PhD Thesis Title: Advanced quality assurance methodologies in image-guided high-dose-rate brachytherapy

Author: Saad Aldelaijan
Email: saad.aldelaijan@mail.mcgill.ca
Institution: McGill University
Supervisors: Dr. Slobodan Devic and Dr. Louis Collins
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ABSTRACT: (two versions: original and short)

Original Thesis Abstract:
Brachytherapy (BT) was the first form of radiotherapy and it is still effectively used because of its unique physical and biological advantages. Although the principles of BT operation are considered to be relatively simple (since it is based on the correct timing and positioning of radioactive sources), BT has also benefitted from technological advances. The rate of technical inventions and their incorporation into BT treatments has necessitated development of more precise quality assurance (QA) tools. The purpose of this thesis is to introduce a robust QA framework based on radiochromic film (RCF) dosimetry for image-guided high-dose-rate (HDR) BT. These films can be digitized allowing for high spatial resolution visualization of the source dosimetric trace, which can be used to reconstruct the source positions and evaluate the dose distribution simultaneously.

To increase the HDR source-tracking reliability, a film-digitization protocol was developed. This protocol evaluates issues related to film scanning and handling, and specifies parameters of film response and mathematical models that relate this response to absorbed dose. The protocol is based on a new linear response function, ‘normalized pixel value’ (*nPV*), and it was designed to achieve high accuracy while maintaining practicality. It was further improved by using all RGB (Red, Green, Blue) color information available in RCF scanned images, to correct for scanning-related issues. This protocol was tested and validated for six independent RCF dosimetry systems in three different clinics, demonstrating robustness of the method and its ability to mitigate systematic response shifts.

The first application of this dosimetry protocol was in the QA of Freiburg Flap (FF) based treatments in HDR surface BT. The current standard of care in the treatment planning of surface BT does not take into account the lack of the backscatter above the FF and the patient skin, since it assumes the HDR source is always surrounded by water. Before comparing the planned and delivered doses, the film response was calibrated and a detailed uncertainty budget was discussed. The RCF dosimetry system was able to report the difference between the calculated and the delivered doses for different setups and to evaluate the use of bolus to reduce these differences.

Subsequently, the source-tracking algorithm was developed to precisely localize the HDR source within catheters based on the acquired 2D distribution from the RCF. The algorithm relies on measured-features of the relative isodose lines (blob analysis) such as area, perimeter, weighted-centroid, elliptic orientation, and circularity. A reference library of features was prepared based on the AAPM TG-43 datasets and the correlations were derived between these features and the source coordinates (x, y, z, ϑ_y, ϑ_z). The measured features are then compared to the referenced ones and the most probable source coordinates are reported. The source-tracking algorithm was verified experimentally with an accuracy of 0.1 mm by having two film sets on opposing ends of the source.

This technique offers a novel method having the potential to be used for source QA of commercial and customized applicators.

This thesis addressed the acquisition of accurate 2D dose maps with RCF which is essential for the detection of the HDR source dosimetric trace when using the source-tracking algorithm. This included the calibration of RCF for HDR BT dosimetry and their use in dose verification. The thesis also demonstrated the potential incorporation of these findings into a comprehensive image-guided HDR BT QA framework. In the future, the framework is intended to encompass all the software and strategies developed thus far and adapt new algorithms by taking advantage of the simple irradiation patterns yet revealing many QA metrics accurately.

Short Modified Abstract:
Brachytherapy (BT) was the first form of radiotherapy and it refers to the placement of radioactive sources temporarily or permanently into or near target tumor volumes giving a high dose of radiation to them while sparing surrounding healthy tissues and organs-at-risk. Although technological advancements in man-made external beam radiotherapy (EBRT) aimed to create BT-like dose distributions, BT remains unparalleled in dose conformality and unsurpassed in clinical outcome for many body sites. Yet, BT is still underutilized because of unfavorable logistics and reimbursement policies compared to EBRT. Nonetheless, with more accumulating clinical evidence, BT is going through a renaissance and more resources are being invested to improve it. Nowadays, image-guided brachytherapy (IGBT) is the state-of-the-art form of BT allowing further dose escalation protocols to tumor volumes. However, despite the rate of technical innovations and their incorporation into BT treatments, its quality assurance (QA) protocols are more than two decades old. The purpose of this thesis was to design and implement a robust low-cost QA framework based on radiochromic film (RCF) dosimetry for contemporary applications of IGBT. These films can be digitized using inexpensive document scanners allowing for high spatial resolution visualization of the source dosimetric trace. This data is then used to precisely reconstruct the source positional and dosimetric information simultaneously, while assuring safe and high quality treatments to cancer patients. To increase the radioactive source tracking reliability, a RCF digitization protocol was developed. This protocol evaluates issues related to RCF scanning and handling, and specifies parameters of RCF response to the absorbed dose. Subsequently, the source-tracking algorithm was developed to precisely localize the BT source within catheters based on the acquired 2D RCF images. The algorithm relies on benchmarking measured-features of the relative isodose lines, such as their area, perimeter, centroid and circularity. Accurate knowledge of the source position and its associated dose distribution constitutes a QA benchmark for testing current and future IGBT sources and auxiliary equipment. This innovative approach provides new effortless QA insights commensurate with today's IGBT challenges, which in turn empowers its use and comes timely since the scientific community is advocating IGBT based on current clinical benefits.

References to author publications that relate specifically to the dissertation:

1. **Aldelaijan, S**., Devic, S., Bekerat, H., Papaconstadopoulos, P., Schneider, J., Seuntjens, J., Cormack, R.A. and Buzurovic, I.M., "Positional and angular tracking of HDR ^{192}Ir source for brachytherapy quality assurance using radiochromic film dosimetry." *Med. Phys*. 47(12), 6122-6139 (2020) https://doi.org/10.1002/mp.14540

2. **Aldelaijan, S.,** Devic, S., Papaconstadopoulos, P., Bekerat, H., Cormack, R.A., Seuntjens, J. and Buzurovic, I.M., "Dose–response linearization in radiochromic film dosimetry based on

multichannel normalized pixel value with an integrated spectral correction for scanner response variations.” *Med. Phys.*, 46(11), 5336-5349 (2019) https://doi.org/10.1002/mp.13818

3. **Aldelaijan, Saad** and Devic, Slobodan, “Comparison of dose response functions for EBT3 model GafChromic^{TM} film dosimetry system,” *Phys. Med.* 49, 112-118 (2018). https://doi.org/10.1016/j.ejmp.2018.05.014

4. **Aldelaijan, S.,** Bekerat, H., Buzurovic, I.M., Devlin, P.M., DeBlois, F., Seuntjens, J. and Devic, S., “Dose comparison between TG-43–based calculations and radiochromic film measurements of the Freiburg flap applicator used for high-dose-rate brachytherapy treatments of skin lesions.” *Brachytherapy*, 16(5), 1065-1072 (2017) DOI: 10.1016/j.brachy.2017.06.011