Innovation Crossover Preliminary Research Report
Life Sciences/Biomedical – Medical Imaging

Context/Scope

This paper represents research conducted by OVO Innovation for the NSWC Crane Innovation Crossover event October 12-13, 2016. This research is intended to provide more insight into key challenges that were identified within the four technology clusters (Advanced Manufacturing, Cyber/IT, Life Sciences and DoD Technologies) first documented in the Battelle report. OVO consultants interviewed subject matter experts (SMEs) from the private sector, academia and the government identified by NSWC Crane to gather insights into key challenges in each cluster. This report is meant to inform the participants of the Innovation Crossover event and identify new research and new technologies that might address the key challenges.

This research was collected during August and September, 2016. The reports were submitted by OVO to NSWC Crane in late September 2016.

Introductory Narrative

The Innovation Crossover event, scheduled for 12-13 October 2016 in Bloomington is the culmination of months of planning and hard work. Some of this preparatory work involved the initial Battelle study which identified key technology clusters (Advanced Manufacturing, Life Sciences, Cyber/IT and DoD Technologies) in southern Indiana. From these clusters NSWC Crane and its contractor OVO Innovation conducted further, more detailed research, to examine detailed challenges and opportunities in each technology cluster. The reports attached document the research OVO conducted with subject matter experts identified by NSWC Crane in academia, industry and in the government. The reports are meant to document specific challenges within each technology cluster that could become areas of joint research and cooperation across the three constituents in southern Indiana. The reports are provided to you to help you prepare for your participation in the upcoming Innovation Crossover event and to frame both the challenges and active research underway to address these challenges.

Problem Context

Problem or Challenge: Imaging

Most current devices and materials are based on making them radiopaque. New techniques are needed to allow imaging via alternative methods so that other types of tools and materials can be utilized.

Problem Context

Problem or Challenge: Mechanisms

Transform advances in knowledge of cellular and molecular disease mechanisms into precise medical diagnostics and therapeutics.

Overview: Mechanisms

Early stages of research into mechanisms at the cellular/molecular level

- Biomarkers for disease states
  - Research exists for decades, but opening up new frontiers
  - Challenge is translating knowledge into therapeutic action
- Extraordinary complexity of human biology/physiology
  - Systems don't operate independently; difficult to design effective experiments
- Models needed to explain how materials interact with cells/tissues in ways that can be "seen"

Technologies: Imaging

- Imaging technologies for diagnostics are largely based on ionizing radiation (i.e. x-ray)
  - Pros: High resolution; deep penetration
  - Cons: tissue damage (acute and cumulative, particularly in younger patients); clinician exposure

- Imaging technology also used to guide procedures (needle placement, biopsies, vascular procedures, surgery, etc.)
  - Visible optical techniques; ultrasound

Technologies: Imaging (II)

Non-ionizing imaging techniques:

- Magnetic Resonance Imaging (MRI)
  - Functional MRI (fMRI)
- Ultrasound
- Optical (visible and non-visible wavelengths like IR)
- Positron Emission Tomography (PET)
- Fluorescence

- Research areas – materials to enhance imaging, preferential binding sites, excite visibility in targeted tissue/cells, nanomaterials

Problem Relevance

Benefits of non-ionizing imaging technologies include:

- Improved patient and clinician safety
- Lower costs (equipment are related facilities)
- Greater availability of tests (more centers or offices)
- Improved user experience

Scope

- For the purposes of this research, we've defined the scope of the challenge to be the complete set of technologies that can be used as alternatives to imaging techniques based on the use of ionizing radiation.

- This includes imaging techniques themselves, as well as the related technologies such as probes, markers, particles, materials, etc.

Research

Objective of imaging technologies: Identify sites of disease or damage to determine accurate diagnosis leading to therapy or treatment.

- Direct observation of the physical structure (polyp during colonoscopy, e.g.)
- Indirect observation through the use of dyes, particles, or other markers that highlight a particular structure or function (indocynanine green for cardiac fucntion, e.g.)
  - Considerable research is directed toward these later technologies (measured by papers submitted to journals)

Research

Direct observation technologies:

- Laparoscopy
- Diffusive optical tomography
- Acoustic (ultrasound)
- Photoacoustic
- MRI/fMRI

With exception of MRI, penetration depths are low, meaning techniques are useful only for superficial observations.

Research

Indirect observation technologies:

- Coated ferrous oxide particles
- Injectable biologics
  - Make tumor cells “glow in the dark” for excision
- Nanoparticles for targeted delivery
- Contrast enhancements
- Computer-aided imaging enhancement

Advances in these areas require better understanding of cellular and molecular mechanisms

Research

Scenario provided by Cook Medical: In-situ surgical MRI (biopsy; stent placement are two examples)

- Materials research becomes essential: guide wire example
  - Need stiffness and flexibility
  - Ferrous metals become antennas
  - Nitinols, other non-ferrous metals create artifacts
  - Need new conductive materials (i.e. polyimides)

Research

"**Indiana Consortium for Innovation in Biological Imaging:** Creating the Premier Biomedical Imaging Network in the United States"

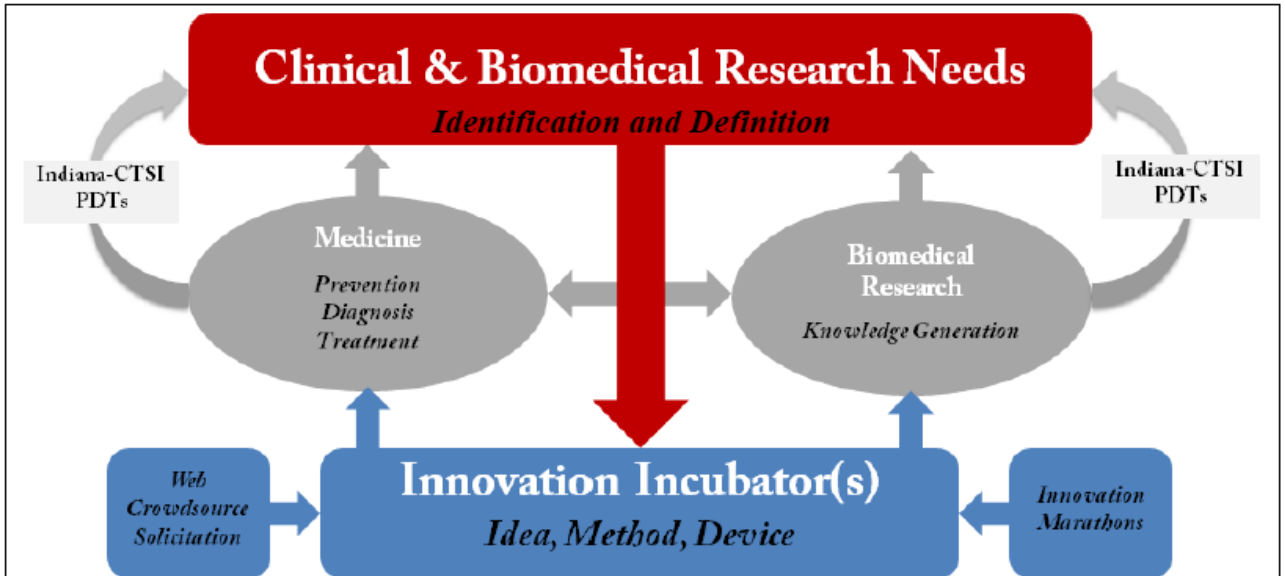
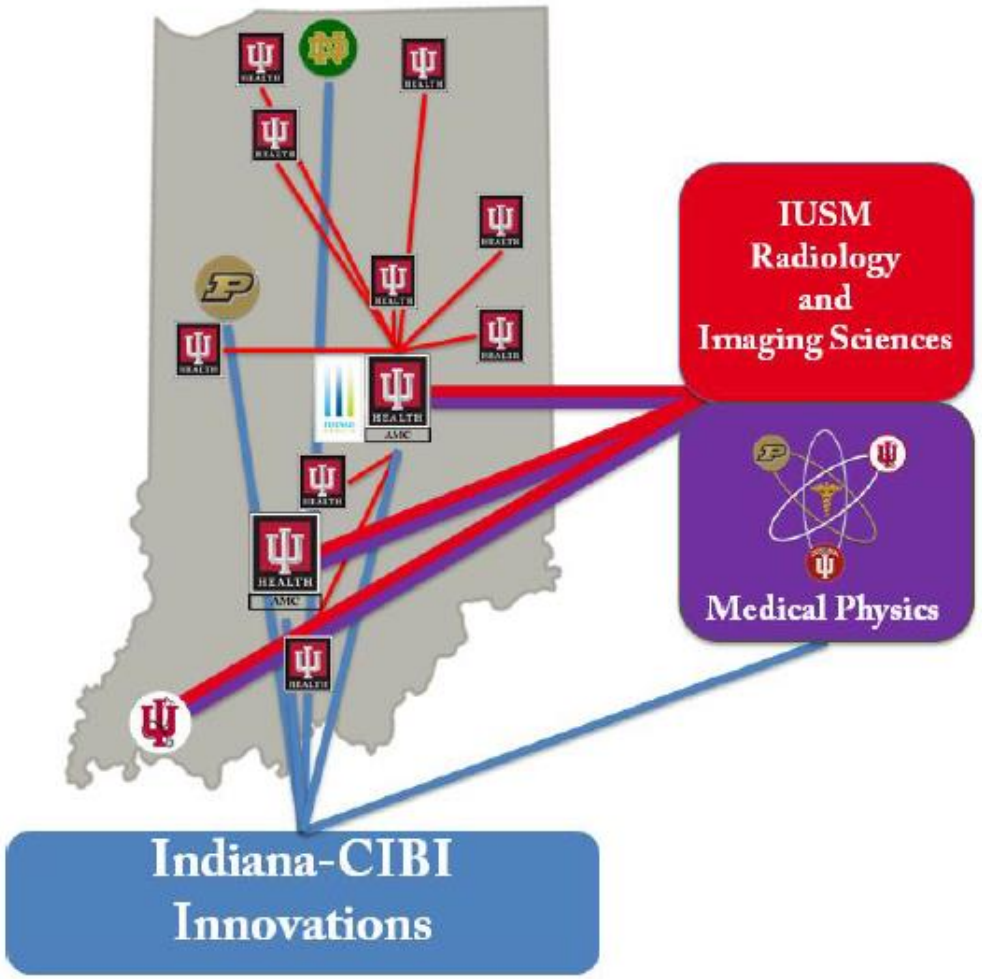


Figure 3. Indiana-CIBI Operational Model.

Research

Statewide network of centers of expertise ranging from research through pre-clinical to clinical implementation forms a “Translation-to-Practice Network”



Summary

- High level of interest in using safer forms of imaging in medical diagnostics and treatment
- Optical methods suffer from poor depth of penetration
- Methods involving particles, biologics, and nanomaterials to interact with tissue and highlight targeted areas are subject of significant research effort
  - Translation challenges pose obstacle
- Greater understanding of cellular and molecular disease mechanisms needed to better design new materials

Sources

Subject Matter Experts consulted / interviewed

- Rajesh Naik, PhD (Air Force Research Laboratory)
- David Puleo, PhD (University of Kentucky)
- David Daleke, PhD (Indiana University)
- Sean Chambers, PhD (Cook Medical, Inc.)

Sources

- Indiana Consortium for Innovation in Biomedical Imaging (report)

Inter-related challenges

Life Sciences/Biomedical

Three inter-related areas of research

1. Non-radiation based imaging
2. Informatics technology
3. Cellular and molecular disease mechanisms

Inter-related purposes

- **Imaging**: Observation
- **Informatics**: Measure and monitor
- **Mechanisms**: Prevention and healing

Overall goal: Personalized or precision medicine

Mechanisms support all

- **Imaging**: What to observe?
- **Informatics**: What to measure?
- **Mechanisms**: How does it work?