Finite Element Analysis of Customized Alternating Electric Field (AEF) Transducers for Small Animal Applications

Ha Nguyen

PI: Dr. Keith Schubert

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LOMA LINDA UNIVERSITY School of Medicine

THE UNIVERSITY OF TEXAS MD Anderson ~~Cancer~~ Center

Stanford University

UNIVERSITY OF DELAWARE

Keck Medicine of USC

Overview

Introduction

➢ Glioblastoma (GBM)

  ○ High mortality and morbidity
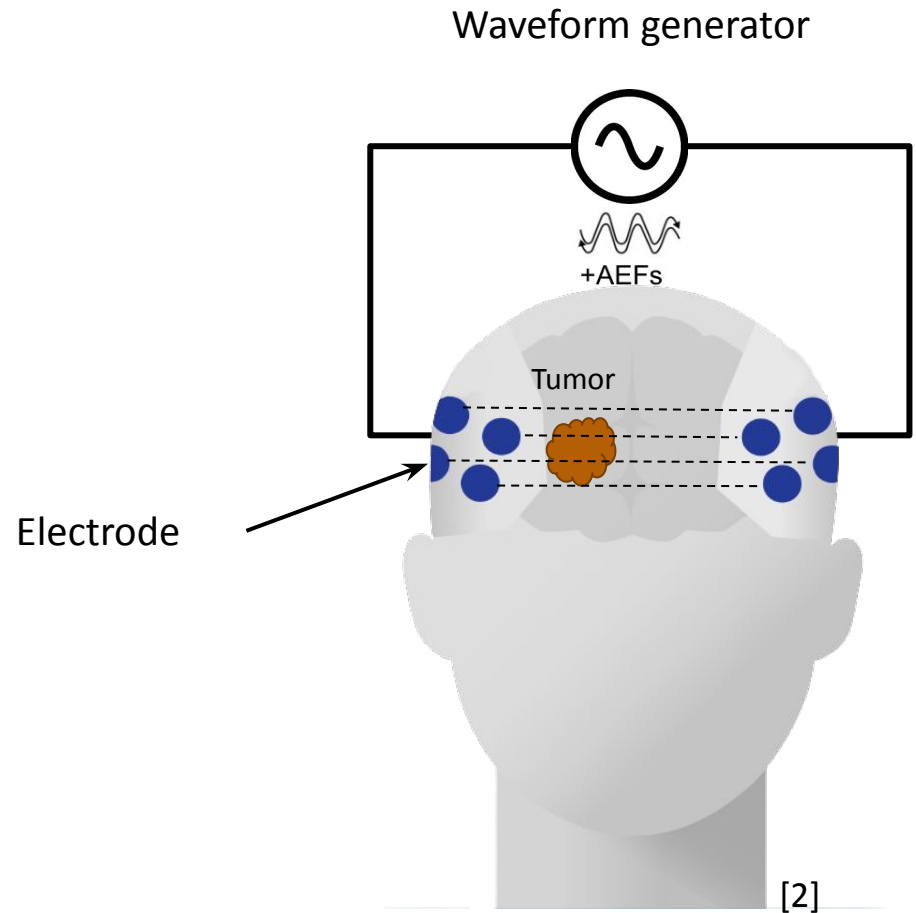
[1]
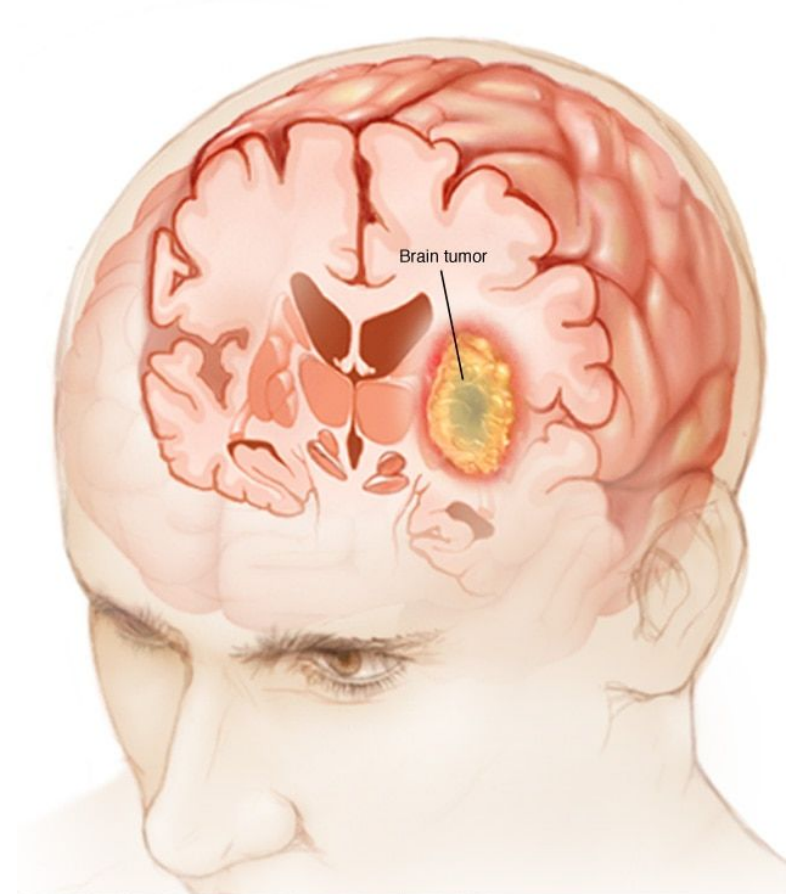
Introduction

➤ Glioblastoma (GBM)

  ○ High mortality and morbidity

  ○ Standard treatment

    ■ Surgery

    ■ Radiation

    ■ Chemotherapy

➤ Alternating electric field (AEF) therapy

Alternating Electric Fields (AEF) Therapy

➢ Alternating electric fields

- ○ 100-300 kHz
- ○ 1-3 V/cm

Waveform generator

+AEFs

Tumor

Electrode

[2]

Alternating Electric Fields (AEF) Therapy

➢ Alternating electric fields

  ○ 100-300 kHz

  ○ 1-3 V/cm

➢ FDA-approval

  ○ EF-11 trial

    ■ 2011 for recurrent GBM

  ○ EF-14 trial

    ■ 2015 for newly diagnosed GBM

Motivation

➢ Limited of in vivo studies

  ○ Incomplete knowledge of AEFs

inovitro[TM] Lab Research System   [3]

Motivation

➢ Limited of in vivo studies

  ○ Incomplete knowledge of AEFs

➢ Ultimate goal

  ○ A systematic AEF platform for small animal applications

➢ Computational work

  ○ Customized AEF transducers
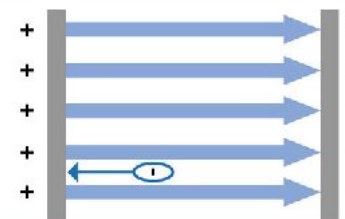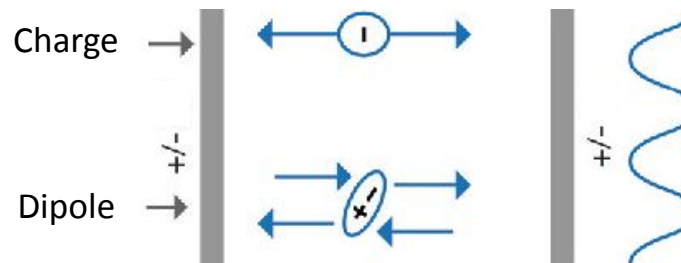
    ■ Titanium screws and metal caps

Overview

❏ **Introduction**

❏ **Literature Review**

❏ **Methodology**

❏ **Results and Discussion**

❏ **Conclusion**

Fundamental Principles of AEFs

➢ Electric field
  ○ Intermediate frequency
    ■ 100-500 kHz
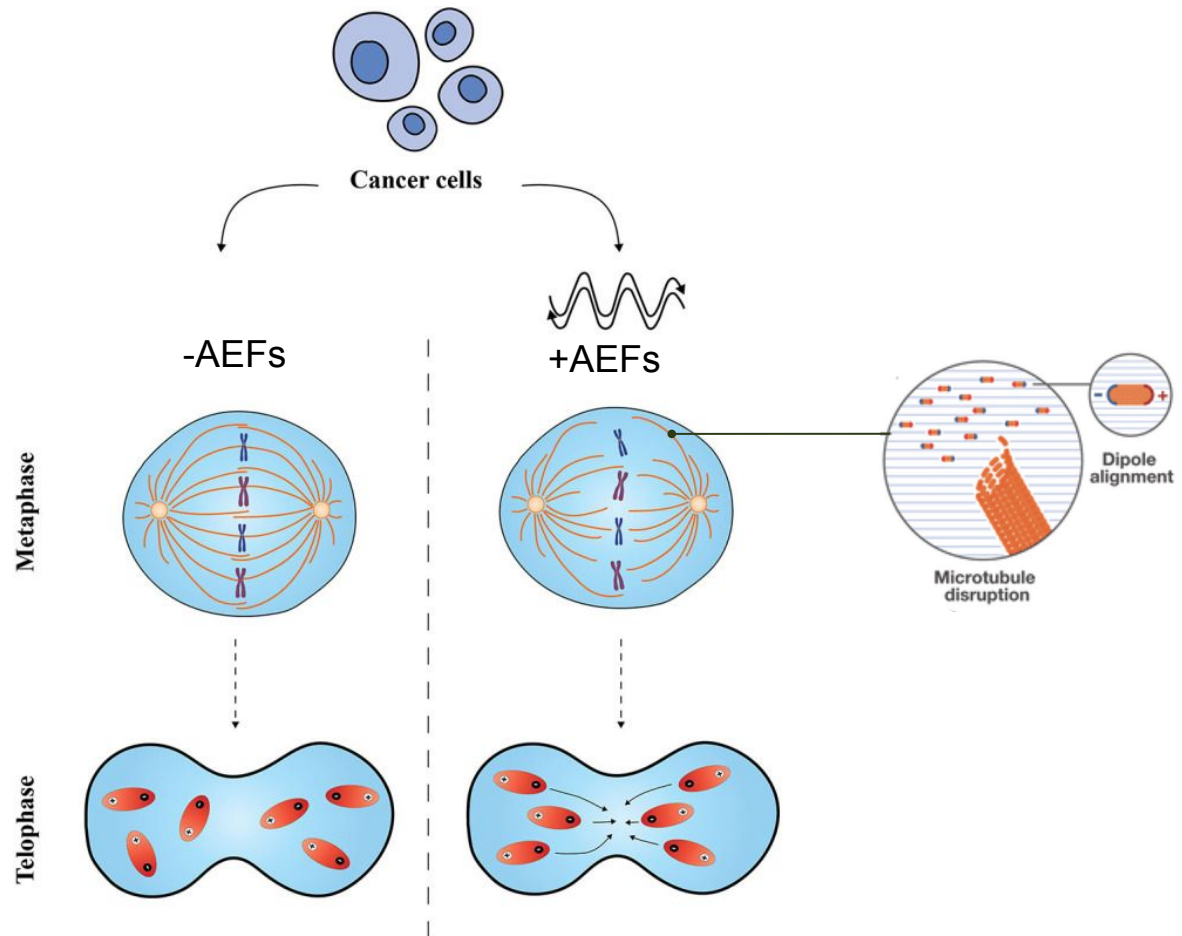   ■ Kirson and Palti
      ● 1.5 V/cm at 200 kHz
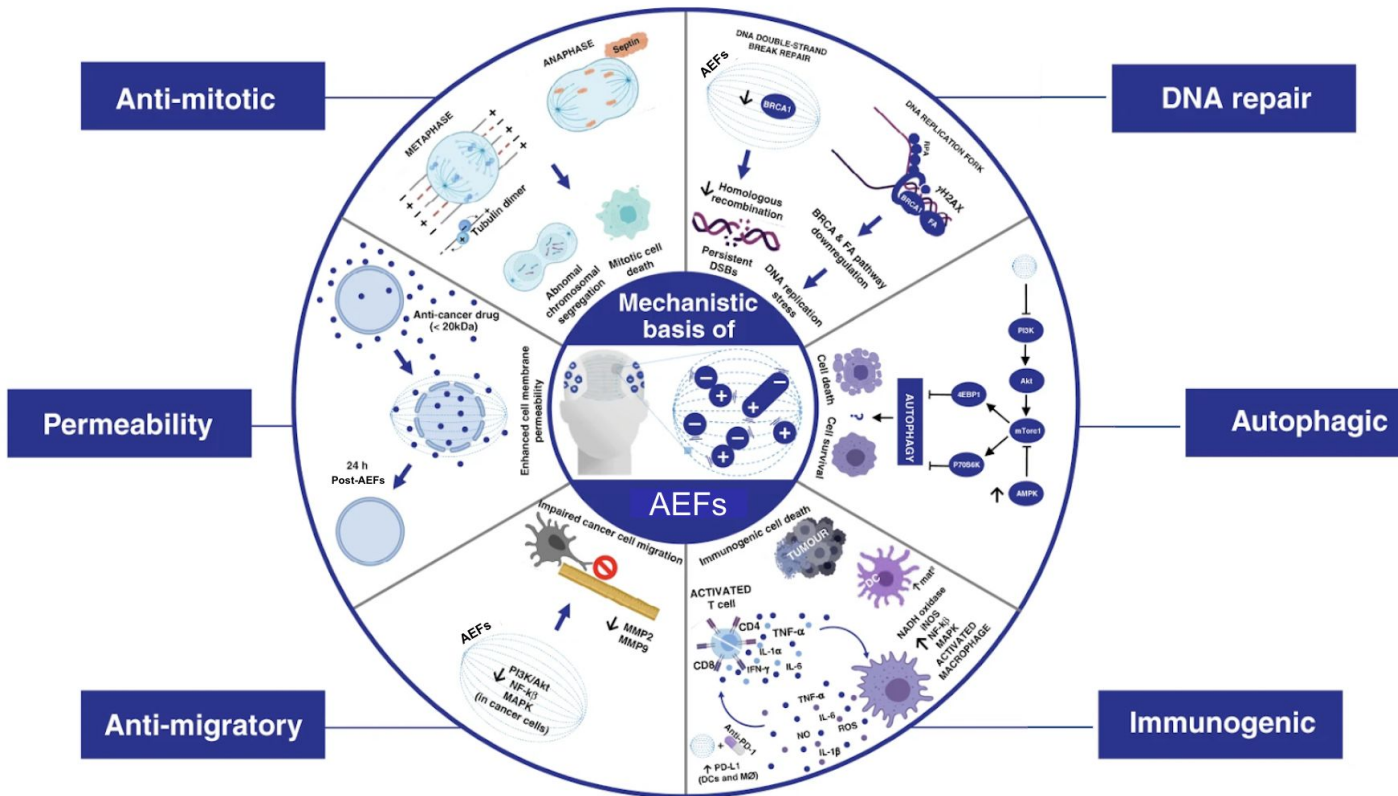
Constant, uniform electric field

Charge →

Dipole →

Alternating electric fields   [4]

Biological Effects of AEFs

Mitosis

[5]

Biological Effects of AEFs

[6]

Clinical AEF Apparatus

➢ Optune™ System
  ○ Novocure Ltd.

(A)

(B)

[6]

Clinical AEF Apparatus

➢ Optune™ System

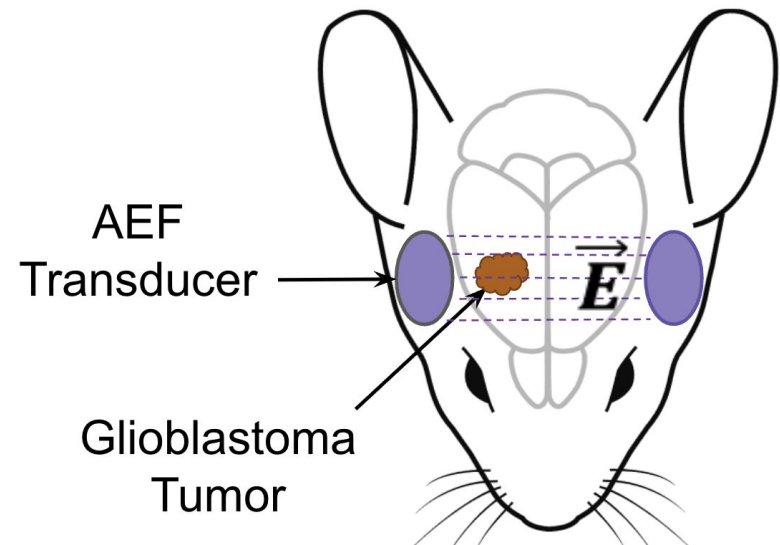   ○ Electrode (i.e. PMN-PT, ε_r =5000)
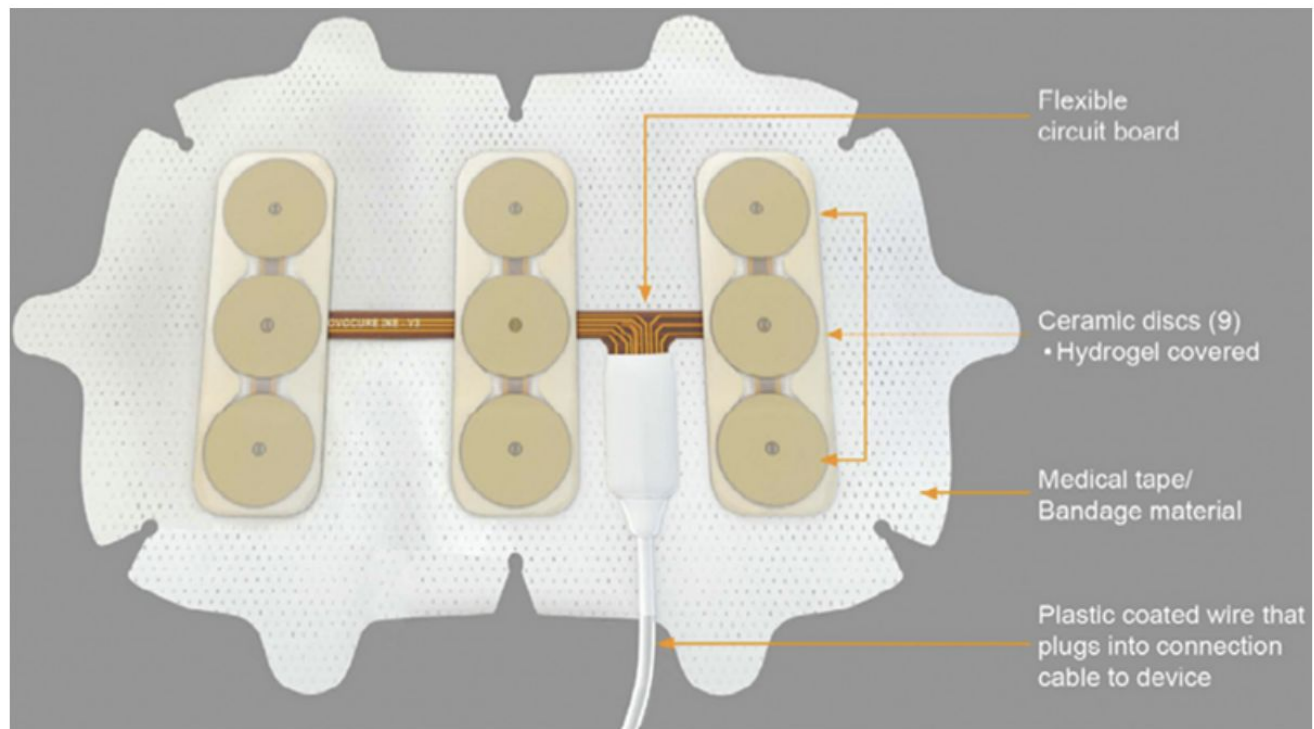
[7]

Overview

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❑ **Results and Discussion**
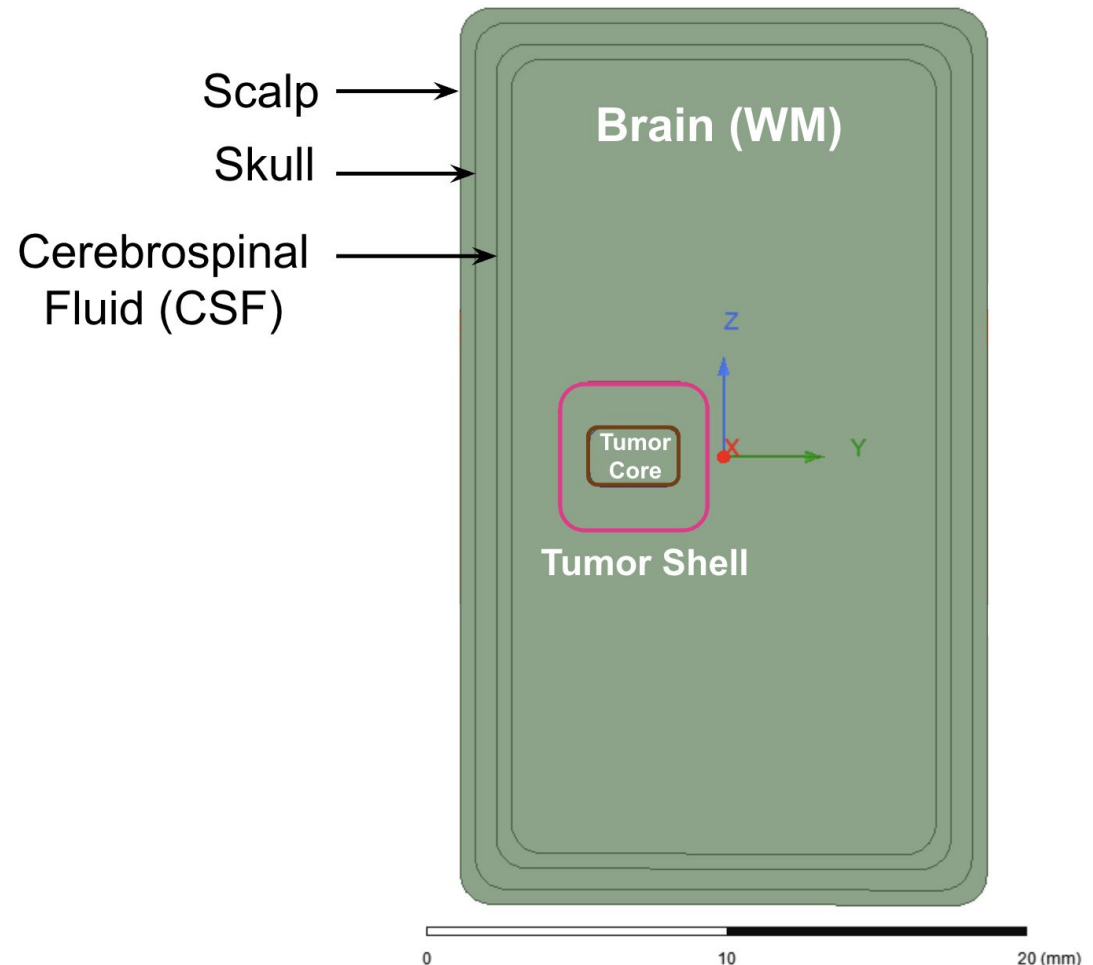
❑ **Conclusion**

Computational Simulations

➤ Ansys Electronics

➤ Simulation models

    ○ A simplified rat head model with a tumor and AEF electrodes

        ■ Three AEF electrode models

AEF Transducer

E

Glioblastoma Tumor

Computational Modeling

➢ Simplified rat head model

- ○ 17.4 mm H x 30 mm D
- ○ 4 layers
- ○ Human glioblastoma

Scalp

Skull

Cerebrospinal
Fluid (CSF)

Brain (WM)

Tumor
Core

Tumor Shell

Z

X

Y

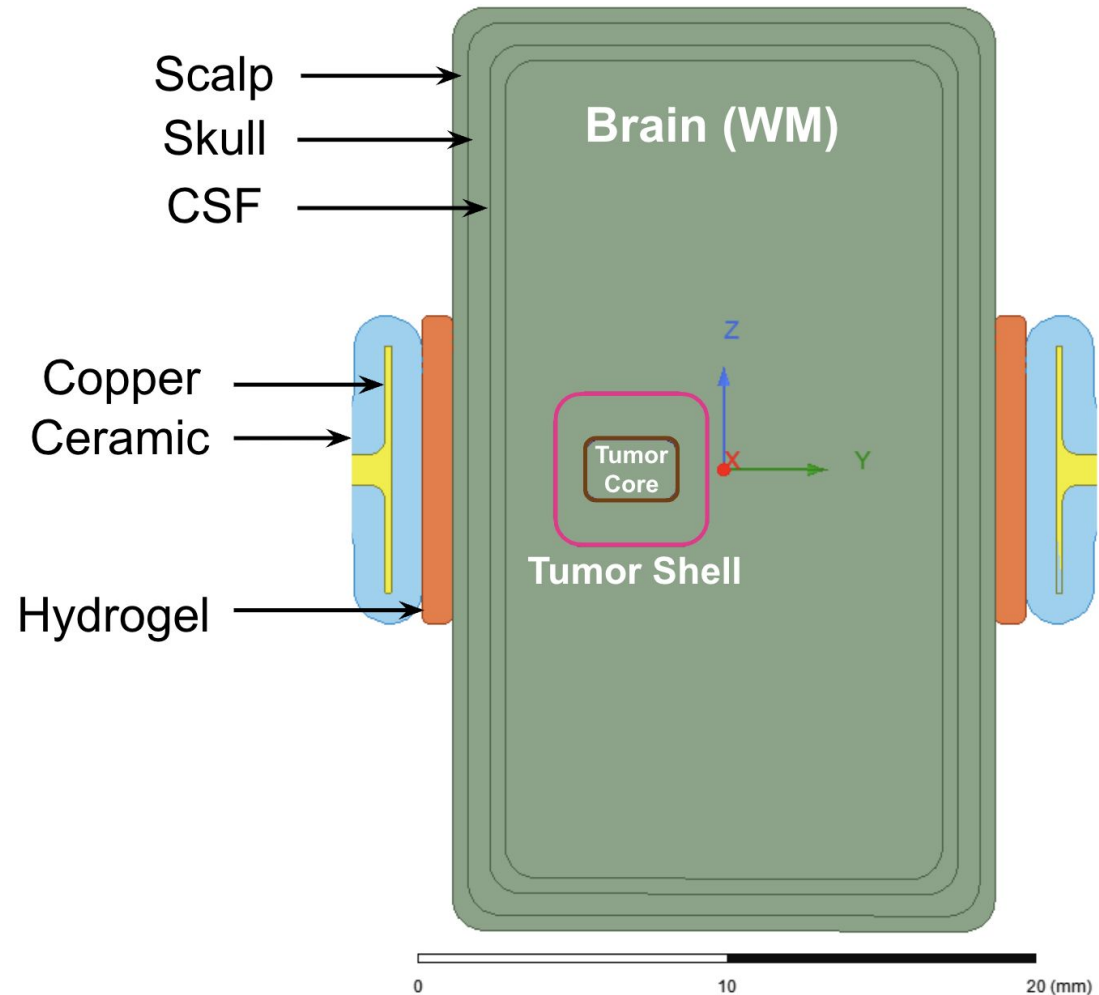0   10   20 (mm)

Computational Modeling

➢ Three AEF electrode models

   ○ Model 1 - Baseline transducers

   ○ Model 2 - Baseline transducers mounted to titanium screws
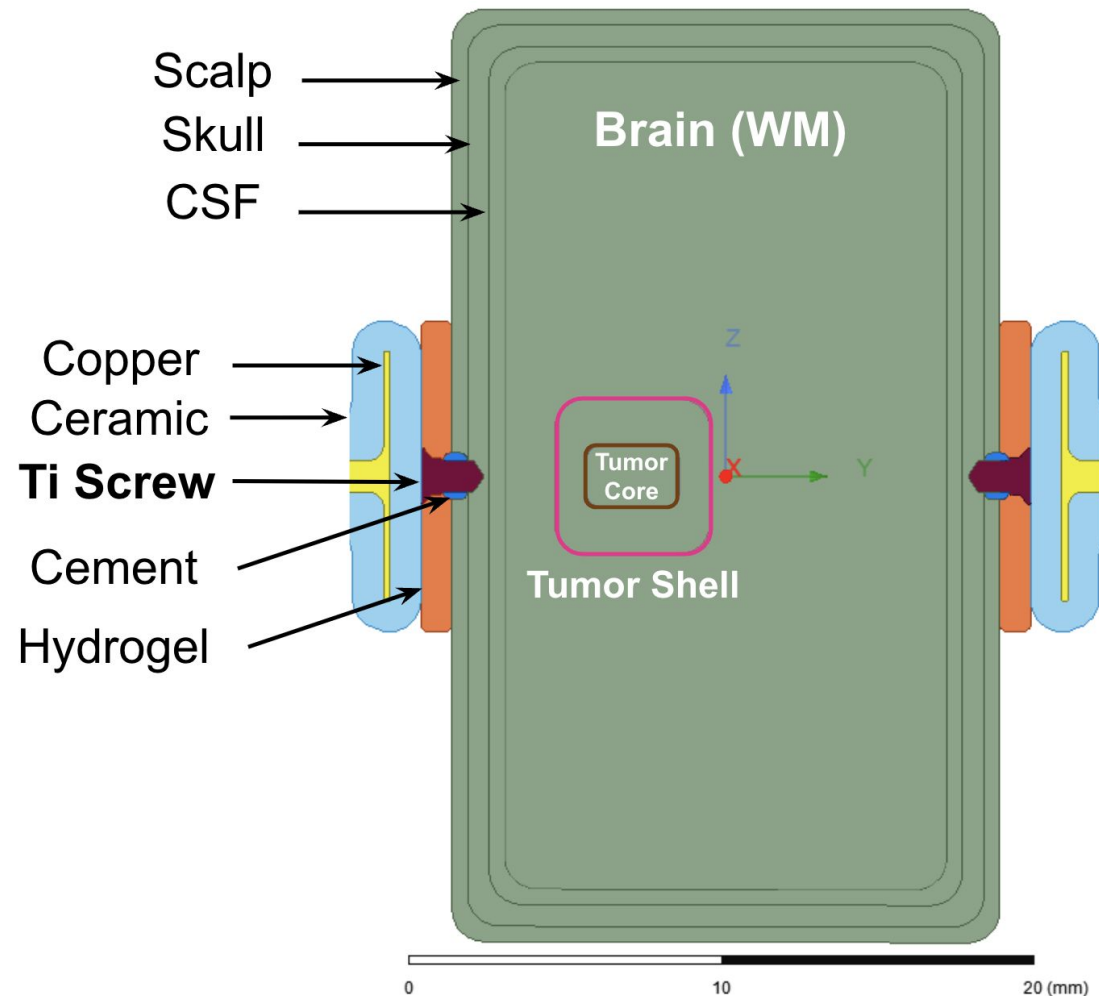
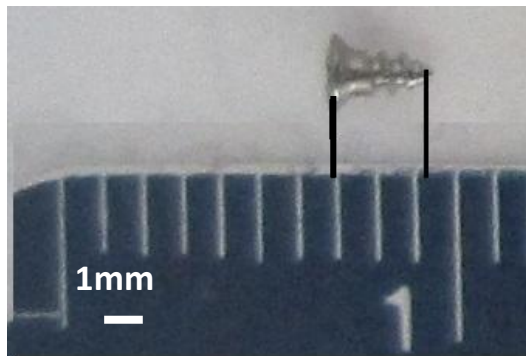   ○ Model 3 - Customized transducers

Computational Modeling

➤ Model 1

   ○ "Baseline" transducers

      ■ 10 mm diameter

      ■ Copper plate

      ■ Ceramic
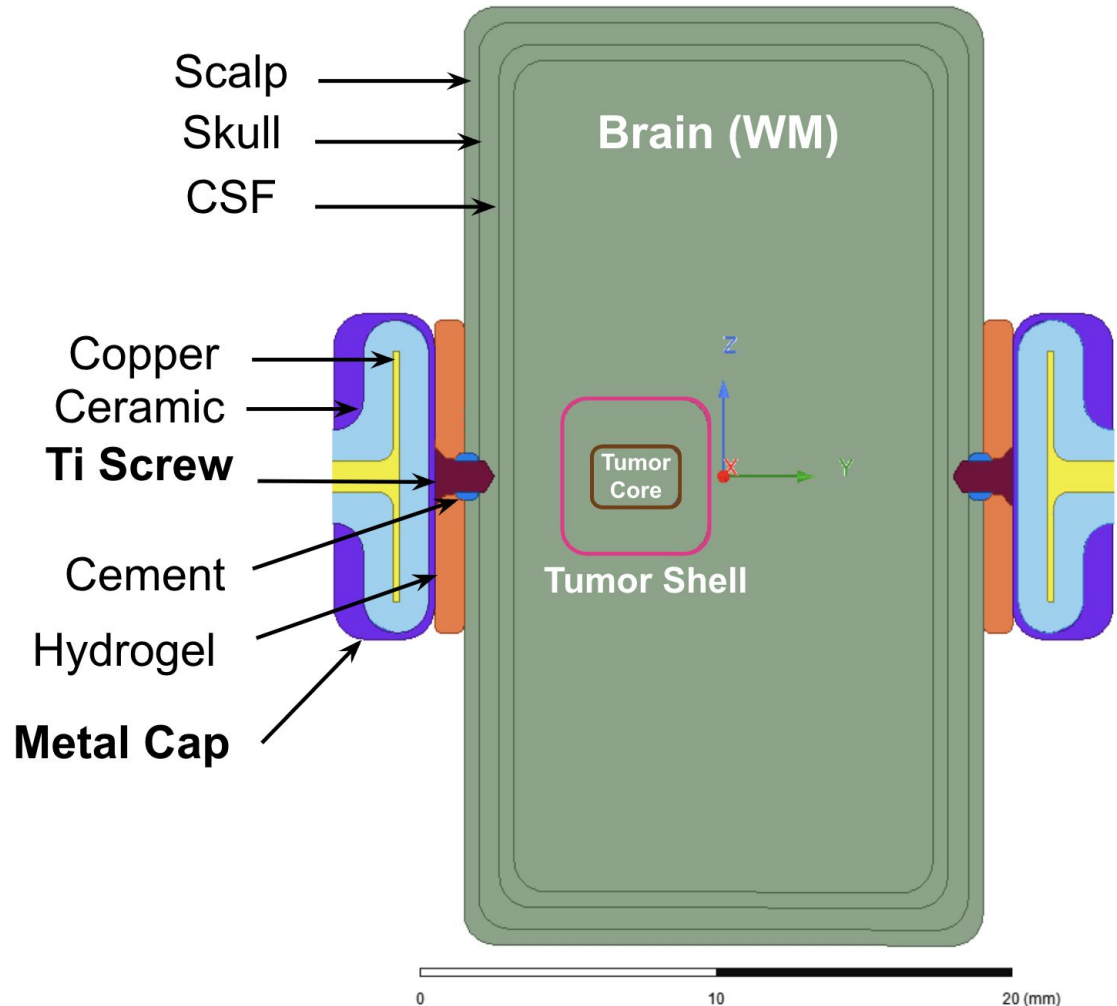
      ■ Hydrogel

Computational Modeling

➤ Model 2
- ○ Baseline transducers
  - ■ Titanium (Ti) screws
    - ● OsteoMed, TX

Computational Modeling

➢ Model 3

  ○ Customized transducers

    ■ Ti screws

    ■ Metal caps

      ● Aluminum

Scalp

Skull

CSF

Brain (WM)

Copper

Ceramic

Ti Screw

Cement

Hydrogel

Metal Cap

Tumor Core

Tumor Shell

0   10   20 (mm)

Testing Parameters

➢ Three simulation models

   ○ Model 1 - Baseline transducers

   ○ Model 2 - Baseline transducers mounted to titanium screws

   ○ Model 3 - Customized transducers

➢ Ansys Electronics

   ○ HFSS

      ■ 42 V at 200 kHz

   ○ Icepak

      ■ Room temperature at 24°C

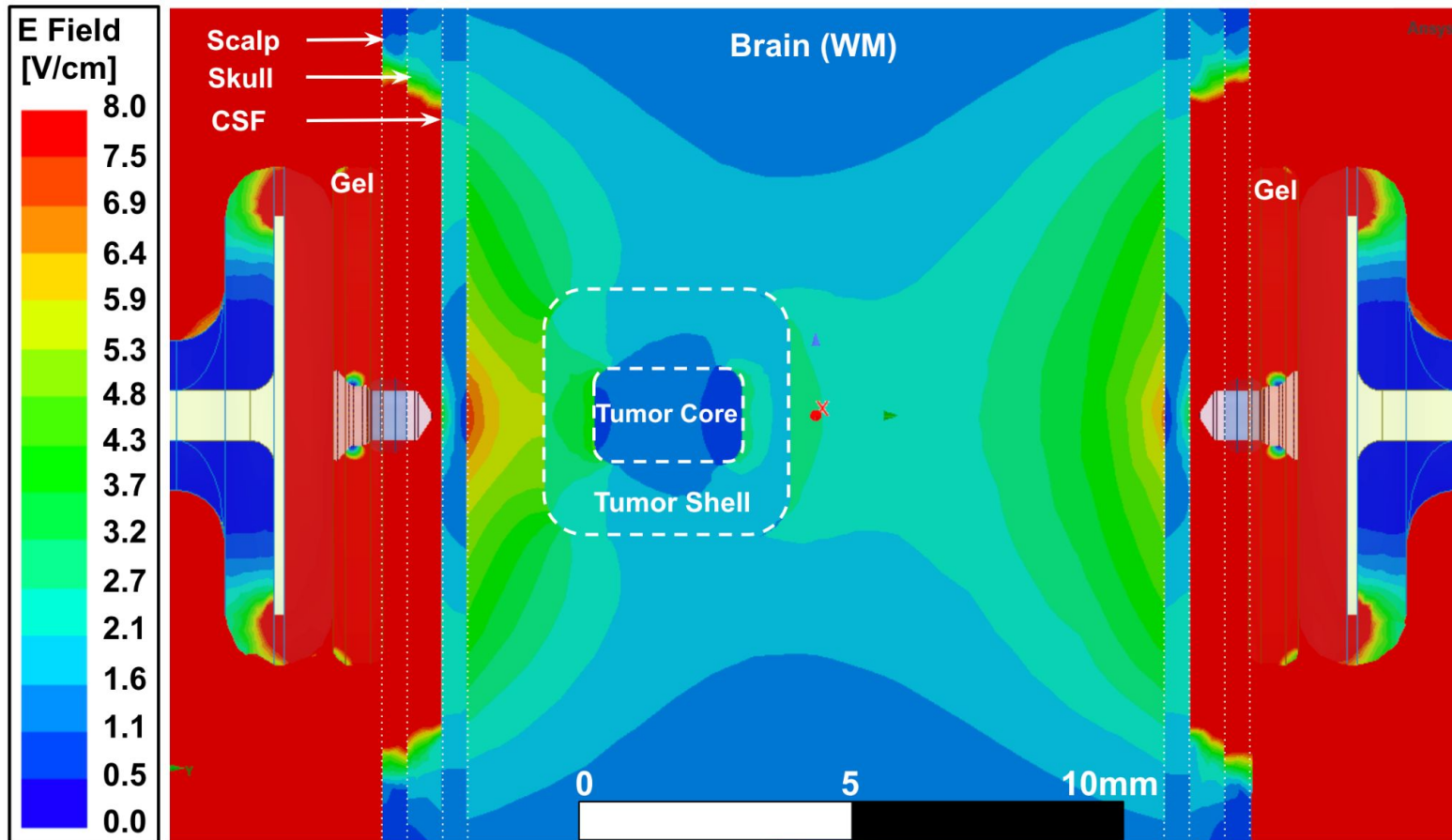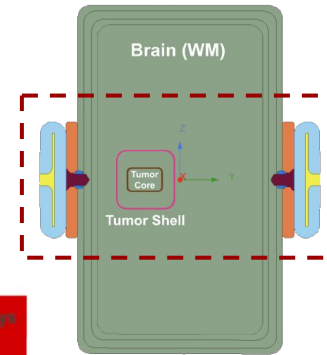   ■ No physiological processes (blood flow and metabolic heat)

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Model 1 - Baseline AEF Transducers
(no Ti screws, no metal caps)
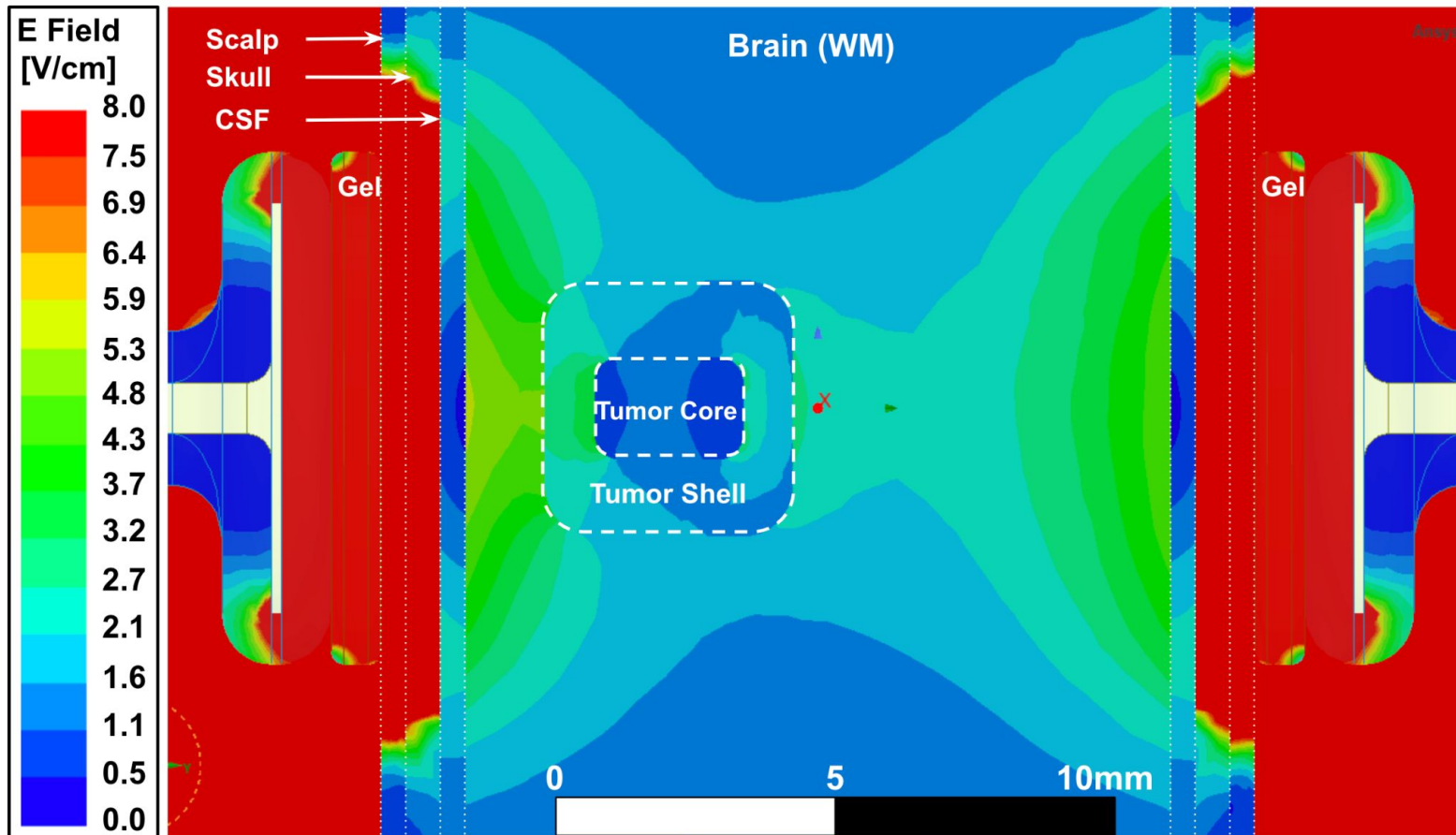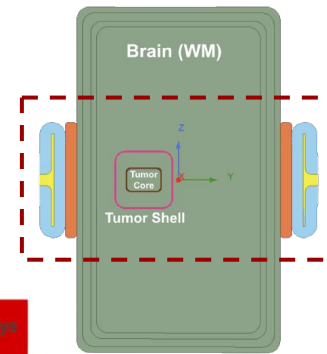
Model 2 - Baseline AEF Transducers mounted to Ti screws (no metal caps)

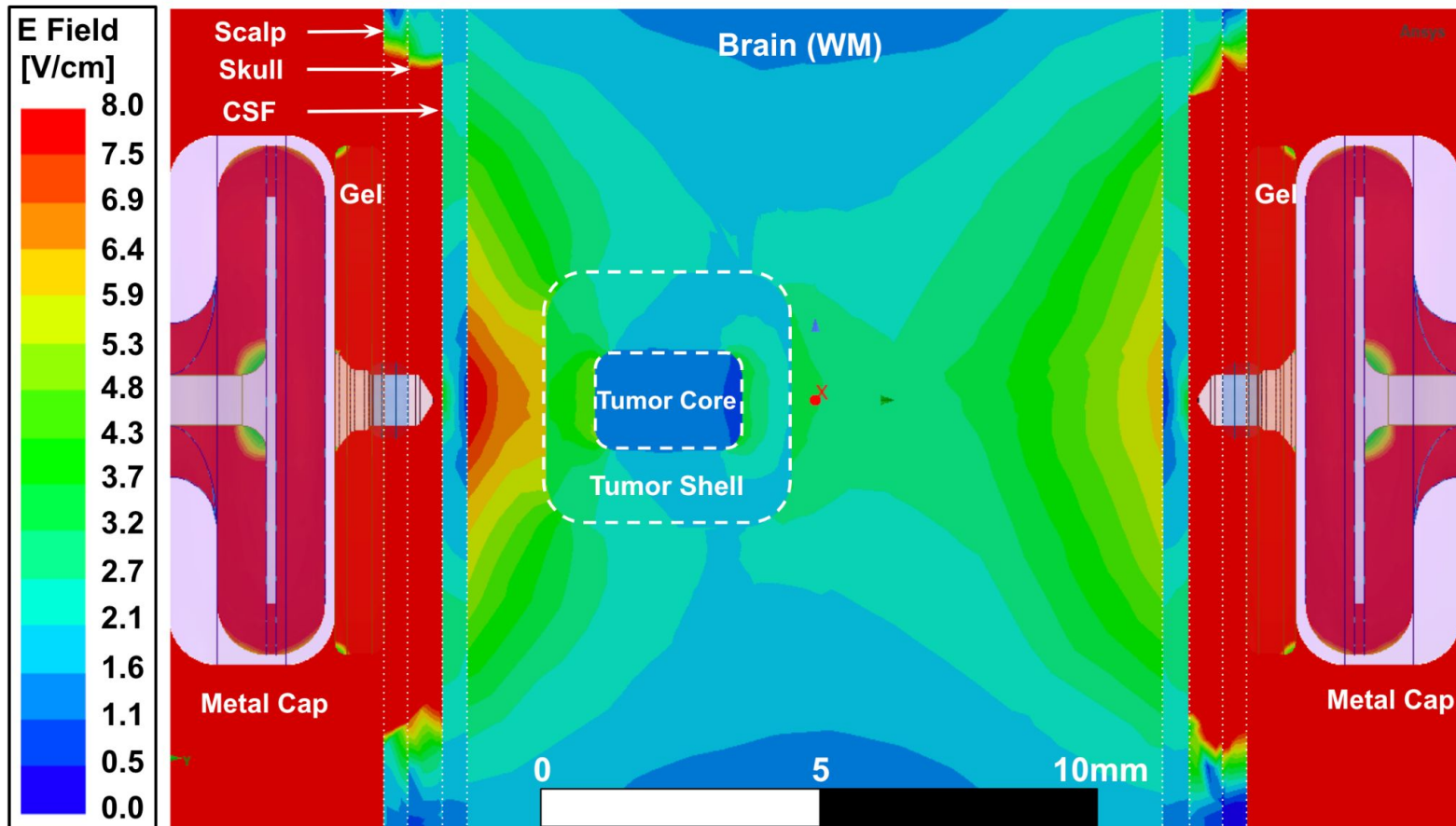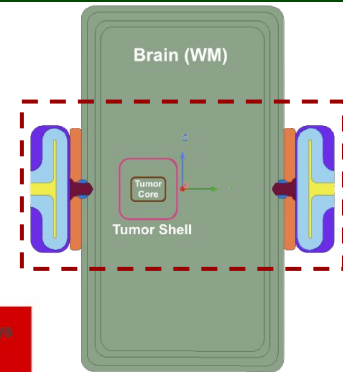# Model 3 - Customized AEF Transducers (Ti screws and metal caps)

Table 2. Mean AEF strength (V/cm) in the brain (WM), tumor shell, and tumor core

Model	Simulation Description	Mean AEF strength (V/cm)		
		Brain (WM)	Tumor shell	Tumor core
1	Baseline AEF transducers	1.2	1.8	1.1
2	Baseline AEF transducers mounted to titanium screws	1.2	1.9	1.1
3	Customized AEF transducers	1.5	2.4	1.4

➢ Tumor shell: ~26% improvement in mean field strength
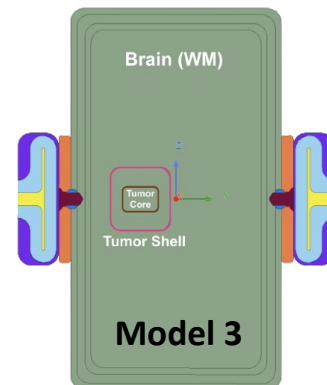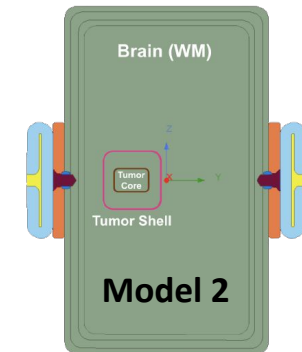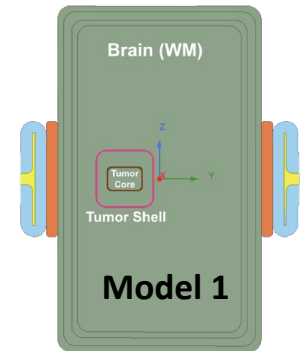

Model 1

Model 2

Model 3

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➢ Tumor shell: ~26% improvement in mean field strength

Table 3. Other measurements

Model	Simulation Description	Thermal load (°C) on scalp	Power (W) across the electrodes
1	Baseline AEF transducers	9.1	0.2
2	Baseline AEF transducers mounted to titanium screws	9.5	0.2
3	Customized AEF transducers	6.3	0.3

➢ Scalp: ~30% reduction in thermal load
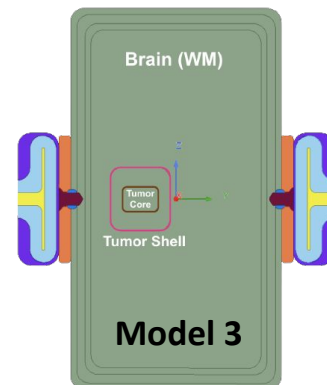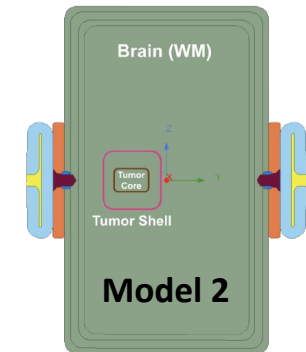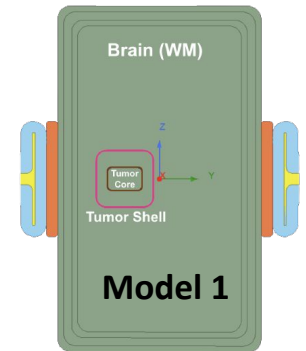
Model 1

Model 2

Model 3

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Summary

➢ Computational work

  ○ Mean AEF strength >2 V/cm in the active shell

  ○ Thermal load reduction of 30% on the scalp
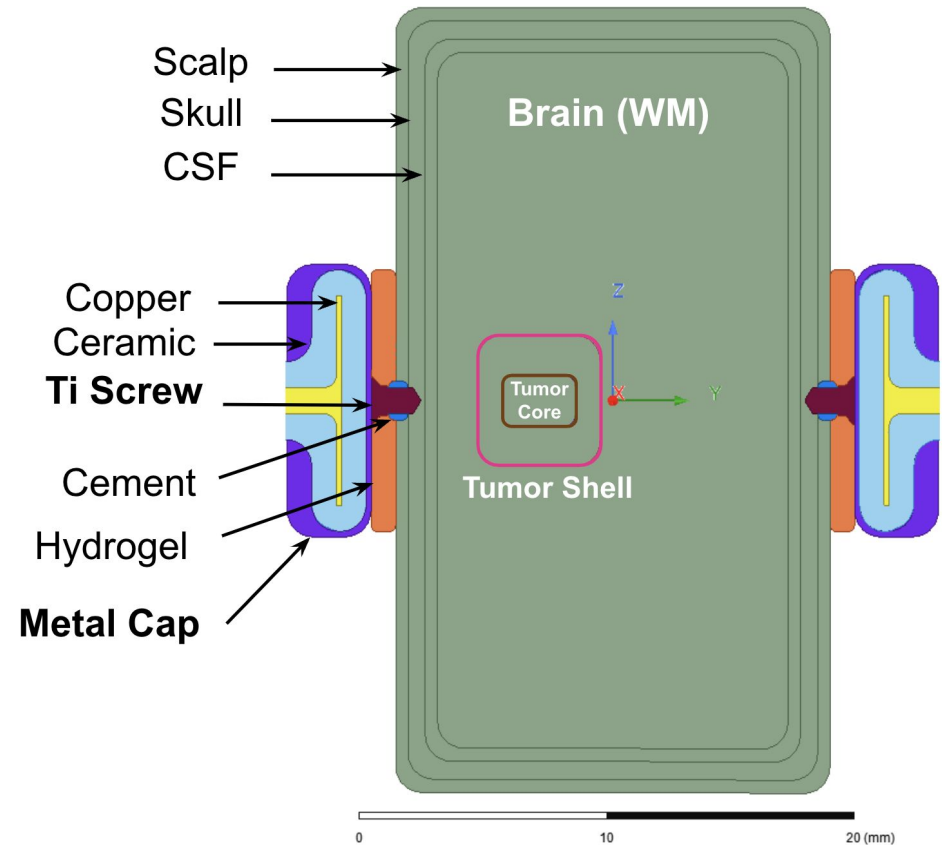
Future Research

➢ Verify the performance of the proposed AEF device in tissue-mimicking phantoms

➢ MCU-based AEF device

  ○ Animal testings

Acknowledgment

I would like to thank our collaborators: Dr. Reinhard Schulte from Loma Linda University; Dr. Chirag Patel from MD Anderson; Dr. Christoph Pohling, Dr. Ying Nie, and Dr. Vladimir Bashkirov from Loma Linda University; Dr. Edwin Chang from Stanford University; Dr. Yuping Zeng from University of Delaware; and Dr. Vicky Yamoto from University of Southern California.

I would like to thank Ansys for their generous support

References

[1] https://www.mayoclinic.org/diseases-conditions/glioma/multimedia/glioma/img-20129420

[2] https://www.novocure.com/our-therapy/

[3] Y. Porat *et al.*, "Determining the Optimal Inhibitory Frequency for Cancerous Cells Using Tumor Treating Fields (TTFields)," *JoVE (Journal of Visualized Experiments)*, no. 123, p. e55820, May 2017, doi: 10.3791/55820.

[4] M. Saria and S. Kesari, "Efficacy and Safety of Treating Glioblastoma With Tumor-Treating Fields Therapy.," *Clinical journal of oncology nursing*, 2016, doi: 10.1188/16.CJON.S1.9-13.

[5] F. A. Carrieri, C. Smack, I. Siddiqui, L. R. Kleinberg, and P. T. Tran, "Tumor Treating Fields: At the Crossroads Between Physics and Biology for Cancer Treatment," *Front Oncol*, vol. 10, p. 575992, Oct. 2020, doi: 10.3389/fonc.2020.575992.

[6] O. Rominiyi, A. Vanderlinden, S. J. Clenton, C. Bridgewater, Y. Al-Tamimi, and S. J. Collis, "Tumour treating fields therapy for glioblastoma: current advances and future directions," *Br J Cancer*, vol. 124, no. 4, pp. 697–709, Feb. 2021, doi: 10.1038/s41416-020-01136-5.

[7] A. A. Rehman, K. B. Elmore, and T. A. Mattei, "The effects of alternating electric fields in glioblastoma: current evidence on therapeutic mechanisms and clinical outcomes," *Neurosurgical Focus*, vol. 38, no. 3, p. E14, Mar. 2015, doi: 10.3171/2015.1.FOCUS14742.

Thank you!

Contact Info:

ha_nguyen3@baylor.edu