Affordable Cancer Technologies Program

Translational Research in Global Oncology

NCAB Subcommittee on Global Cancer Research

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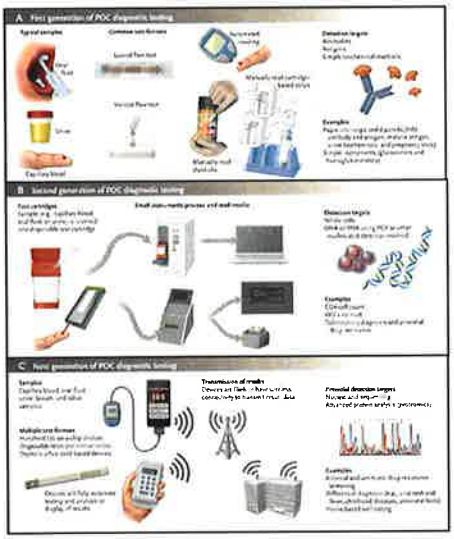
Motivations

- Rapid progress in several fields is contributing to the development of a new generation of point-of-care technologies (POCT).
- Affordable Cancer Technologies (ACTs) program created to support translational research focused on adapting such technologies to address cancer in LMICs.



Jani V. Ilesh, June 13, 2013 N. Engl J Med

Program Overview

- Three issuances (RFA-CA-13-015, RFA-CA-15-001, RFA-CA-15-024)
  - First awards made in 2014.
  - 20 active grants in the ACTs portfolio
- Awards are managed by program staff from
  - Division of Cancer Diagnosis and Treatment
  - Division of Cancer Prevention
  - Division of Cancer Control and Population Sciences
  - Office of HIV and AIDS Malignances
  - National Institute for Biomedical Imaging and Bioengineering

ACTs Performance Sites

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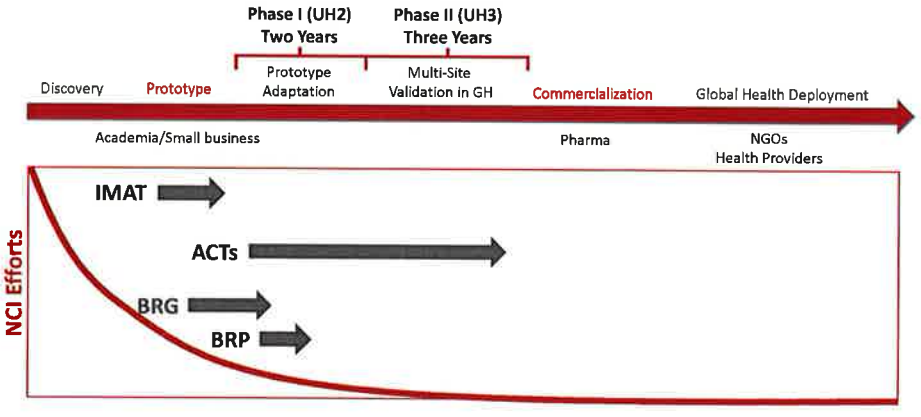
Program Structure

- **Multi-PI Mechanism:** oncology, engineering, business development, global health
- **Phase I (UH2) - two years:** Demonstrate clinical potential in a global health setting
- **Phase II (UH3) - three years:** Validate device in global health setting .



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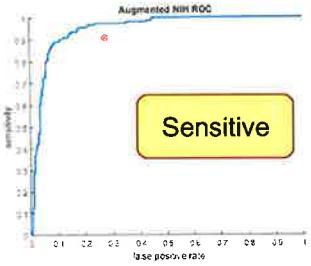
Example

Investigator and support: Dr. Susan Love, UH2EB019889/UH3CA189966, cooperative agreement with Dr. Susan Love Research Foundation
Device: a hand-held, low cost ultrasound system and analytical software to characterize palpable breast masses for triage.

Figure 8: (8a) GE Vscan (8b) Philips Lumify

Portable



Sensitive

minimally trained (1-3 hours) health care workers

Lesion capture by Trainee

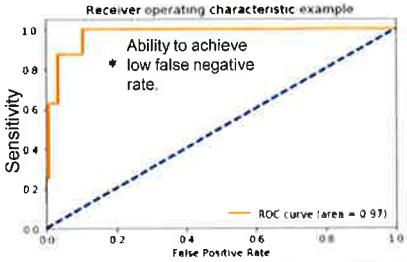
Lesion capture by radiologist

radiologist

Easy to Use

Progress and Achievements

- Investigators developed, preliminarily validated, and are now prospectively validating software for "reading" breast lump images captured by a low cost ultrasound transducer.
- Current Aims:
  - Complete recruiting 500 patients with palpable breast lumps to train and test the software on images from the low cost system vs. clinical ultrasound.
    - Goal: ROC curve operating point corresponding to 85% sensitivity and specificity corresponding to correctly identifying 40% of benign lesions.
  - Start recruiting 600 patients to determine clinical effectiveness with portable low-cost ultrasound imaging, where *results will guide patient management.*
- Results to Date:
  - 148 patients enrolled, 80 images analyzed.
  - AUC = 0.97; 100% sensitivity; 64% imputed benign biopsy reduction



Example 2

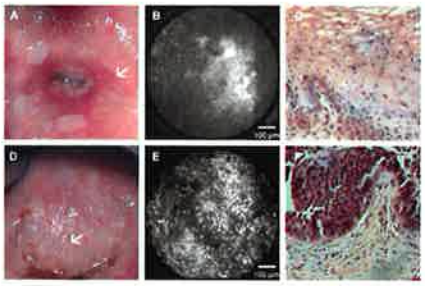
Investigator and support: Dr. Rebecca Richards-Kortum and Dr. Kathleen Schmeler, UH2CA189910/UH3CA189910, cooperative agreement with Rice University and MD Anderson

Device: Same visit screening, diagnosis, and treatment of cervical neoplasia.

High resolution microendoscope (HRME)

Portable

Easy to Use



Colposcopy HRME Histology

Goal: Same Visit Treatment or Referral

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Progress and Achievements

- Investigators successfully demonstrated implementation of the HRME in a mobile diagnostic and treatment unit for real-time diagnosis and treatment of cervical precancer in screen positive women.
- Current Aims:
  - Study of >12,000 women to validate the diagnostic sensitivity and specificity of HRME compared to VIA and colposcopy.
    - Outcome measures: proportion of women needing treatment (CIN2+) who actually received it and the proportion of women treated who actually required treatment (CIN2+).

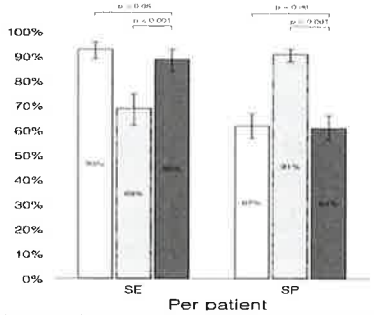
- Results to Date:

UH2 Accrual (additional staff hired for scale up)

	July 2018	Sept 2018
Enrolled	XXX (XX% complete)	855 (46% complete)
Pathology Complete	328 (35% complete)	871 (30% complete)

Comparable CIN2+ Detection to Colposcopy for Low-Grade Cytology

(based on the limited data so far)



Sensitivity and specificity of colposcopy and four-quadrant HRME for detecting CIN2+. Error bars represent binomial exact 95% confidence intervals. Significance testing was performed using McNemar's test.

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Overall Program Achievements

- Awardees from two RFAs have transitioned to UH3 (12 of the 14 successfully).
- Contributions to the literature, including several in high-impact journals.
- Grants have taken advantage of and contributed to state-of-the-art science, including deep learning for image interpretation, holographic imaging, advanced microfluidics, and lens-free microscopy.
- In-country experiences have led to new iterations of devices that are better suited to the end-users and environments of use (e.g., Erickson Lab's TINY).

- *USAID's Global Development Lab has created a program focused on later stage translation of such technologies to address cervical cancer in Malawi and Mozambique based largely on the technologies we have supported.*

Assessment

Team-Science Approach

- Multidisciplinary team structure has resulted in active collaborations and learning, especially for the engineers now working in LMICs and for LMIC PIs.

Mechanism

- UH2/UH3 mechanism lacks flexibility and arbitrarily constrains grantees to award timing.
- Variability in the entry points of technologies and varying experience in-country in LMICs, makes a one size fits all approach challenging.
- Awardees with promising technologies may either structure their applications to meet award requirements artificially or fail to meet their milestones because of the nature of the local context rather than the quality and appropriateness of the technology.

Cooperative Agreement

- Argument for increased NIH staff involvement pertains to the complexity of the projects, and the ability of NIH staff to provide scientific, technical, and regulatory guidance.
- Creates significant management burden for program and additional reporting for PIs.

Business and Regulatory

- Requiring business plans increased the complexity of the program overall.
- Regulatory approval needs varied significantly across the technologies.

Recommendations

- **ACTs is a potentially high-reward endeavor.**
  - If even if a small percentage of funded projects are validated clinically and implemented in LMICs, the benefit related to decreasing mortality could be substantial.
  - Some technologies may also be applicable to limited- resource settings in the United States, leading to domestic benefits.
- **No other USG-funded program has the scope and mission of ACTs.**
  - Due to lacking market drivers, efforts that extend beyond preliminary clinical validation are needed to ensure that such technologies can be inserted successfully into the continuum of care in LMICs.

Primary Recommendations:

1. Continue to pursue funding avenues to support this research community.
2. Maintain high-level scope, inclusive of interventions spanning the cancer control continuum and technologies including imaging tools, in-vitro tests, and ablative treatments/tools to enhance treatment effectiveness.

Additional Recommendations

- Move from phase-transition award to de-linked awards.
  - 1) An exploratory award for device/assay adaptation (i.e., R21, UH2)
  - 2) A longer phase for clinical validation (i.e., R01, U01)
- Potentially keep the cooperative agreement structure for the awards.
- Focus programmatic goals on clinical validation and translation/implementation of new technologies in LMIC health systems and leave commercialization and business development to other targeted programs. We're trying to do too much in this program.
- Make changes to application and review criteria:
  - Address the potential for different points of entry and different clinical validation requirements depending upon the nature of the technology.
  - Place greater emphasis on design thinking and understanding the continuum of care associated with proposed technologies.

Conclusions

Ongoing

- Last UH3 closeout in 4/2022.
- Active SBIR/STTR program:
  - PAR-18-801:
    Cancer Prevention, Diagnosis, and Treatment Technologies for Low-Resource Settings (R43/R44 - Clinical Trial Optional)
  - PAR-18-802:
    Cancer Prevention, Diagnosis, and Treatment Technologies for Low-Resource Settings (R41/R42 - Clinical Trial Optional)

Future

- Outcomes evaluation
- Investigating possibility for future similar programs.

Appendix

Active ACTs Grants

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Cervical Cancer

HPV Diagnostics

Louise Kuhn, Columbia University

Setting: South Africa

Kristin Weidemaier, Becton Dickinson

Setting: Kenya, China, Brazil

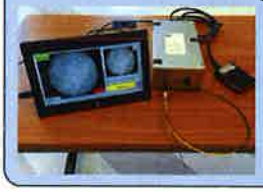
Rolando Herrero, IARC

Setting: Colombia, Argentina, Honduras, Costa Rica, Mexico, Paraguay, Uruguay, Peru, and Bolivia

Karen Anderson, Arizona State

Setting: India

POC Imaging



Kathleen Schmeler, MD Anderson; Rebecca Richards-Kortum, Rice University

Setting:Brazil

Ablative Therapies

Miriam Cremer, Basic Health International

Setting: Peru, Columbia, El Salvador

Jean Anderson, Johns Hopkins

Setting: Philippines

Partha Basu, IARC

Setting: Zambia

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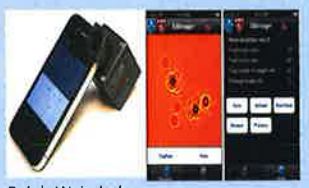
HIV-Associated, Oral, and Liver Cancers

Diagnostics for HIV Associated Malignancies



Ralph Weissleder,
Massachusetts General Hospital

Setting: Botswana

David Erickson,
Cornell University

Setting:
Uganda, Kenya

Detection and Treatment of Oral Cancer

Rongguang Liang,
University of Arizona

Setting: India

Tayyaba Hasan, MGH
Jonathan Celli, UMass Boston

Setting: India

Detection of Serum Markers for Liver Cancer

Ashutosh Chilkoti,
Duke

Setting: China

Marc Porter,
University of Utah

Setting: Mongolia

Other Cancer Sites and Radiotherapy

Breast Cancer Triage

Susan Love,
Dr. Susan Love Research Foundation

Setting: Mexico

Esophageal Cancer Screening

Stephen Meltzer, Johns Hopkins

Setting: Uganda

Colorectal Cancer Diagnostic

Peter Kingham,
Memorial Sloan Kettering

Setting: Nigeria

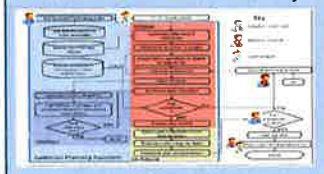
Digital PCR CML Diagnosis and Monitoring

Daniel Chiu, University of Washington

Setting:
Nigeria, Malawi, Uganda

Radiotherapy

Semi-Automated RT Dosimetry



Laurence Court, MD Anderson

Setting: Philippines, South Africa

Compensator for Cobalt 60 RT for Targeted Therapy

Eric Ford,
University of Washington

Setting:
India