Biomedical Engineering for Global Health

Lecture Seven

Plagiarism: Why Talk About It?

- Serious crime which can end your career
- DHHS Office of Research Integrity
  - Plagiarism is involved in over 50% of the complaints received for investigation of scientific misconduct.

Plagiarism: What is it?

1. Direct, verbatim lifting of passages
2. Rewording ideas from the original in the purported author's own style
3. Paraphrasing the original work without attribution
4. Noting the original source of only some of what is borrowed

American Medical Association Manual of Style

Plagiarism: How to prevent

- Use quotation marks when more than 6 words are lifted verbatim from another source
- Cite the original source when paraphrasing material
- Credit the original source for all the information borrowed.
- Unpublished material is the exclusive property of the original author.
- Written permission is required for the use of all cartoons, drawings, figures etc.

Four Questions

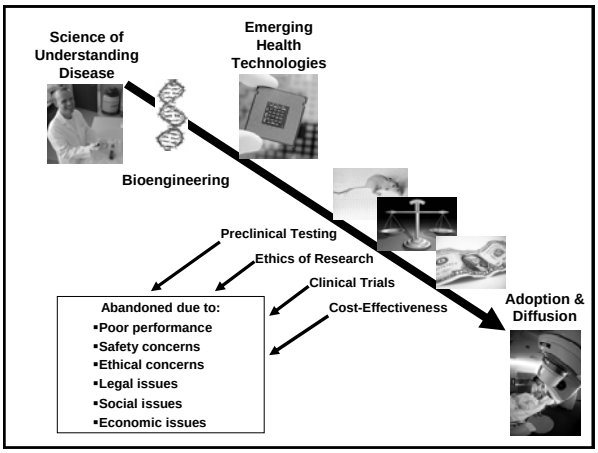
- What are the problems in healthcare today?
- Who pays to solve problems in healthcare?
  -
- How can we use science and technology to solve healthcare problems?
- Once developed, how do new healthcare technologies move from the lab to the bedside?

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:

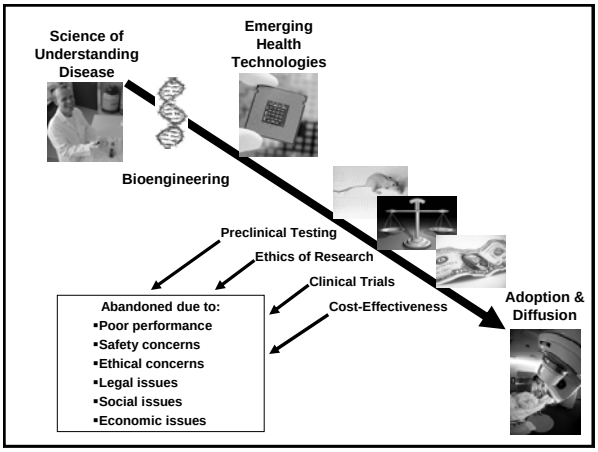
The process of developing a new medical technology



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

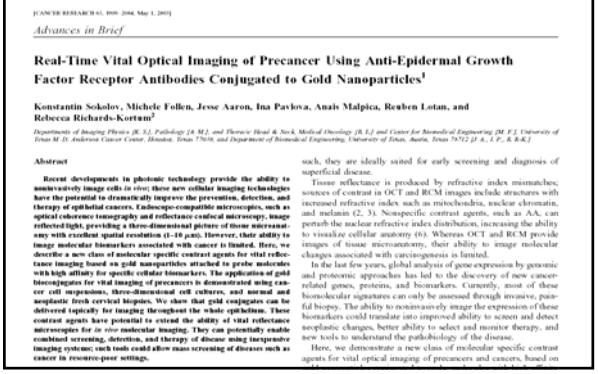
Engineering Design Method

- 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



[CANCER RESEARCH 61, 1999–2004, May 1, 2001]

Advances in Brief

Real-Time Vital Optical Imaging of Precancer Using Anti-Epidermal Growth Factor Receptor Antibodies Conjugated to Gold Nanoparticles[1]

Konstantin Sokolov, Michele Follen, Jesse Aaron, Ina Pavlova, Anais Malpica, Reuben Lotan, and Rebecca Richards-Kortum[2]

Departments of Imaging Physics [K. S.], Pathology [A. M.], and Thoracic Head & Neck Medical Oncology [R. L.] and Center for Biomedical Engineering [M. F.], University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, and Department of Biomedical Engineering, University of Texas, Austin, Texas 78712 [I. A., I. 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. Endoscope-compatible microscopies, 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 μm). 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 probe molecules with high affinity for specific cellular biomarkers. The application of gold bioconjugates 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 topically for imaging throughout the whole epithelium. These contrast agents have potential to extend the ability of vital reflectance microscopies for *in vivo* molecular imaging. They can potentially enable combined screening, detection, and therapy of disease using inexpensive 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 (6). 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 biopsy. 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
- Diagnostic Imaging Patent

Class Activity #2

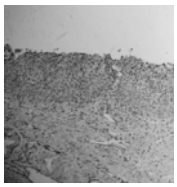
Example: Cervical cancer detection

- 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

Science of Precancer

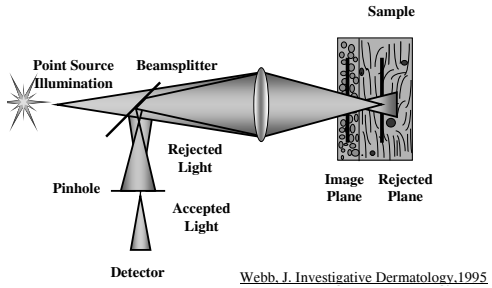
Normal Cervical Tissue

Cervical Pre-Cancer



- Diagnosis based on morphologic features
  - Nuclear size, shape, texture
  - Nuclear-to-cytoplasmic ratio

Technology: Confocal Microscopy

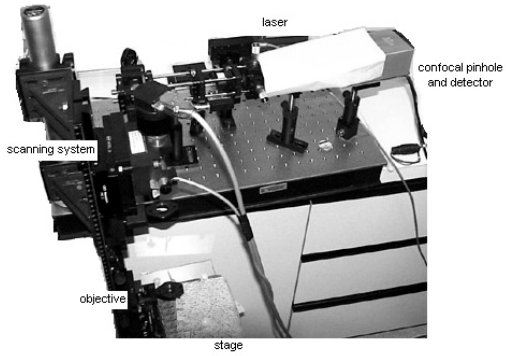


Webb, J. Investigative Dermatology,1995

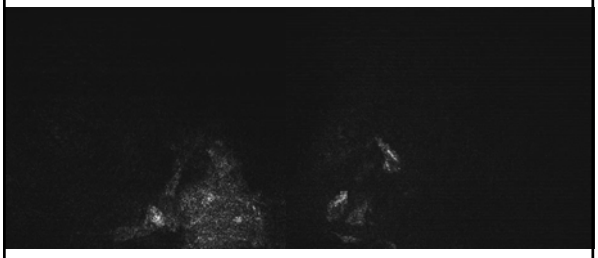
Example: Cervical cancer detection

- 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

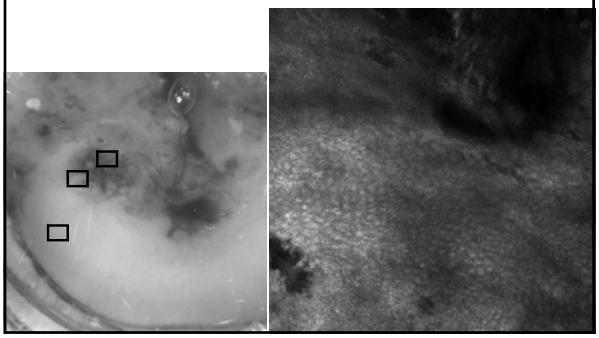
Confocal Microscope



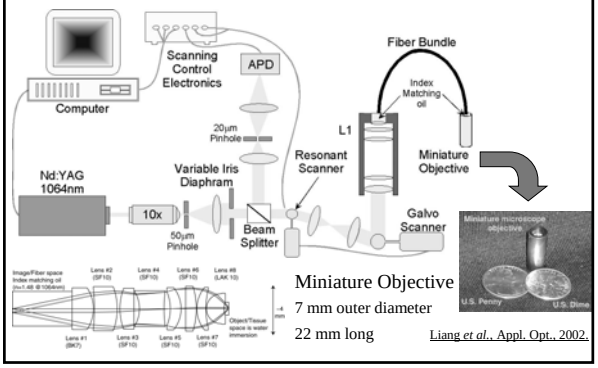
Imaging Endogenous Contrast



LEEP Study

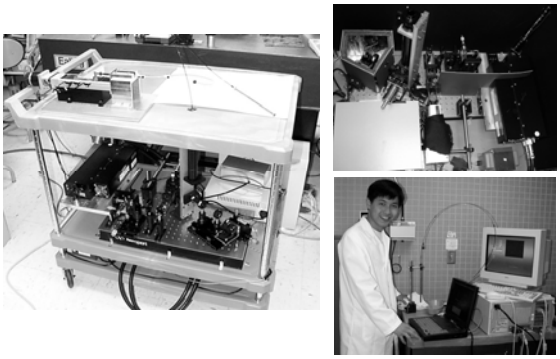


In Vivo Fiber Optic Confocal Microscope

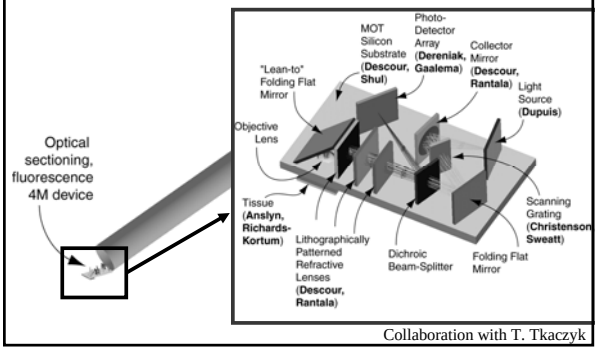


Liang *et al.*, Appl. Opt., 2002.

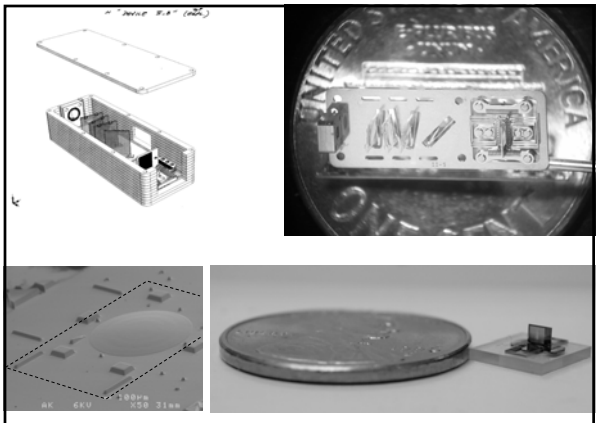
Portable system for clinical studies



Miniature Microscopes



Collaboration with T. Tkaczyk



Example: Cervical 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

Summary of Lecture 7

- Science
  - **"Science** is the human activity of seeking natural explanations for what we observe in the world around us."
- Engineering
  - Systematic design, production and operation of technical systems to meet practical human needs under specified constraints
  - Six steps of the engineering design method