Novel Approach to RCC Early Diagnosis and Therapeutic Monitoring using Volatile Organic Compounds

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Clinical and Translational Research for Renal and Prostate Cancers

Early Phase Clinical Trials / Novel Therapeutics

Investigator Initiated Trials

- Phase 1b Avelumab / Gemcitabine for sarcomatoid mRCC
- Phase II Maintenance Niraparib for Biomarker Selected mCRPC
- Phase 1 First-in-Human PSMA Re-directed / TGFb-resistant CART for mCRPC
- Randomized neoadjuvant IO v. IO/TKI in high-risk RCC

Industry & Cooperative Group Trials

Cardiac Toxicity in GU Malignancies

- Multi-Institutional Prospective Study of Sunitinib-Induced Cardiac Toxicity
- Pilot Cohort Study of Myocardial Blood Flow Reserve using Rb82 Myocardial PET in Prostate Cancer
- Two Multi-Institutional Randomized Trials of CV Risk Mitigation Strategies
  - Intensive BP control vs Standard Care in mRCC
  - Modified Cardiac Rehab program in PCa

Translational / Biomarker

- Peripheral Blood Predictive Biomarkers in mRCC receiving anti-PD1 therapy
- Optimization / Validation and Early Clinical Testing of Novel Diagnostic/Classifier for Localized RCC

Brief Background:

- Up to 25% of incident RCC presents with locally advanced or metastatic disease
  - Initial clinical staging significantly impacts long-term clinical outcomes

- Critical need for early diagnostic, as well as improved methods for post-nephrectomy surveillance and therapeutic monitoring in advanced disease

- No current tools exist to efficiently conduct targeted screening in an average-risk population

Brief Background:

- Concept inspired by natural abilities of mammalian olfaction
  - Capitalizes on differential production of Volatile Organic Compounds (VOCs / ‘odorants’) by tumor cell metabolism
  - Controlled studies demonstrate sensitivity of canine detection in variety of localized malignancies

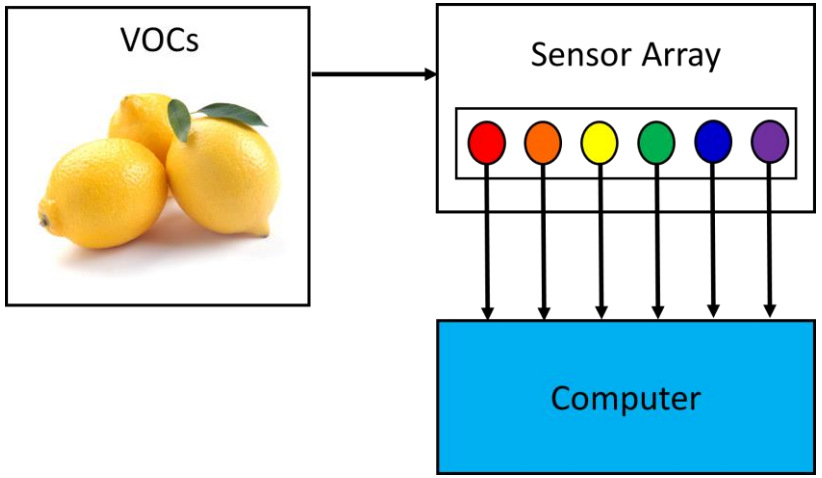
- Potential untapped target for early detection, surveillance, therapeutic monitoring?

CONCEPT OVERVIEW of VOC Detection

- Hypothesis: VOCs from healthy cells differ from benign tumor cells which differ from malignant cells

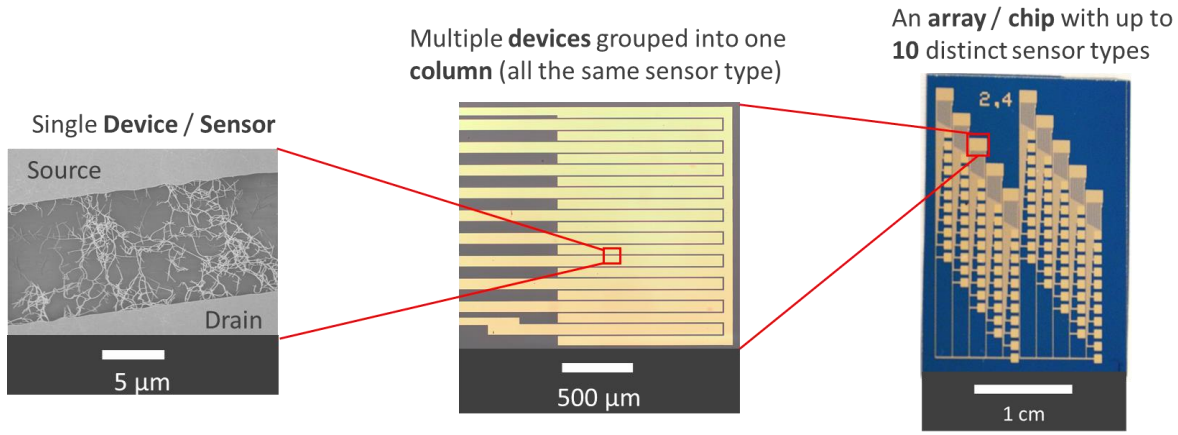
- Sensors have overlapping selectivity and are not specific to a chemical compound

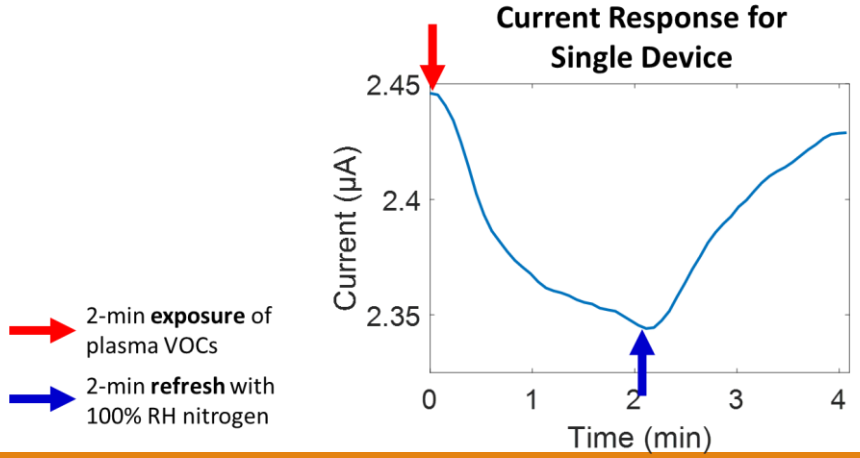
- Electronic signals are analyzed using pattern recognition via machine learning to build a classification algorithm

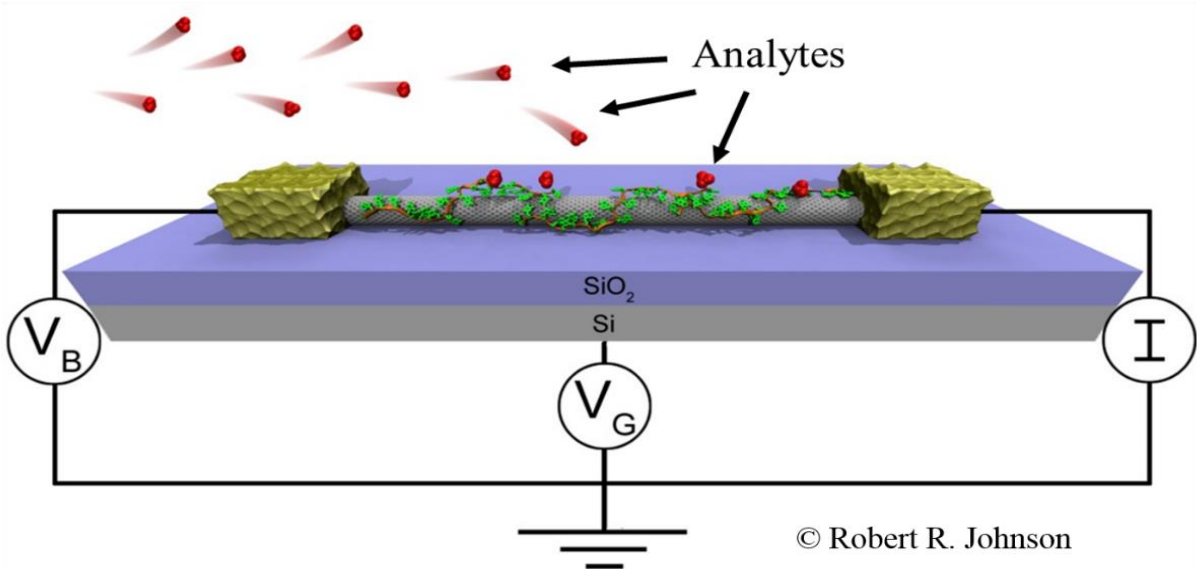


Assay Design:

- Carbon nanotubes (CNT) connect the source and drain electrodes of a single field effect transistor (FET)
- CNTs are functionalized with single stranded DNA which increases response to VOCs by introducing binding sites
- Each CNT-FET is functionalized with the same DNA oligomer to form a unique odorant sensor type
- Sensor array comprises 10 CNT-FETs, yielding 10 sensor types per array
- VOC analytes interact with the DNA, altering the electrical properties of the FET, resulting in measurable shift in the current



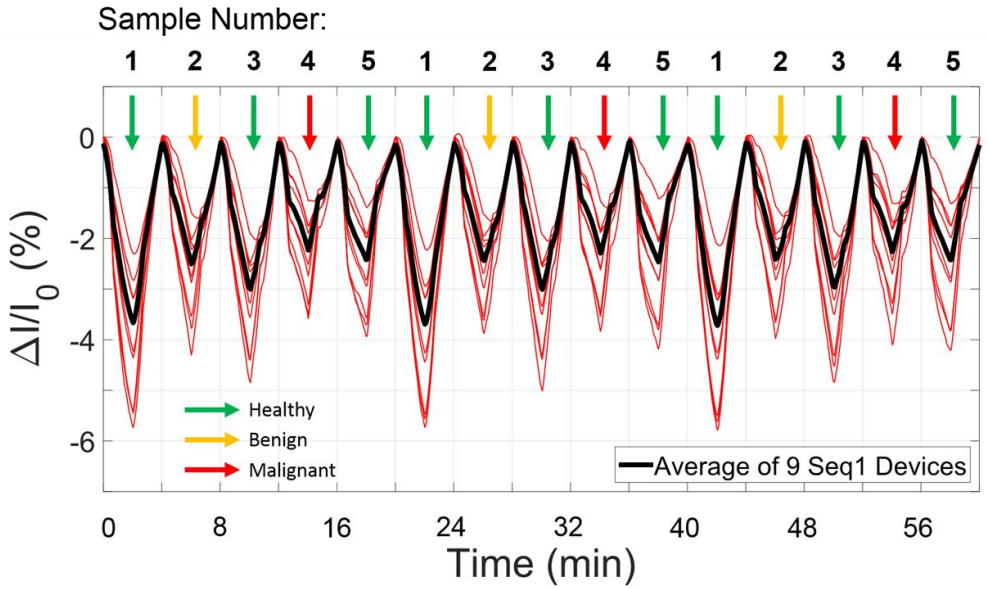




Preliminary Experience with Ovarian Cancer:

Training Set: 24 plasma samples.
~ 8 each: Malignant (1 early stage), Benign, Control

Validation Set: 34 plasma samples.
11 Malignant (**5 early stage**), 11 Benign, 12 Control



Using Machine Learning for Classification and Statistical Validation:
(N=58 samples)

Stratified K-Fold Cross-validation
Success Rate: 95%
Early Stage Rate: 100%
False Positive: 0%
False Negative: 5%

		CLASSIFIED		
		Cancer	Benign	Healthy
ACTUAL	Cancer	10	1	0
	Benign	0	8	3
	Healthy	0	0	12

Preliminary Aims:

AIM 1: Evaluate for detection of VOC signature using DNA-NT sensor array technique in RCC patient samples.

- Further refine the DNA-NT sensor array for RCC by screening against large number of patient samples (from benign, healthy control, localized and metastatic disease settings).

AIM 2: Validate and benchmark the VOC sensor array

- Assessment of reproducibility, classification accuracy, population differences

AIM 3: Preliminary assessment of assay in clinical testing

- Presurgical clinical staging – correlation with T-stage, histopathology, nuclear grade
- Potential utility for post-nephrectomy surveillance