

# BIOE 301

## Lecture Seven



## Four Questions

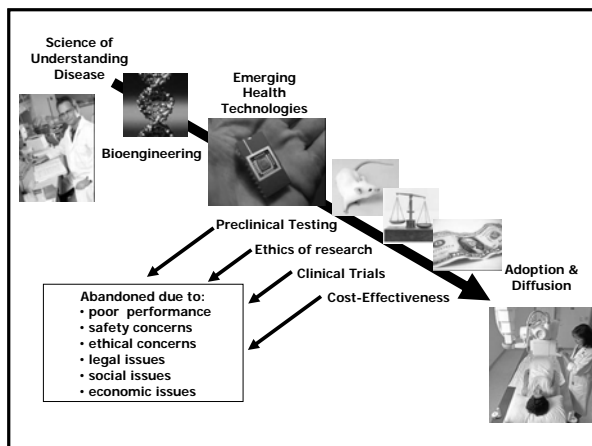
- What are the problems in healthcare today?
- Who pays to solve problems in healthcare?
- How can we use science and technology to solve healthcare problems?
- Once developed, how do new healthcare technologies move from the lab to the bedside?

## Three Case Studies

- Prevention of infectious disease
  - HIV/AIDS
- Early detection of cancer
  - Cervical Cancer
  - Ovarian Cancer
  - Prostate Cancer
- Treatment of heart disease
  - Atherosclerosis and heart attack
  - Heart failure

## Today:

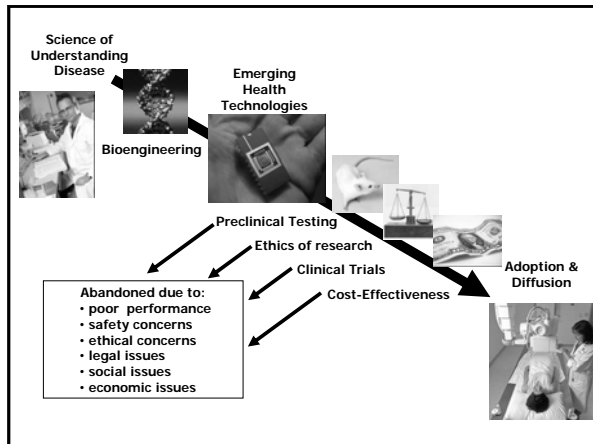
The process of developing a new medical technology



## Class Activity #1 – Gene Therapy

### Directions:

- Place the articles in correct chronological order
  - Contextual clues in the selections
  - Your knowledge of the science of DNA and genes
  - Your recollection of events in the media.
- Articles reflect current thought for the time
- First article published in 1953; the last in 2003
- Discuss in group; come to consensus
- Choose one member of your group to speak
  - Did your ideas about the sequence match each other?
  - What clues or events prompted you to make choice?
- Do not discuss your ideas with other groups



Question:

- What is the difference between science and engineering?

Definitions

- Science
  - Body of knowledge about natural phenomena which is:
    - Well founded
    - Testable
  - Purpose is to discover, create, confirm, disprove, reorganize, and disseminate statements that accurately describe some portion of physical, chemical, biological world
- "Science is the human activity of seeking natural explanations for what we observe in the world around us."

Definitions

- Engineering
  - Systematic design, production and operation of technical systems to meet practical human needs under specified constraints
    - Time
    - \$\$
    - Performance
    - Reliability
  - "Engineering. . . in a broad sense. . . is applying science in an economic manner to the needs of mankind "

Definitions

- What is the difference between science and engineering?
  - Science
    - Inquiry to better understand world around us
    - No practical goal necessary
  - Engineering
    - Use of science to solve real world problem in practical way

Engineering Design Method

- Fashioning a product made for a practical goal in the presence of constraints
- Six design steps:
  1. Identify a need
  2. Define the problem (goals, constraints)
  3. Gather information
  4. Develop solutions
  5. Evaluate solutions
  6. Communicate results
    - Papers, patents, marketing

→ SPECS

↻ Refine Design

## Journal Article

12187 • JUNE 15, 2006 • Vol. 13, No. 24 • *Journal of Clinical Investigation*

*Advances in Brief*

### Real-Time Vital Optical Imaging of Precancer Using Anti-Epidermal Growth Factor Receptor Antibodies Conjugated to Gold Nanoparticles<sup>1</sup>

Konstantin Sokolov, Michele Follen, Jesse Aaron, Inna Pavlova, Anais Malpica, Reuben Lotan, and Rebecca Richards-Kortum<sup>2</sup>

<sup>1</sup>Departments of Imaging Physics (K.S.), Pathology (J.A.M.), and Therapeutic Radiology (J.A.), and Center for Biomedical Engineering (M.F.), University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, and <sup>2</sup>Department of Biomedical Engineering, University of Texas, Austin, Texas 78712 (J.A., J.P., R.R.K.)

#### Abstract

Recent developments in photonic technology provide the ability to noninvasively image cells *in vivo*. These new cellular imaging technologies have the potential to dramatically improve the prevention, detection, and therapy of epithelial cancers. Endoscopic-compatible microscopes, such as optical coherence tomography and reflectance confocal microscopy, image reflected light, providing a three-dimensional picture of tissue microanatomy with excellent spatial resolution (1–10  $\mu\text{m}$ ). However, their ability to image molecular biomarkers associated with cancer is limited. Here, we describe a new class of molecular specific contrast agents for vital reflectance imaging based on gold nanoparticles attached to protein antibodies with high affinity for specific cellular biomarkers. The application of gold nanoparticles for vital imaging of precancers is demonstrated using cancer cell suspensions, three-dimensional cell cultures, and normal and neoplastic fresh cervical biopsies. We show that gold conjugates can be delivered optically for imaging throughout the whole epithelium. These contrast agents have potential to extend the ability of vital reflectance microscopes for *in vivo* molecular imaging. They can potentially enable combined screening, detection, and therapy of disease using integrative imaging systems; such tools could allow mass screening of diseases such as cancer in resource-poor settings.

such, they are ideally suited for early screening and diagnosis of superficial disease.

Tissue reflectance is produced by refractive index mismatches; sources of contrast in OCT and RCM images include structures with increased refractive index such as mitochondria, nuclear chromatin, and melanin (2, 3). Nonspecific contrast agents, such as AA, can perturb the nuclear refractive index distribution, increasing the ability to visualize cellular anatomy (4). Whereas OCT and RCM provide images of tissue microanatomy, their ability to image molecular changes associated with carcinogenesis is limited.

In the last few years, global analysis of gene expression by genomic and proteomic approaches has led to the discovery of new cancer-related genes, proteins, and biomarkers. Currently, most of these biomolecular signatures can only be assessed through invasive, painful biopsies. The ability to noninvasively image the expression of these biomarkers could translate into improved ability to screen and detect neoplastic changes, better ability to select and monitor therapy, and new tools to understand the pathobiology of the disease.

Here, we demonstrate a new class of molecular specific contrast agents for vital optical imaging of precancers and cancers, based on

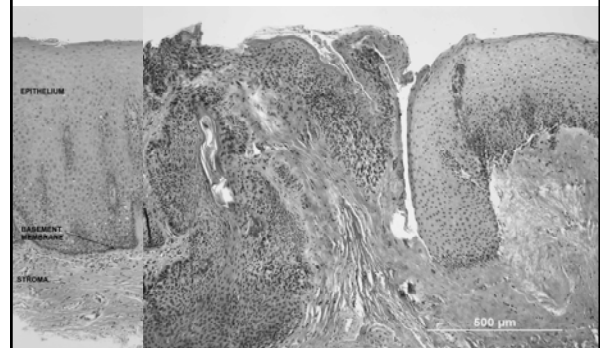
## Patent

- [www.uspto.gov](http://www.uspto.gov)
- [Diagnostic Imaging Patent](#)

## Example: Oral cancer detection

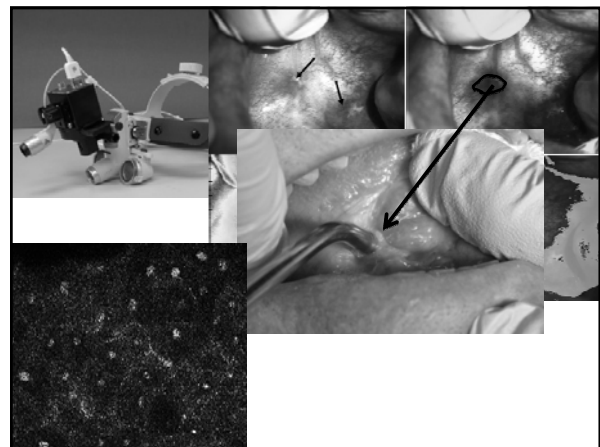
- Science of precancer
- Engineering solutions for precancer detection
  - 1. Identify a need
  - 2. Define the problem (goals, constraints)
  - 3. Gather information
  - 4. Develop solutions
  - 5. Evaluate solutions
  - 6. Communicate results

## Histology of Oral Cancer



## Clinical Needs

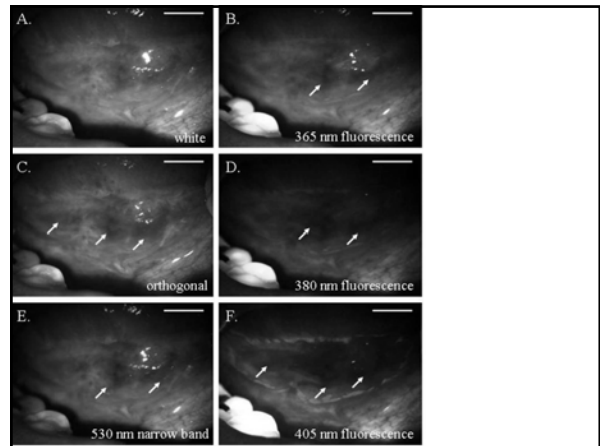
- High sensitivity and specificity
  - Relative to standard of care
  - Relative to clinical impression or gold standard
- Survey all tissue at risk
- Detect precursor or early disease



# Multispectral Digital Microscope



- Imaging modes:
- Reflectance
    - Multispectral
    - Polarized
  - Fluorescence



Site	Pathology
a.	CIS
b.	Mild Dysplasia
c.	CIS
d.	CIS
e.	Normal
f.	CIS

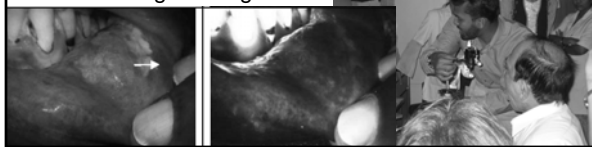
Predicted Probability  
50% 75% 100%

# Portable Screening System

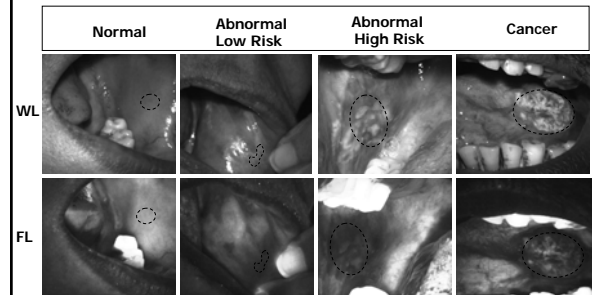
LED light source  
Battery powered

3 Image Modes:  
White light  
Fluorescence  
Polarized

Records digital images

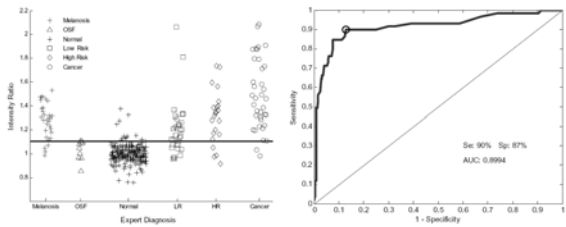


# Typical Lesions of the Four Diagnostic Categories

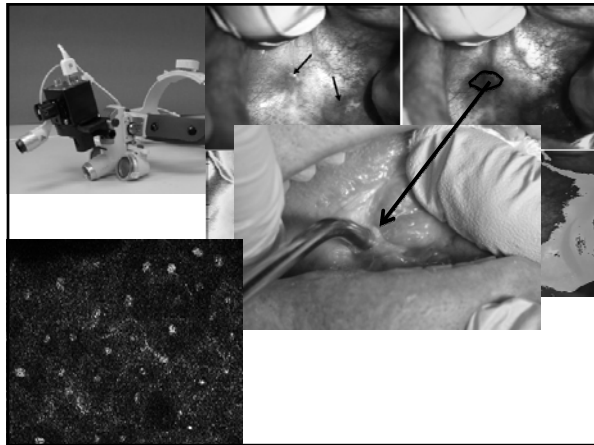
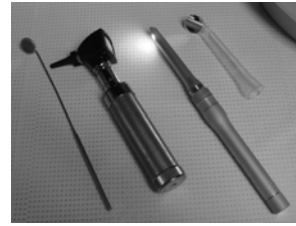


## Image Analysis

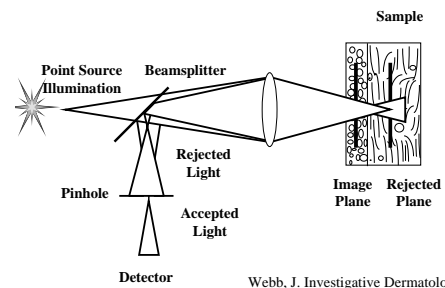
### Normalized Ratio of Red to Green MFI



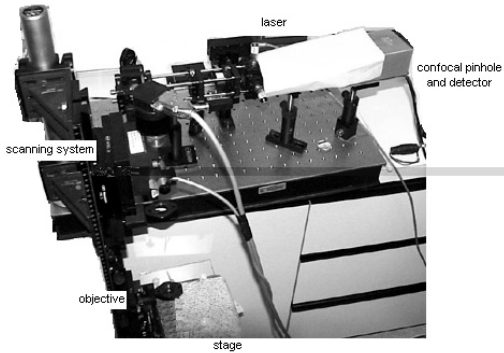
## Commercial Device



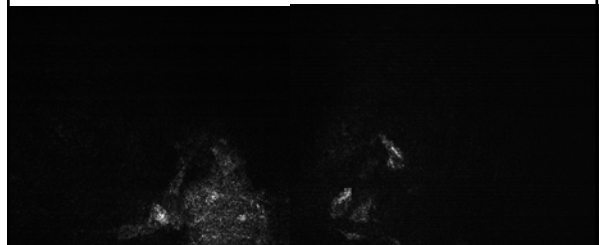
## Technology: Confocal Microscopy

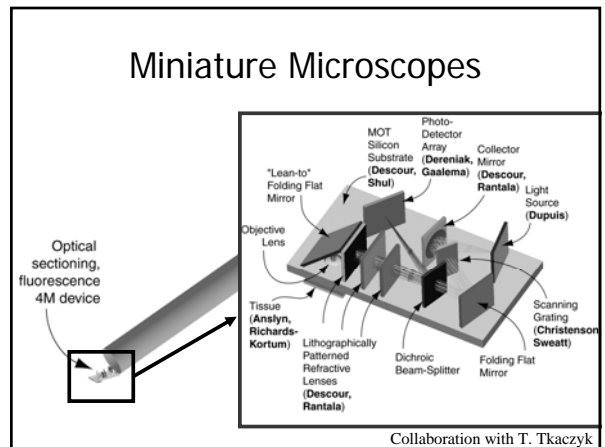
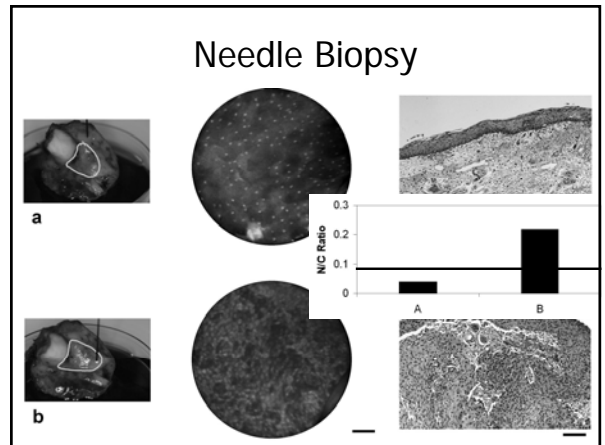
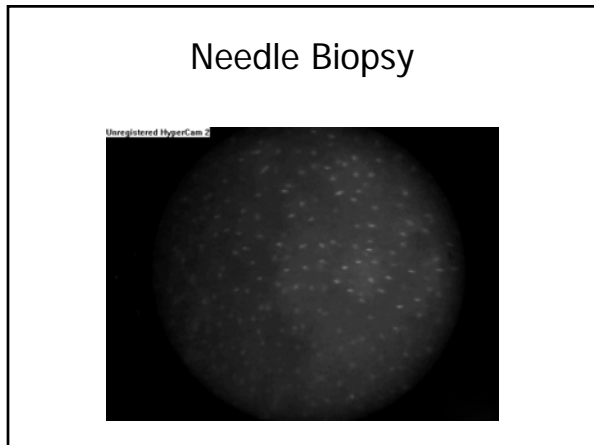
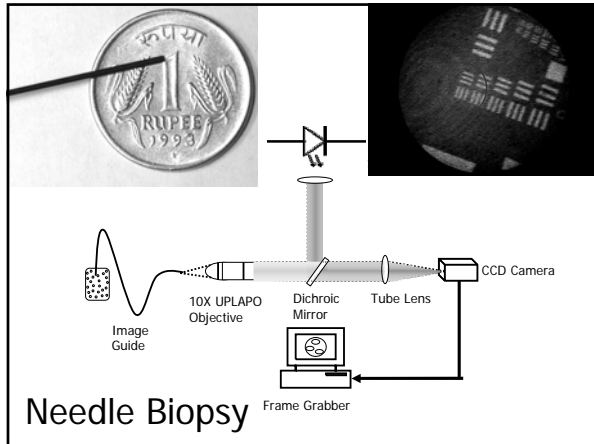


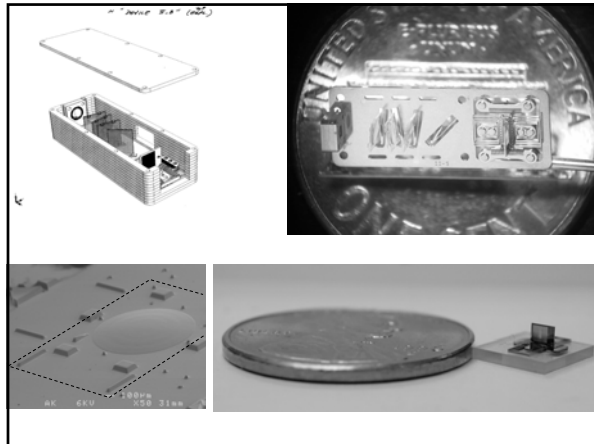
## Confocal Microscope



## Imaging Endogenous Contrast







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### Assignments Due Next Time

- None!