

The Role of the Radiologist in the 21st Century Healthcare



**Sam Gambhir M.D., Ph.D.
Stanford University**

In memoriam



**Dr. Juergen Willmann
(5/24/1972 – 1/8/2018)**

Disclosures

Abbvie, AlphaSource, Biogen, BMS, Bracco, CellSight Inc.*, Click Diagnostics, Cytomx, Earli Inc.*, Endra Inc.*, GE Health Care, Grail, ImaginAB, Infinitus, Kite Pharma, Konica-Minolta, Life Molecular Imaging, MagArray, Nine-Point Medical, Nines Inc., Novartis, Novocure, NuvOx, Philips Medical, Piramal MI, Pliant, Puretech, Reflexion Inc., Rio Inc.*, Site-One Therapeutics, Sanofi Aventis, TauMark, Third Rock Ventures, Vave Inc., Verily Life Sciences, Visualsonics, Vor Biopharma

*** Founder / Co-Founder**

Special Thanks



Dr. Garry Gold

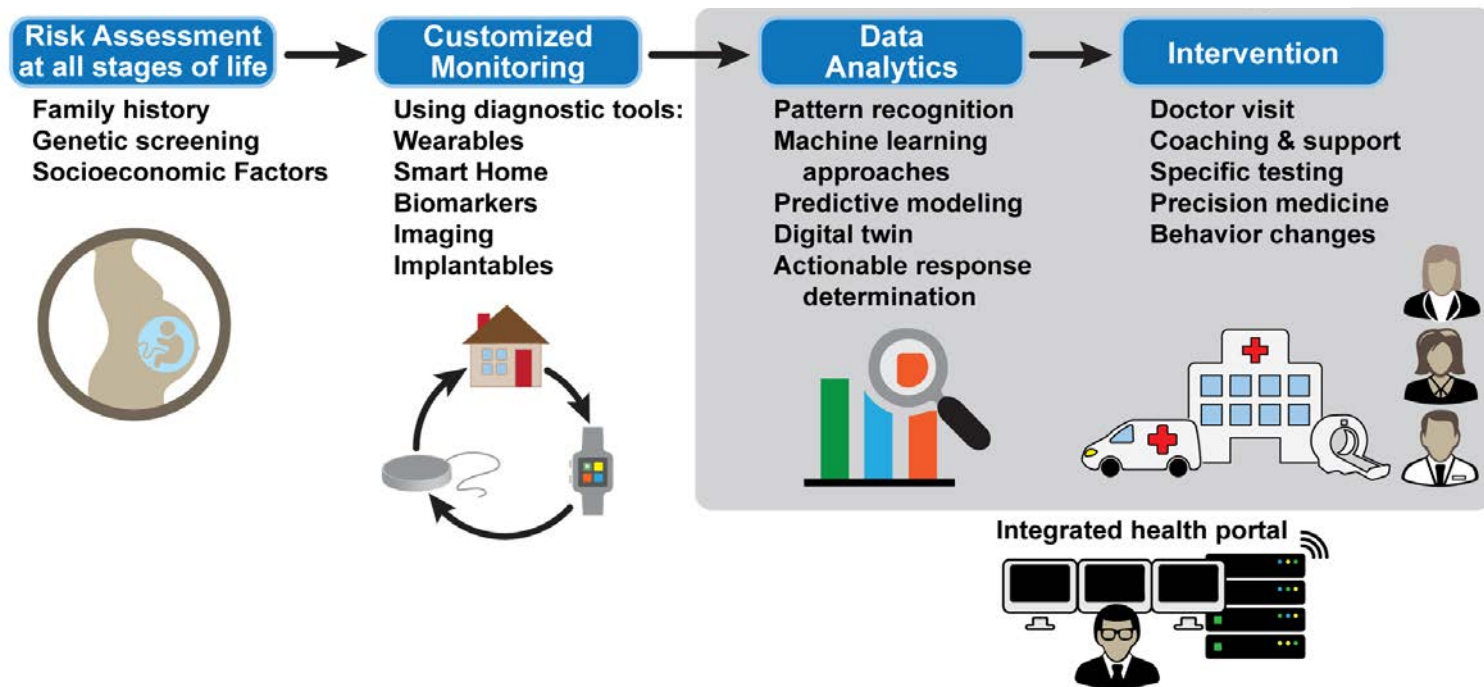


Dr. David Larson

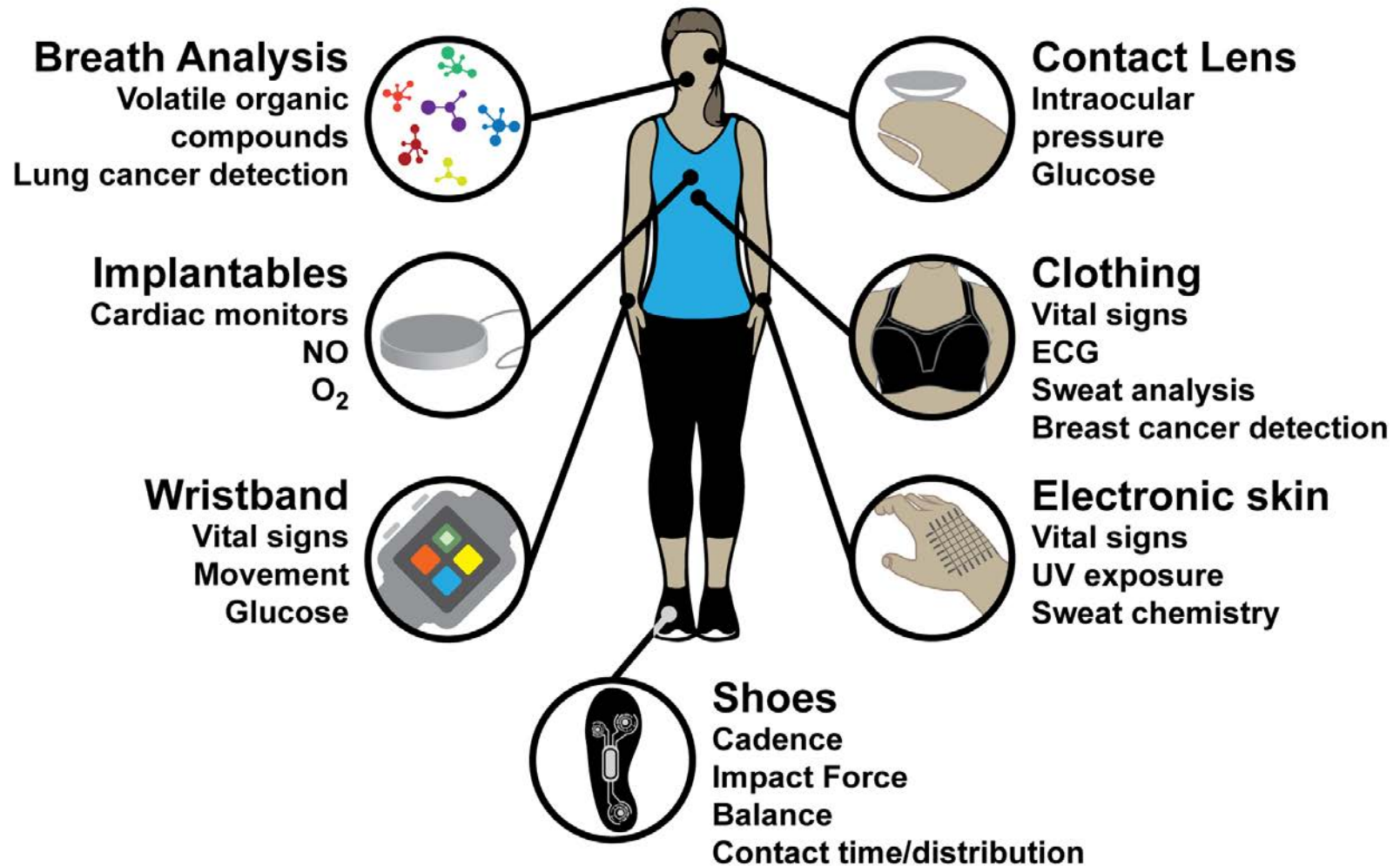
Modern Day Healthcare



Precision Health

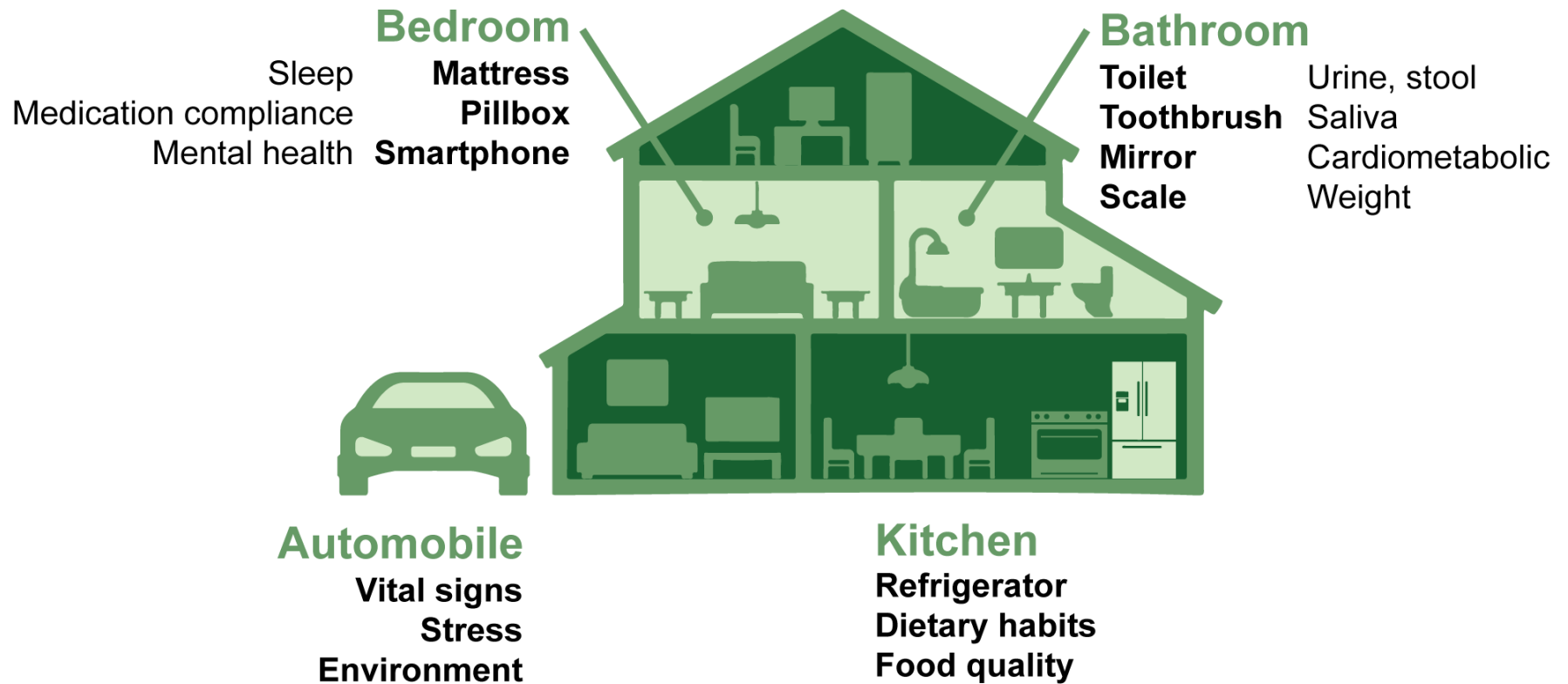


S.S. Gambhir et al, Science Translational Medicine, 2018



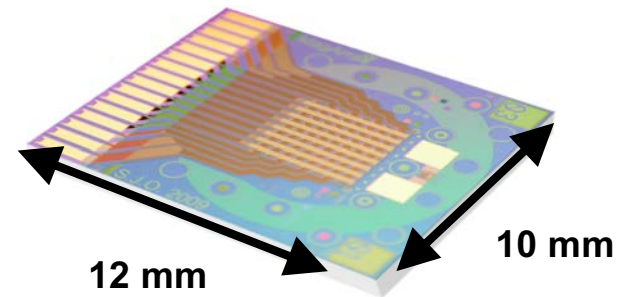
S.S. Gambhir et al, Science Translational Medicine, 2018

Smart Home



S.S. Gambhir et al, Science Translational Medicine, 2018

Smart Toilet Technology



**Simple, ultra-sensitive, multiplex system.
Diseases: Renal Ca, Bladder Ca, Colorectal Ca,
Prostate Ca, Diabetes, Infections**

S.M. Park et al/ Gambhir Lab (Patent Pending)



Apple Heart Study

In partnership with  **Stanford** | MEDICINE

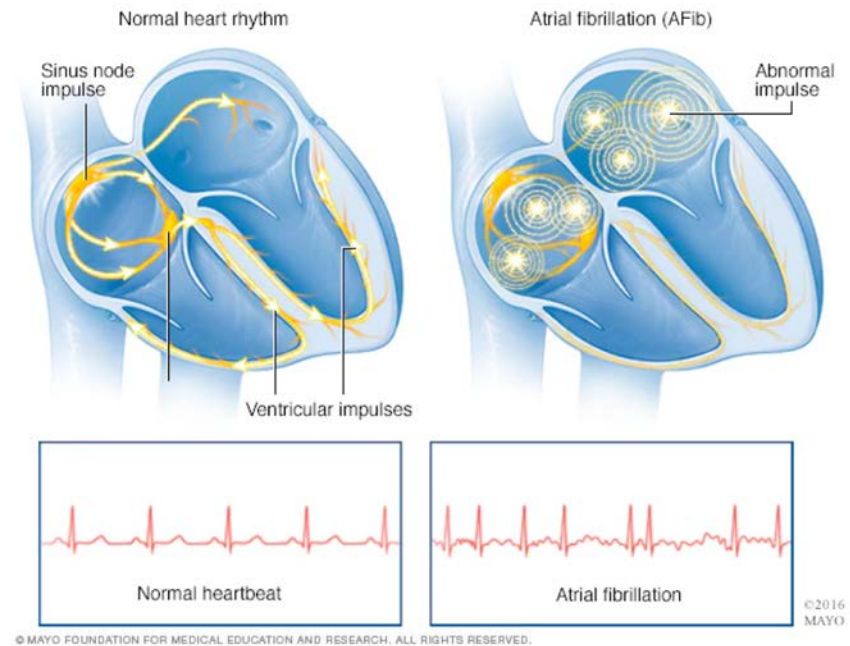
Early detection of irregular heart rhythms may prevent more serious health issues

- The goal of the study is to understand the test characteristics of a smartwatch algorithm for photoplethysmography-based detection of atrial fibrillation (AF) and to estimate the diagnostic yield in a large, US-based population.
- The study launched Nov 29th, 2017 – Jan 31st 2019
- Currently 419,093 participants enrolled
- The study is funded by Apple, and performed in partnership with Stanford School of Medicine including Stanford Center for Clinical Research (SCCR) and the Quantitative Science Unit (QSU)



Background

- 1 in 4 in the US has AF during their lifetime
- Over 5 million people in the US are affected by AF, increasing one's risk of stroke (5-fold) and heart failure.
- An estimated 700,000 of these people don't even know they have AF.
- AF has an incremental cost burden of 3.2 billion.
- This study is the largest screening study of AF ever performed.
- A similar Swedish study, Stroke stop study, is screening 25,000 participants for mass arrhythmia.
<https://www.ncbi.nlm.nih.gov/pubmed/25910800>
- In the US 77% of people have smart phones, 13% have smart watches, and 40% express interest in purchasing one.



Data and Measures

Data Collected

- Smart watch
- Smart phone
- Telehealth study visits
- Ambulatory ECG patch
- Participant reported outcome surveys
- Research adjudication portal
- Study safety desk

Tachograms are not visualized or provided to the participant, and analyses are run in the background.

Data Access:

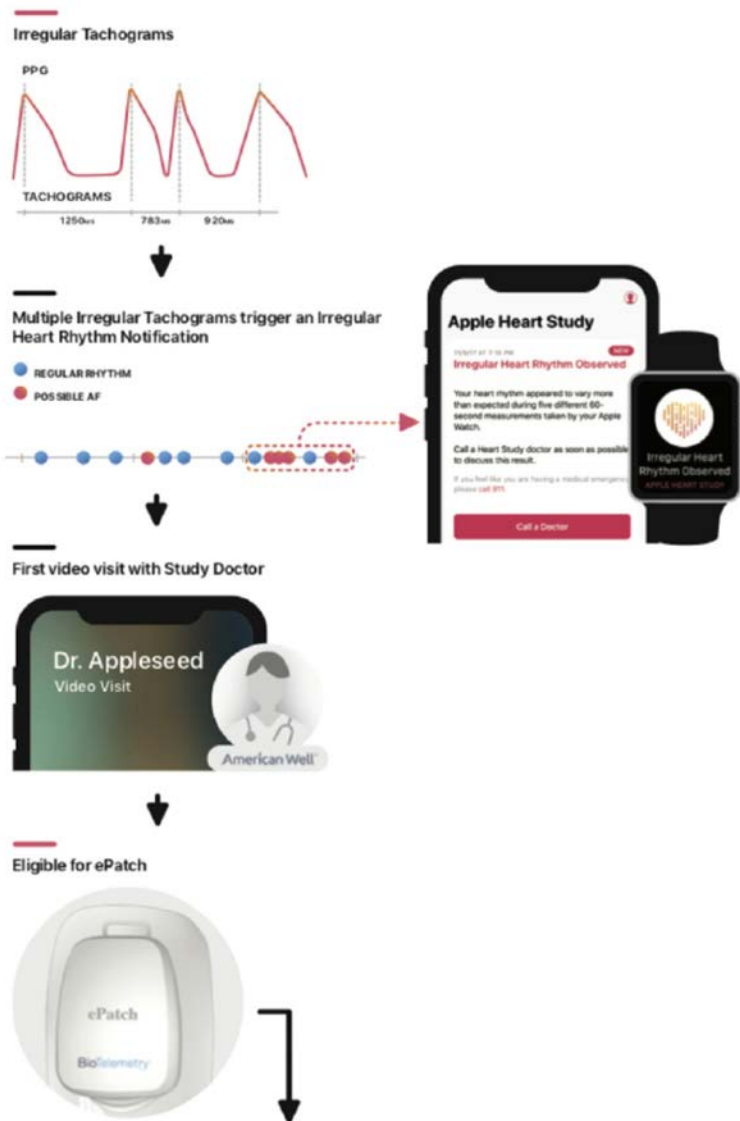
Apple Inc., Stanford University, Schulman Institutional Review Board (ethics committee), American Well and its clinical partner, Online Care Group (Study Telehealth Provider), Biotelemetry (ePatch provider), and its subsidiaries/affiliates, Data Safety Monitoring Board, Office for Human Research Protections in the U.S. Department of Health and Human Services, the FDA (Food and Drug Administration) and other international regulatory agencies may have access to your data.



Study Design (part 1)

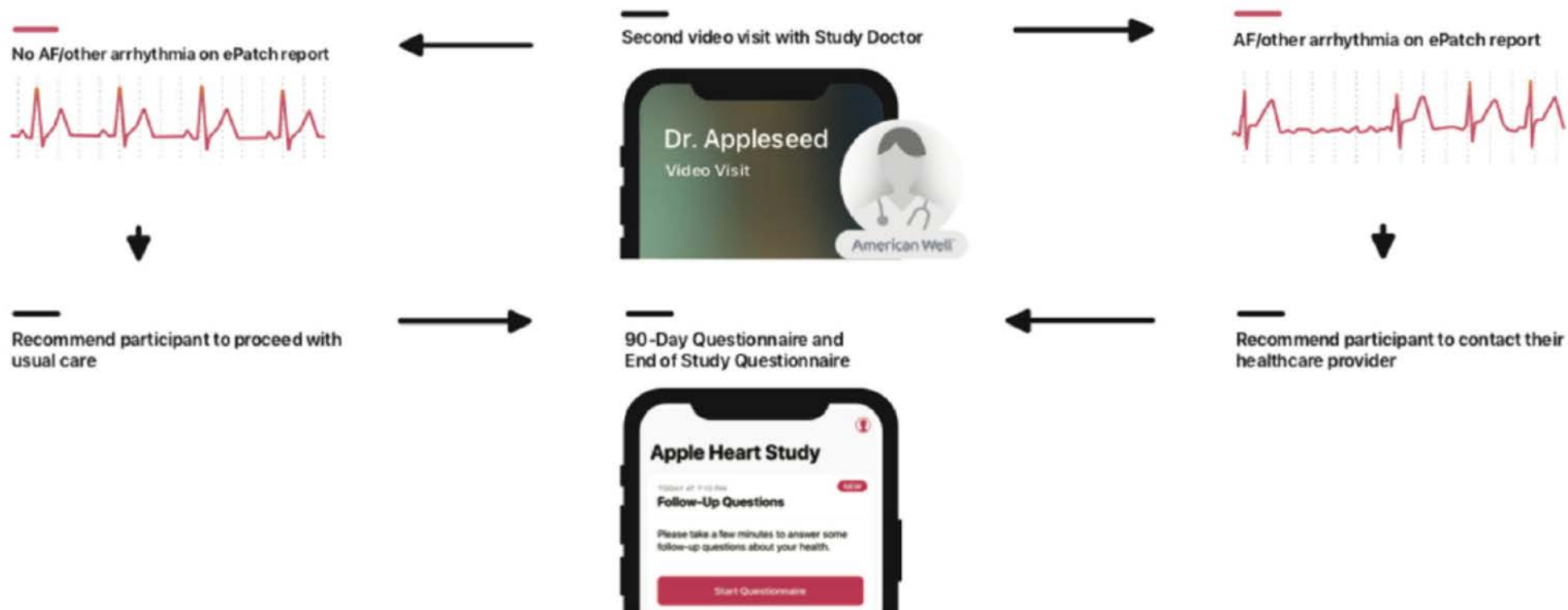


Study Design (part 2)



ePatch given if irregular heart Rhythm is detected

Study Design (part 3)



Precision Health



Precision Medicine \neq Precision Health

Precision Medicine

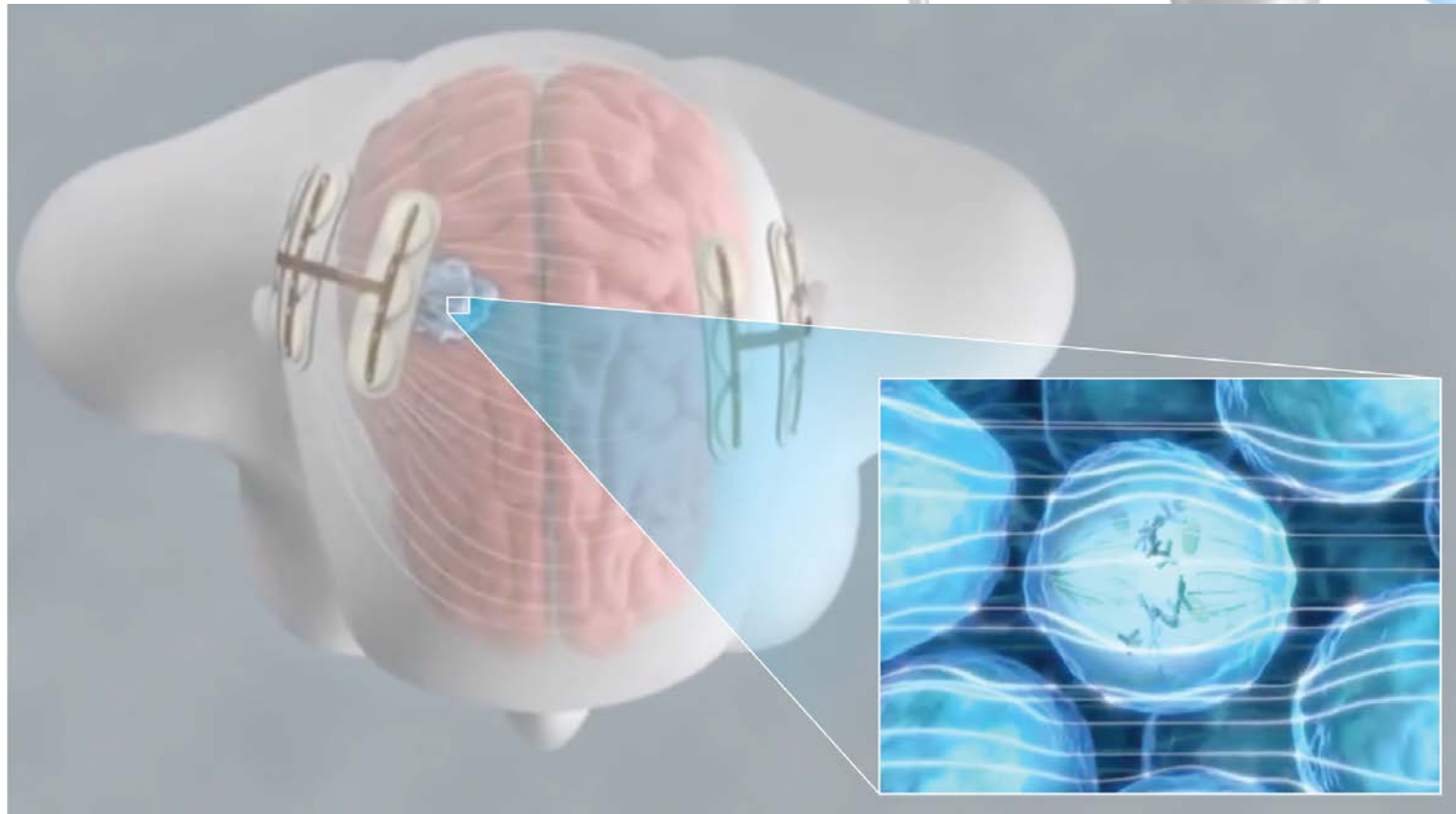
**Right Treatment
Right Person
Right Time**



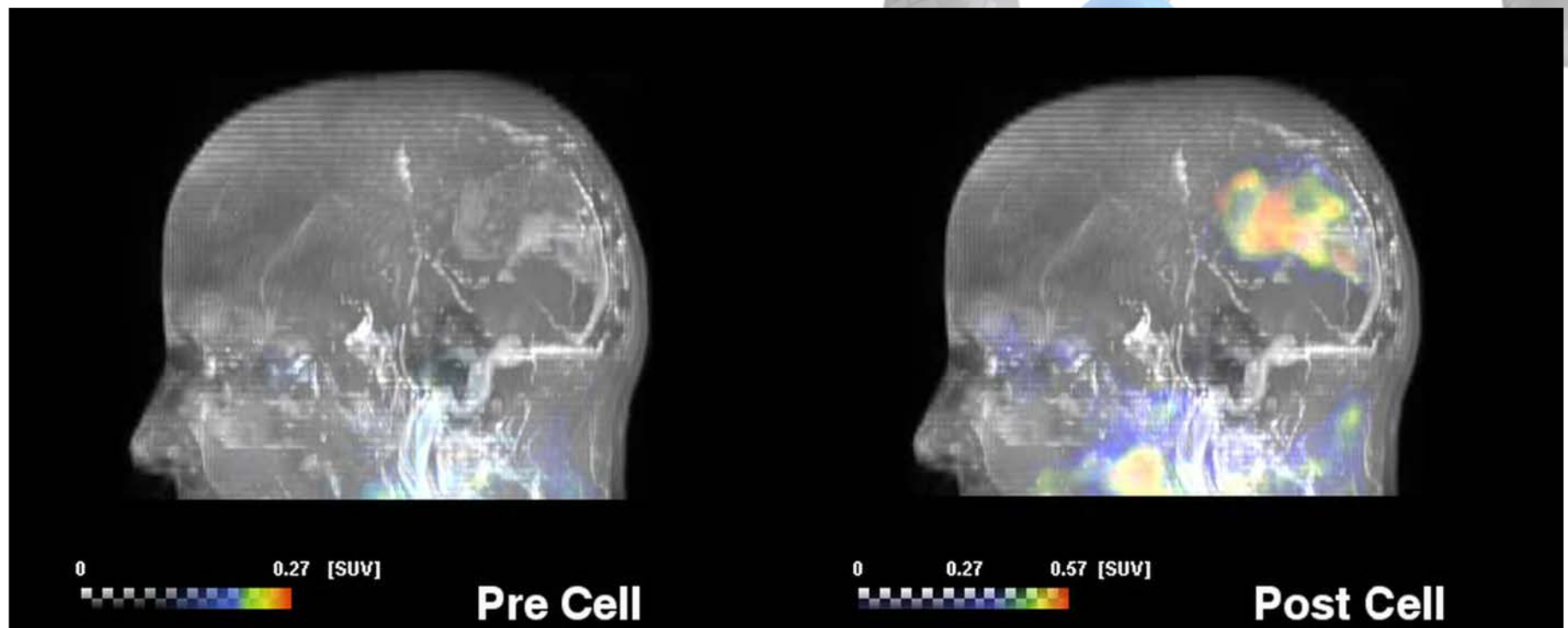
The Future of Precision Medicine

Entirely new therapies will become available and they will be driven by fundamental technological advances linked to our increasing knowledge of biology

Tumor Treating Fields (TTF)

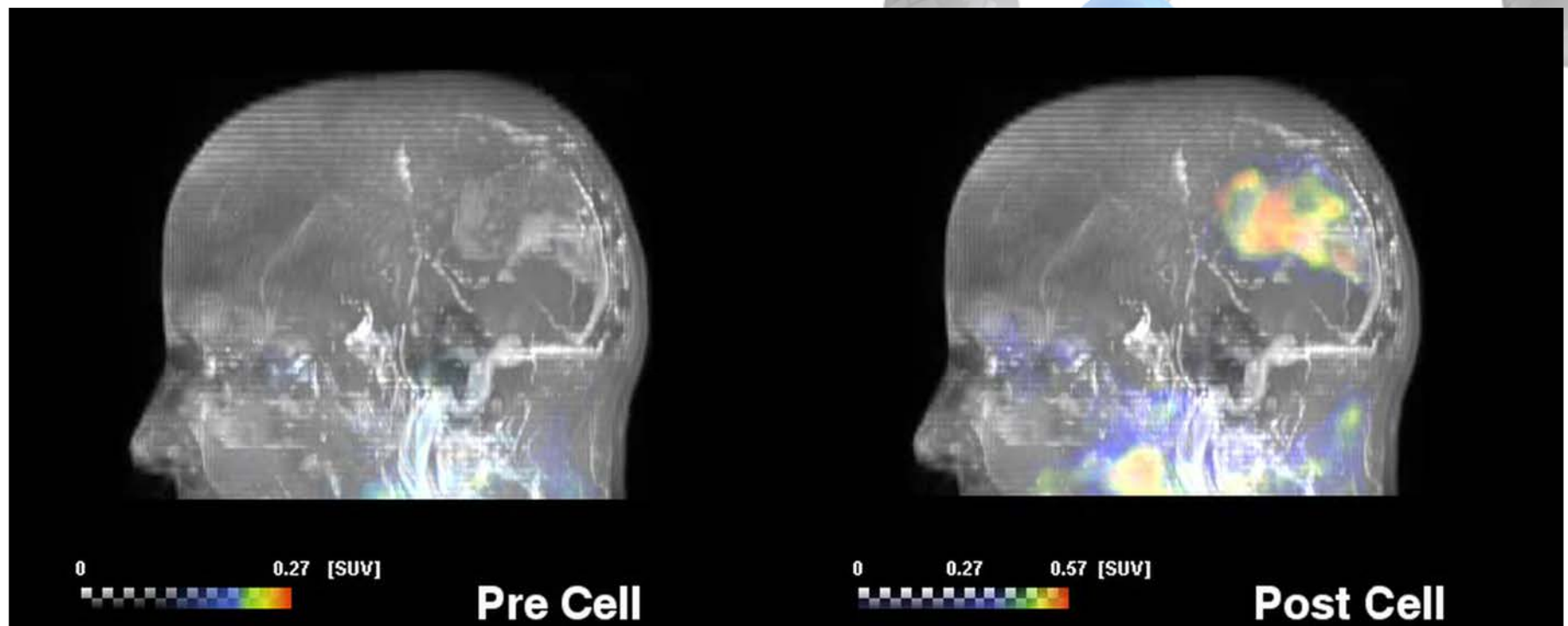


Harnessing the Immune System for Therapy



K. Keu et al/ Gambhir Lab; Sci Trans Med (2017)

Harnessing the Immune System for Therapy



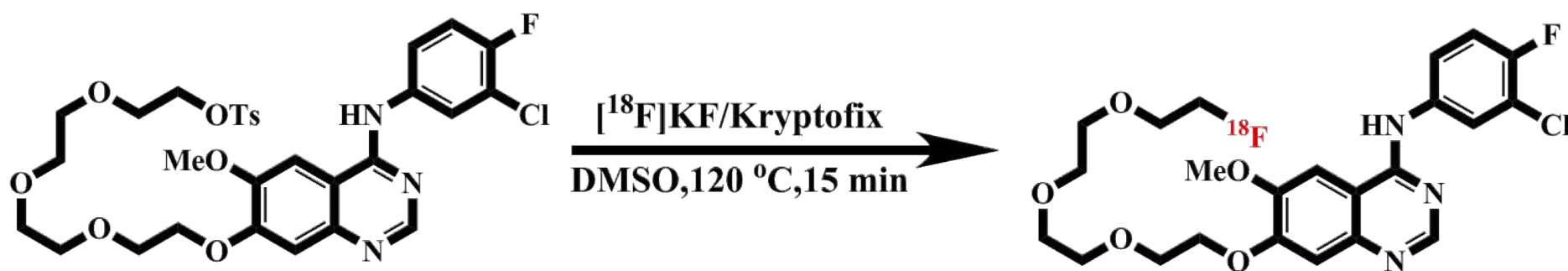
K. Keu et al/ Gambhir Lab; Sci Trans Med (2017)



**For both precision health and precision medicine to
succeed precision diagnostics will be the key**

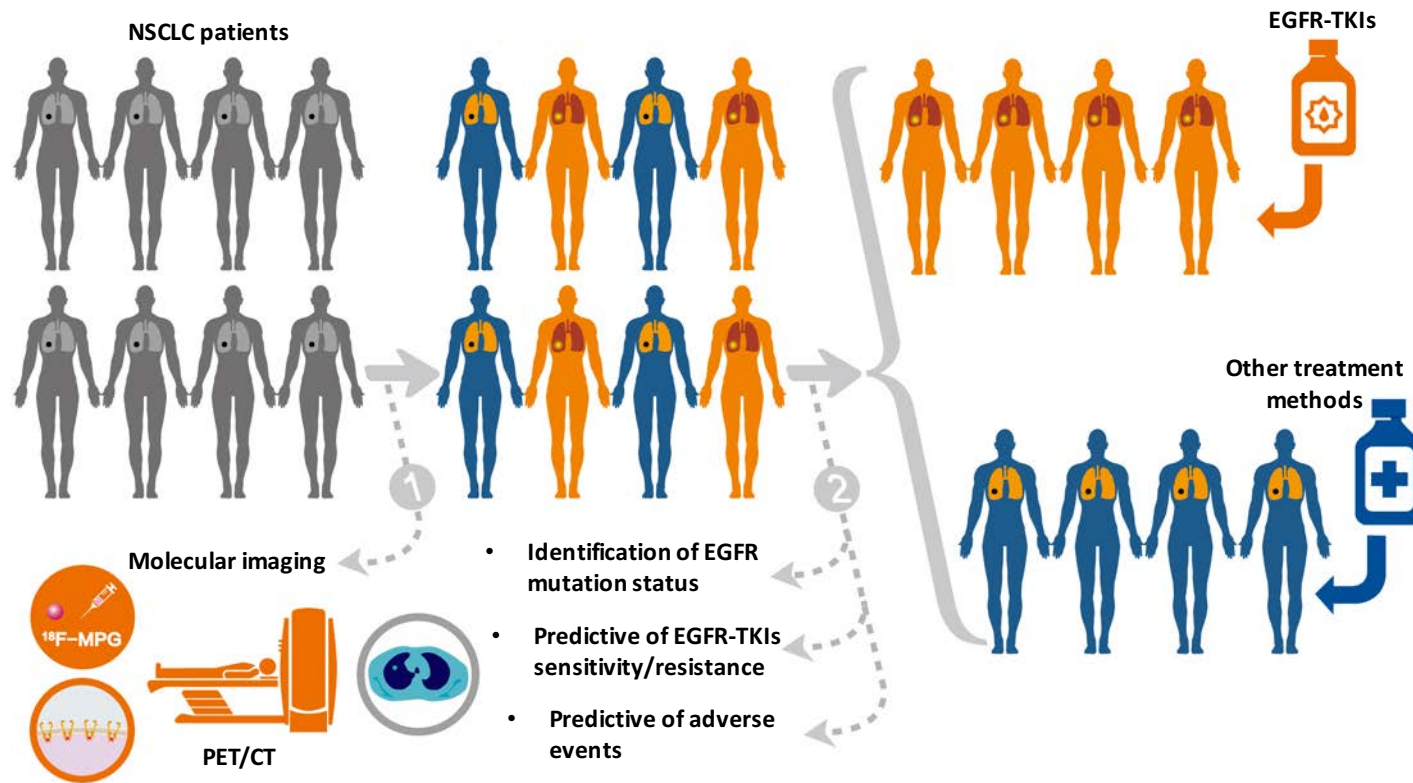
Molecular Imaging can Lead the Way in Predicting Response to Therapies

Clinical Trial of ^{18}F -MPG in Lung Cancer



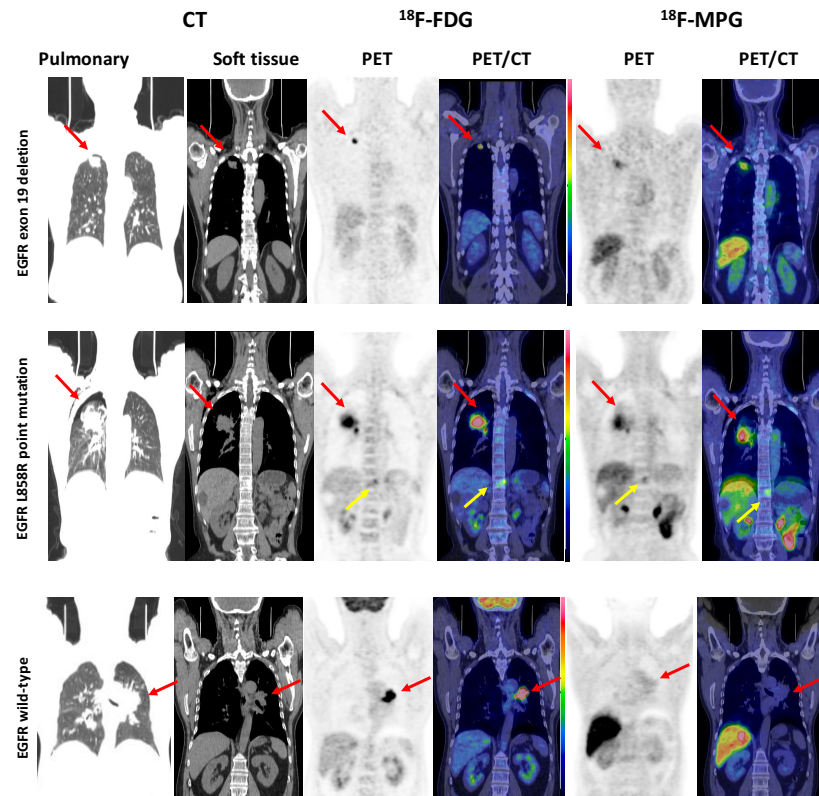
X. Sun, Z. Cheng, S.S. Gambhir, Science Translational Medicine, 2018

Novel Molecular Imaging Strategy with ^{18}F -MPG PET

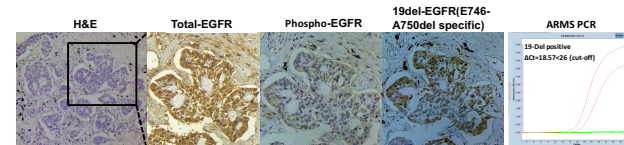


Determining EGFR mutation status for improved lung cancer patient management

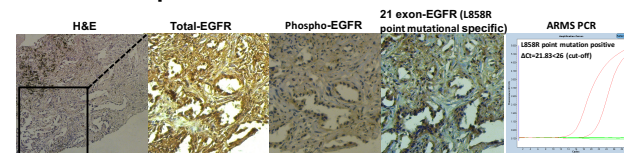
Clinical Trial of ^{18}F -MPG in Lung Cancer



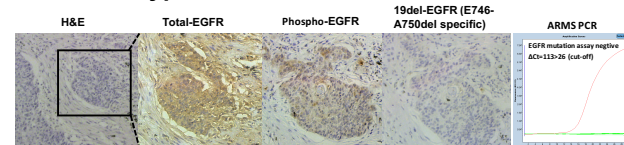
EGFR exon 19 deletion



EGFR L858R point mutation



EGFR wild-type

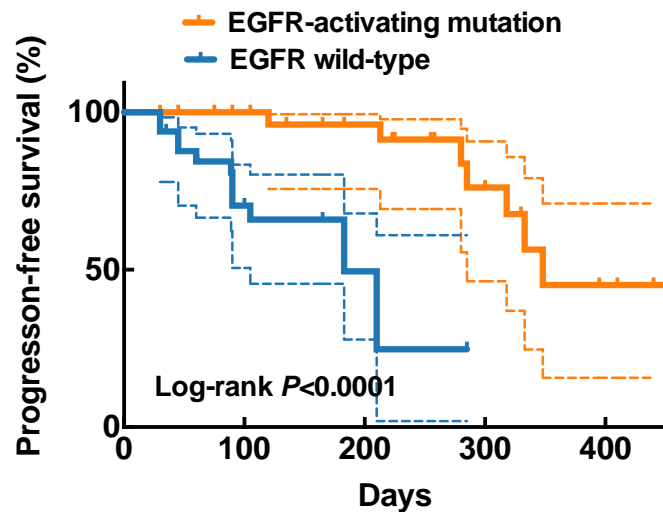


^{18}F -MPG successfully delineated EGFR-activating mutant tumors, showing visually appreciable higher contrast than EGFR wild-type tumors.

X. Sun, Z. Cheng, S.S. Gambhir, Science Translational Medicine, 2018

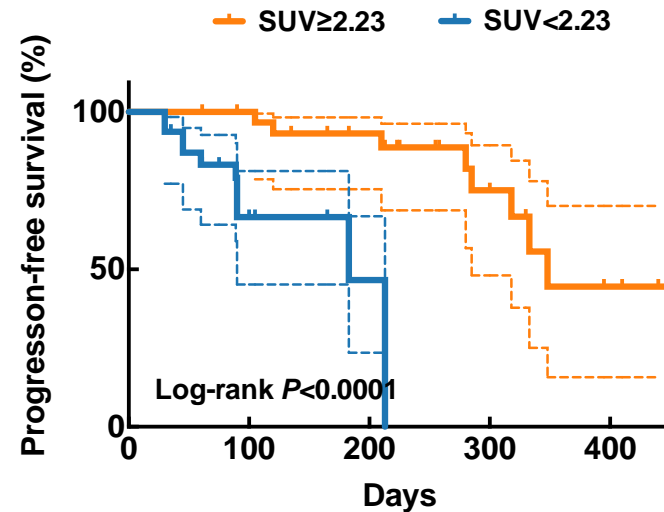
NSCLC Patients with High 18F-MPG SUVmax Benefited from EGFR-TKI Treatment

A: PFS according EGFR mutation status



Patients with EGFR-activating mutations had longer PFS than those carrying EGFR wild-type

B: PFS according ^{18}F -MPG PET/CT SUV_{max}



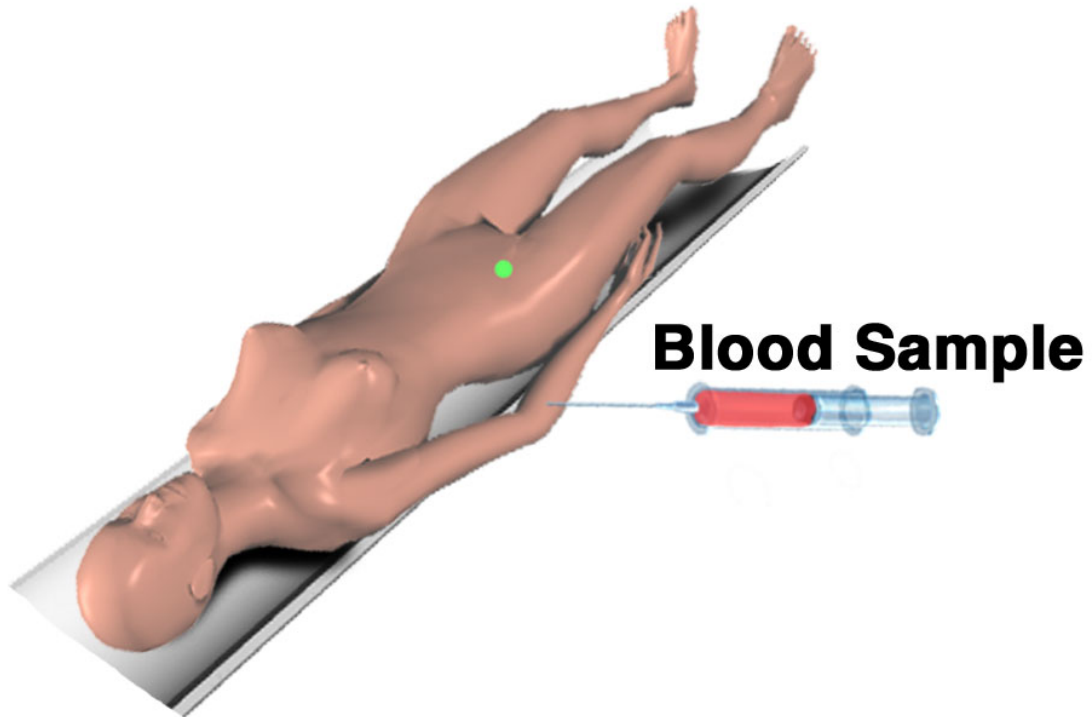
When using a cutoff of 2.23 for ^{18}F -MPG SUV_{max} , a significant association with PFS was observed

$\text{SUV}_{\text{max}} \geq 2.23$ 348 days
 $\text{SUV}_{\text{max}} < 2.23$ 183 days

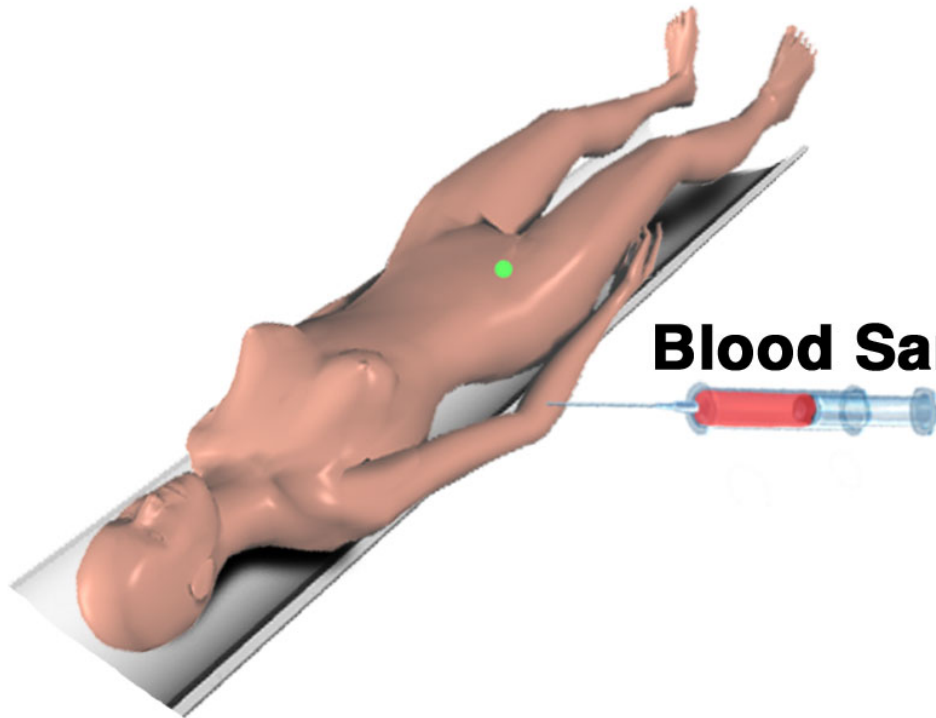
X. Sun, Z. Cheng, S.S. Gambhir,
Science Translational Medicine, 2018

***In Vitro* Diagnostic Strategies are
Rapidly Growing and will Challenge
the role of Imaging in Patient
Management**

Remote Sensing / Liquid Biopsies

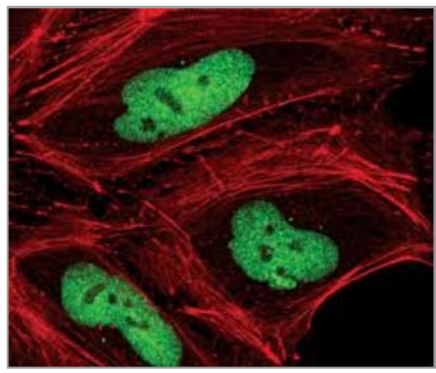


Remote Sensing & Liquid Biopsies



- Proteins
- DNA / RNA / microRNA
- Small molecules
- Circulating tumor cells
- Microvesicles/Exosomes
- Platelets

Techniques for Molecular Classification



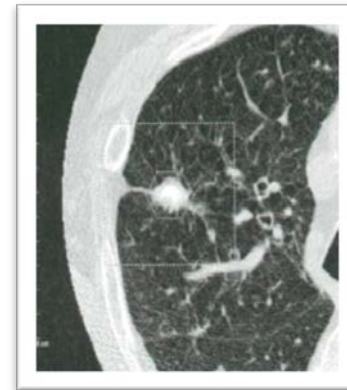
Biopsied samples

often fail or have poor reproducibility because of insufficient material for mutation analysis



Blood samples

Sometimes cannot address the issue of expression heterogeneity in primary or metastatic tumors

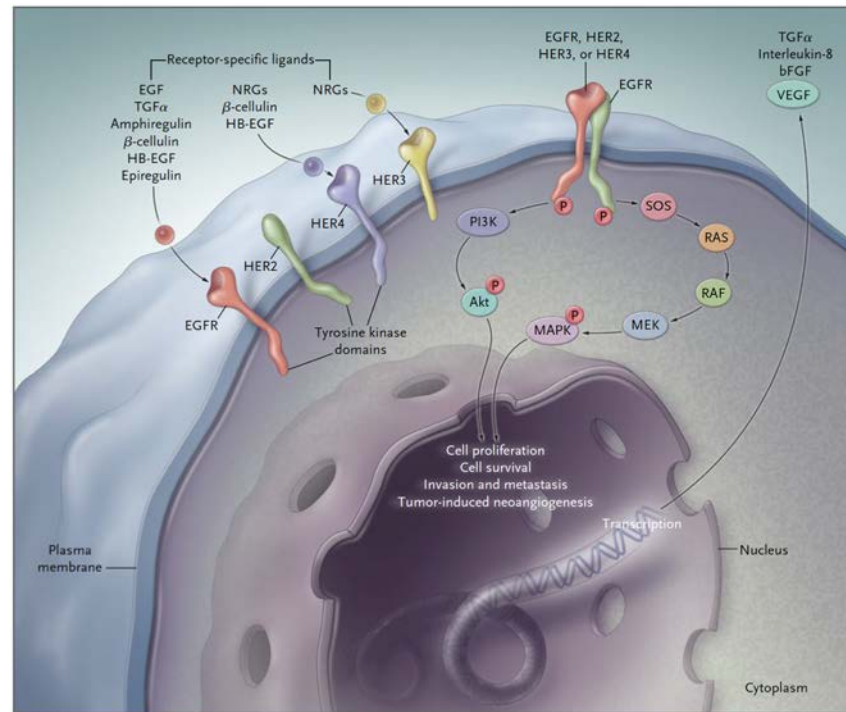
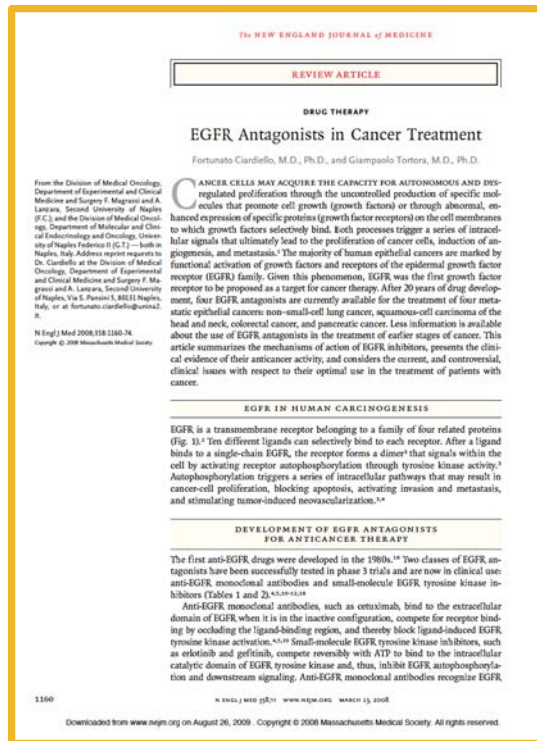


Traditional Imaging

does not show the gene and protein level changes of tumors

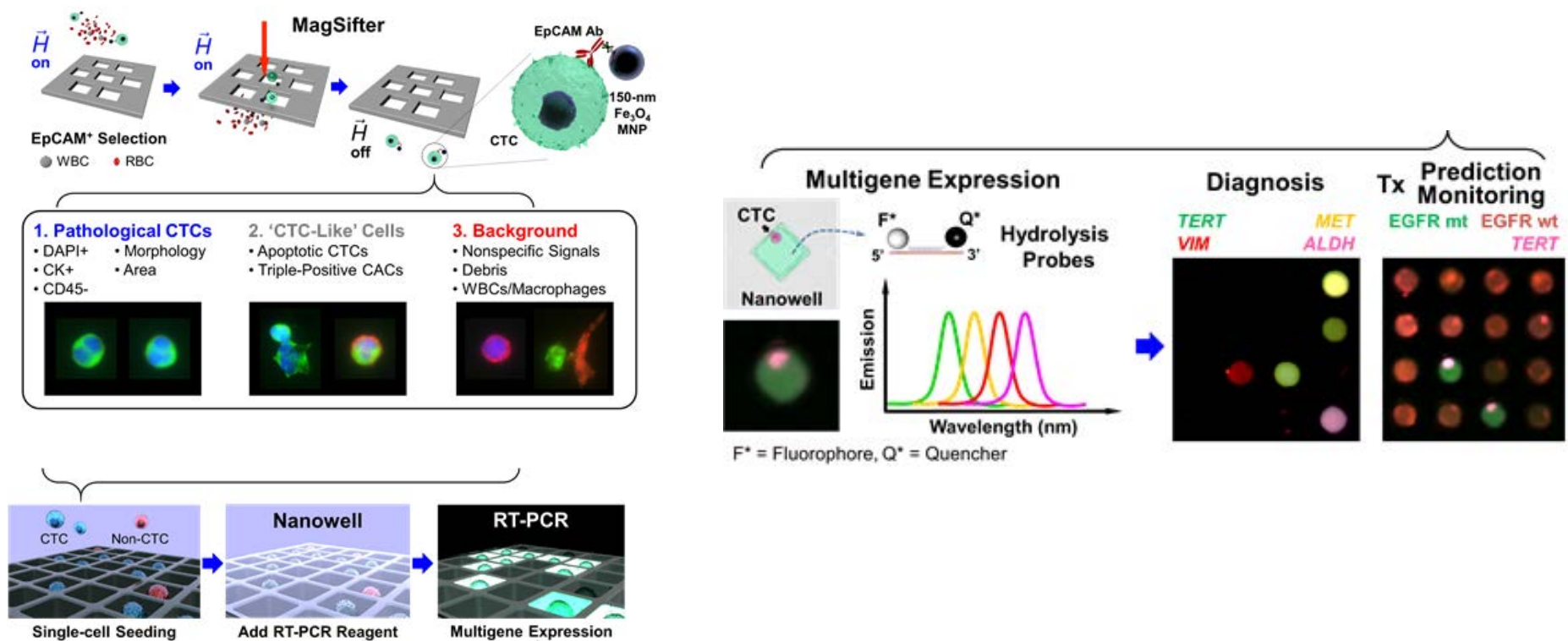
There is an urgent need to develop techniques for comprehensive tumor EGFR profiling in real-time, particularly in lung cancer precision medicine trials

Lung Cancer and EGFR Mutation Status



Estimation of EGFR mutation status is essential for the identification of NSCLC patients who may benefit from treatment with EGFR-TKIs, and hence for improving prognosis and EGFR-TKI therapy efficacy

Monitoring Response to Therapy by Analysis of Circulating Tumor Cells in Lung Cancer Patients

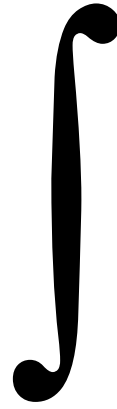


Park *et al.* / Gambhir Lab **PNAS**, 2016, 113, 52, E8379–E8386.

The Role of the Future Diagnostic Radiologist



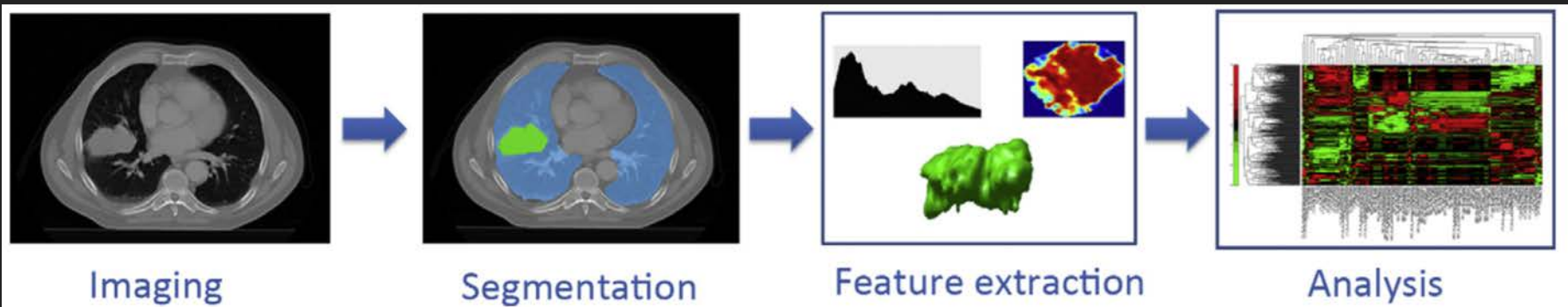
The Role of the Future Diagnostic Radiologist



Radiomics

Radiomics: Extracting more information from medical images using advanced feature analysis

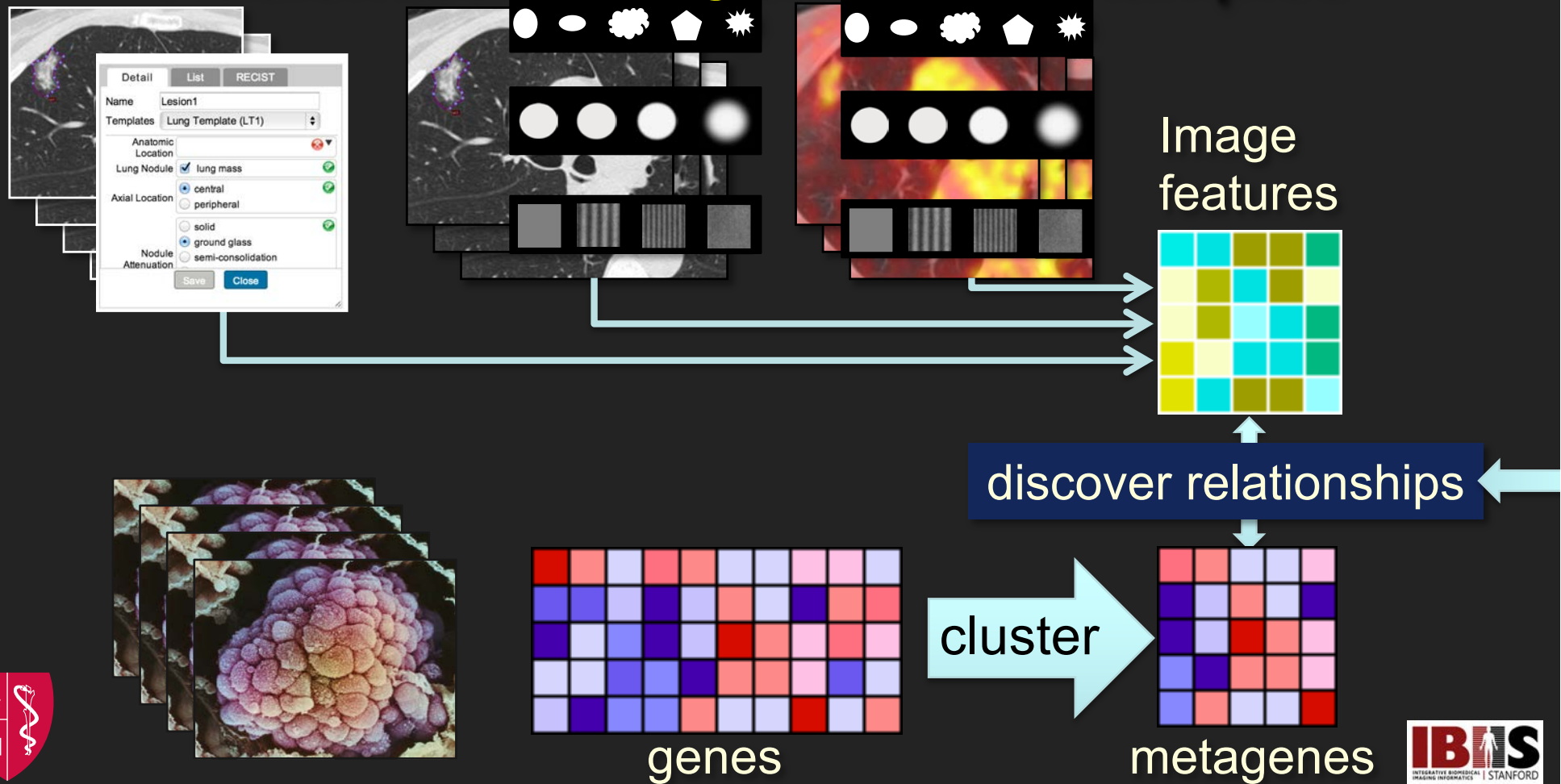
Philippe Lambin^{a,*,e,f}, Emmanuel Rios-Velazquez^{a,e}, Ralph Leijenaar^{a,e}, Sara Carvalho^{a,e}, Ruud G.P.M. van Stiphout^{a,e}, Patrick Granton^{a,e}, Catharina M.L. Zegers^{a,e}, Robert Gillies^{b,e}, Ronald Boellard^{c,e}, André Dekker^{a,e}, Hugo J.W.L. Aerts^{a,d,e}



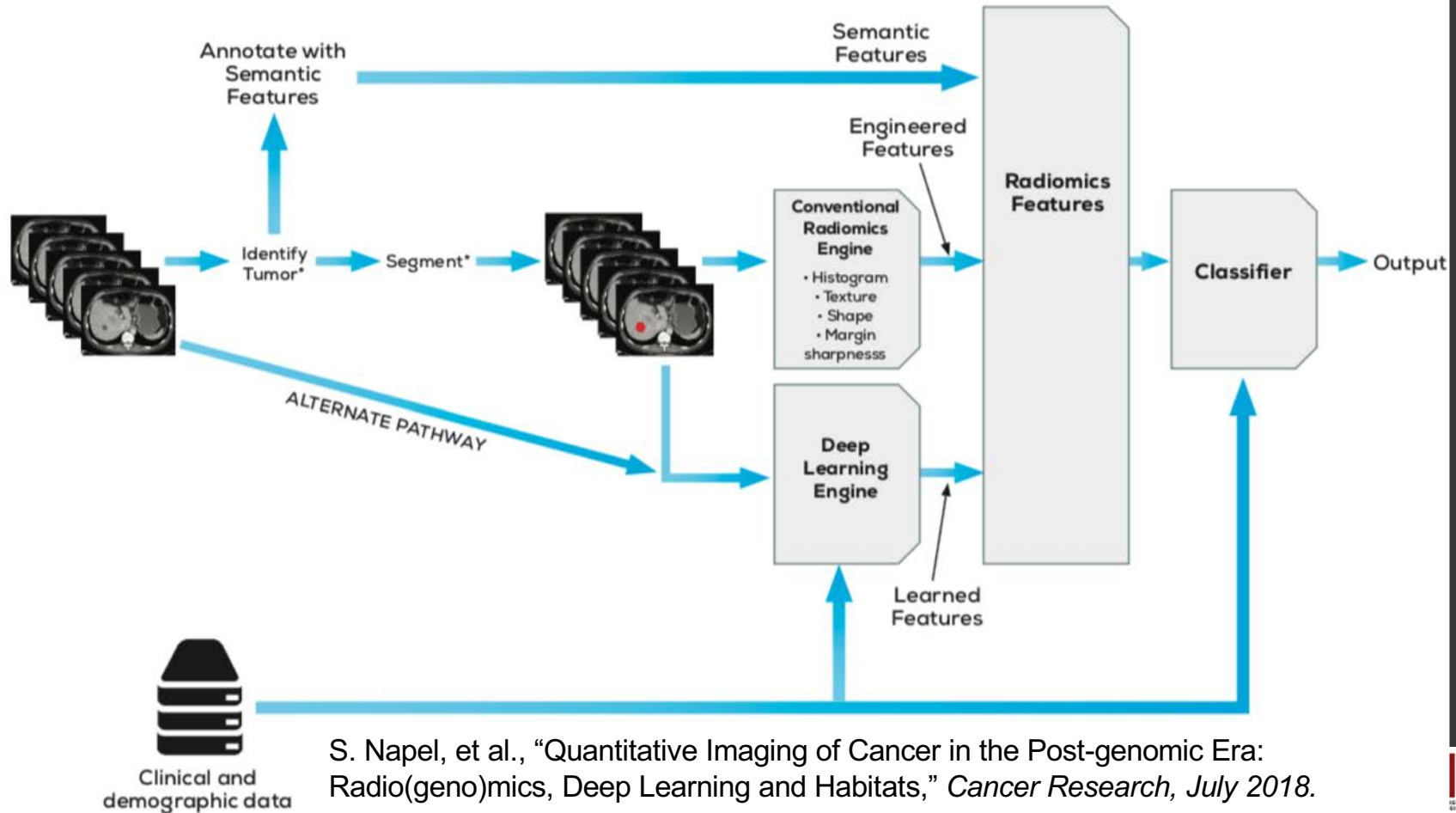
European Journal of Cancer (2012) 48:441–446



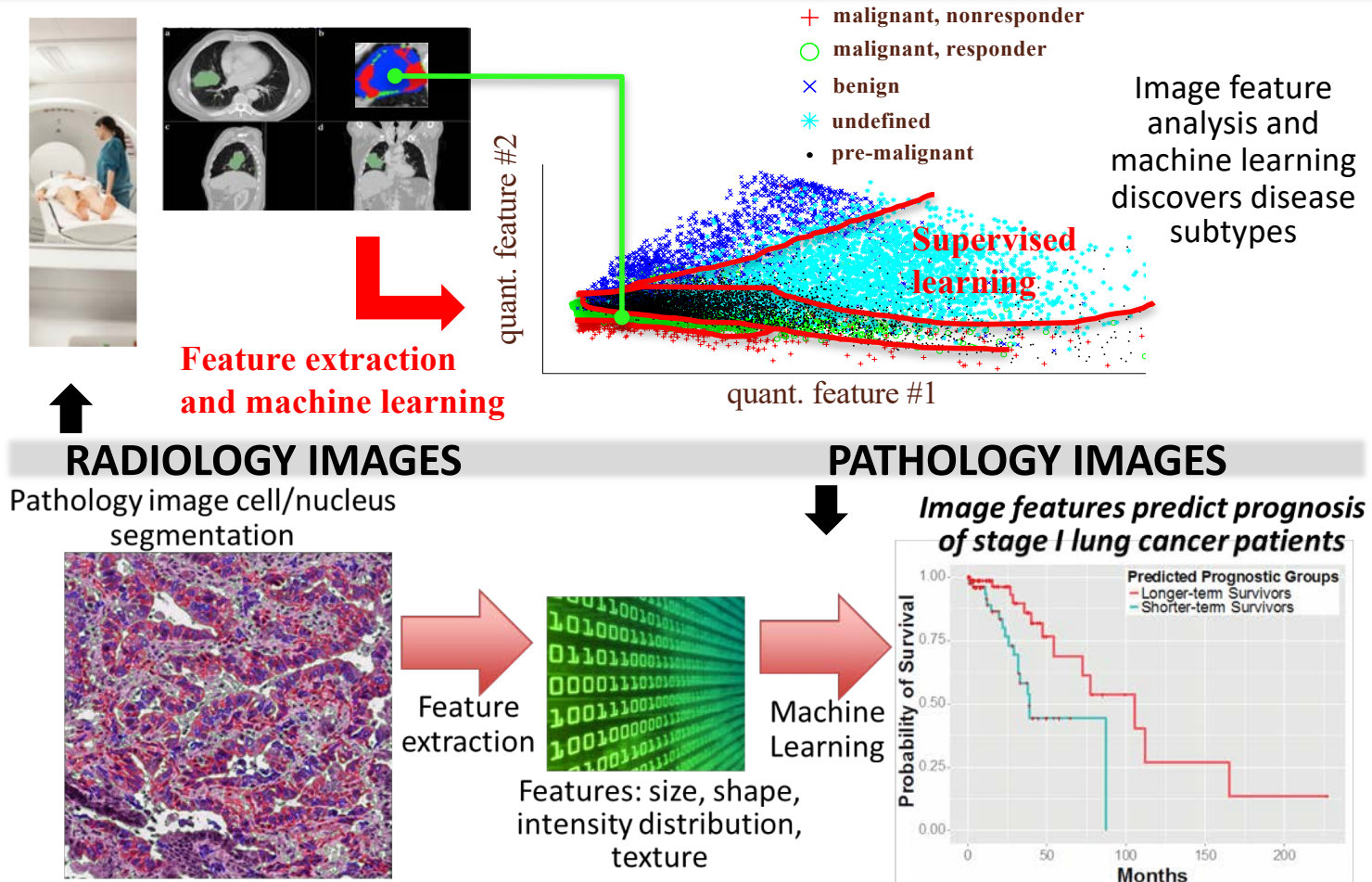
Radiomics/Radiogenomics Examples



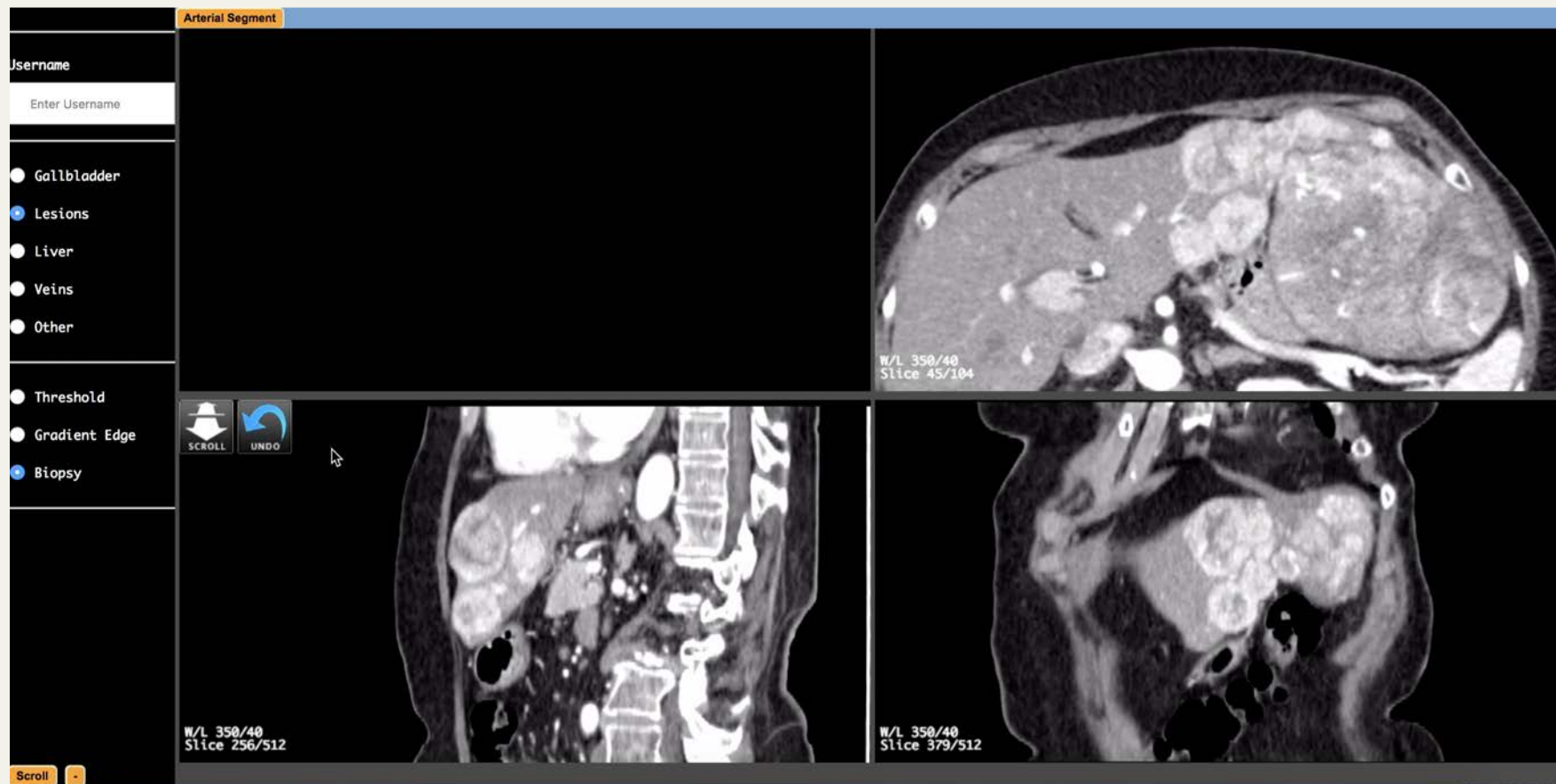
Radiomics Workflow



Electronic phenotyping of images for discovering best treatments



A Radiomic Biopsy Tool



100

1. *Journal of the American Medical Association*, 2000; 284: 2689-2695.





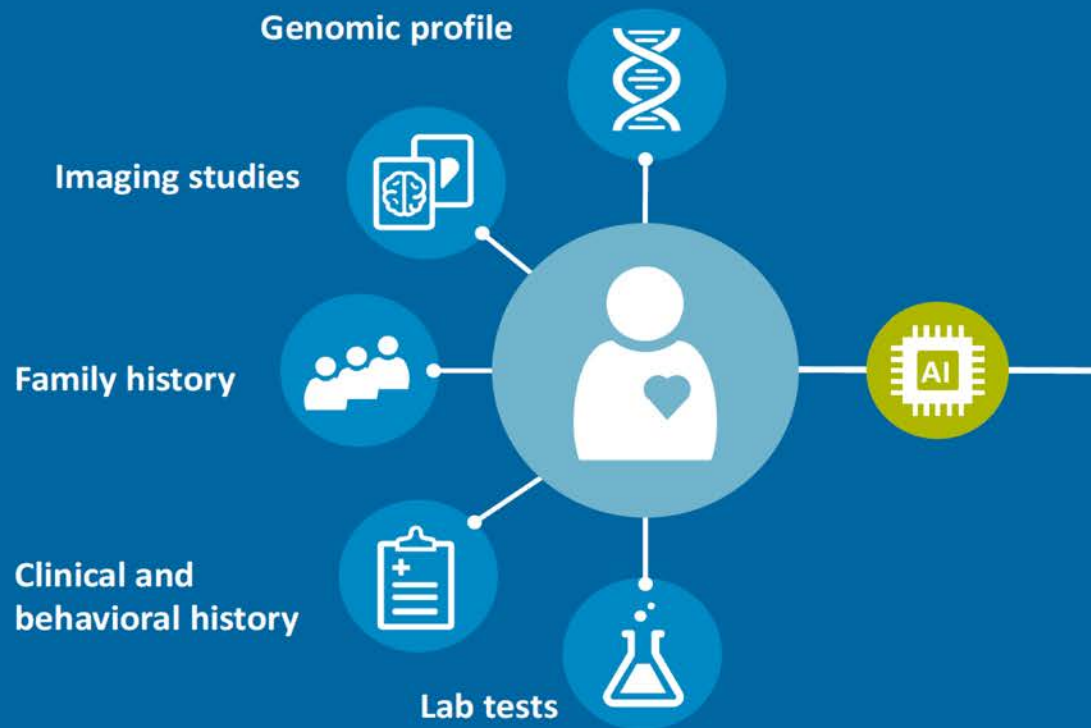
Digital Twin

Detailed digital models of anatomy, physiology, and pathology

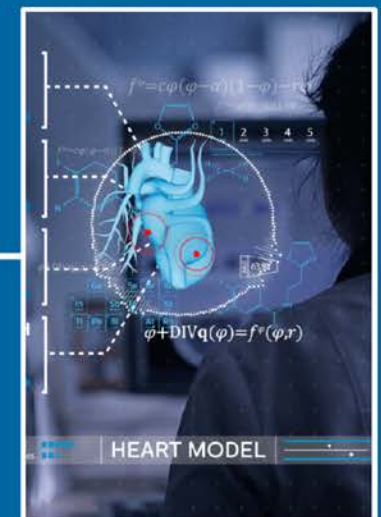


Deriving a Single Patient View

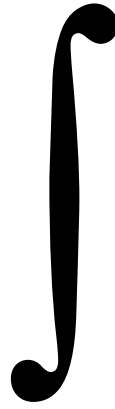
The right diagnosis, at the right time, leading to the right therapy



Digital twin



The Role of the Future Diagnostic Radiologist



Additional Points

- **It is estimated that the doubling time of medical knowledge in 1950 was 50 years; in 1980, 7 years; and in 2010, 3.5 years. In 2020 it is projected to be ~60 days**
- **Technology is well ahead of the biology**
- **Being focused primarily on radiology images alone will likely set our field up for long-term failure**
- **The diagnostic radiologist role could evolve into a “diagnostician” that integrates multiple sources of data with the help of AI**
- **We will need to have more strategic interactions with our colleagues in pathology**

Additional Points

- **Radiology residents need education in bioinformatics, data management and cell/molecular biology**
- **Radiology and pathology training programs need to be combined over time**
- **Our systems for data integration can become learning healthcare systems so that we and AI systems learn from each health encounter so that for future patients we can truly learn from past patients with very similar characteristics**
- **The diagnostician role as an integrator of health and medical information may put us at odds with the role of the medical internist**
- **Industry-academic collaborations will be key to the future evolution of our field**

Conclusions

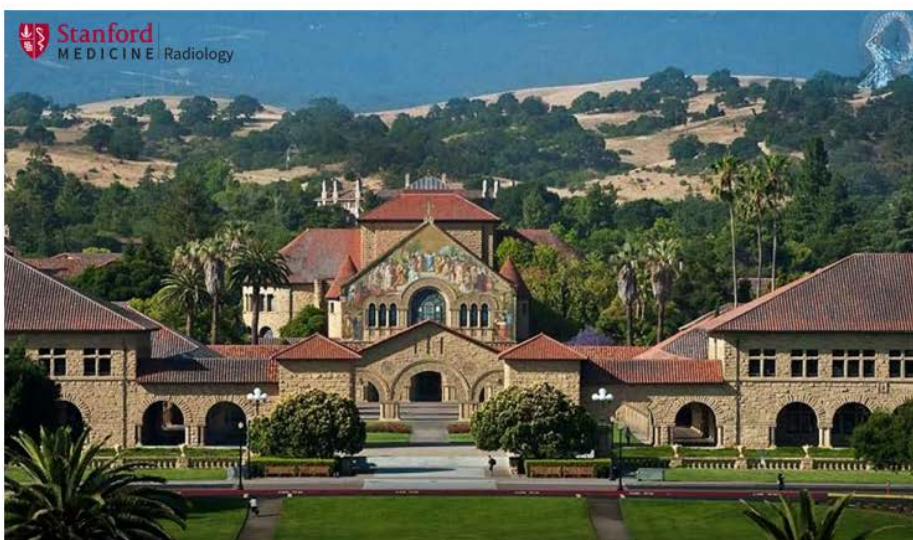
“The best way to predict your future is to create it”

Abraham Lincoln



INTERNATIONAL
SOCIETY
FOR STRATEGIC
STUDIES IN
RADIOLOGY

2020 Interim Meeting



International Summit
Disruptive Healthcare
September 24-25, 2020
Stanford University, Stanford CA

For the first time, thought leaders from academia, traditional diagnostic imaging companies and Bay Area tech giants will come together to envision highly disruptive approaches to healthcare.

As the lines are blurring between healthcare and other industries, this summit will unite companies hoping to revitalize the field and devise fresh approaches to medical diagnostics.

- Invitation only - 250 Attendees
- Participating Companies: GE, Siemens, Philips, Canon, Verily, Apple, Google, Amazon, Bay Area Startups
- Break out sessions on areas such as AI, home based and wearable devices, data standards, healthcare economics
- Tours of New Stanford Hospitals, PHIND, Bay Area companies

Hosted by:
Stanford Medicine, Department of Radiology
The International Society for Strategic Studies in Radiology (IS3R)
Precision Health and Integrated Diagnostics Center at Stanford (PHIND)
Canary Center at Stanford for Cancer Early Detection

Special Thanks



Dr. Gabriel Krestin