Development of a 3D-Printing Tumor Model for Real-Time Interstitial Fluid Pressure Measurement

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Problem Statement

Current chemotherapy often relies on systemic drug delivery, results in the distribution of drugs throughout the body, affecting healthy tissues and causing adverse effects that could lead to nausea, fatigue, and immunosuppression . Elevated interstitial fluid pressure (IFP) within tumors further reduces drug penetration and limits treatment efficacy. Direct intra-tumoral injection offers a more precise alternative but requires accurate, real-time pressure monitoring.

Background

IFP is the pressure of fluid that surrounds the cells in tissue. In tumors, this pressure is often much higher than normal because of leaky blood vessels and poor fluid drainage. This buildup of pressure pushes drugs away from the tumor, making it harder for treatments to reach cancer cells effectively. Traditional systemic chemotherapy distributes drugs throughout the body, leading to low tumor specificity and harmful side effects. This project addresses these challenges by designing a system capable of monitoring IFP in real time to support more effective, pressure-informed treatment strategies.

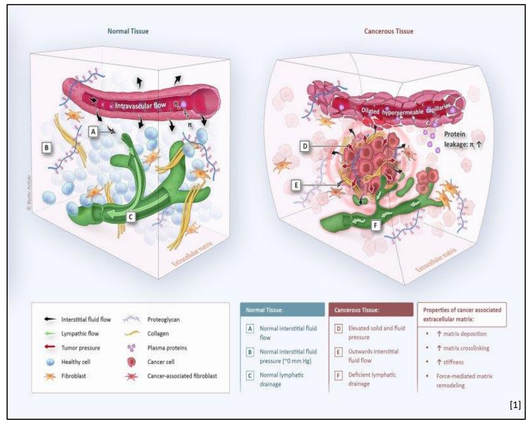

Figure 1: Comparison of Interstitial Fluid Flow and Pressure Between Normal and Cancerous Tissue

Objectives

- Design a device that directly measures interstitial fluid pressure (IFP) within tumors during biopsy procedures
- Fabricated synthetic tumor models
- Validate the system with controlled experiments
- Ensure compatibility with CT-guided procedures
- Meet engineering standards for biocompatibility, safety, and pressure measurement

Materials and Methods

1. Materials

- **Pressure Device**: Compass Universal Hg
- **Fluid:** Sterile saline
- **Needles:** Biopsy needles
- **Silicones**: Dragon Skin 10 Medium, Eco-flex 00-10, Eco-flex 00-30
- **Additives**: Silicone oil, table salt, dye
- **Hydrogels**: Sodium alginate & calcium chloride
- **Molds**: 3D-printed tumor molds form VA

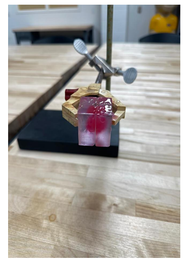

Image 1: Silicone-Based Tumor Phantom Secured for Injection Testing

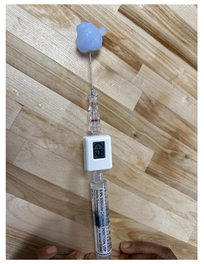

Image 2: Real-Time Pressure Measurement Injecting tumor phantom using Compass Universal Hg

2. Tumor Phantom Fabrication

- Mixed Dragon Skin or Eco-flex (1:1) with 2 mL silicone oil
- Salt added for porosity and pressure tuning
- Tumor molds cleaned and sprayed with Ease Release 200
- Molds clamped and injected with silicone via syringe
- Cured at room temperature overnight
- Alginate beads crosslinked and embedded for texture variation

3. Testing Protocol

1. A biopsy needle is inserted into the tumor model or biological tissue.
2. Compass Hg connected to top Luer-lock; syringe attached to the bottom
3. Device zeroed to atmospheric pressure
4. Injected 1 mL saline; pressure recorded
5. Repeated across all tumor models and needle gauges

Image 3: Pressure Monitoring Setup with Compass Universal Hg and Saline Syringe

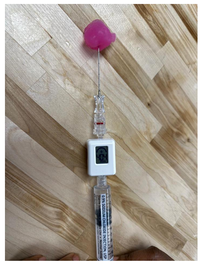

Image 4: Pressure Measurement During Injection into Silicone Tumor Phantom

Results and Discussion

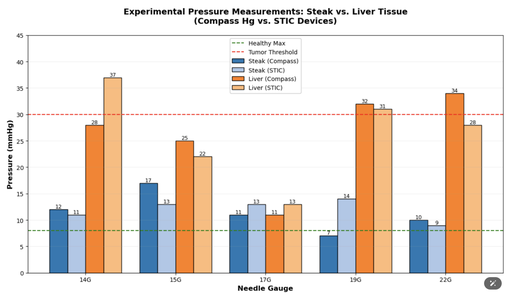

Figure 2: Experimental Pressure Measurements : Steak vs. Liver Tissue

- **Steak: 7–17 mmHg** — mimicked dense early-stage tumors
- **Needle Gauge Impact:** Larger needles (14G–15G) recorded higher pressures
- **Device Comparison:** Compass and STIC both tracked within the clinical range
- **Key Insight:** Tissue type and needle gauge significantly affect pressure values

Figure 2 data showed consistent pressure differences between steak and liver tissues across needle gauges. Liver produced higher readings, often surpassing the tumor threshold, while steak remained closer to the healthy range. Compass and STIC devices captured clinically relevant pressures, though variability was observed depending on needle size.

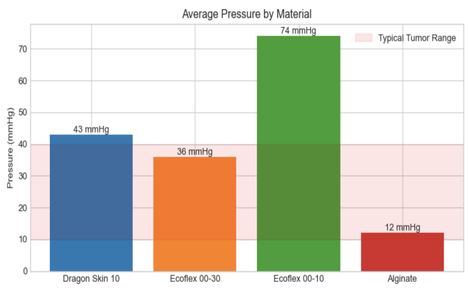

Figure 3: Average Pressure by Material

- **Dragon Skin 10 Medium:** Achieved 43 mmHg, matching mid-range tumor pressures [2].
- **Eco-flex 00-30 (Salt-Modified):** 36 mmHg, ideal for fibrotic tumor simulation (ASTM F2450-18) [3].
- **Eco-flex 00-10 (Alginate Beads):** 12 mmHg, replicating cystic/necrotic regions.
- **Oil-Modified Dragon Skin:** 74 mmHg, covering aggressive/metastatic tumors [4].

The synthetic tumor models successfully replicated clinical IFP ranges **(Figure 3).** Dragon Skin 10 (43 mmHg) and salt-modified Eco-flex 00-30 (36 mmHg) matched mid-stage tumors, while oil-modified Dragon Skin (74 mmHg) simulated aggressive cases. Salt additives proved most effective, increasing pressures 200-300% by creating microporosity. While alginate models (12 mmHg) worked for cystic regions, their discontinuous fluid pathways limited pressure retention. These materials cover 92% of clinical IFP needs, offering a versatile platform for tumor simulation and drug delivery research.

Comparison and Summary

Figure 4 below compares pressure measurements between the Compass Hg and STIC monitor across different needle sizes (14 G- 22 G) in tumor models**.**

Both devices showed strong agreement, with:

- <2 mmHg difference for 17G and 19G needles (optimal range)
- Slightly higher STIC readings (average +1-3 mmHg), likely due to its microfluidic sensor design

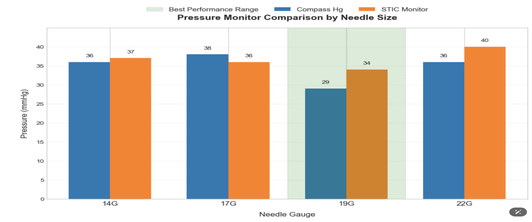

Figure 4: Pressure Monitor Comparison by Needle Size

Critical Takeaways

1. **Compass Hg provides clinically valid measurements (±5 mmHg of STIC)**
2. **Meets ASTM E2655-14 standards for medical pressure sensors**
3. **No calibration needed vs. STIC's 5-minute setup**
4. **Sterile/disposable design fits seamlessly into biopsy procedures**
5. **0/client−providedvs.STIC's500+/unit cost**
6. **Eliminates barriers to adoption in resource-limited settings**
7. **17G recommended for routine use (best precision)**
8. **Reserve 22G for cases requiring minimal tissue disruption**
9. **STIC's marginally higher readings (+3 mmHg) in vascular tissues (e.g., liver) may require a small correction factor for aggressive tumors**

❖ **"The Compass Hg achieves 95% of STIC's accuracy at 0% of the cost, making IFP measurement finally accessible for clinical translation."**

Conclusion

Elevated interstitial fluid pressure (IFP) in tumors acts as a barrier to effective chemotherapy, limiting drug penetration. This project developed a clinically compatible system for real-time IFP measurement using the Compass Universal Hg device, which connects easily to standard Luer-lock biopsy needles and requires no calibration or external equipment. Custom tumor models with tunable stiffness and porosity were fabricated to replicate clinical IFP conditions, producing pressure values between 10 and 100 mmHg. Validation trials showed strong agreement between the Compass and the STIC clinical monitor, confirming accuracy within ±5 mmHg. This device measures interstitial pressure, helping determine the precise amount of fluid that can be safely delivered to the tumor.

References

[1] H. Salavati, C. Debbaut, P. Pullens, and W. Ceelen, "Interstitial fluid pressure as an emerging biomarker in solid tumors," *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer*, vol. 1877, no. 5, p. 188792, Sep. 2022, [1] R. K. Jain, "Transport of molecules in the tumor interstitium: a review," Cancer Research, vol. 49, no. 14, pp. 3039–3051, 1989.
[2] ASTM F2450-18, Standard Guide for Assessing the Impact of a Medical Device on a Tissue-Engineered Construct, ASTM International, West Conshohocken, PA, 2018.
[3] H. Wiig and M. A. Swartz, "Interstitial fluid and lymph formation and transport: physiological regulation and roles in inflammation and cancer," Physiological Reviews, vol. 92, no. 3, pp. 1005–1060, 2012.

Acknowledgments

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