Development of System and Models for Measurement of Intra-Tumoral Pressures for Drug Delivery Planning

Vera Peters, Alexander Stone, Tracy Lin, Dr. Jaime Ramirez-Vick, and Dr. Vic Middleton

WRIGHT STATE UNIVERSITY
Biomedical Engineering
Industrial and Systems Engineering

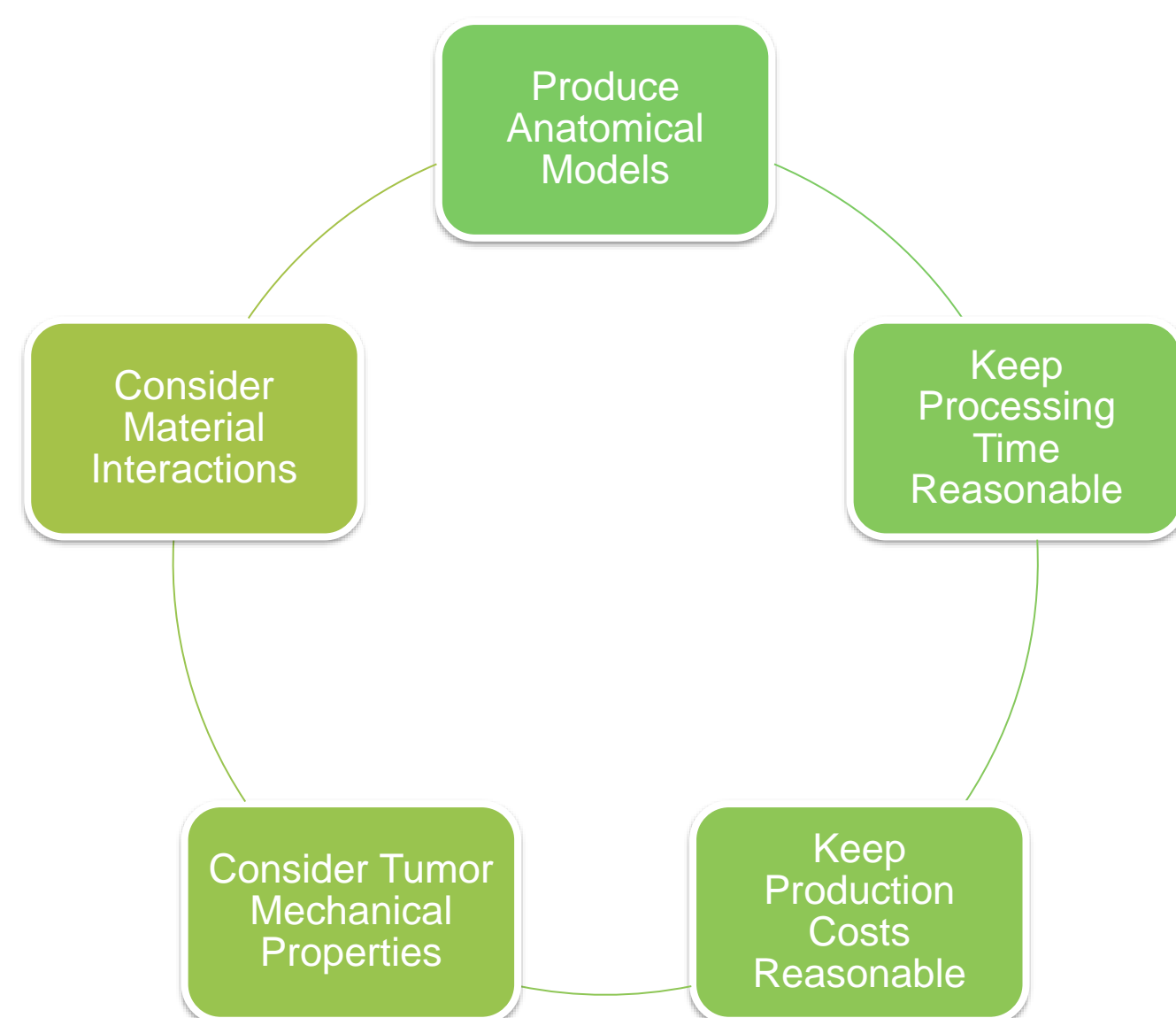**VA | U.S. Department of Veterans Affairs**

Problem Statement

Data on intra-tumoral pressures is limited, and evaluation methods are not well established. Due to this lack of data, minimal tumoral evaluation can be performed externally to the patient. Data concerning intra-tumoral pressures would further the clinician's ability to investigate image-guided therapy for tumors of various sizes and shapes.

Background

The Dayton VA is leading the charge for the development of new technologies in the Interventional Radiology field. By developing and dispersing a tumor modeling procedure, the team offers a method for developing anatomical models on which clinicians to practice procedures on before interacting with patients, and potentially, a model for measuring intratumoral pressures.

The project scope will encompass the creation of a methodology for developing these models, with the methodology including: instructions to manipulate the DICOM scan of the tumor in a 3D modeling software called MIMICS; instructions to convert the DICOM to an STL file; instructions for how to properly manipulate the file to ensure the correct features are present (i.e., a stand to hold the tumor model or creating a negative of the tumor); instructions for filling the molds and the materials necessary to do this task; and any relevant Safety Data Sheets (SDS) of the materials used.

Objectives

- Produce Anatomical Models
- Keep Processing Time Reasonable
- Keep Production Costs Reasonable
- Consider Tumor Mechanical Properties
- Consider Material Interactions

Materials and Methods

Following protocol was employed:
- CT from public domain was obtained.
- Utilizing the program MIMICs, the tumor was processed and turned into an STL file.
- The STL file of the tumor was downloaded onto the VA biomedical engineering lab laptop and processed within Meshmixer to add additional structures. This step was omitted if no additional steps were needed.
- Files were opened on Preform to prepare for printing on Formlabs 3BL resin printer. For printing surrogate tumors, Formlabs 3BL printer was exclusively used.
- The models were placed in Formlabs Wash machine, prefilled with isopropyl alcohol and washed for approximately 10 minutes.
- Models were air dried and then cured for an additional 20-30 minutes in Formlabs Cure L device.
- 3x3 model model boxes created in Solidworks were printed using ABS on the AON M2+ in advance.
- Silicon as the primary material was mixed with a 1:1 ratio of Silicon and Silicone curing agent (Part A and Part B).
- Agar model was mixed in a 1:1.5 ratio (cup:tsp) between water and agar.
- 8 models were made based on silicon and agar, and resin, agar, or silicon representing as tumor centers. 7 of those models stayed intact.

Image 1. Visual display for filling the box half-way with agar, allowing it to set, placing the permanent tumor model within the box on top of the agar, and filling the remaining space with agar to create one whole model.

Image 2. Example of removing Tumor 3 silicon model from the 3x3 inch box.

- Models created: Tumor 1 (Grey V4) in agar, Tumor 1 (50A) in silicon, Tumor 1 (80A) in silicon, Tumor 2 (Grey V4) in silicon filled with agar, Tumor 2 (Grey V4) in agar filled with silicon, Tumor 2 (50A) in agar, Tumor 3 (Grey V4) in silicon filled with agar, Tumor 3 (50A) in agar.
- Finished models were transported to VA for Ultrasound testing.

Results

	Time to Print	Volume of Resin	Cost per Print
Grey V4	5 hr 5 min	109.14 mL	$16.37
Elastic 50A	11 hr 29 min	102.69 mL	$20.54

Table 1. Time to print, volume of resin used, and overall cost to print Tumor 1 on a stand using various materials.

	Time to Print	Volume of Resin	Cost per Print
Elastic 50A	5 hr 15 min	24.31 mL	$4.86
Flexible 80A	5 hr 37 min	23.76 mL	$4.75

Table 2. Time to print, volume of resin used, and overall cost to print Tumor 1 without a stand using various materials.

Table 3. Time to print, volume of resin used, and overall cost to print Tumor 2 on a stand using various materials

	Time to Print	Volume of Resin	Cost per Print
Grey V4	4 hr 24 min	100.69 mL	$15.10
Elastic 50A	9 hr 55 min	93.10 mL	$18.62

Table 4. Time to print, volume of resin used, and overall cost to print Tumor 2 without a stand using various materials

	Time to Print	Volume of Resin	Cost per Print
Elastic 50A	3 hr 43 min	9.99 mL	$2.00
Flexible 80A	3 hr 58 min	9.97 mL	$1.99

	Time to Print	Volume of Resin	Cost per Print
Grey V4	4 hr 0 min	102.22 mL	$15.33
Elastic 50A	8 hr 37 min	94.57 mL	$18.91

Table 5. Time to print, volume of resin used, and overall cost to print Tumor 3 on a stand using various materials

	Time to Print	Volume of Resin	Cost per Print
Elastic 50A	2 hr 45 min	9.45 mL	$1.89
Flexible 80A	2 hr 53 min	9.31 mL	$1.86

Table 6. Time to print, volume of resin used, and overall cost to print Tumor 3 without a stand using various materials

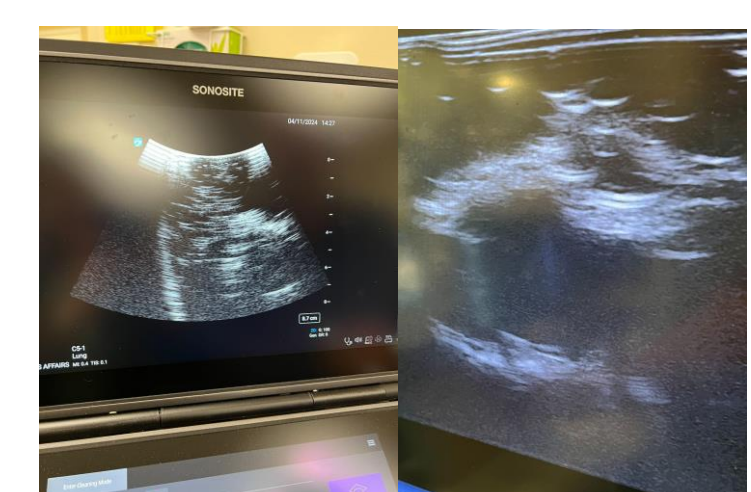**Image 3.** Tumor 1 (Grey V4) model being removed from agar.

Image 4. (*Left*) Sonosite ultrasound with Tumor 1 (50A). (*Right*) GE ultrasound with Tumor 1 (50A), both in silicon. The black mass is the tumor. The tumor also stayed in place without any issues, the only problem that arose was during the ultrasound process. The Sonosite Ultrasound had a hard time finding the tumor, as shown in images 4. To verify, it was assessed by GE ultrasound on right.
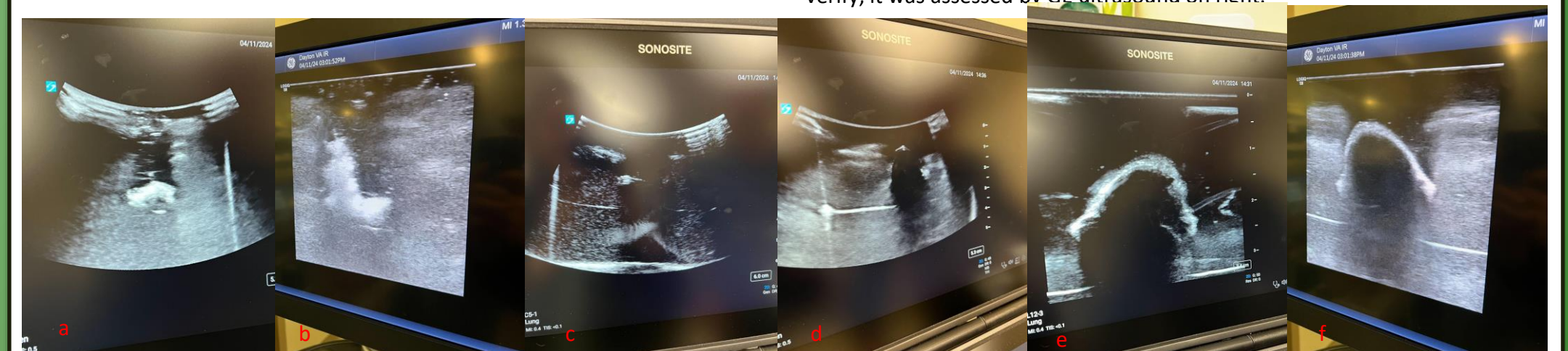

Image 5. a and b) Evaluating Tumor 2 (Grey V4) in agar with silicon center scanned with the Sonosite Ultrasound (*a*) and GE ultrasound (*b*). **c-d)** Evaluating Tumor 2 (50A) using the Sonosite ultrasound with the C5-1 head. **e-f)** Evaluating Tumor 2 (50A) using the Sonosite ultrasound with the head L12-3 (e) and the GE ultrasound (f).

Conclusion

With more time, the team could test the models produced and compare them to any available data on the properties of tumors and the surrounding tissue. It might be necessary to test the tumors directly by performing the tests in vivo. However, this would require extensive approval processes and the collaboration of Dr. Short and his patients. The team were unable to use patient-specific CT scans to produce the tumor models due to patient safety concerns and therefore scans available from online sources were used instead.

Based on the results, the Grey V4 material is currently the best choice for printing the 3D tumors for developing a model. The agar is currently the better option for developing models that can be used concurrently with ultrasound; however, as stated above, developing other materials that will be able to withstand more force would overall improve these physical models.

Acknowledgments