Academic-Industrial Partnerships (AIP) to Translate and Validate in vivo Imaging Systems (R01 Clinical Trial Optional)

Reissuance of PAR-17-093

NATIONAL CANCER INSTITUTE
Division of Cancer Treatment & Diagnosis

Chris Hartshorn

BSA Meeting

Dec 2019

Academic-Industrial Partnerships (AIP) to Translate and Validate in vivo Imaging Systems

Co-Sponsored via NCI (DCTD-CIP, DCP, DCB) and other ICs (NIDDK, NIBIB, NIDCR)

- Primary requirement: *Formation of an Academic-Industrial partnership to identify and translate an imaging solution*

- Enables more focused / pragmatic clinical application of novel solutions

- *Offers a unique translational funding mechanism not offered elsewhere at the NIH*

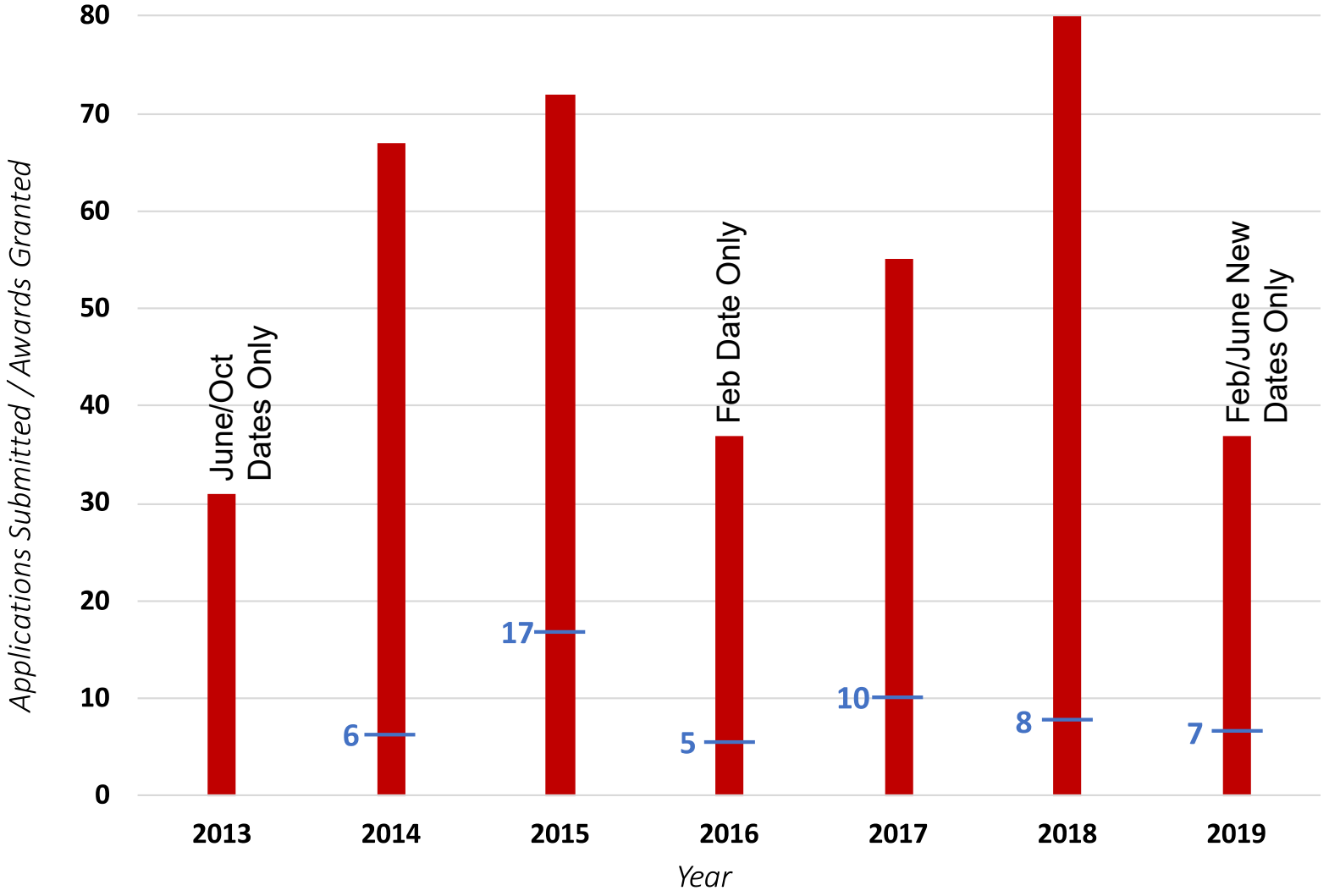
    1. Participation by companies beyond "small" are also needed
    2. Opens short-cut to commercialization / marketing
    3. Provides opportunity for companies to participate in novel R&D, even if investment strategy opposes it

- Standard 3 receipt dates per year and offers up to 500K / yr over 5 years for the partnership

- Translational outlet for NCI programs including QIN, image-guided therapy, SBIR/STTR as well as parent R01

- **Special emphasis panel under NIH CSR that enables necessary reviewer experience for its *additional translationally-focused requirements and review / research plan criteria*. Thus, continues to need issuance of PAR vs. R01 Parent**

Applications and Award Stats 2013-present



Applications → Awards

= 67 (submitted / year) → 9 (funded / year)

***Human subjects* = 71% → 79%**

***Software Development* = 37% → 48%**

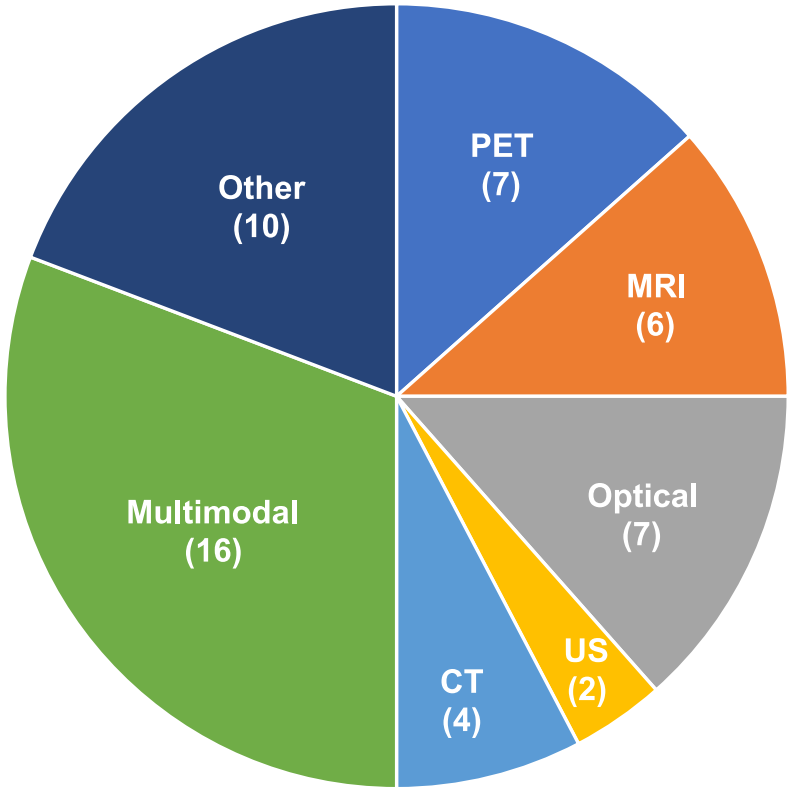
***Machine Intelligence (ML/AI)* = 7% (25% in 2019) → 6%**

***Academic : Industrial $ allocation* = 75:25**

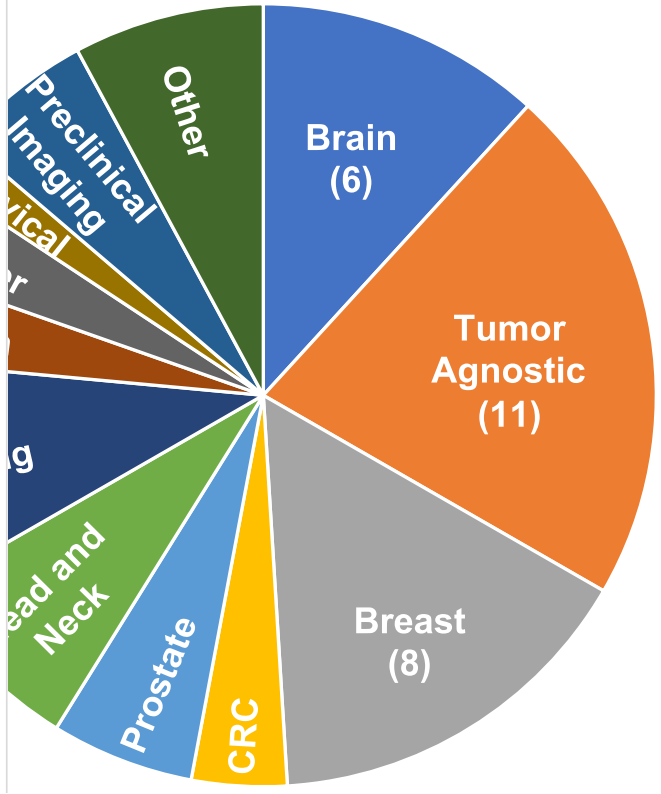
***Large : Med/Small Company* = 48:52**

Award Statistics 2013-present

AIP Imaging Systems Funded:
Imaging Modality



AIP Imaging Systems Funded:
Tumor Type



Investigator Productivity

- ***Clinical Trials*** = >20
- ***Patents*** = >80
- ***Regulatory Approvals*** = >25
- ***Products to Market*** = >20
- ***Publications*** = >350

Large to smaller companies involved:

Medtronic, GE Global Health, Siemens, Toshiba, Philips to Caliber ID, Curadel, Multifunctional Imaging, Intuitive Surgical and many others

AIP Example: *Novel Imaging Agent*

Image-guided diagnosis and therapy of neuroendocrine tumors

(*M. Sue O'Dorisio and Yusuf Menda*)

(*University of Iowa, Molecular Insight Pharmaceuticals and Iowa City VA*)

Modality: PET/CT

"Image-guided, molecularly-targeted therapy of neuroendocrine tumors (NETs) can be made widely available for patients in the United States within the five year time period of this Academic-Industry award through the collaborative…"

- **Approvals = 1 NDA and 2 INDs**
- **Clinical Trials = 7 complete**
- ***Enabled first ever FDA Approval for Peptide Receptor Radionuclide Therapy (PRRT) 2018 (Lutathera®)***

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FDA Approves New Treatment for Certain Neuroendocrine Tumors

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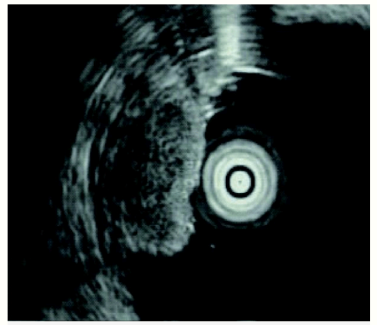
February 8, 2018, by NCI Staff

People with certain cancerous neuroendocrine tumors (NETs) affecting the digestive tract now have a new treatment option.

On January 29, the Food and Drug Administration (FDA) approved a new targeted treatment, lutetium Lu 177 dotatate (Lutathera®), for adult patients with advanced NETs that affect the pancreas or gastrointestinal tract, known as GEP-NETs. Lutetium Lu 177 dotatate is the first radioactive drug approved to treat these rare cancers.



An endoscopic ultrasound of a neuroendocrine tumor (NET) in the upper gastrointestinal tract (duodenum).
Credit: BMC Gastroenterol 2011. doi: 10.1186/1471-230X-11-67 CC 2.0.

Patients with GEP-NETs have limited treatment options if initial therapy fails to keep the cancer from growing or progressing.

"This is a major advance for patients with neuroendocrine tumors and provides a new treatment alternative for a good number of patients who don't respond to other treatments," said Electron Kebebew, M.D., chief of the Endocrine Oncology Branch in NCI's Center for Cancer Research.

The new drug consists of a radioactive isotope, Lu-177, attached to dotatate—a molecule that binds to GEP-NET cells that have a molecule called a somatostatin receptor on their surface. The drug then enters these somatostatin receptor–positive tumor cells, and radiation emitted by Lu-177 helps kill the cells.

New Approval Supported by Two Studies

The FDA approval was based on results from two clinical studies. The first study was a randomized clinical trial of 229 patients with inoperable, somatostatin receptor–positive NETs in the midgut that had gotten worse after treatment with standard-dose octreotide LAR (Sandostatin® LAR Depot). The multisite trial, called NETTER-1, compared lutetium Lu 177 dotatate plus standard-dose octreotide LAR with high-dose octreotide LAR, and was funded by the drug's manufacturer, Advanced Accelerator Applications.

AIP Example: *Novel Imaging Device*

Quantitative 3D Ultrasound Breast Scanner for Breast Cancer Detection and Diagnosis

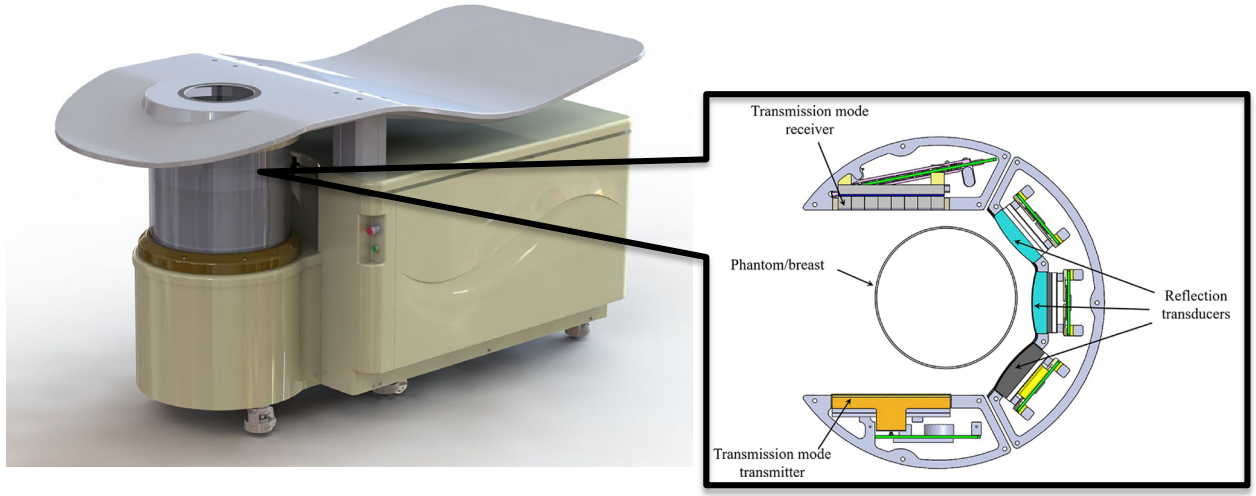
(*James Wiskin and Bilal Malik*)

(*UCSD/UT Southwestern and Techniscan/QT Ultrasound*)

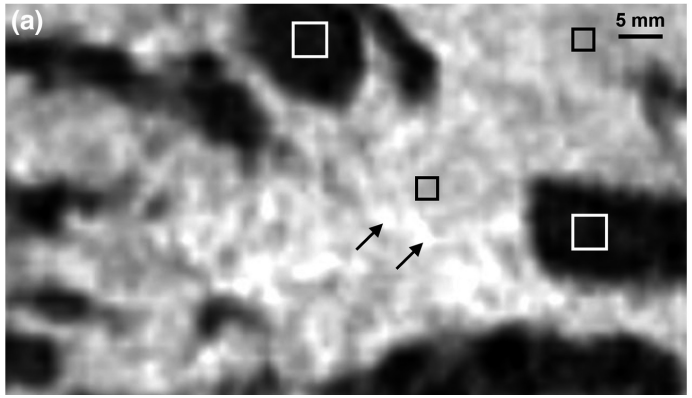
Modality: Combined Transmission Tomography (IST) and Reflection Tomography US

"Pre-clinical and clinical trials to date show that TechniScan's Warm Bath US system provides both improved sensitivity and specificity compared to targeted breast ultrasound, and with the addition of new features described herein, its clinical and diagnostic value is expected to be further enhanced."

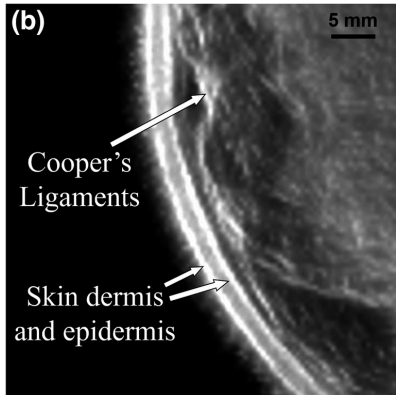
- **Patents = 11 granted and 13 more filed / in process**
- **Clinical Trials = 2 multisite complete**
- ***2018 FDA Breakthrough Device designation***



Techniscan's Warm Bath 3D Ultrasound platform



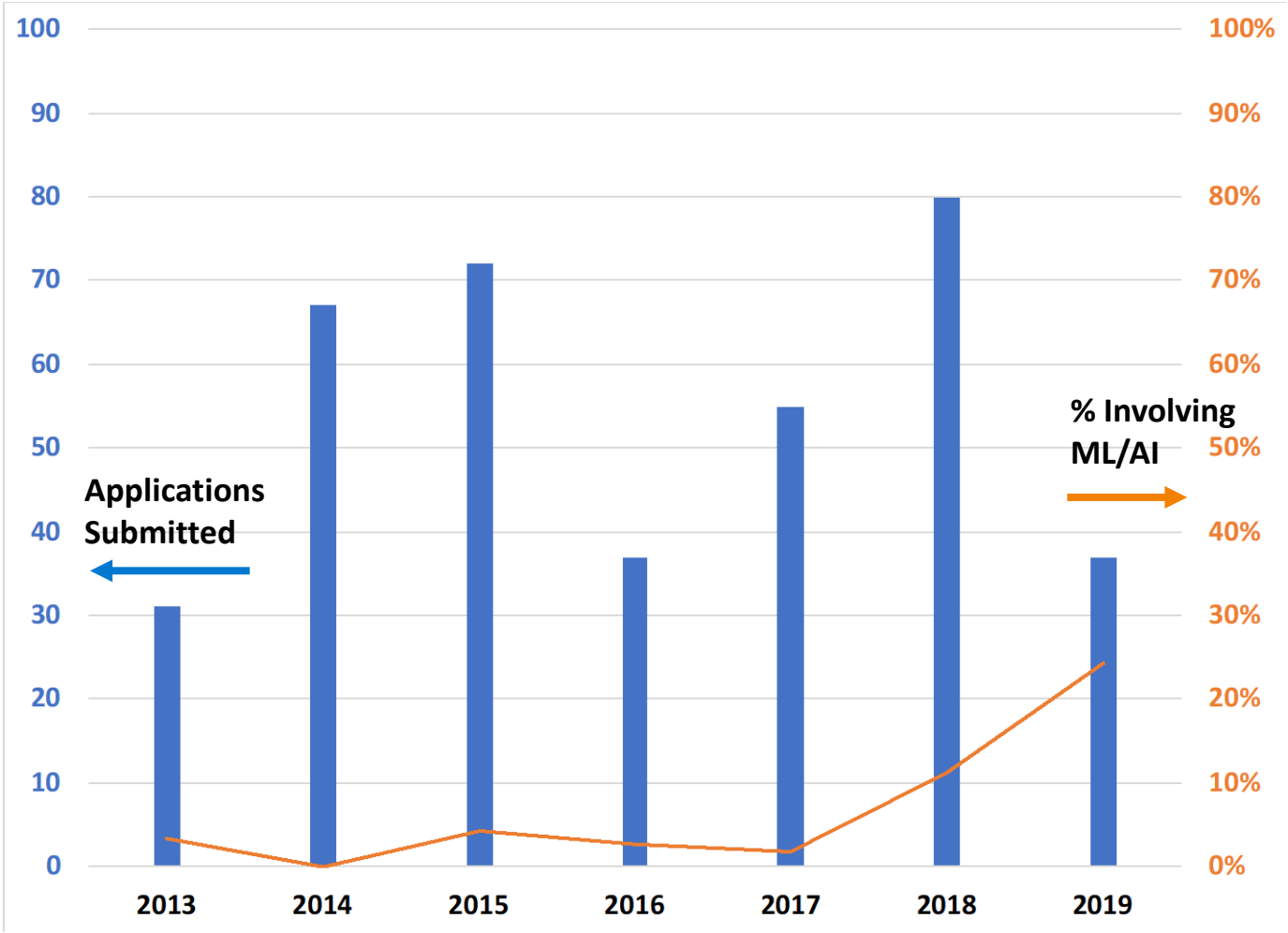
Transmission Tomography Component



Reflection Tomography Component

Evolving Area of Machine / Artificial Intelligence in Medical Imaging

ML/AI displaying large increase in applicant pool. Utility / Value proposition to industry for enhancing existing hardware with big data and unsupervised learning to enable better detection, quality control, streamlining workflow, etc



- ***Apps 2013-17*** = **2%**
- ***Awards 2013-17*** = **2**
- ***Apps 2018 -> 2019*** = **11% -> 25%**
- ***Awards 2018-current*** = **2**
- **"Confocal video-mosaicking microscopy to guide surgery of superficially spreading skin cancers"**
- **"Artificial Intelligence for Improved Breast Cancer Screening Accuracy: External Validation, Refinement, and Clinical Translation"**

Research Directions for Re-issuance

- Imaging platforms for anatomical, molecular, functional, or metabolic analysis;
- Multimodality imaging platforms or spectroscopic tools;
- Imaging tools to improve analysis, acquisition, lesion visualization, navigation guidance, or measurement of treatment response;
- Image guided interventions;
- Contrast agents;
- Development, optimization, and or implementation of methods to harmonize data collection across sites, quality assurance tools/methods, modeling methods, image data processing or display, structured reporting tools, and clinical workflow or other tools to aid clinical decision support;

✓ Integration of modern computational or informatics methods (e.g., machine learning/vision to 'Machine Intelligence', integrated bioinformatics, predictive analytics, etc.) into preclinical and clinical imaging methods to enhance / optimize utility for detection, diagnosis, or treatment monitoring.

In Summary

- FOA continues to receive strong interest from the community (*67 apps / yr*) and continued competitiveness (*9 awards / yr*)
- FOA offers unique mechanism to translate novel imaging tools via collaborative efforts of academia and industry, small to large
- FOA continues as translational outlet for NCI programs including QIN, image-guided therapy, SBIR/STTR as well as parent R01
- PAR is necessary to continue the highly specialized nature of the review requirements with the proper per round breadth of expertise

Re-issuance request

- Request FOA to *continue as R01 on standard receipt dates* and *extend 2 more years*
- Additional focus towards 'machine / artificial intelligence' projects
- Anticipated cost at $4-5M / year from 2-3 awards / round

More Examples

Name	PI(s)	Institutions	Products	Trials	Patents	Approvals
Real-Time in vivo MRI Biomarkers for Breast Cancer Pre-operative Treatment Trials	Nola Hylton	UCSF and Sentinelle Medical (bought by Hologic)	1 product	1 multisite (20) trial	1 patent	1 IDE and 1 510K
Clinical Translation of ^{19}F MRI to Visualize Cancer Immunotherapeutic Cells	Eric Ahrens	Carnegie Mellon Univ., Univ of Pittsburgh, and Celsense Inc	1 commercial prototype	1 trial		1 IND and 1 IRB
Non-invasive Image-Guided HIFU for Breast Cancer Therapy	Dennis Parker	Univ. of Utah, Image Guided Therapy, and Siemens Healthcare	1 product	1trial	6 patents + 2 pending	1 IDE and 1 IRB
Incorporating Real-Time Localization in Radiation Therapy Planning	Parag Parikh	Wash. Univ. and Nuclear Medical Systems	1 product and 1 prototype	1 trial	2 patents	1 IDE and 1 IRB
Culturally appropriate screening and diagnosis of cervical cancer in East Africa	Nirmala Ramanujam, Olola Oneko and Daniel Stevenson	Duke University, Becton Dickinson and Company, Kilimanjaro Christian Medical Centre, and Zenalux Biomedical, Inc	30 protype devices now being coupled to mobile phone	2 clinical studies at two international sites		
Software to Facilitate Multimode, Multiscale Fused Data for Pathology and Radiology	Michael Feldman	Univ. of Penn., Case Western Reserve Univ., Siemens Corp Research, and SUNY Buffalo	1 open source product		11 patents + 2 pending	
Whole Body PET/CT Assessment of Tumor Perfusion Using generator-Produced ^{62}Cu	James Fletcher	Purdue Univ., Univ. of Indianapolis, and Proportional Technologies	1 prototype	1 trial		1 IND and 1 IRB
Academic-Industrial Partnership for Non-invasive Barrett's Esophagus Detection	Stephen Meltzer and Martin von Dyck	Johns Hopkins University and CapNostics	2	1		