What Are the Optimal SFRT Geometric Parameters? Examining through an In-Vitro Study

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Introduction

Spatially Fractionated Radiotherapy (SFRT) is a treatment technique in which the tumor receives an alternating pattern of high and low doses often referred to the peaks and valleys.

One of the biggest challenges in the SFRT community is the lack of standardization across cancer centers and within the same cancer center. A crucial question still left to be answered is: "What is the optimal SFRT geometric pattern for optimal treatment outcomes?" We hypothesize that **<u>different patterns may induce more/less indirect cell kill.</u>**

METHODS AND MATERIALS

- Two cancer cell lines (UM-SCC-2 and UM-SCC-6) and one non-cancerous cell line (MCF-10A) were used in this study.
- These cell lines were first uniformly irradiated at 4 different dose points to derive their uniform derive α and β values.
- Next, these cell lines were irradiated with 10 different SFRT patterns at a prescription dose of 5, 10, 15, and 20 Gy.
  - These 10 patterns consisted of high-dose diameters of 0.5, 1.0, 1.5, and 2.0 cm with a center-to-center spacing (CTC) of either 1.0, 1.5, 2.0, 2.5 cm. This is shown in Figure 1.

The linear-quadratic (LQ) model was fitted for each pattern for each cell line to derive the SFRT α and β values.

Evaluation of the optimal SFRT pattern was performed using relative effectiveness factor (REF) and therapeutic ratio as defined below, evaluated at a range of equivalent uniform dose (EUD) values of 1-9.0 Gy.

$$REF = \frac{D_U}{EUD} = \frac{\left(\alpha/\beta\right)_U}{2EUD}\left(-1 + \sqrt{1 + \frac{4EUD}{\left(\alpha/\beta\right)_U}\left(1 + \frac{EUD}{\left(\alpha/\beta\right)_U}\frac{REF_{HD}^2}{REF_{LD}}\right)}REF_{LD}\right)$$

$$TR = \frac{SF_{normal}\,(EUD_{SFRT})}{SF_{normal}\,(D_U)}$$

$$SF_{Tumor}\,(EUD_{SFRT}) = SF_{Tumor}\,(D_U).$$

Monte Carlo sampling was performed to determine the optimal pattern based on the probability of having the largest TR and REF.

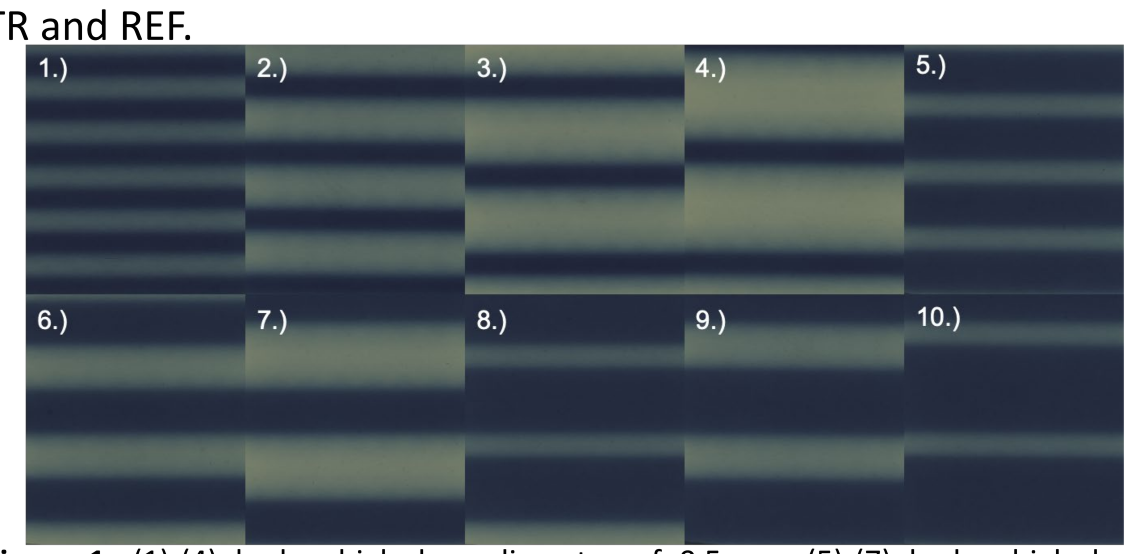

Figure 1: (1)-(4) had a high-dose diameter of 0.5 cm. (5)-(7) had a high-dose diameter of 1.0 cm. (8)-(9) had a high-dose diameter of 1.5 cm. (10) had a high dose diameter of 2.0 cm.

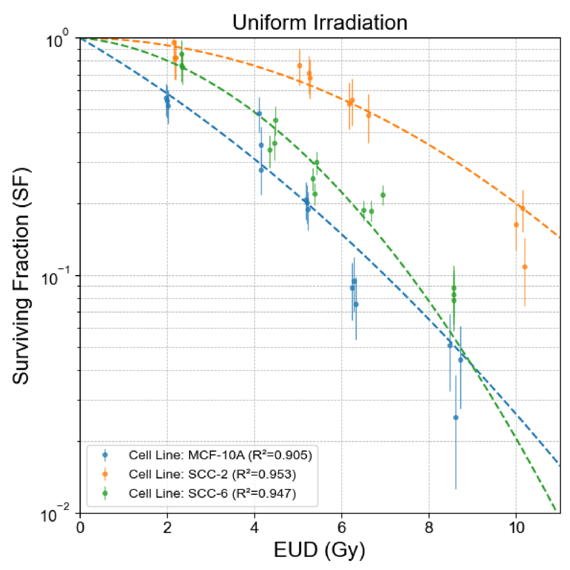

Figure 2: Resulting LQ curves fitted to cell lines irradiated with uniform irradiation. Shown is that UM-SCC-6 is the most radioresistant of the three cell lines used in this study.

RESULTS

The resulting LQ curves for the uniformly irradiated cell lines are shown in Figure 2. Figure 3 shows the resulting LQ curves for all three cell lines when irradiated with the 10 SFRT patterns.

- The UM-SCC-2 cell line was the most radioresistant cell line, while UM-SCC-6 and MFC-10A had similar radiosensitivities.
- The enhanced SFRT cell kill was mostly demonstrated in the UM-SCC-2 cell line, demonstrating SFRT benefits radioresistant cell lines more. The MCF-10A cell line did demonstrate marginal benefits when irradiated with a SFRT pattern.

REF: For the UM-SCC-2 cell line, pattern 6 was the best at an EUD below 3.5 Gy. For EUD values greater than 3.5Gy, pattern 4 was optimal. For the UM-SCC-6 cell line, pattern 10 was best for EUD values less than 1.7 Gy, and pattern 5 was best for EUD > 1.7 Gy. The results of the MC sampling is depicted in Figure 4.

TR: When considering UM-SCC-2, pattern 6 had the best TR at EUD < 3.6 Gy. Past this EUD value, there wasn't a clear optimal pattern. For the UM-SCC-6 cell line, pattern 5 was best overall. The results of the MC sampling is depicted in Figure 5.

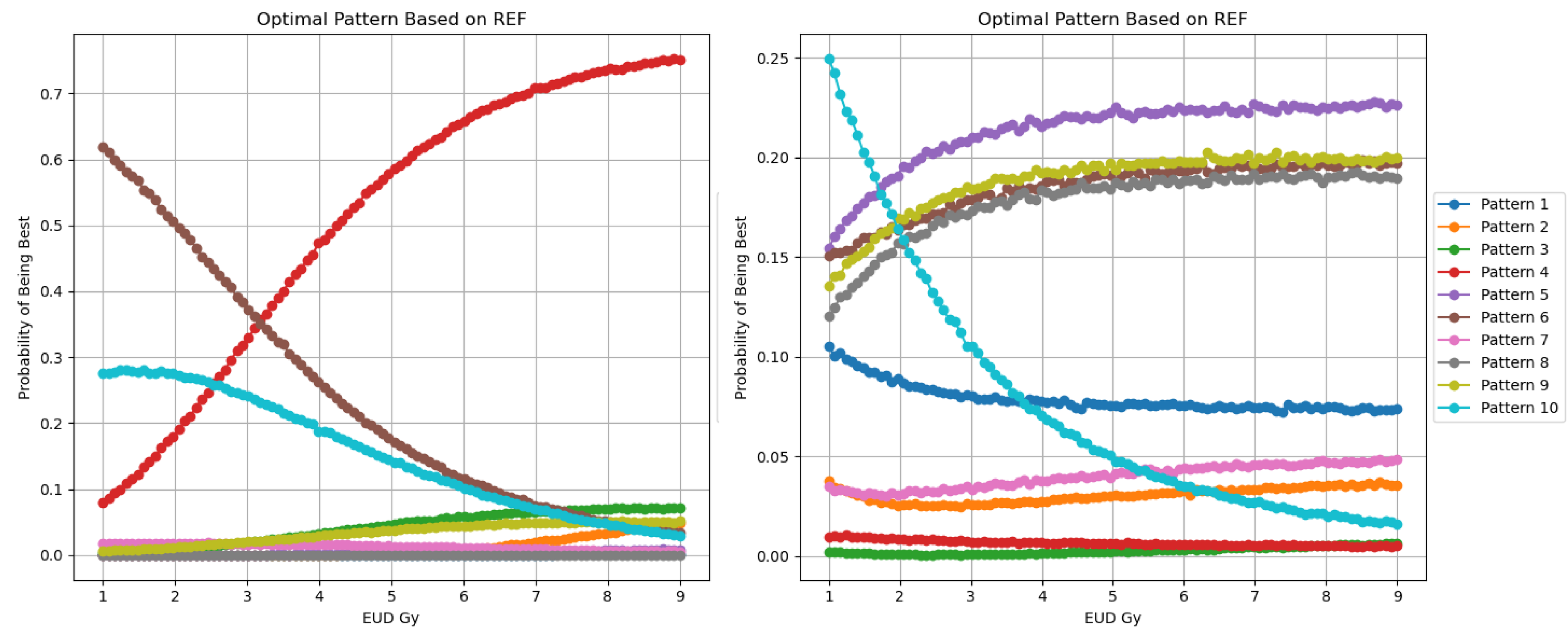

Figure 4: Resulting MC results of the probability of each pattern being the best in terms of REF. EUD range of 1-9 was evaluated.

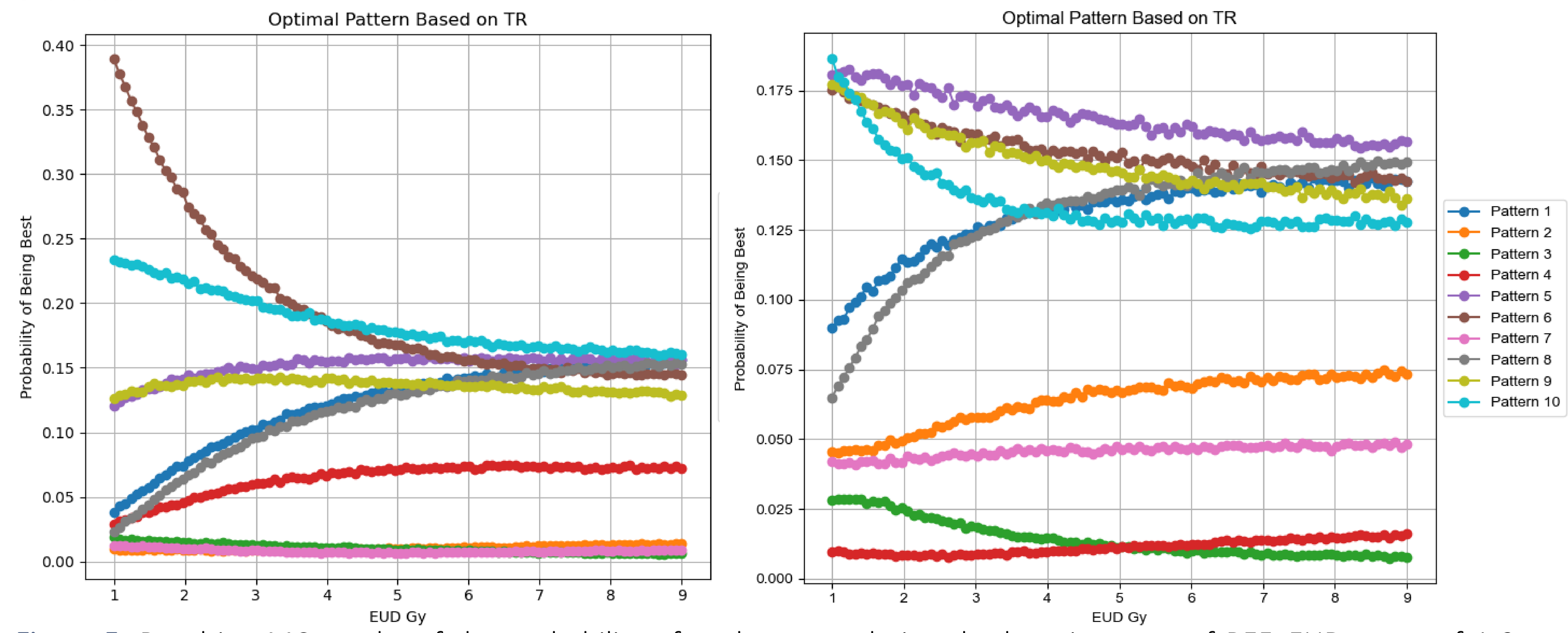

Figure 5: Resulting MC results of the probability of each pattern being the best in terms of REF. EUD range of 1-9 was evaluated.

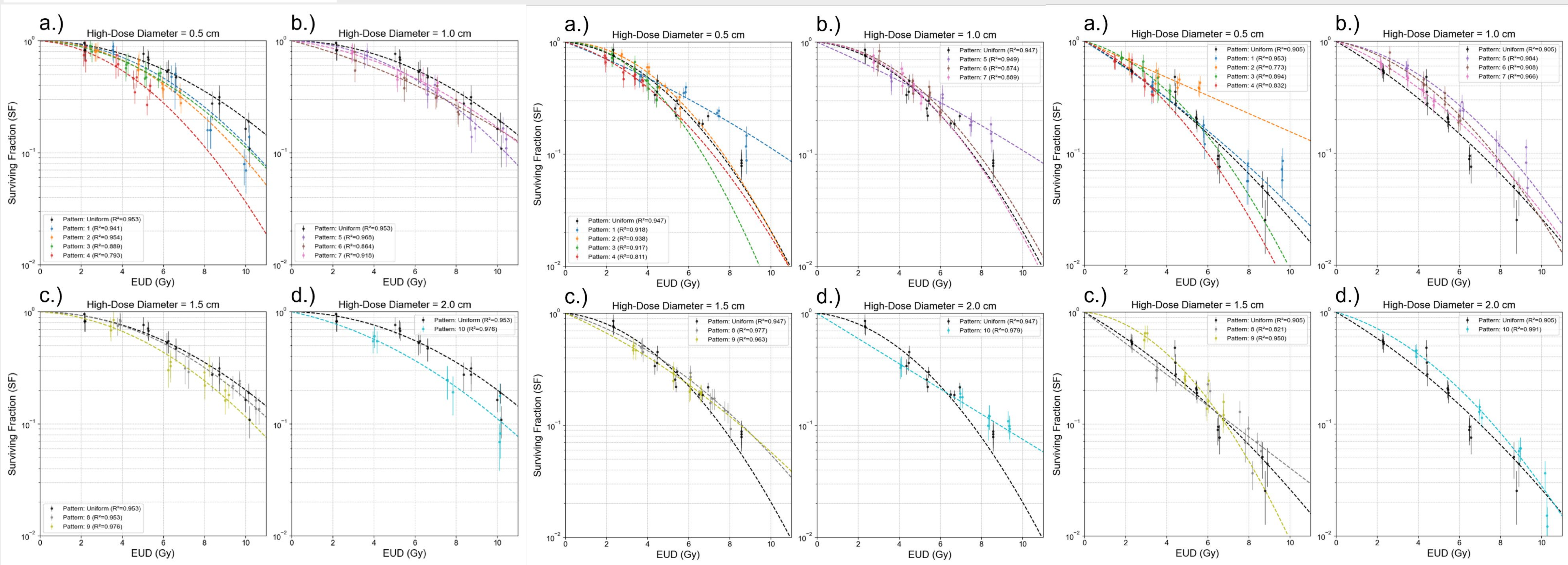

Figure 3: Resulting LQ curves fitted to cell lines irradiated with differing SFRT patterns. Left 4 panels comes from UM-SCC-2, middle 4 comes from UM-SCC-6, and rightmost panels are from the MFC-10A data. (a) are patterns with a high-dose diameter of 0.5cm, (b) is using a high-dose diameter of 1.0 cm, (c) are patterns using a high-dose diameter of 1.5 cm, and (d) are patterns with a high-dose diameter of 2.0 cm.

CONCLUSIONS

- SFRT is shown to be more effective for radioresistant tumors
- For radioresistant tumors, a high-dose diameter of 1.0 cm and a CTC of 2.0 cm is recommended.
- For radiosensitive tumors, a high-dose diameter of 1.0 cm and a CTC of 1.5 is recommended.
- Optimal pattern depends on the EUD that can be achieved and the tumor cell sensitivity.

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