(Regulatory) Science and the Medical Physicist

Joint Council Symposium: Science and the Medical Physicist

Aldo Badano

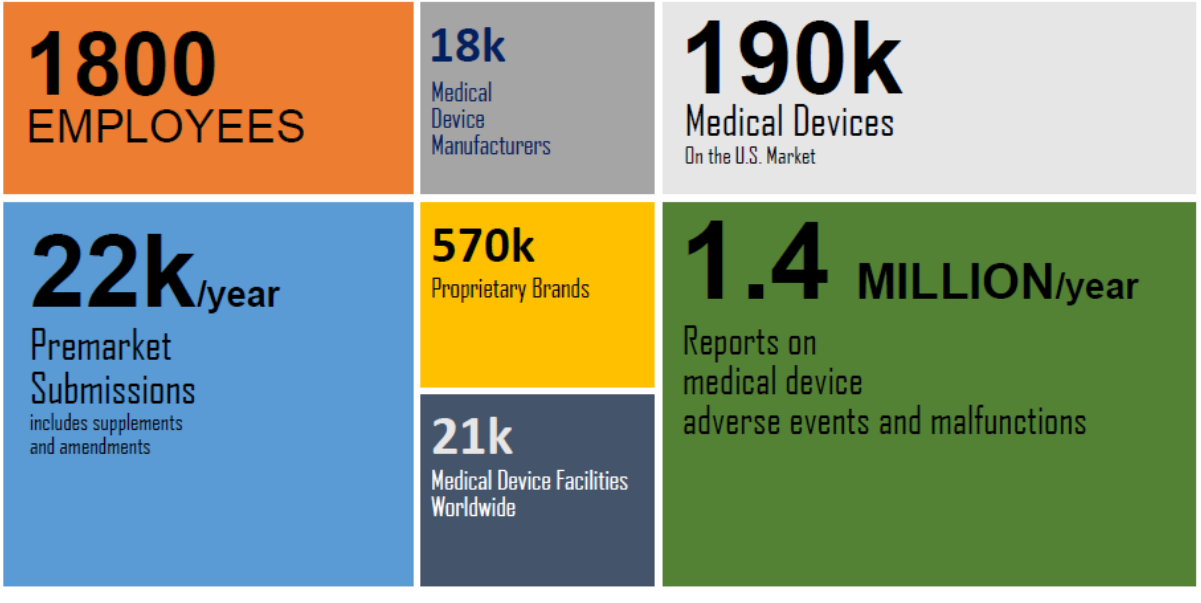
Division of Imaging, Diagnostics, and Software Reliability
Office of Science and Engineering Laboratories
Center for Devices and Radiological Health
US Food and Drug Administration

Outline

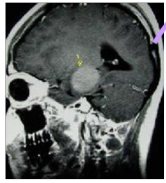
Regulatory science at FDA

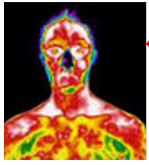
Development of methods and tools to assess the safety, efficacy, quality, and performance of FDA-regulated products.

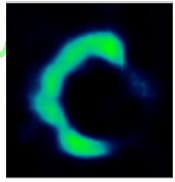
1. Identify priorities for new research for continued mission success
2. Prepare for tomorrow's challenges
3. Ensure decisions are scientifically sound, least-burdensome, and contribute to public health
4. Highly multidisciplinary (engineering, medicine, chemistry, toxicology, statistics and social sciences)

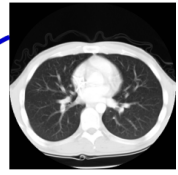

1800
EMPLOYEES
18k
Medical
Device
Manufacturers
190k
Medical Devices
On the U.S. Market
22k/year
Premarket
Submissions
includes supplements
and amendments
570k
Proprietary Brands
21k
Medical Device Facilities
Worldwide
1.4 MILLION/year
Reports on
medical device
adverse events and malfunctions

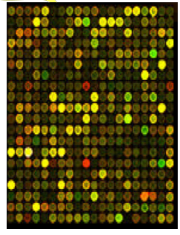
Regulatory science and the medical physics (imaging)







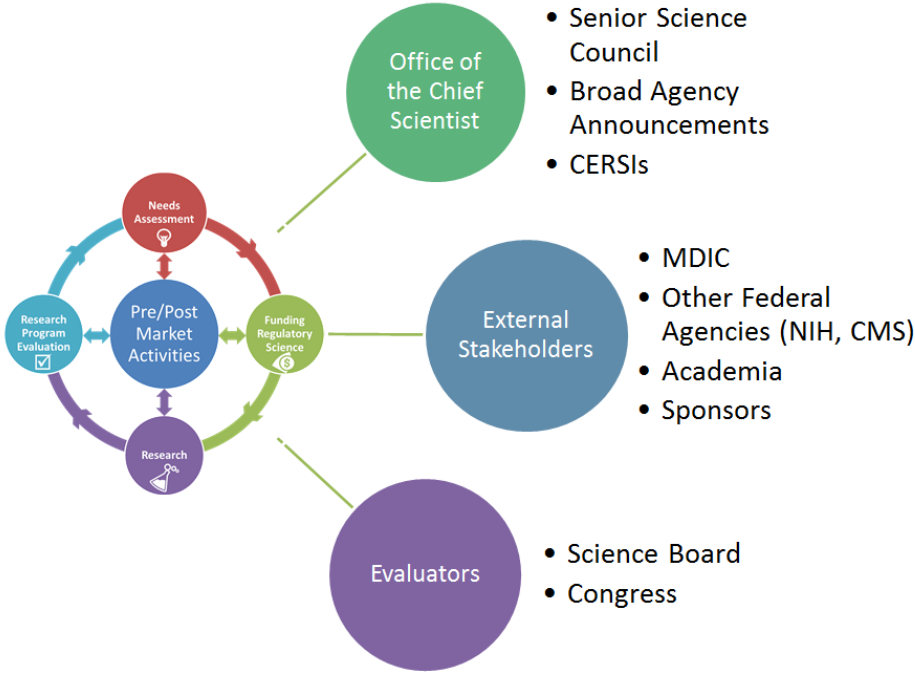




LDH --------- 167	AST (SGOT) ----- 17
ALK PHOS ----- 44	TOT. BILI ------ 0.9
ALBUMIN ----- 4.4	GLOBULIN -------- 2.5
GLUCOSE ------ 66	BUN ------------- 16
CREATININE -- 1.0	PLATELETS ------- 185

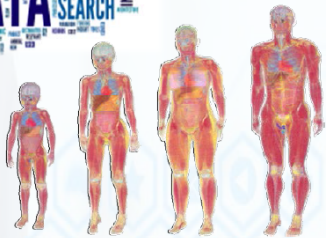
Outline

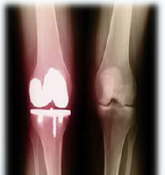

Needs Assessment
Pre/Post Market Activities
Funding Regulatory Science
Research
Research Program Evaluation


Office of the Chief Scientist
• Senior Science Council
• Broad Agency Announcements
• CERSIs
Needs Assessment
Research Program Evaluation
Pre/Post Market Activities
Funding Regulatory Science
Research
External Stakeholders
• MDIC
• Other Federal Agencies (NIH, CMS)
• Academia
• Sponsors
Evaluators
• Science Board
• Congress

FY 2017 Regulatory Science Priorities

- Big Data
- Biocompatibility
- Real-World Evidence
- Clinical Trial Design
- Computational Modeling
- Digital Health and Cybersecurity
- Infection Control
- Patient Input
- Predicting Clinical Performance
- Precision Medicine and Biomarkers





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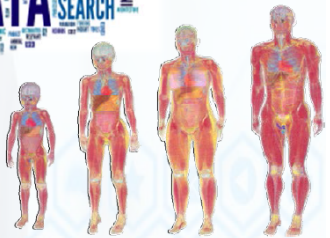
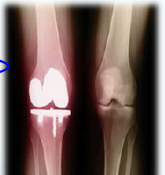
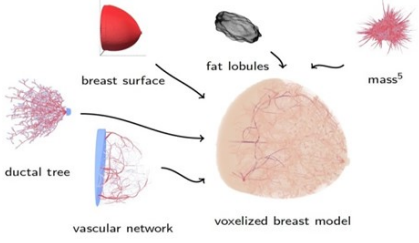


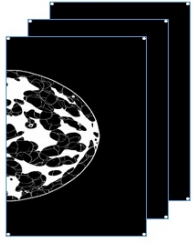


Outline

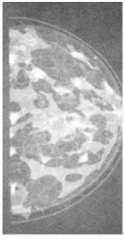
Fabricating Anthropomorphic Breast Phantoms Using Inkjet Printing (Ikejimba et al, Med Phys 2017)

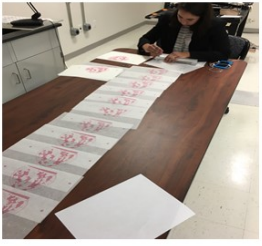


Graff CG, SPIE Proc 9783, 2016.



Digital Phantom



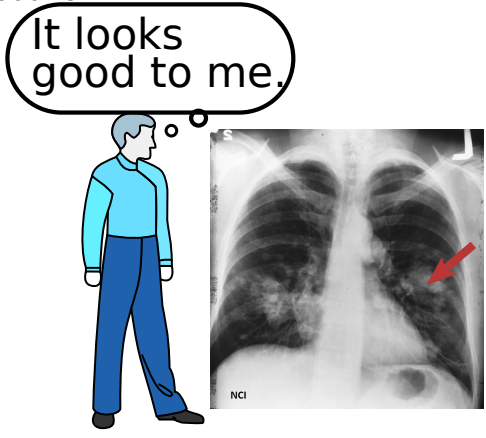


Adapted from talk by Steve Glick.

Outline

Evaluation of AI in imaging devices

Denoising low-dose images - Artifact reduction - k-space interpolation - Faster and sparse recons



How confident are you that the enhancement on the image really exists inside the patient?

- Subjective evaluations are meaningless.
- We need to measure how much information images depict about patients.
- How well can human or machine readers diagnose, measure lesion volume, or detect lesions?

Adapted from talk by Frank Samuelson.

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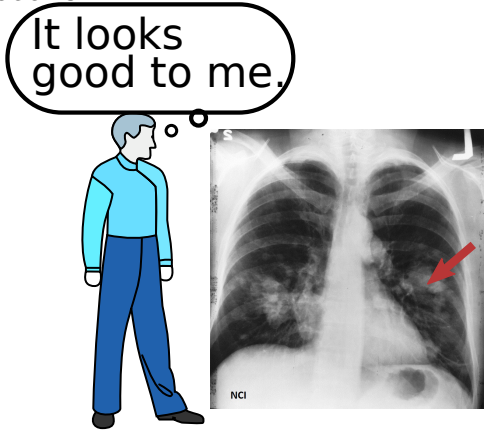

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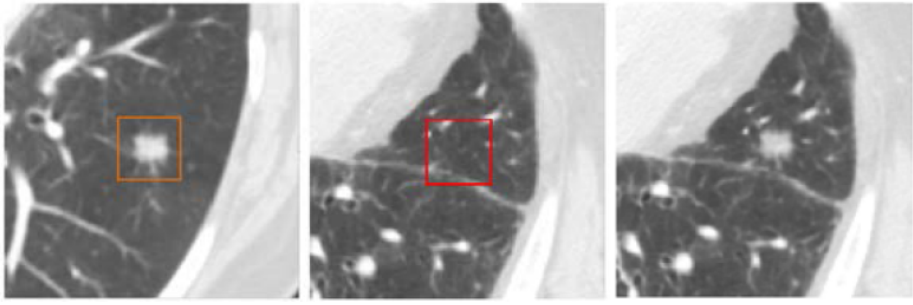
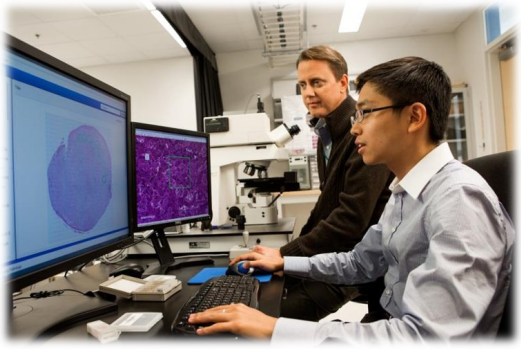
Facilitating training and testing by data augmentation

Augment datasets with insertion of lesions extracted from patient images into normal cases.[1]



[1] A. Pezeshk et al., "Seamless insertion of pulmonary nodules in chest ct images.", IEEE transactions on bio-medical engineering **62**, 2812–2827 (2015), A. Pezeshk et al., "Seamless lesion insertion for data augmentation in cad training.", IEEE transactions on medical imaging **36**, 1005–1015 (2017).

High-throughput truth annotation of large datasets[2]

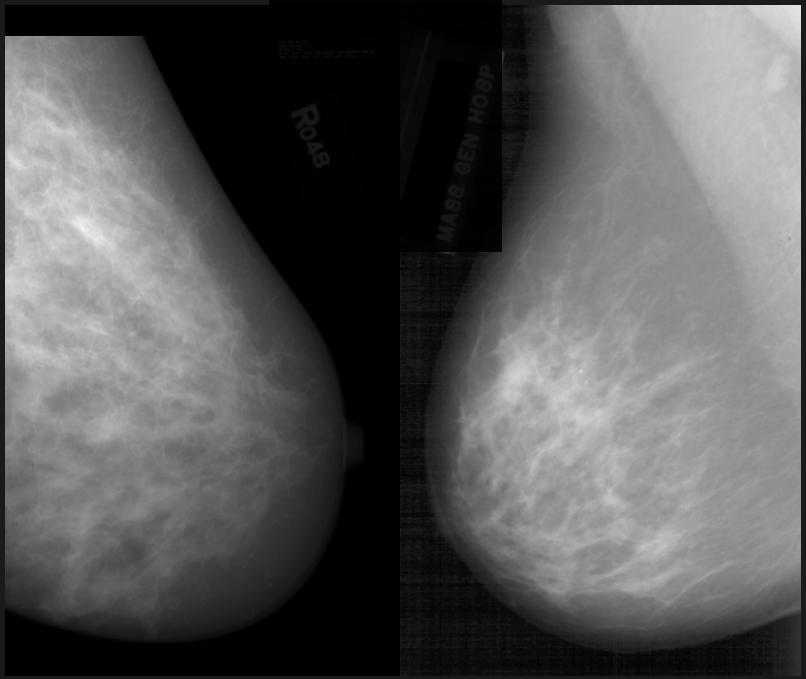


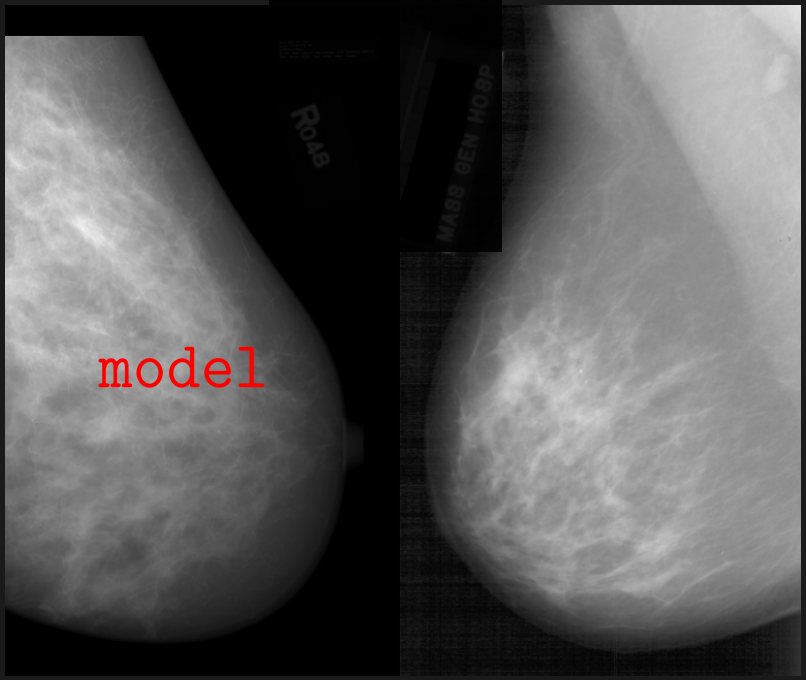
eeDap: An evaluation platform for digital and analog pathology evaluation.

12 pathologists marking (on paper) the locations of the mitotic figures in 40 ROIs and classifying 128 pre-determined candidate mitotic figures on a multi-level confidence scale (all done in 120 min).

[2] B. D. Gallas et al., "Evaluation environment for digital and analog pathology: a platform for validation studies.", Journal of medical imaging (Bellingham, Wash.) **1**, 037501 (2014).

Outline


ROAB
MASS GEN HOSP


ROAB
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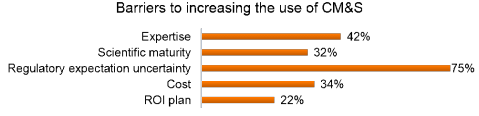
model

FDA viewpoint

"In the future, computer-based modeling may change the way we think about device validation . . . allowing for much smaller clinical trials, or may change the way we think about running trials, in that some 'clinical' information may be derived from simulations."[a]

[a] O. Faris and J. Shuren, "An FDA viewpoint on unique considerations for medical-device clinical trials", New England Journal of Medicine **376**, PMID: 28379790, 1350–1357 (2017).



However, barriers remain . . .

How can we stimulate or speed up adoption of *in silico* trials while ensuring scientifically sound regulatory decisions?[a]

[a] mdic.org/computer-modeling/.

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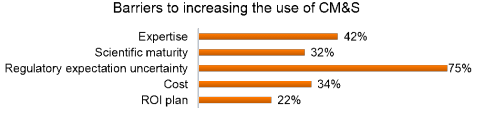

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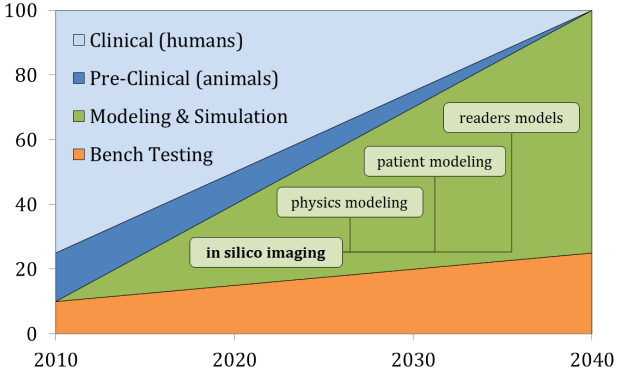
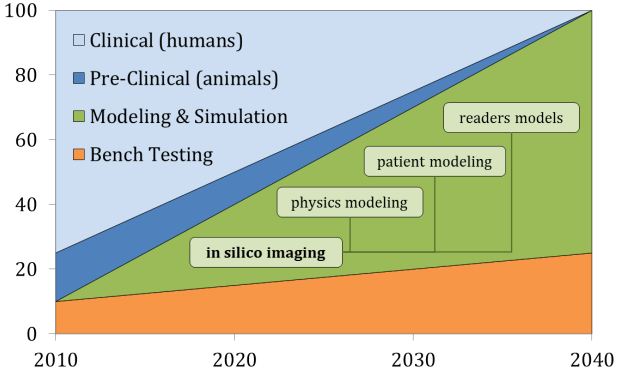


Note: No actual data was collected to inform this prediction. A TPLC, least-burdensome approach is sought as opposed to increased requirements. The question of whether or not traditional trials will in the future be needed at all is philosophical and beyond the scope of this presentation.

- How to increase the role of *in silico* trials?
- Why subject humans to clinical trials when we can reach the same regulatory decision with in silico trials?



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Imaging clinical trials for regulatory evaluation

Patients

Imaging

Radiologists

A premarket imaging clinical study (P140011)

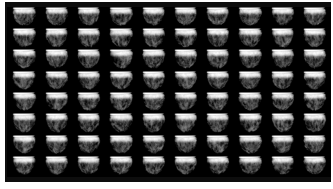
- 400+ women double-exposed
- Some biopsied (follow-up as truth)
- Screening population

- DM/DBT imaging systems

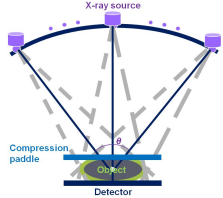
- 30+ radiologists
- 6+ clinical sites
- 6+ years

In silico imaging trial

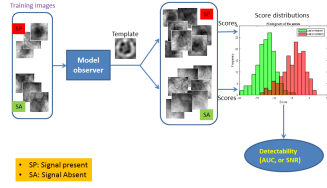
- Unlimited subjects based on procedural models



- State-of-the-art Monte Carlo x-ray transport



- Computer image interpretation



What is the research program VICTRE?

VICTRE aims at demonstrating that computational modeling can play an increasingly predominant role in the regulatory assessment of imaging products. See talk by Dr. Badal (TU-AB-202-3).

Why?

- Expensive and lengthy clinical trials delay regulatory evaluation.
- This burden can stifle innovation affecting patient access to novel, high-quality imaging technologies.

How?

Before: incremental development and validation.

VICTRE: *in silico* replication of an existing clinical trial[a] with demonstration of savings and benefits for stakeholders.

[a] P140011: Comparative trial in summary of safety and effectiveness.

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Outline

Consensus development

Role of standards

- Actively supports international and national standards
- CDRH liaisons to 29+ IEC/ISO TCs and participates in 400+ WGs in 20+ organizations
- CDRH has 1000+ recognized standards

AAPM leadership participation

- AAPM/TG196: display color
- AAPM/TG270: display QC
- AAPM/TG260: handheld displays
- AAPM/TSC Tomosynthesis
- AAPM/TG245
- AAPM/IPC

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the end