A CPS approach to tumor immunomodulation: sensing, analysis, and control to prime tumors to immunotherapy

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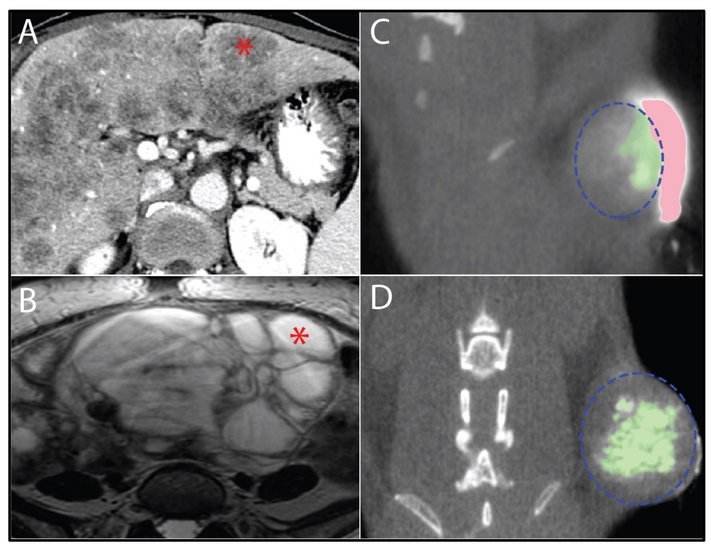
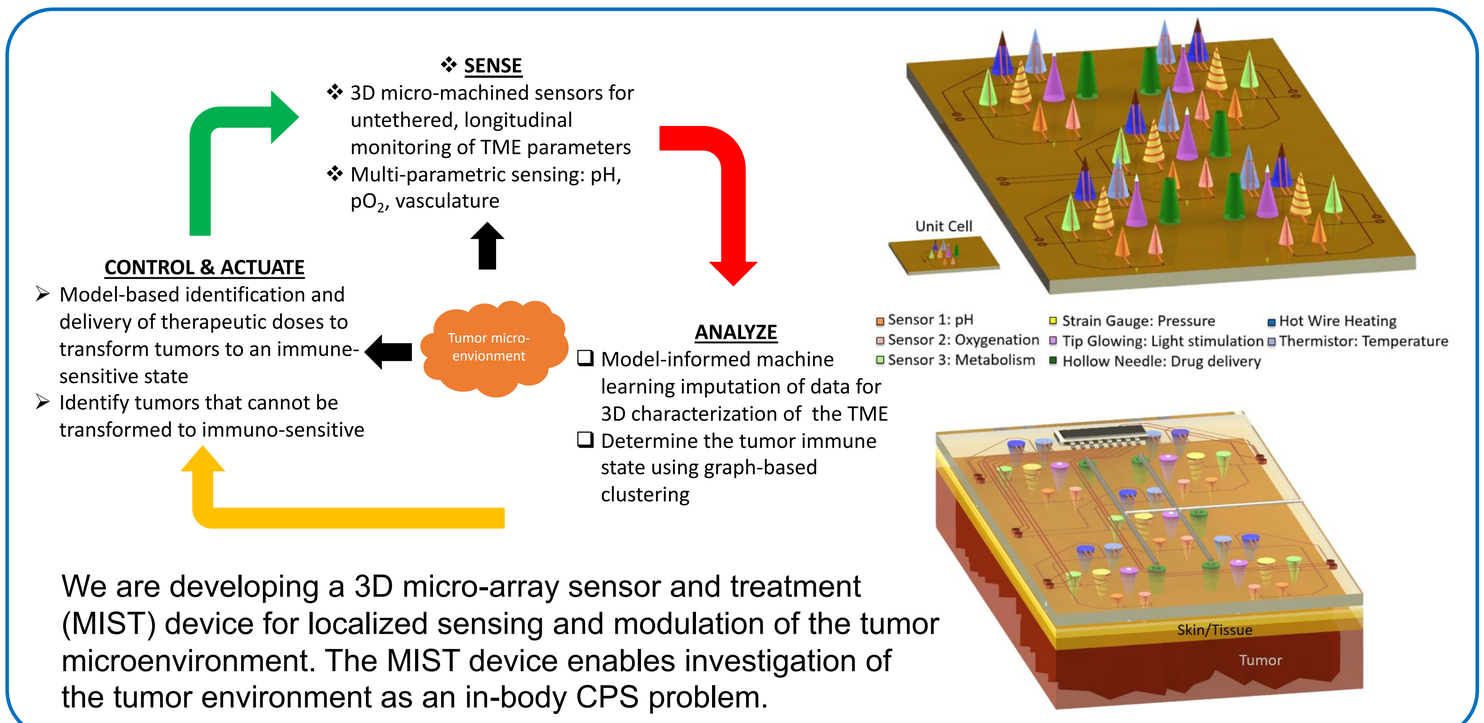
KEY PROBLEMS:

- *Design*: Formulation of intra-tumoral immunotherapy as an in-body CPS problem
- *Microsensor fabrication*: Development and demonstration of an advanced diffraction lithography technique to fabricate complex 3D structures and surface-integrated microsensors
- *Model-informed machine learning*: Inductive graph-neural tensor completion for data imputation and state estimation



Tumor interstitial pressure (TIP) correlates with tumor characteristics: fibrotic metastases such as the target liver lesion in A (*) had high TIP resulting in inferior drug delivery when injected using the same technique as low TIP tumors such as the target lesion in B (*). Analogous murine models of high (C) and low (D) TIP tumors were injected with drug, with micro-CT imaging confirming off-target (red) relative to on-target deposition (green) when injected in the same manner.

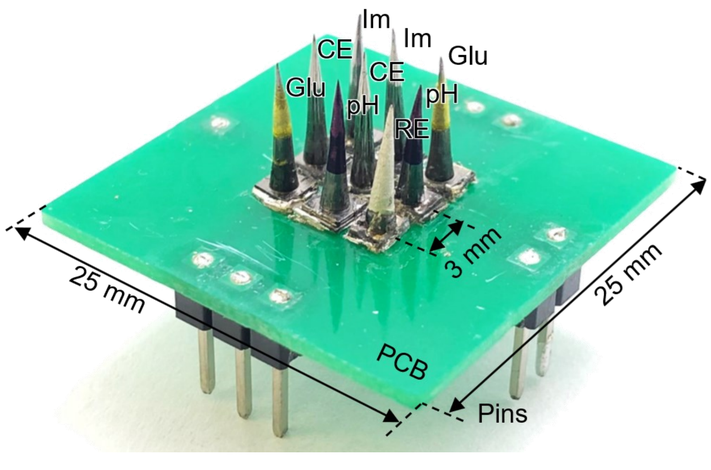


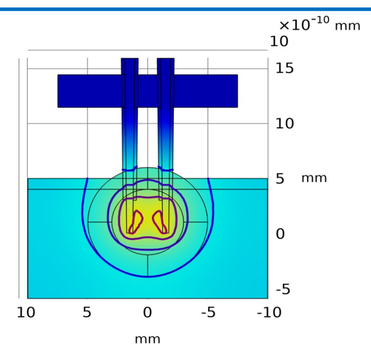
We are developing a 3D micro-array sensor and treatment (MIST) device for localized sensing and modulation of the tumor microenvironment. The MIST device enables investigation of the tumor environment as an in-body CPS problem.

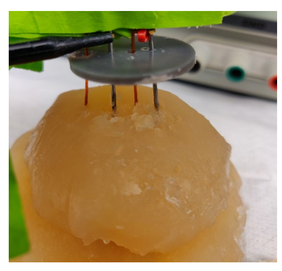
SCIENTIFIC IMPACT:

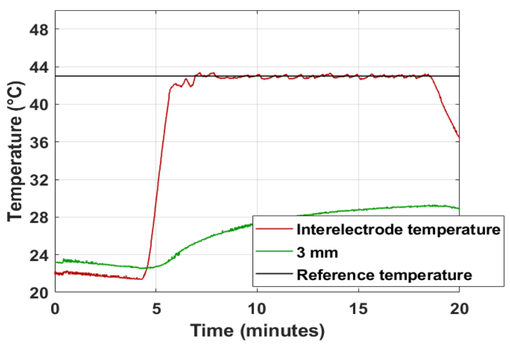
- Design principles providing a CPS framework for longitudinal control of the biological state
- Establish integrated micro-sensing and treatment/actuation arrays for modulating the state of in-body CPS
- Situational awareness tools for sparsely observable CPS

pH, glucose concentration, and impedance are measured on a single platform.



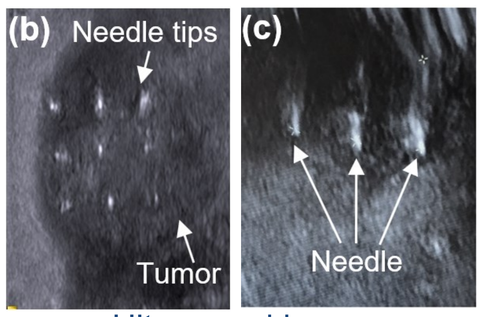




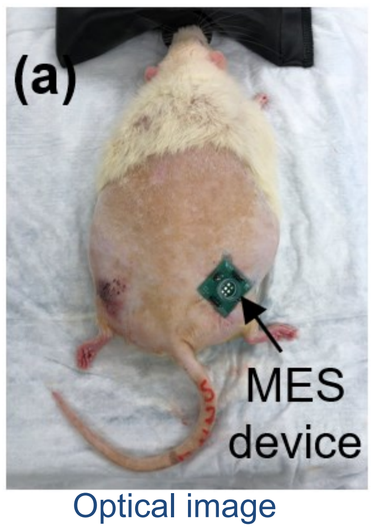


Computational models and bench experiments support feasibility of delivering mild hyperthermia to tumors in rodents *in vivo* with RF currents applied to microneedles

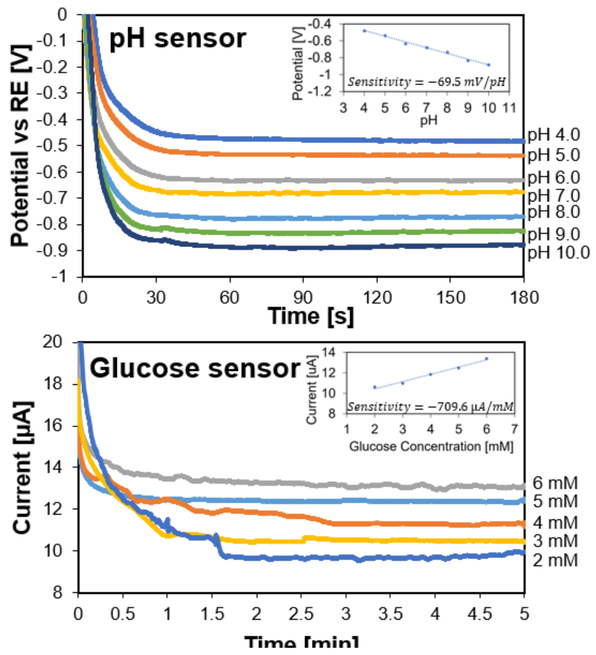
Insert the MES device through the guiding holes



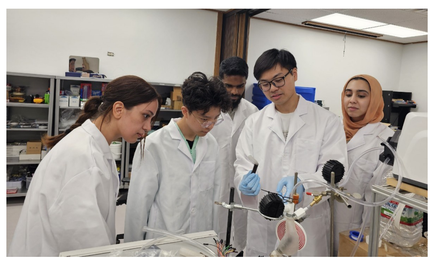
Ultrasound images



Optical image



3D Microneedle fabrication activity: KAWSE GROW program for 6th-8th graders



Microfabrication activity: High school and College students

Award ID#: 2039014 (KSU); 2038851 (MD Anderson)