Electroporation-based proteome sampling *ex vivo* enables the detection of brain melanoma protein signatures in a location proximate to visible tumor margins

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Introduction

Needle-based biopsies main concern:

- Misdiagnosis may occur, specifically in needle-based biopsies that provide information limited to the needle size.

E-biopsy

- Molecular harvesting with electroporation.
- E-biopsy enables extraction of specific biomarkers in vivo.
- Can increase the sampled tissue volume in comparison to tissue sampling by a needle alone.
- Minimally invasive.
- Enables multiple probing in different locations of the lesion.

The e-biopsy method for molecular harvesting from brain solid tumors *ex vivo* using electroporation

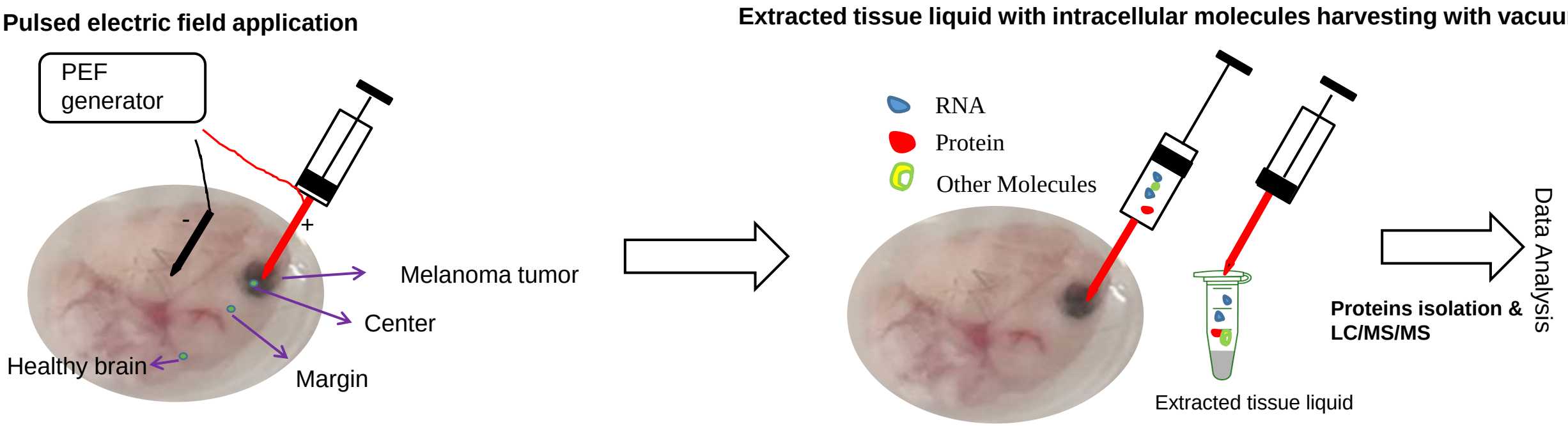
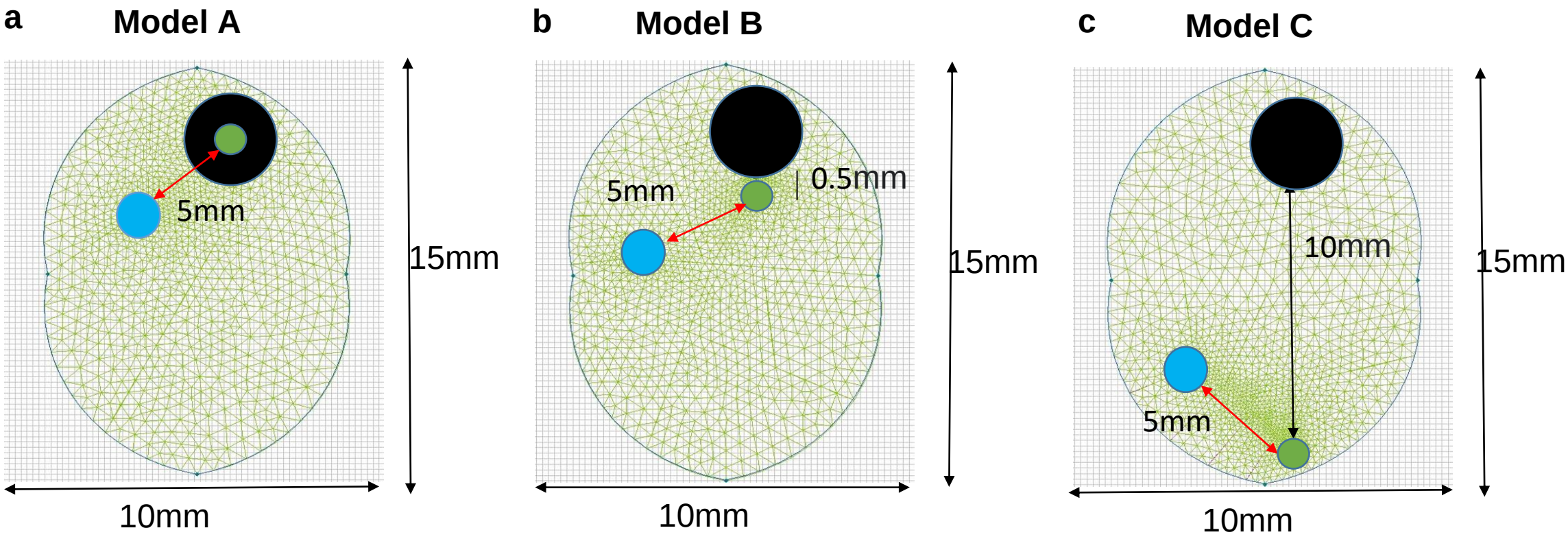


Figure 1. e-biopsy technique

1. **Pulsed electric field**
2. **Vacuum**
3. **Molecular analysis**

Model Geometry



0.642 mm ground radius

0.312 mm e-biopsy needle radius

Melanoma tumor

Equation and boundary conditions

Numerical solutions for a Laplace equation that result in the electric field distribution in the brain and brain melanoma models were performed in QuickField (Tera Analysis, Denmark).

To calculate the electric field distribution, we used Laplace equation:

$$\nabla^2 U = 0$$

with the following potentials:

$$V_{Short,\, high\ voltage\ pulse} = 1000V\ ,\ V_{Long,\, low\ voltage\ pulse} = 50V\ ,\ V_{Ground} = 0V$$

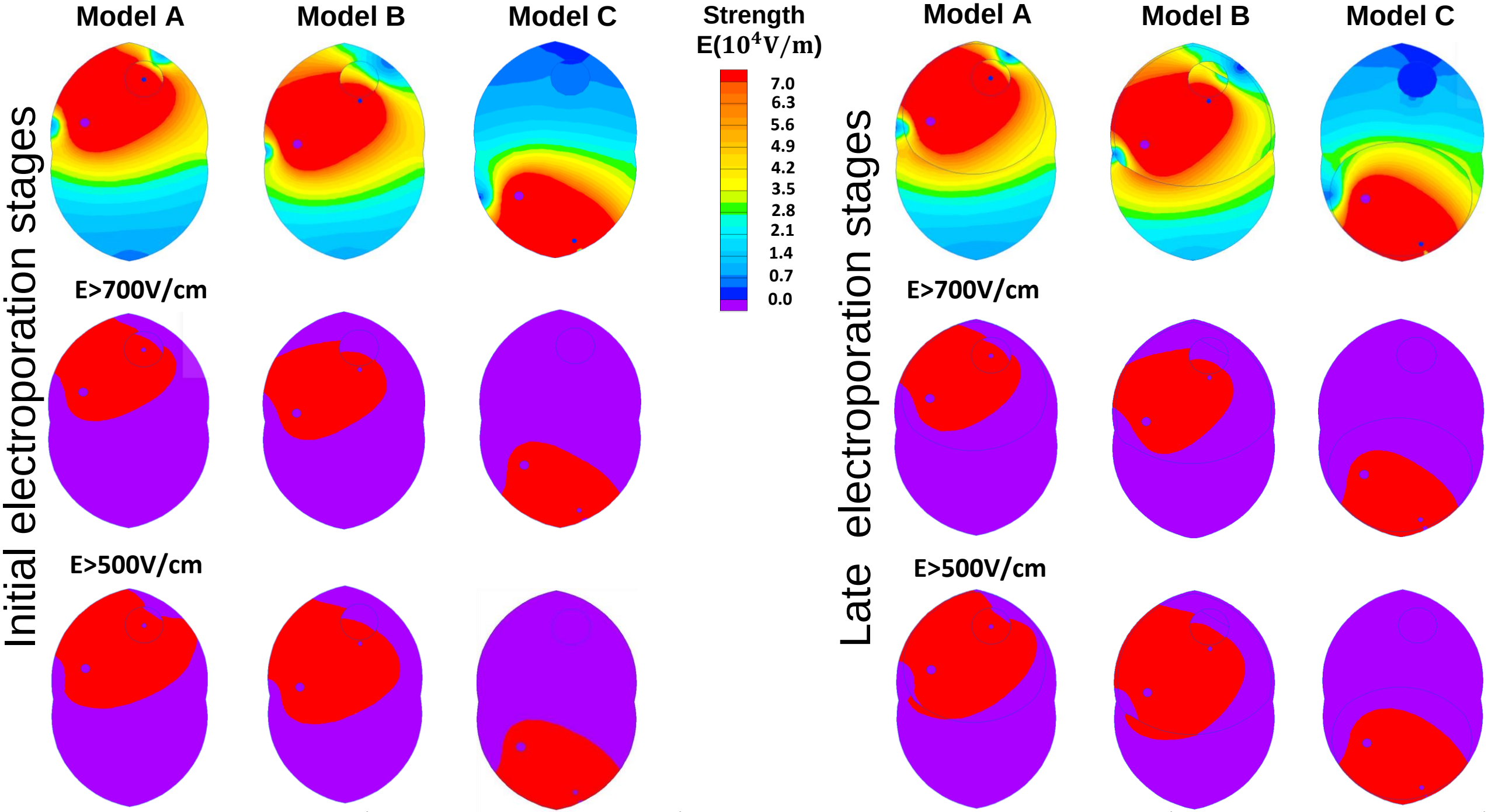


Figure 3 brain conductivity **0.258 S m^{-1}**, melanoma conductivity **0.43 S m^{-1}** brain conductivity **0.882 S m^{-1}**, melanoma conductivity **1.47 S m^{-1}**

Thermal effects

To calculate the power supplied by the pulsed electric field, we used the following equation:

$$Q_{avg} = \frac{V_{RMS}^2}{R} = \frac{V^2 t_p f}{R}$$

where Q_{avg}(W) is the total average power delivered by square pulse electric field, R (ohm) is the resistance, V_{RMS} is the root mean square voltage, V (Volt) is the applied voltage,t_p is the duration of the pulse and f (Hz) is the frequency of the pulse wave.

To calculate the thermal distribution, we solved the transient heat transfer equation :

$$\frac{\partial}{\partial x}\left(\gamma_x \frac{\partial T}{\partial x}\right) + \frac{\partial}{\partial x}\left(\gamma_y \frac{\partial T}{\partial y}\right) + \frac{\partial}{\partial z}\left(\gamma_z \frac{\partial T}{\partial z}\right) = -q - c_p \frac{\partial T}{\partial t}$$

Where T is the temperature (K), γ(W $K^{-1}m^{-1}$) is the thermal conductivity, c_p ($J\ K^{-1}\ kg^{-1}$) is the specific heat capacitance, t (s) is time, q (Wm^{-3}) is the volume power of heat sources. In our problem q is the average volume power supplied by a pulsed electric field. We assume that heat is transferred by convection between the air, and mouse brain, and he convection coefficient with air is α = 5 W K^{-1} m^{-2}

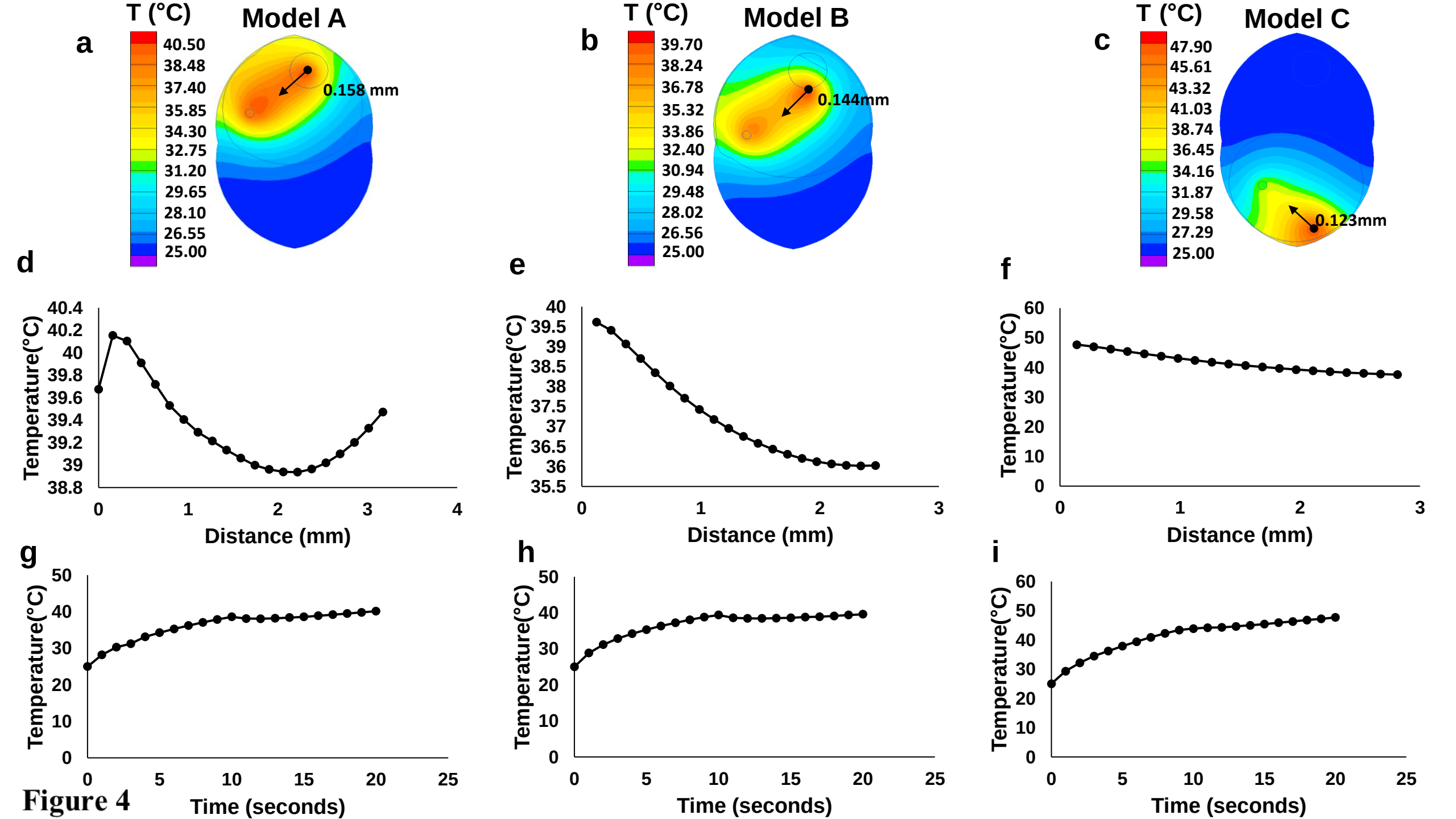

a
T (°C)
Model A
40.50
38.48
37.40
35.85
34.30
32.75
31.20
29.65
28.10
26.55
25.00
0.158 mm
b
T (°C)
Model B
39.70
38.24
36.78
35.32
33.86
32.40
30.94
29.48
28.02
26.56
25.00
0.144mm
c
T (°C)
Model C
47.90
45.61
43.32
41.03
38.74
36.45
34.16
31.87
29.58
27.29
25.00
0.123mm
d
Temperature(°C)
Distance (mm)
e
Temperature(°C)
Distance (mm)
f
Temperature(°C)
Distance (mm)
g
Temperature(°C)
Time (seconds)
h
Temperature(°C)
Time (seconds)
i
Temperature(°C)
Time (seconds)

Figure 4

Electroporated tissue volume

In this work, we calculated the areas of tumor covered by electric field above two thresholds E_c: 500Vcm^{-1} and 700Vcm^{-1}. As a first approximation we calculated the visible tumor coverage% as described in the equation:

$$Visible\_Tumor\ coverage\% = 100\% \frac{A_{E>E_c}}{A_t}$$

Where A_t is the total area of the tumor in the 2D simulation, E_c is the threshold of the electric field above which the tissue is electroporated, $A_{E>Ec}$ is the area of the tumor in which the electric field is larger than the threshold electric field required for electroporation.

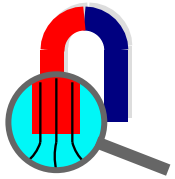
	Model A	**Model B**	**Model C**
Visible_Tumor electroporated area $(\mathbf{mm^2})$ (E>500 V cm^{-1})	4.41±0.02	2.219±0.05	0
Visible_Tumor coverage (%) for Ec= 500 V cm^{-1}	92.47	46.52	0
Visbile_Tumor electroporated area $(\mathbf{mm^2})$ (E>700 V cm^{-1})	3.91±0.01	1.346±0.03	0
Visible_Tumor coverage (%) for Ec= 700 V cm^{-1}	82.1	28.26	0

Conclusions

E-biopsy probed proteome signature differentiates between melanoma tumor center and healthy brain in mice.

E-biopsy provide a possibility to detect tumor margins or detect tumor presence near the biopsy needle .

These findings were corroborated with numerical models.



This recording is over

More recordings and simulation examples at www.quickfield.com