Assessing Tumoral Volume in a Murine Colorectal Cancer Model Using MRI Technology

Introduction

Preclinical models, such as murine models, are essential for evaluating the efficacy of therapeutic treatment in oncology research. Recently, novel murine models with surgically implanted orthotopic tumor allow a more accurate representation of human cancer than traditional subcutaneous models. Orthotopic models however require *in vivo* evaluation. This shift necessitates the use of non-invasive imaging techniques to monitor tumor growth, as caliper measurements used for subcutaneous tumors are no longer applicable.

Monitoring the tumoral volume or its follow-up is often imprecise. It is also difficult to attribute weight changes to tumor progression or other confounding factors. One of the key endpoints in these studies is the assessment of tumoral volume, which allows researchers to monitor not only tumor growth but also response to treatments over time. MRI has emerged as a non-invasive and precise imaging technique providing detailed anatomical and functional information, making it particularly useful in oncology research.

This white paper, meant as a proof of concept, discusses the pertinence of using MRI technology to assess tumoral volume in an orthotopic murine colorectal cancer model.

Materials and Methods

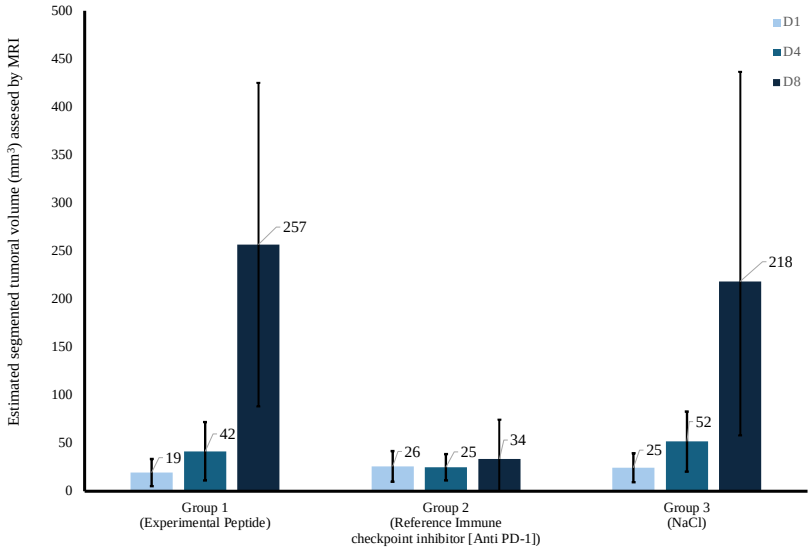
Experimental Design

- **Model**: Female murine model (C57BL/6).
- **Surgery**: Tumor surgically implanted orthotopically on the colon segment between two blood vessels 7 days before D0.
- **Groups**: Mice were divided into three groups:
    1. **Group 1** (Experimental Treatment): Treated with a new experimental peptide.
    2. **Group 2** (Positive Control): Treated with a known immune checkpoint inhibitor (Anti PD-1).
    3. **Group 3** (Negative Control): Treated with saline solution (NaCl).
- **Sample Size**: 8 mice per group.
- **Imaging**: MRI data acquisition was performed at three time points (D1, D4, and D8) - to assess changes in tumoral volume.

MRI Acquisition and Segmentation

Each Tumor volume at D1, D4 and D8 were manually segmented, as automated algorithms do not perform well due to the irregular nature of tumor shape, by two experts, to ensure precise delineation of tumor limits.

Data Analysis and Results



Graphic 1: *Mean tumor volumes (mm^3) were calculated for each group at each time point.* Standard deviations (error bars) represent the variation of the tumoral volume within each group.

	Group 1 Experimental peptide	**Group 2** Reference immune checkpoint inhibitor [Anti PD-1]	**Group 3** [NaCl]
Tumor Volume D1 (mm^3)	19	26	25
Tumor Volume D4 (mm^3)	42	25	52
Tumor Volume D8 (mm^3)	257	34	218

Table 1: Estimated tumoral volume assessed using MRI after segmentation

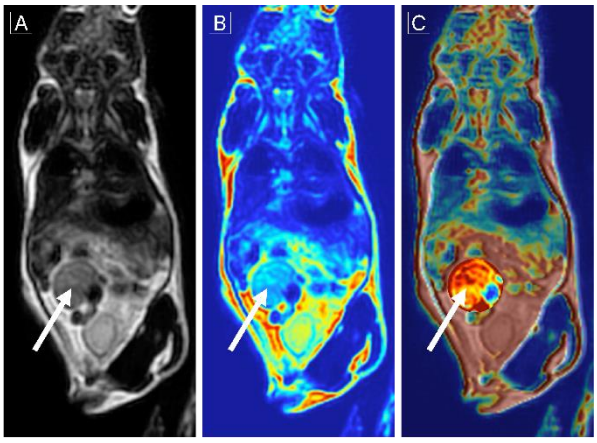


Image 1: *In-vivo monitoring of a colorectal cancer orthotopic preclinical model. MRI enabled real-time monitoring and quantification of the evolution of the volume of an orthotopic tumor lesion. The white arrow indicates the orthotopic lesion 8 days post-implantation.*

(A) *T1-weighted MRI was able to in vivo monitor and quantify the evolution of the volume of an orthotopic tumoral lesion.* ***(B)*** *and* ***(C)*** *Different lookup tables were used to better define the lesion. The white arrow indicates the orthotopic lesion 8 days after implantation.*

Discussion

MRI: A Powerful Tool for Non-Invasive Tumor Volume Assessment

Our results underscore the invaluable role of MRI in tracking tumor growth over time without the need for invasive procedures. Compared to traditional methods like caliper measurements or histological analysis, MRI offers several key advantages:

- **Precision:** MRI's 3D volumetric capabilities enable accurate measurement of irregularly shaped tumors, which are frequently observed in cancer models.
- **Non-Invasive Nature:** Unlike histological assessments that necessitate animal sacrifice at multiple time points, MRI allows for longitudinal studies in the contemporaneous cohort, minimizing variability and reducing the number of animals required.
- **Early Detection:** MRI's sensitivity in detecting small tumor volumes as early as day 1 is crucial for evaluating the early efficacy of therapeutic interventions.
- These advantages make MRI an indispensable tool for preclinical research, providing valuable insights into tumor biology and the effectiveness of potential treatments.

Interpretation of Results

A significant increase in tumor volume was observed in Group 1 by Day 8, suggesting that the experimental treatment may be less effective in controlling tumor progression in rapidly growing tumor models, such as MC38 model, compared to the positive control group. Conversely, Group 2, treated with the well-established immune checkpoint inhibitor anti-PD-1, exhibited a slight reduction in tumor volume, demonstrating the efficacy of this control treatment in suppressing tumor growth. The NaCl control group displayed consistent tumor growth, with a substantial increase in volume by Day 8, confirming the aggressive nature of tumor progression in this untreated model.

Relevance to Cancer Research

The use of MRI for measuring tumoral volume provides valuable data for early-phase drug development in cancer research. The ability to visualize and quantify tumor progression or regression offers critical insights into the efficacy of novel therapeutic agents. Moreover, the non-invasive nature of MRI means that researchers can obtain frequent, reliable measurements from the same animals, thereby increasing the statistical power of the study and reducing animal usage.

Conclusion

The results from this colorectal cancer murine model underscore the pertinence of using MRI technology for tumoral volume assessment. The high accuracy, non-invasive nature, and ability to monitor tumor growth longitudinally make MRI a gold standard for preclinical cancer studies. While the experimental treatment group exhibited significant variability in tumor response, the positive control group demonstrated the efficacy of an anti-tumoral agent, and the NaCl control group showed typical aggressive tumor progression. These findings reinforce the value of MRI in preclinical evaluations and its role in advancing the development of effective cancer therapies.

This white paper provides a foundation for further studies that can refine the experimental design, optimize the treatment regimen, and expand on the use of MRI in oncology research.