Leaving the Ivory Tower: Efforts to Bring Spectral Methods of Diagnostics to the Market

Max Diem

Laboratory for Spectral Diagnosis (LSpD)
Department of Chemistry and Chemical Biology,
Northeastern University,  Boston, MA 02115

Oct 19, 2010 RICC Conference
Outline

• Spectral Methods of Diagnosis

• Prior Art (2006 and earlier)

• Intellectual Property, 2008 – present

• Commercialization Efforts
Classical diagnostics: cytopathology and histopathology

Subjective diagnosis based on staining pattern, morphology, nucleus/cytoplasm ratio, etc. of exfoliated cells. Drawback: low accuracy and reproducibility

Subjective diagnosis of tissue sections based on staining pattern, tissue architecture, cell morphology, nucleus/cytoplasm ratio, etc. Drawback: lack of objectivity; requirement for special stains
Optical Diagnosis based on physical (optical) measurement

Reproducible, objective, operator independent…

• Fluorescence

• Light scattering (visible / near-IR range)

• Vibrational Spectroscopy (infrared and Raman spectroscopy)

PI’s laboratory involved in Spectral Diagnosis since 1996 (at CUNY), since 2006 at Northeastern University, Laboratory for Spectral Diagnosis
Infrared Spectral Diagnostics:

- Collect entire infrared absorption spectrum of a cell, or from pixels of tissue
- Infrared spectrum is a snapshot of total biochemical composition of sampled area (genome, proteome, metabolome…)
- Analyze spectra by methods of multivariate statistics

Spectral Cytopathology (SCP): automatic differentiation between normal and dysplastic cells
Spectral Histopathology (SHP): automatic detection of tissue structures and cancer
Outline

• Spectral Methods of Diagnosis

• Prior Art (2006 and earlier)

• Intellectual Property, 2008 – present

• Commercialization Efforts
2006¹: Distinction of human (○) and canine (●) epithelial cells (500 cells each, indistinguishable by morphological methods)

2005²: Detection and diagnosis of metastatic cancer (colon adenocarcinoma) in human lymph node section

2006 State-of-the-art data collection / analysis

Spectral Cytopathology

• Visual selection of cells
• Definition of aperture size and orientation;
• Automatic data acquisition
• ~ 200 cells /day
• Principal component analysis

Spectral Histopathology

• Large areas at low spatial resolution
• Presence of scattering artifacts
• Image reconstruction (hierarchical cluster analysis): 1 day / image

Good for research, not yet useful for commercial application…
2005: Offer from C&CB at NEU

- Potential for real – life application of research
- Potential for IP for NEU
- Interaction with CenSSIS
- (two R01 grants from NIH)

- Academically successful four years:
  - 3 patents, 6 book chapters, 32 papers
Outline

• Spectral Methods of Diagnosis
• Prior Art (pre-2006)
• Intellectual Property, 2008 – present
• Commercialization Efforts
Fixed cells are spin-deposited on low-emissivity ("low-e") slide.

4 mm x 4 mm area is imaged automatically, resulting in a 409,600 spectra dataset.

Subsequently, cells are stained and imaged, and images and spectra are linked and stored in database.

PapMap calculates average IR spectra of all cells from pixel spectra.
SCP of Cervical Cells (Spectral “Pap” Test):

Good separation between normal and pre-cancerous exfoliated cells. The “hysteresis” could be linked to viral infection.

Higher Sensitivity and Spatial Resolution in SHP: detection of breast cancer micro-metastases and single metastatic cells in axillary lymph nodes

12 mm  
1 mm  
15 μm
Acceleration of Database Construction for SHP: Tissue Microarrays

Slide may contain over 100 tissue cores with TNM diagnosis, and disease outcome, for several disease types and from dozens of patients
Computational Acceleration

• Datasets are very large (up to 400,000 spectra, 2.5 Gbyte)
• Multivariate analysis requires large contiguous RAM space on computer (matrix size in excess of 2 Gbyte)
• Without vectorization and parallelization, analysis took 45,000 s using compiled MATLAB
• Vectorization of MATLAB code produces a reduction of execution time by a factor of 300 (150 s)
• Parallelization: nVIDIA Tesla 1060C graphic accelerator: 240 processors, AccelerEyes Jacket 1.4, MATLAB interface (factor 100 gain in execution speed: 1.5 sec)
Outline

• Spectral Methods of Diagnosis
• Prior Art (pre-2006)
• Intellectual Property, 2008 – present
• Commercialization Efforts
PR and Intellectual Property Efforts
Blue Slate LLC and Northeastern University

Sept 2007: NEU files provisional patent on PapMap procedure
Sept 2008: NEU files full patent application for PapMap
2008: key success milestones in two new Blue Slate startups reached
2008: Blue Slate LLC initiates internal Cancer-Dx program
2009: Blue Slate goes wide and deep on Cancer-Dx in public domain

July 2009: Press release for oral cancer screening
Oct 2009: Blue Slate follows up on internal findings and contacts LSpD for review
Dec 2009: PapMap PCT
PR and Intellectual Property Efforts
Blue Slate LLC and Northeastern University, continued

Jan 2010: 2 papers in Nature Publishing Group Journals
May 2010: NEU files 2 provisional patent Applications for data collection and analysis
2010: Blue Slate centers effort around LSpD technology
Aug 2010: Blue Slate forms NJ-based LLC for development and commercialization; trademark filed for new company
Oct 2010: Northeastern and Blue Slate LLC reach technology and commercial collaboration agreement
Commercial Goals:

New diagnostic methods for

- Early and more accurate cancer detection
- Spectral cancer staging
- Spectral cancer prognosis
- Therapeutic intervention based on spectral diagnostics

Advise for colleagues at a similar juncture:

Use university resources for PR (e.g., for press releases) and IP (patent committee, Technology Transfer Center)

Don’t let reviewers at the NIH distract you…..

Arm yourself with endless patience !!!!!!