Electroporation-Based Molecular Sampling for Brain Diagnostics: A Novel Approach to Reduce False Negatives and Enable Spatial Proteomics

Executive Summary

False-negative outcomes in needle biopsies remain a real barrier to timely, precise oncology care because a single needle pass samples only a narrow tissue column and can miss aggressive tumor subclones. Electroporation-based molecular harvesting ("**e-biopsy**") uses pulsed electric fields to permeabilize cell membranes around the needle, enabling intracellular proteins to be collected from a **larger effective sampling volume** with **minimal invasiveness**. In murine brain melanoma models, **e-biopsy pulled tumor-like proteomic signatures from 0.5 mm outside the visible tumor margin**, while clearly differing from healthy brain tissue—suggesting a path to reduce false negatives and improve margin detection.

Background & Clinical Need

- **Biopsy limitations.** Standard needle biopsies risk missing lethal clones because they only sample the tissue directly intersected by the needle; scaling needle size can reduce false negatives but increases risks like bleeding and infection.
- **Liquid biopsy constraints.** Circulating biomarkers provide systemic data but often lack **organ specificity** and **spatial resolution** needed for margin assessment or subclone mapping.

Technology Overview: e-biopsy by Electroporation

Concept. Pulsed electric fields transiently permeabilize membranes in tissue surrounding a sampling needle, allowing intracellular proteins to diffuse toward gentle vacuum in the needle and be captured for proteomic analysis—expanding sampled volume without increasing hardware invasiveness.

Protocol (preclinical). In the study: 40 pulses at **1000 V for 40 µs (4 Hz)** followed by 40 pulses at **50 V for 15 ms (4 Hz)**; sampling positions included **tumor center**, **0.5 mm outside the visible margin**, and **≥10 mm away (healthy brain)**.

Key Findings

Proteomic detection beyond visible margins

- **Margin sampling (0.5 mm)** captured **protein patterns similar to tumor center** and **distinct from healthy brain**, indicating tumor-relevant molecular signatures outside the visible lesion.
- Across **15 samples** (5 mice × 3 sites), **5,072 proteins** were detected; **4,743** appeared in at least 3 mice. A set of **183 proteins** matched a "tumor-present" pattern (P10) in **all 5 mice**, and **5 proteins** matched the stricter center+margin pattern (P110) in **4/5 mice**—including **DDX3X**, **FUBP2**, and **RPS9**.

Electric-field coverage & thermal profile

Finite-element modeling showed that e-biopsy pulses can **electroporate substantial portions of the tumor** even when the needle is placed at the margin, expanding the effective sampling volume. Using brain electroporation thresholds of **500 V/cm (reversible)** and **700 V/cm (irreversible)**:

- **Center placement:** ~**92.5%** coverage at 500 V/cm; ~**82.1%** at 700 V/cm.
- **Margin (0.5 mm outside):** ~**46.5%** coverage at 500 V/cm; ~**28.3%** at 700 V/cm.
- **Healthy (10 mm away): 0%** coverage at both thresholds.
- **Thermal safety (simulated peak temperatures).** ~**40.15°C** (center), ~**39.61°C** (margin), and ~**47.7°C** (healthy-away), underscoring the need for protocol optimization and placement to minimize heating.

Clinical & Operational Implications

- **Reduce false negatives.** Sampling tumor-associated molecules **beyond the needle path** may lower the chance of missing aggressive clones.
- **Spatial molecular cartography.** Multi-site probing can map tumor/microenvironment biochemistry at **higher spatial resolution**.
- **Complement to histopathology.** Provides **biochemical context** alongside imaging/pathology during stereotactic or intraoperative workflows.

- **Margin assessment potential.** Early evidence suggests feasibility for detecting **tumor presence near margins**; clinical validation is the next step.

Safety & Risk Considerations

- **Thermal rise & electrochemistry.** Optimize pulse parameters, electrode materials, and placement to limit heating, pH shifts, and metal ion release.
- **Transport confounders.** Sampling efficiency depends on intracellular abundance, diffusion, and extracellular transport—factors to be engineered/controlled.
- **Regulatory stage.** Current evidence is **ex vivo in murine brain tissue**; human safety/efficacy will require rigorous trials. **Not yet cleared for clinical use.**

Limitations of Current Evidence

Findings derive from **ex vivo** murine models and **2D** simulations; 3D transport, clinical heterogeneity, and workflow variables remain to be quantified in multi-center trials assessing diagnostic yield, sensitivity/specificity, and health-economic impact.

Translational Roadmap

1. **Preclinical optimization**: pulse parameters, electrode geometry, proteomic pipelines.
2. **First-in-human feasibility**: safety endpoints, sampling yield, histology concordance.
3. **Pivotal studies**: performance vs. standard biopsy, impact on false negatives/margin assessment.
4. **Integration**: workflow standardization, training, reimbursement & cost-effectiveness.

Why e-biopsy by Elsy Medical

- **Larger effective sampling volume** with **minimally invasive** hardware.
- **Proteomics-ready extracts** for deep molecular characterization.
- **Intraoperative/stereotactic adjunct** potential.
- **Designed to complement** existing imaging and pathology workflows.

Reference

Genish I., Gabay B., Ruban A., Goldshmit Y., Singh A., Wise J., Levkov K., Shalom A., Vitkin E., Yakhini Z., Golberg A. (2022). **Electroporation-based proteome sampling *ex vivo* enables the detection of brain melanoma protein signatures in a location proximate to visible tumor margins.** *PLOS ONE* 17(5): e0265866.

Collaborate With Us

The E-biopsy research platform is available for collaboration and experimental use. We are seeking research partners to explore new applications in oncology, pharmacology, and regenerative medicine.

Contact us to design your next study:

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