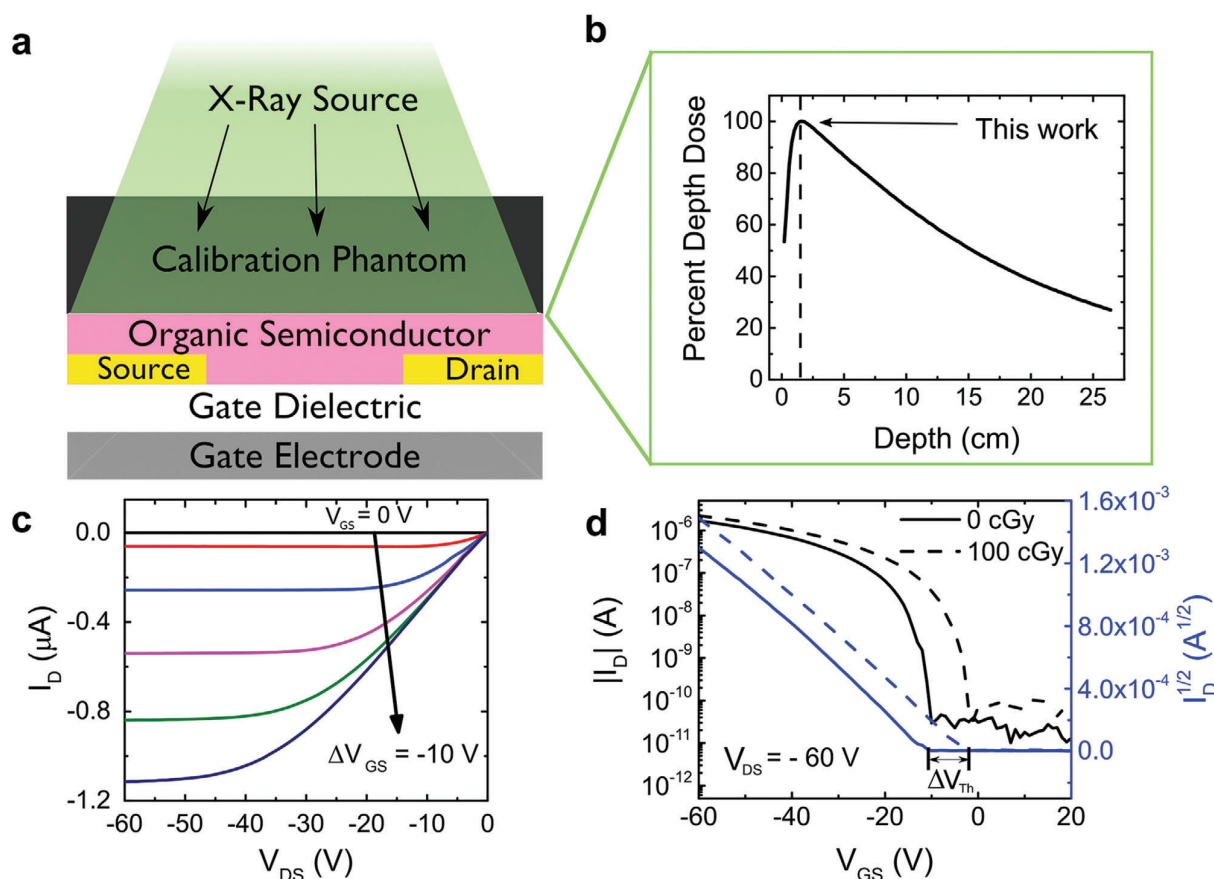


Figure 2. Experimental setup for radiation exposure and current-voltage characteristics of a RAD-OFET. a,b) Illustration of the experimental setup (a), the tissue equivalent phantom slab above the OFET ensures a calibrated dose (b) is delivered to devices during the experiment. c) Typical I - V characteristics of an OFET such as the ones used in this study. d) The threshold voltage shift induced by radiation exposure in a device. The geometry for this device was $L = 90 \mu\text{m}$ and $W = 800 \mu\text{m}$.

tumors requires doses between 100 to 200 cGy per fraction.^[4] To the best of our knowledge, this is the first example of using organic thin-film devices as dosimeters for radiation procedures used for cancer diagnosis and treatment.

The organic field-effect transistors used in this work had a bottom-gate, bottom contact geometry.^[23] This device architecture allows for direct exposure of the organic semiconductor to the radiation beam. We started with a rigid structure, with a SiO_2 layer playing the role of bottom-gate dielectric, and later expanded to large-area flexible substrates with a Cytop gate dielectric. The contacts were made of Au and the semiconductor was 2,8-difluoro-5,11-bis(triethylsilyl)ethynylanthradithiophene (diF-TES ADT), a material that has shown remarkable electrical properties, with charge carrier mobilities close to $20 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ in devices with near ideal current-voltage characteristics,^[24] and strong sensitivity to X-rays, although past work has focused on much higher doses and used different methods for detection.^[5,25] The OFETs were fabricated using standard procedures and their electrical properties were first characterized in air and dark, prior to exposure.^[24] The devices were sandwiched without compression between two slabs of tissue-equivalent calibration layers and irradiated through the top layer. The experimental set-up is shown in Figure 2a. The X-ray radiation was supplied by a

medical-grade linear accelerator (Elekta Versa HD, Wake Forest University Baptist Medical Center), and the corresponding relative dose as a function of depth is shown in Figure 2b. Test samples consisting of arrays of OFET devices were placed in the center of the X-ray field, as described in the Experimental Section. This setup reproduces the reference irradiation geometry used for radiation beam calibration in the clinical setting. The samples were exposed to radiation doses in increments of 0.2 Gy between 0 and 1 Gy, and in increments of 2 Gy from 2 to 10 Gy, at a nominal dose rate of 6 Gy min^{-1} . Control samples were fabricated using identical procedures, but were not exposed to X-rays, and were tested along with the irradiated ones, to be able to decouple the aging effects from the interaction with radiation (see Figure S1, Supporting Information).

Typical device output characteristics are shown in Figure 2c, where we plot the drain current I_D as a function of drain-source voltage V_{DS} for fixed gate-source voltages, V_{GS} . In Figure 2d we show the dependence of I_D on V_{GS} at constant V_{DS} before exposure to radiation (solid line, see Figure S2 in the Supporting Information for forward and reverse sweeps) and after absorbing 100 cGy of radiation (dashed line); the curves obtained after other exposure doses are included in Figure S3 in the Supporting Information. It can be clearly observed that irradiation caused

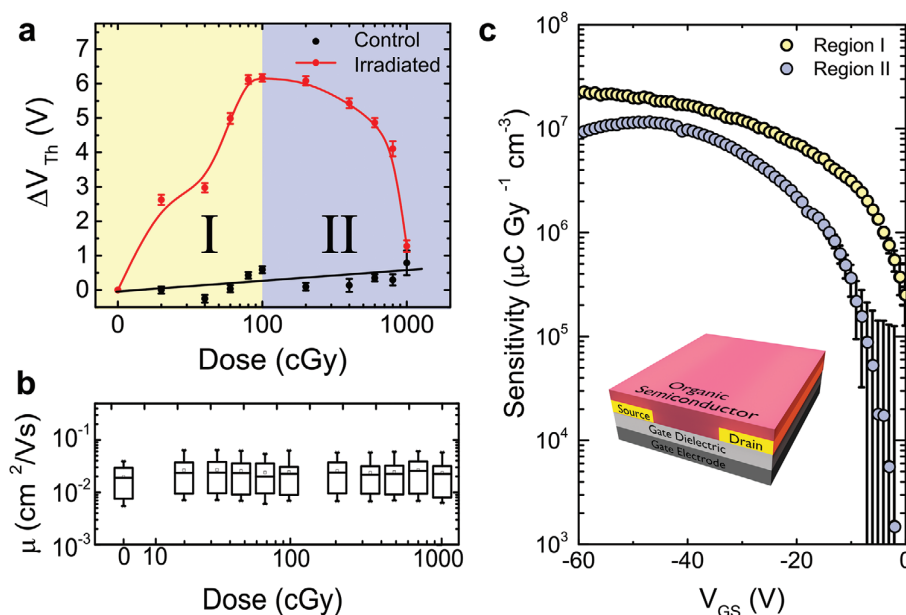


Figure 3. OFET response as a function of radiation dose. a) Threshold voltage shift versus applied radiation dose for the irradiated samples (red) and the control devices (black). In region I (yellow area) the shift is positive, while in region II (blue area) the shift is negative for the irradiated sample. No significant changes were recorded for the control sample. b) Box plot showing that the charge carrier mobility remains unchanged as a function of dose. c) Average device sensitivity as a function of gate-source voltage in the two dose regimes. Averages for threshold voltage shift and mobility were performed over a sample size of $n = 10$.

a shift in the threshold voltage of the OFET, i.e., the intercept of square-root-of-drain-current curve (blue) and the V_{GS} -axis, as marked in Figure 2d (more details about the analysis can be found in Figure S4, Supporting Information). This shift ΔV_{Th} is described by Equation (1)

$$\Delta V_{Th} = V_{ThD} - V_{Th0} \quad (1)$$

where V_{ThD} represents the threshold voltage at the target dose and V_{Th0} the threshold voltage at zero dose, i.e., before irradiation. To ensure that the threshold voltage was uniformly determined for each measurement, we adopted the method of the second derivative of I_D with respect to V_{GS} .^[24] This type of dosimetry, where the measurements are taken after exposing the sample to radiation, is referred to as passive. Passive sensors rely on the detection of changes induced in the sample upon exposure to radiation and that persist after exposure; on the contrary, active sensors monitor in real time by recording the photoconductive gain.^[26] In this case, a passive detection ensures that the irradiation and device testing take place sequentially, i.e., there is no voltage applied to the RAD-OFET while it is placed on a patient.

In Figure 3a we plot the shift in the threshold voltage as a function of radiation dose, in red, along with the changes recorded in the control sample. While the control samples exhibit negligible changes, a shift in the threshold voltage can be observed upon irradiation, with two regions being clearly distinguished. At low irradiation doses, Region I—between 0 to 1 Gy, the irradiated OFETs exhibited a positive shift in the threshold voltage, up to a value of 6.1 ± 0.2 V, obtained at 1 Gy. The aver-

age sensitivity of the detector, defined as $S_v = \Delta V_{Th}/\text{Dose}$, was determined to be $S_v = 60 \pm 8$ mV cGy⁻¹ for region I, a value which corresponds to $S_1 = (2.2 \times 10^7 \pm 0.2 \times 10^7)$ $\mu\text{C Gy}^{-1} \text{cm}^{-3}$, where $S_1 = (I_D - I_{D,0})/(\text{Detector Volume} \times \text{Dose Rate})$, I_D is the current measured after exposure, and $I_{D,0}$ is the current prior to irradiation (both currents correspond to an applied gate-source voltage of $V_{GS} = -60$ V). This sensitivity value is similar to that obtained at high doses with other dosimeters based on organic semiconductors,^[5,11] but in our case the performance was obtained under clinically relevant conditions for radiation treatment, where typical doses applied to patients do not exceed 200 cGy per treatment. In Region II, from 1 to 10 Gy, a negative shift in the threshold voltage is observed, with a sensitivity of $S_v = 4.6 \pm 0.9$ mV cGy⁻¹ ($S_1 = (8.9 \times 10^6 \pm 0.2 \times 10^6)$ $\mu\text{C Gy}^{-1} \text{cm}^{-3}$).

To gain more insight into the processes responsible for the observed threshold voltage shifts, we also evaluated the evolution of the charge carrier mobility (μ) in response to sample irradiation. The mobility was calculated from the slope of the square-root of the drain current curve with respect to the gate-source voltage (blue curves in Figure 2d), using Equation (2)

$$I_D = \frac{W}{L} \frac{C_i}{2} \mu (V_{GS} - V_{Th})^2 \quad (2)$$

where L and W are the channel length and the channel width, respectively, and C_i the capacitance per unit area of the dielectric.^[23] Figure 3b shows the response of μ to cumulative dose; it is notable that the mobility did not change over the course of the treatments, suggesting that the organic semiconductor layer

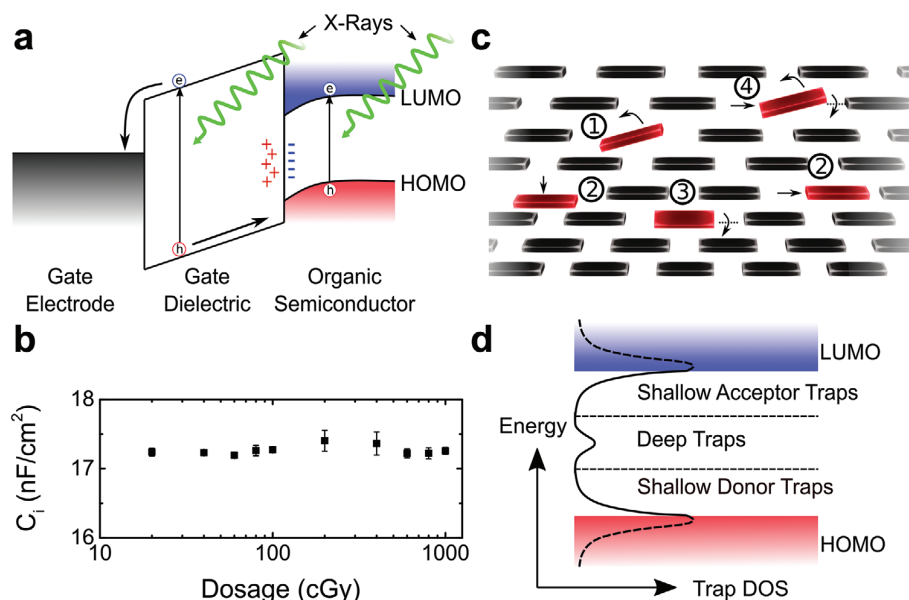


Figure 4. Mechanism for RAD-OFET operation. a) Band energy diagram illustrating the generation of electron-hole pairs when the device is irradiated, and the accumulation of deeply trapped holes at the interface. b) Capacitance measurements of the SiO₂ dielectric suggesting that holes are not trapped in the bulk of the dielectric (sample size $n = 10$). c) Illustration of positional disorder in the diF-TES ADT lattice, showing rotation (1,3), translation (2), and a mixture (4). d) The density of states in the bandgap of the organic semiconductor.

does not experience major chemical changes. Indeed, nuclear magnetic resonance spectroscopy, gas chromatography, UV-vis spectroscopy, and thin-layer chromatography indicated that no degradation occurs in the organic semiconductor film. We do not exclude, however, that chemical changes take place, but the resulting impurity is below the detection limit of our techniques. Attempts to restore the device properties by thermal annealing or room-temperature annealing resulted in partial recovery, while the solvent annealing results were inconclusive (see Figure S5, Supporting Information). The evolution of sensitivity with the gate-source voltage for the low and high dose rates is included in Figure 3c in yellow and blue, respectively. At low bias the sensitivity is hampered by multiple trapping and de-trapping events, which also impact the accuracy of reading, as demonstrated by the large error bars. When the voltage exceeds a critical value, which allows most of the holes accumulated in the transistor channel to be free, only a small dependence of the gate-source voltage is recorded, thus the RAD-OFET response is independent on the applied voltage.

The experimental results obtained upon controlled X-ray irradiation of the OFETs allowed us to propose a mechanism for the operation of the RAD-OFET dosimeters. The invariance in charge carrier mobility, along with partial recovery upon annealing, encouraged us to consider interfacial effects and structural defects as possible causes for the observed changes. The positive threshold voltage shift recorded upon exposure to low dose rates (Regime I) is indicative of electron trapping, a phenomenon that can occur either in the dielectric or in the organic semiconductor, close to the semiconductor/dielectric interface. The interaction of X-rays with the OFETs results in a cascade of events. First, ionizing radiation causes the formation of an electron-hole pair, i.e., an exciton, in the organic semiconductor and in

the SiO₂ layers (see Figure 4a).^[27–29] A fraction of these photo-generated charges will immediately recombine, while the rest will dissociate, resulting in free electrons and holes. The electrons are trapped at the semiconductor/dielectric interface by hydroxyl groups or other impurities and defects present here, while the holes, which are more resilient to trapping events, contribute directly to transport.^[30] There will be two contributions to the hole density: one from the processes occurring within the organic semiconductor layer, and the other from the dielectric, where the holes move through a series of hopping states toward the dielectric/semiconductor interface to contribute to transport (Figure 4a). The effect can be reduced if a high density of holes remains trapped in the oxide, a process that would contribute to a negative shift in the threshold voltage, which counteracts the effect of the holes that migrate to the interface and contribute to a positive shift. By performing capacitance measurements on the SiO₂ dielectric layer (Figure 4b), we concluded that the hole trapping in the oxide is minimal, since the dielectric capacitance remained constant at the dose levels used in this study, at an average value of $C_i = 17 \pm 1$ nF cm⁻². Some of the holes that reach the interface may, however, become deeply trapped here, creating long-lived states which persist over longer time scales (e.g., days, months) and contribute to a negative shift in threshold voltage. While in Region I the photogeneration of holes overcomes the trapping events, resulting in a shift toward more positive threshold voltages, the higher doses (>100 cGy) experienced by the OFETs in Regime II appear to generate significant hole trapping and lead to a negative shift. This shift results from the eventual build-up of deeply trapped holes at the interface and the structural defects occurring in the semiconductor, although we do not exclude the possibility of material degradation at levels below the detection limit of our

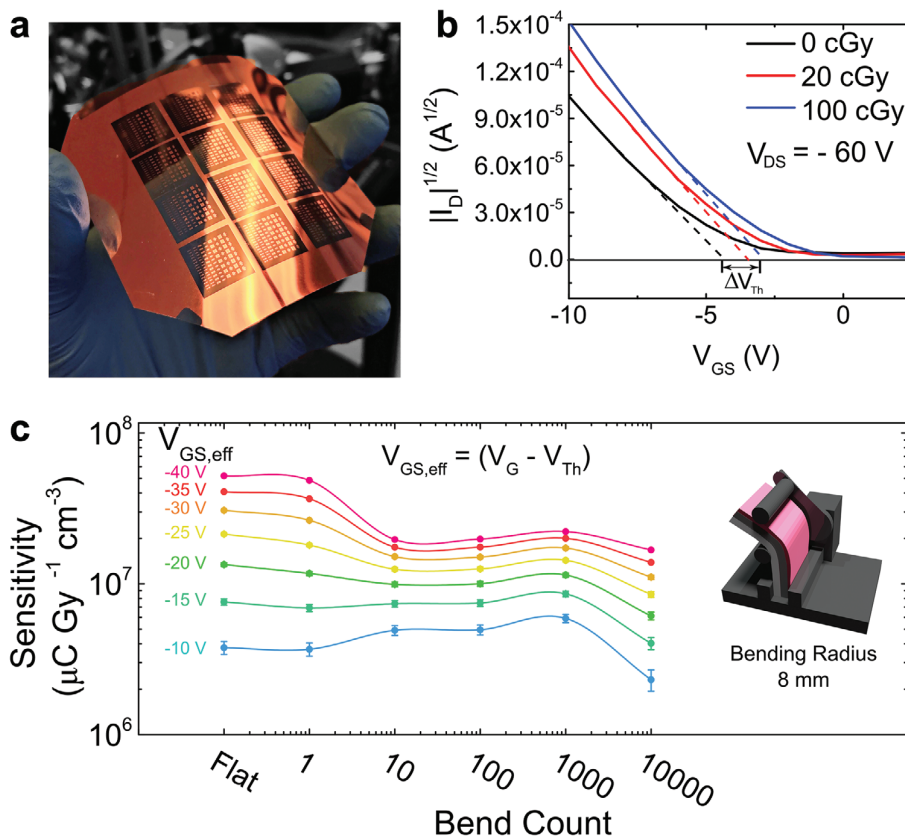


Figure 5. OFET radiation sensor on flexible substrates. a) Photo of an array of diF-TES ADT OFET devices on PET/ITO substrates. b) Square root of I_D versus V_{GS} illustrating the shift in threshold voltages as a function of dose. The geometry for this device was $L = 80 \mu m$ and $W = 1000 \mu m$. c) RAD-OFET sensitivity after repeating bending cycles, for different effective V_{GS} (each point is an average of a sample size $n = 12$). The inset shows a schematic of the computer-controlled bending set-up.

chemical analysis techniques, but that are relevant to electronic transport.

Trap generation in organic materials upon interaction with ionizing radiation has sparked great interest lately. Batlogg and co-workers showed that proton irradiation results in cleaving of the C–H bond in single crystal rubrene, a process that generates deep trap states.^[31] They also found that X-ray irradiation yields local structural disorder, which is a common source of traps in organic semiconductors.^[32] Proton irradiation of triisopropylsilyl ethynyl (TIPS) pentacene OFETs resulted in positional disorder,^[33] and electron irradiation of rubrene thin films induced n-doping and a negative threshold voltage shift.^[34] Podzorov et al. used air-gap rubrene OFETs to eliminate the interfacial effects and concluded that the shifts recorded in the threshold voltage upon interaction with X-rays result from the deep traps created in the crystal.^[35] Figure 4c includes a sketch of possible molecular re-orientations leading to positional disorder in the diF-TES ADT film. The solid-state packing was elucidated in our past work,^[36] and the distortion is exaggerated here for clarity: it includes rotations (1, 3), translations (2), and a combination of both (4). Such defects have been shown to be the origin of electronic traps with an energetic distribution that is dependent on the material and the exact nature of the defect.^[37,38] A schematic

representation of the energetic distribution of the trap density of states is included in Figure 4d, with shallow traps creating acceptor-like and donor-like tail states in the vicinity of the frontier orbitals and deep traps laying in the middle of the bandgap. Since we have not observed changes in charge carrier mobility upon exposure to radiation (Figure 3b), we hypothesize that the molecular re-arrangements generate deep traps. De-trapping of charge carriers residing here is highly unlikely since the trap depth is high, and thus they cannot contribute to transport.^[32]

The tests performed on samples fabricated on silicon substrates provide robust perspectives for OFET adoption in medical radiation dosimetry. To take full advantage of the unique properties of organic semiconductors, next we integrated them with flexible substrates. Large-area, flexible dosimeters can be placed directly onto the patient without the need for additional hardware, allowing for a higher accuracy and resolution of radiation detection and reducing the complexity and cost of the medical equipment. These devices were fabricated in a bottom gate, bottom contact configuration, onto polyethylene terephthalate (PET) flexible substrates with a predefined indium tin oxide (ITO) layer, which played the role of the gate electrode, and Cytop gate dielectric (Figure 5a). Due to the hydrophobic nature of the fluorinated polymer Cytop, an additional surface treatment was applied to

increase its surface energy and allow solution deposition of the organic semiconductor, as described elsewhere.^[39] These devices exhibited similar shifts in the threshold voltage, and the resulting sensitivity was $(5.2 \times 10^7 \pm 0.3 \times 10^7) \mu\text{C Gy}^{-1} \text{cm}^{-3}$. To test the mechanical robustness of the flexible OFET dosimeter, devices were flexed using a computer-controlled servo (Figure 5c, inset) to a bending radius of 8 mm. Devices were exposed to a dose of 100 cGy and the sensitivity was measured as a function of the number of folding and unfolding cycles; the results for different effective gate-source voltages are included in Figure 5, where the effective gate-source voltage is the difference between the applied gate voltage and the device threshold voltage $V_{GS,eff} = V_{GS} - V_{Th}$.

The dependence of sensitivity on gate-source voltage is in agreement with the results presented in Figure 3c. As for the tolerance to bending, a slight decrease in sensitivity occurs after 10 bends, most likely due to mechanical strains created at device interfaces and partial layer delamination, followed by a region of constant response between 10 and 10 000 bending cycles. A drastic decrease in sensitivity is observed after 10 000 cycles. Optical inspection of the films suggests that the micro-cracks that formed in the film are responsible for the performance degradation. Nevertheless, the good tolerance to folding exhibited by our OFET radiation detectors for the first 1000 bending cycles makes them attractive for incorporation in large area flexible radiation detectors.

We introduced a new concept for fabricating passive radiation dosimeters for medical applications, which we named the RAD-OFET. The device is based on organic thin-film transistors, and the radiation dose is detected as a shift in the threshold voltage. The sensor is robust and highly sensitive for doses relevant to a variety of medical radiation procedures, including patient dose monitoring during cancer diagnosis and therapy. To understand the results, we proposed a model based on photogeneration of charges upon X-ray exposure, followed by charge trapping at the semiconductor/dielectric interface. The hole dynamics is governed by a competition between the accumulation of the photo-generated holes and deep trapping within the organic semiconductor, a process which is highly depended on the radiation dose. For RAD-OFETs fabricated on silicon substrates, at low doses, below 200 cGy, trapping is minimal, and a positive shift is recorded in the threshold voltage, with a sensitivity of $60 \pm 8 \text{ mV cGy}^{-1}$ ($(2.2 \times 10^7 \pm 0.2 \times 10^7) \mu\text{C Gy}^{-1} \text{cm}^{-3}$). At high doses the trap formation prevails, leading to a negative shift and a sensitivity of $4.6 \pm 0.9 \text{ mV cGy}^{-1}$ ($(8.9 \times 10^6 \pm 0.2 \times 10^6) \mu\text{C Gy}^{-1} \text{cm}^{-3}$). Solution processing allowed for integration with flexible substrates for the development of conformal RAD-OFETs with high sensitivities, $(5.2 \times 10^7 \pm 0.3 \times 10^7) \mu\text{C Gy}^{-1} \text{cm}^{-3}$. Placement of the sensor directly onto the human body, coupled with the similarity in the atomic number between the electronically active layer and the human tissue, may greatly enhance the precision and reduce the complexity of the medical equipment, facilitating high quality measurement of patient doses. The application of therapeutic radiation with high precision increases the effectiveness on treating cancerous tissue and minimizes the impact on the surrounding healthy cells. The sensitivity of the proposed devices can be further enhanced with fine tuning the molecular structure of the organic semiconductor layer. These findings uncover new opportunities for organic circuits that will not only improve the quality of patient care, but they can have applications even beyond the

cancer therapy. Such applications include OFET dosimeter placement in unique irradiation geometries and types, monitoring of personnel dose in hazardous environments, and measurement of space radiation.

Experimental Section

Device Fabrication: Bottom-gate, bottom-contact devices were fabricated on both highly doped silicon substrates with a 200 nm SiO₂ dielectric layer, and PET substrates with ITO gate electrodes and a protein-modified dielectric layer, as described in earlier work.^[39] The SiO₂ substrates were cleaned by immersion in hot acetone (85 °C) for 10 min, followed by a thorough rinse in acetone and immersion in hot isopropyl alcohol (IPA, 85 °C) for 10 min. The substrates were then rinsed in IPA and dried by a stream of nitrogen. Next, they were exposed to a UV-ozone treatment for 10 min, rinsed with deionized water, and dried in a nitrogen stream. For both substrate types, the source and drain electrodes were patterned by shadow masks and consisted of a 5 nm titanium adhesion layer deposited by electron beam deposition at a rate of 1 Å s^{-1} , followed by thermally evaporated gold at a rate of 0.5 Å s^{-1} . The contacts were treated for 30 min using a $30 \times 10^{-3} \text{ M}$ solution of room-temperature pentafluorobenzene thiol (PFBT) in ethanol, rinsed with ethanol, and dried in a stream of nitrogen. The diF-TES ADT semiconductor film was deposited by spin coating from a 16.5 mg mL^{-1} solution in chlorobenzene at 104 rad s^{-1} (1000 rpm) for 80 s, then placed in vacuum for 18 h to remove additional solvent. The CYTOP 809-M dielectric layer was spin coated at 208 rad s^{-1} (2000 rpm) for 60 s, then annealed at 55 °C overnight, yielding a $1.4 \mu\text{m}$ film.

Device Characterization and Threshold Voltage Extraction: Transistor characterization was carried out in a nitrogen environment in dark using an Agilent 4155 C Semiconductor Parameter Analyzer. Devices were tested immediately after fabrication, as well as after each radiation dose. The control sample was not irradiated, but transported with and kept under similar environment as the irradiated samples. Capacitance measurements were taken using an Agilent E4980A LCR meter on reference and irradiated samples using the quasi-static capacitance voltage measurement technique on samples consisting of the dielectric layer sandwiched between a gold top electrode and a highly doped Si substrate which also played the role of bottom electrode. Threshold voltages were extracted from the plot of the square root of the drain current, I_D , with respect to the gate-source voltage, V_{GS} , using the maximum of the second derivative of I_D with respect to V_{GS} to bracket a linear extrapolation to where $I_D = 0 \text{ V}$, and that voltage taken as the threshold voltage.

X-Ray Irradiation of diF-TES-ADT Radiation Sensors: X-ray radiation was administered to samples using an Elekta Versa HD linear accelerator at a dose rate of 600 cGy min^{-1} . The devices were sandwiched without compression between two slabs of tissue equivalent material, i.e., (Gammex) Solid Water (top layer, to provide maximum percent depth dose to the devices, 1.5 cm thick; bottom layer, to provide backscatter to the devices, 10 cm thick) and irradiated through the top layer in increments of 20 cGy from 0 to 100 cGy, and then in increments of 200 cGy from 100 to 1000 cGy. Test samples, which were $\approx 1.5 \text{ cm} \times 1.5 \text{ cm}$ and contained arrays of OFET devices, were placed in the center of a $10 \times 10 \text{ cm}^2$ field of 6 MV X-rays, 100 cm from the source at depth of 1.5 cm.

Mechanical Durability Testing of Flexible Dosimeters: Repeated bending of devices was accomplished via a computer-controlled servo to ensure a consistent curvature and the substrates were bent to a radius of 8 mm. Devices were electrically characterized for an irradiation dose of 100 cGy, before bending, and after each set of bending cycles, for sets of bending cycles from 1 to 10 000.

Chemical Analysis of Irradiated diF-TES-ADT: Analysis of irradiated samples by gas chromatography / mass spectrometry (Bruker 436 GC / Scion SQ MS) showed diF-TES ADT as the dominant product, along with trace amounts ($<0.1\%$) of the monofluoro and trifluoro derivatives, in the same ratio as in the original un-irradiated sample. Proton NMR analysis of the irradiated sample (400 MHz Bruker Advance NEO) showed traces

of endoperoxide, but this impurity often forms during sample preparation, and the same trace impurity was found when preparing pristine samples of diF TES ADT using the same conditions.

Statistical Analysis: The data used for the extraction of threshold voltage shifts was not pre-processed before the analysis. The sensitivity of the dosimeters was extracted at constant effective gate-source voltage, where the effective gate-source voltage is the difference between the applied gate-source voltage and the device threshold voltage $V_{GS,eff} = V_{GS} - V_{Th}$. Device outliers were excluded prior to analysis based on the reliability of the $I_D^{1/2}$ versus V_{GS} curve, using the coefficient of determination (R^2) value of a linear fit to the data. Values less than $R^2 = 97\%$ were excluded, as the model shown in Equation (2) predicts linear behavior of $I_D^{1/2}$ versus V_{GS} . Results are presented as (mean $\pm$ SD), where SD represents standard deviation, followed by the appropriate units. All experiments had a sample size of at least $n = 10$, and statistical analysis was performed using OriginPro 2016 (OriginLab Corporation).

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

dosimetry, flexible electronics, organic field effect transistors, radiation detection, X-ray detection

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Intensity Modulated Radiation Therapy (IMRT) Quality Assurance (QA)

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Leksell Gamma Knife®(GK) Perfexion™/Icon™ QA

- GAFChromic™ EBT3 film analysis of GK end-to-end tests with anthropomorphic Rando head phantom and solution-filled head phantom for SRS
- GAFChromic™ EBT3 film analysis of GK pin-point tests of coincidence of patient positioning system (PPS) and radiation focal point (RFP) with film holder
- GAFChromic™ EBT3 film analysis of FWHM (and output factors for all three collimators)
- Assisted with annual, monthly and daily QA on Leksell Gamma Knife® Perfexion™/Icon™

Clinical Physics Rotations in Radiation Oncology

- Assisted with inter-campus radioactive materials shipping and transportation for a nonclinical project including package radiation safety survey and wipe test per DOT/NRC regulation
- Assisted with CT scan of Rando head phantom, Solid Water® phantom, thorax phantom and water-filled phantom
- Audited weekly new patient chart rounds including specific chart rounds for SRS/Gamma Knife patients
- Observed/shadowed procedures on Leksell Gamma Knife® Perfexion™/Icon™ including treatment planning, patient head frame installations and skull measurements, mask installations and treatment delivery
- Observed/shadowed procedures for patient scanning with PET/CT/MRI
- Assisted with radiation survey following the Cobalt-60 source change on Leksell Gamma Knife® Icon™
- Assisted with monthly linear accelerator output QA, CBCT image quality QA and light/radiation fields coincidence check with GAFChromic™ RTQA2 film
- Assisted with SNC Daily QA™ 3 array calibration and dose calibration

PUBLICATIONS & PRESENTATIONS

Manuscripts in Preparation, Under Review and Published

Ren T, and Bourland JD, A novel and efficient single-scan lateral artifact correction method combined with dose calibration for multichannel radiochromic film dosimetry, *J. Appl. Clin. Med. Phys.* 2021 [In Preparation]

Ren T, Dezarn WA, Hinson WH, McKee MM, Ververs JD, Black PJ, Parker SA, Zeidell AM, Bourland JD, A channel weighted analytical method for radiochromic film dosimetry, *Med. Phys.* 2021 [Under review]

Zeidell AM, **Ren T**, Filston DS, Iqbal HF, Holland E, Bourland JD, Anthony JE, Jurchescu OD, Organic field-effect transistors as flexible, tissue-equivalent radiation dosimeters in medical applications. *Adv. Sci.* 2020, 2001522.

Conference Abstracts

McKee, M., **Ren, T.**, Bourland, J., "Gamma Knife relative output factor measurements with multichannel radiochromic film dosimetry." *Radiother. Oncol.* (2020), 152, S691-S692

Zeidell, A., **Ren, T.**, Filson D., Haneef, H., Bourland, J., Anthony, J., Jurchescu, O., "Device fabrication and characterization of OFET-RAD for dosimetric response of Megavoltage X-ray." *Med. Phys.* (2020) Vol. 47. No.6

Ren, T., Prajapati, S., Dorand, J., Bourland, J.D., "Source characteristics and loading pattern for a

unique beta irradiation device for preclinical research of cutaneous radiation injury." *Med. Phys.* (2020) Vol. 47. No.6

Ren, T., and J. Bourland. " Triple-channel dosimetry with the channel weighted perturbation method." *Med. Phys.* (2019) Vol. 46. No. 6, pp. e320-e320.

Ren, T., and J. Bourland. " An Improved sensitometric calibration function for radiochromic film dosimetry." *Med. Phys.* (2019) Vol. 46. No. 6, pp. e608-e608.

Ren, T., and Bourland, J., An efficient automatic dose-space registration technique for clinical IMRT/VMAT quality Assurance with radiochromic film dosimetry, *J. Appl. Clin. Med. Phys.* 2019 May 16;20(5):159–159.

Ren, T., and J. Bourland. "Efficient method for combining flatbed scanner calibration and lateral response correction in a single scan for radiochromic film dosimetry." *Med. Phys.* (2018) Vol. 45. No. 6, pp. e608-e608.

Ren, T., and J. Bourland. "Temperature effect during radiation exposure period for radiochromic film dosimetry using flatbed scanner densitometer." *Med. Phys.* (2018) Vol. 45. No. 6, pp. e607-e607.

Other Presentations

D Filston, A Zeidell, **T Ren**, J Bourland, O Jurchescu, *Organic semiconductors as radiation dosimeter for megavoltage X-rays in medical applications*, Wake Forest University Physics Colloquium (presentation session for undergraduate summer research), Winston-Salem, NC, Aug 2019

T Ren, JD Bourland, *On correction of optical path effect from polarized light transmitted by radiation Induced polymer*, 19th Annual Graduate Student and Postdoc Research Day, Wake Forest University, Winston-Salem, NC, Mar 2019

T Ren, JD Bourland, *A novel lateral artifact correction method for triple-channel radiochromic film dosimetry*, (MedPhys SLAM preliminary round) the Southeast Chapter of AAPM 2019 Scientific Meeting, Savannah, GA, Feb 2019

T Ren, JD Bourland, *Characterization of lateral response artifact for radiochromic film dosimetry from flatbed scanner using reflective scanning mode*, (Young Investigator Symposium) the Southeast Chapter of AAPM 2018 Scientific Meeting, Greenville, SC, Feb 2018

T Ren, JD Bourland, *A novel surface dose extrapolation and superficial dose measurement technique for megavoltage X-ray using a single sheet of radiochromic film*, 18th Annual Graduate Student and Postdoc Research Day, Wake Forest University, Winston-Salem, NC, Mar 2018

US patent application

Flexible radiation dosimeters based on organic field effect transistor, US provisional patent pending

Inventors: Andrew M. Zeidell, Oana D. Jurchescu, **Tong Ren**, J. Daniel Bourland; *Assignee:* Wake Forest University

Lateral artifact/parabola effect correction combined with dose calibration for radiochromic film, US provisional patent pending

Inventors: **Tong Ren**, J. Daniel Bourland; *Assignee:* Wake Forest University

PROFESSIONAL AFFILIATIONS

American Association of Physicists in Medicine (**AAPM**) | *Student member* (2016-present)

The Southeast Chapter of the American Association of Physicists in Medicine (**SEAAPM**) | *Student/Trainee member* (2016-present)

Radiation Research Society (**RRS**) | *Scholar-in-training member* (2018-present)

HONORS & AWARDS

- 2018, 2019 -- Alumni Travel Award-Wake Forest University Graduate School of Arts and Sciences
- 2019 -- Graduate Student Travel Award-Wake Forest University Department of Physics
- 2021 -- Best Paper Award-The Southeast Chapter of American Association of Physicists in Medicine

RESEARCH EXPERIENCE

Graduate Research Experience

Graduate School of Arts and Sciences, Wake Forest University
Winston-Salem, NC

- Methodologies on improving the accuracy and efficiency of the analytical triple-channel film dosimetry
 - Development of an improved radiochromic film dosimetry method: triple-channel dosimetry with channel weighted perturbation method
 - Development of a novel and efficient method combining flatbed scanner calibration and lateral artifact correction in a single scan for radiochromic film dosimetry
 - Development of a complete toolkit for efficient IMRT/VMAT QA with film using the state-of-the-art multichannel radiochromic film dosimetry methods and the widely adopted one-scan protocol which include the novel fiducial-mark free, automatic dose space registration, dose difference map, dose profile plot, global/local gamma index mapping/analysis for film dosimetry methods comparison

- Retrospective radiation dosimetry planning for cynomolgus macaques whole body irradiation study using Pinnacle³
- Organic field effect transistor (OFET) as radiation dosimeter
- Stage 2 study on a medical countermeasure of radiological terrorism: “Proof of concept” study using Silverlon® as a mitigator in Yorkshire pigs (sus scrofa) to determine the potential efficacy and safety for a medical countermeasure that provides mitigation of cutaneous radiation injury (Silver based anti-microbial wound dressing for beta-emitter cutaneous radiation syndrome) : Commissioning, acceptance and QA of 2 new beta irradiation applicators, BRD 2.0 and 3.0 (high dose rate solid state Sr/Y-90 sources) beta irradiation devices.
- Cutaneous radiation injury study on dark skin using red duroc porcine model (the same BRD devices used to induce injury)
- Gammacell® 3000 Elan Cesium-137 blood irradiator dosimetry study for irradiating ex-vivo blood for the routine calibration of CytoRADx™ (ASELL, Owings Mills, MD) high-throughput bio-dosimetry system and comparing to the linac based blood irradiation approach

TEACHING EXPERIENCE

Teaching Assistant

Department of Physics, Wake Forest University
Winston-Salem, NC

08/2015-06/2019

- Instructor, PHY 110L Introductory Physics Lab
- Instructor, PHY 113L General Physics Lab I
- Instructor, PHY 114L General Physics Lab II
- Grading Assistant, PHY 771 Radiological Physics
- Grading Assistant, PHY 773 Radiation Therapy Physics

College Physics Tutor

Learning Assist Center & Disabilities Services (LAC-DS), Wake Forest University
Winston-Salem, NC

08/2019-12/2020

- PHY 110 Introductory Physics
- PHY 113 General Physics I
- PHY 114 General Physics II

ADDITIONAL TRAINING

Graduate School of Arts and Sciences, Wake Forest University
Radiation Oncology Department, Wake Forest School of Medicine
Winston-Salem, NC

08/2015-10/2019

Training Descript

Year

- Good Laboratory Practices (GLP) Training 2018, 2019
- Center for the Advancement of Teaching (CAT) training 2018
- Department of Transportation (DOT) Hazardous Materials Training 2018
- Institutional Animal Care and Use Committee (IACUC) Training 2019
- Annual Radiation Safety Training from the Radiation Safety Officer (RSO)
2016, 2017, 2018, 2019
- SBRT training course titled, *Principles and Practice of Image Guided Hypofractionated Radiotherapy* 2019