Implementation and Dosimetric Evaluation of a kV Microbeam X-Ray Irradiation Platform

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ABSTRACT

Purpose:
The purpose of this study was to implement and experimentally characterize a kV microbeam X-ray irradiation platform, with emphasis on spatial dose modulation and dosimetric suitability for future radiobiological applications. Spatially Fractionated Radiation Therapy (SFRT) delivers non-uniform dose distributions that combine regions of very high and low dose within the same irradiation field. Among SFRT techniques, Microbeam Radiation Therapy (MRT) has emerged as a promising preclinical modality, in which a homogeneous X-ray field is segmented into arrays of micrometer-scale beams that produce high-dose peaks separated by low-dose valleys, enabling tumor control while preserving normal tissue function.

Methods:
A tungsten microbeam collimator consisting of 31 parallel slits was implemented in a MultiRad 225/26 orthovoltage X-ray irradiator operating in the 50–200 kVp energy range with added filtration. The collimator was positioned at the central axis of the beam and produced nominal microbeam widths of 40 µm with a center-to-center spacing of 400 µm. Custom 3D-printed holders ensured precise and reproducible alignment within the beam path. Spatial dose distributions were measured using radiochromic films (EBT3 and EBT-XD), which were compared in terms of spatial resolution and dynamic range for peak and valley dose assessment. Lateral dose profiles were analyzed to extract microbeam width, spacing, and peak-to-valley dose ratio (PVDR). Additional measurements investigated the influence of tube voltage, filtration, and backscatter materials.

Results:
Clear and reproducible microbeam dose profiles were obtained, resolving an average of 30 microbeams per profile. The measured full width at half maximum was 152 µm, with a mean center-to-center spacing of 638 µm. Peak doses ranged from approximately 8 to 18 Gy, while valley doses remained below 1 Gy. Peak-to-valley dose ratios ranged from 15 to 34 depending on the analysis method. Peak dose uniformity across the field was high, with a coefficient of variation of 21%, demonstrating stable and well-defined spatial dose modulation.

Conclusion:
This work demonstrates the feasibility of experimentally delivering and characterizing kV microbeam X-ray fields with high spatial precision and large PVDR values using radiochromic film dosimetry. The developed platform provides a robust technical foundation for future depth-dose characterization and preclinical microbeam radiobiology studies, with ongoing percentage depth dose measurements and in-vitro cell irradiation experiments.

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DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

INTRODUCTION

Recent groundbreaking studies in mouse cancer models and few selected patient cases underscored superiority of SFRT (microbeam or minibeam) over conventional X rays (CONV RT) in inducing tumor control and sensitizing to immunotherapy. Consistently, we meta-analyzed respective publicly available omics data and showed that microbeams activate innate immunity pathways earlier than CONV RT. Furthermore, the SFRT-specific gene signatures are associated with higher predictability of long-term patient survival [1].

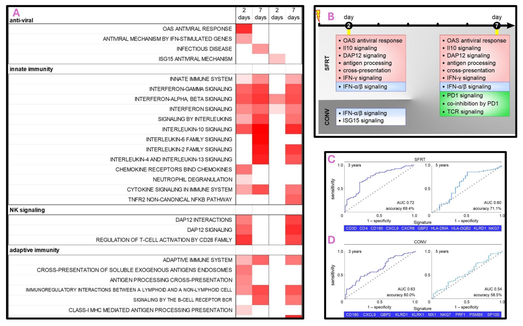

Figure 1. (A) GSEA meta-analysis of microarray RNA data from melanomas excised from B16 mouse models 2 and 7 days after SFRT or CONV RT irradiation. (B) Diagram of the temporal differences in pathway induction between SFRT and CONV RT. (C-D) ROC curves correlating SFRT-induced (C) or CONV RT-induced transcript signatures with survival of melanoma patients from the TCGA SKMC cohort ≥ 3 years (left) and ≥ 5 years (right) after initial diagnosis.

The superior antitumor effects of SFRT appear to be linked with special spatial and temporal features. To dissect this complexity, radiobiology labs will benefit from user-friendly set-ups to convert CONV RT to SFRT for in vitro and in vivo experimentation. Herein, we established a cost-effective, user-friendly benchtop system that produces microbeams in a laboratory setting. The system is expected to significantly support preclinical studies of the enigmatic known molecular mechanisms of responses of tumor cells to SFRT [2].

METHODS AND MATERIALS

The development of a kilovoltage (kV) microbeam irradiation platform utilizing a commercial orthovoltage X-ray unit was undertaken. A custom tungsten microbeam collimator consisting of 31 slits was positioned at the beam central axis using a precision 3D-printed holder to generate spatially fractionated X-ray fields (Figure 2). A dedicated sample and well-plate holder was designed by using Inventor 2024 [3] to ensure reproducible positioning and irradiation geometry for future biological experiments (Figure 3).

Figure 2. 3D Design of microbeam collimator holder ensuring precise central axis alignment.

Figure 3. 3D Design of sample/well plate holder for reproducible biological experiments.

METHODS AND MATERIALS

The experimental characterization of microbeam projections was performed using radiochromic film dosimetry. This study investigates and compares two film types, Gafchromic™ EBT-XD [4] and EBT-4 [4], with the objective of determining their effectiveness in high-resolution spatial dose measurements. Film calibration was performed using known dose irradiations, and lateral dose profiles were extracted from high-resolution scans to evaluate the spatial distribution and modulation of the generated microbeam projections.

Concurrently, a Monte Carlo model, EGSnrc, of the X-ray irradiation system was developed to reproduce the experimental geometry, incorporating the X-ray source, beam-shaping components, tungsten microbeam collimator, and irradiation setup (Figure 4).The simulated geometry was implemented as a framework for future comparison between measured and calculated dose distributions [5].

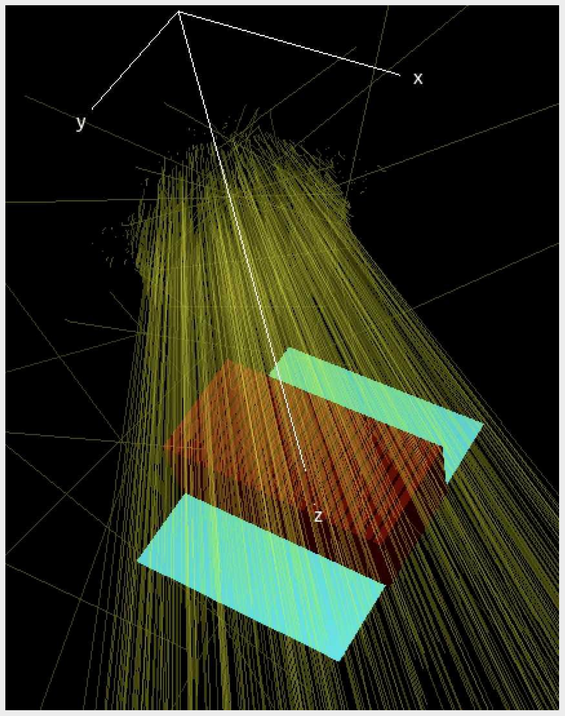

Figure 4. BEAMnrc Monte Carlo model of the experimental microbeam irradiation platform, including the X-ray source, tungsten microbeam collimator, and detector geometry.

RESULTS & DISCUSSION

It was demonstrated that both Gafchromic™ EBT-XD and EBT-4 films produced baseline peak-to-valley dose ratios (PVDRs) exceeding the value of 20. The comparable PVDR values indicate that there is no distinguishing difference on spatial distribution between them. Therefore, due to cost efficiency EBT-4 were selected for this study.

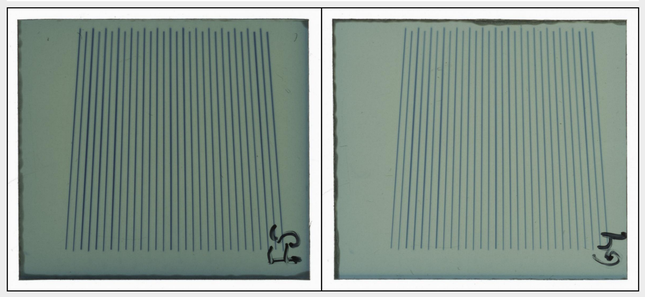

Figure 5. The images above depict microbeam irradiation of EBT-4 film (left) and EBT-XD film (right). No discrete differences on the peaks were detected.

RESULTS & DISCUSSION

The high-resolution radiochromic film measurements demonstrated a mean resolution of 30 microbeams per profile. The full width at half maximum (FWHM) of the beam was measured to be 152 µm, with a mean centre-to-centre spacing of 638 µm, indicative of consistent microbeam generation. The range of peak doses was from 8–18 Gy, while the valley doses remained below 1 Gy, resulting in peak-to-valley dose ratios (PVDRs) of 15–34, depending on the analysis method (Figure 6).

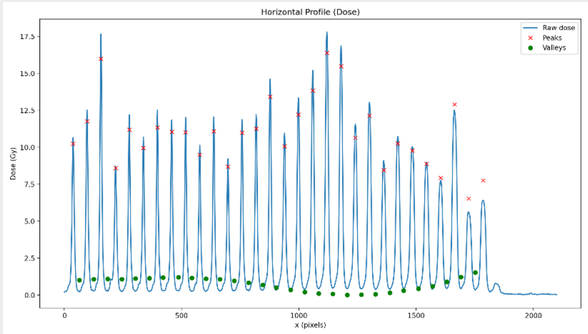

Figure 6. Horizontal Microbeam Dose Profile and PVDR Analysis

The effect of the irradiation geometry was investigated by measuring the PVDR for four film configurations: film inside a well with 1 mL of water, film below the water-filled well, film inside an empty well, and film outside the well without water. In all configurations, the film was covered with parafilm. The measured PVDR values were comparable for all configurations with values of 14.01, 13.54, 14.91, and 14.69, respectively. The findings suggest that the presence of water and the geometry of the well do not exert a significant influence on microbeam dose modulation. This outcome corroborates the maintenance of the peak-to-valley dose structure under varying irradiation conditions..

CONCLUSIONS

The characterization of a microbeam platform was conducted utilizing an X-ray kV irradiator. The PVDR values were found to range from 15 to 34. This renders the system suitable for studies that focus on reducing normal tissue toxicity. The validated platform will be used for biological investigations, including cell and zebrafish embryo irradiation studies, to evaluate the effects of the microbeam pattern. In order to ascertain the most effective platform for the irradiator, a new platform would first be constructed and validated using Monte Carlo simulations. Subsequent research will concentrate on correlating dose rate and biological response to enhance comprehension of the FLASH effect.

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