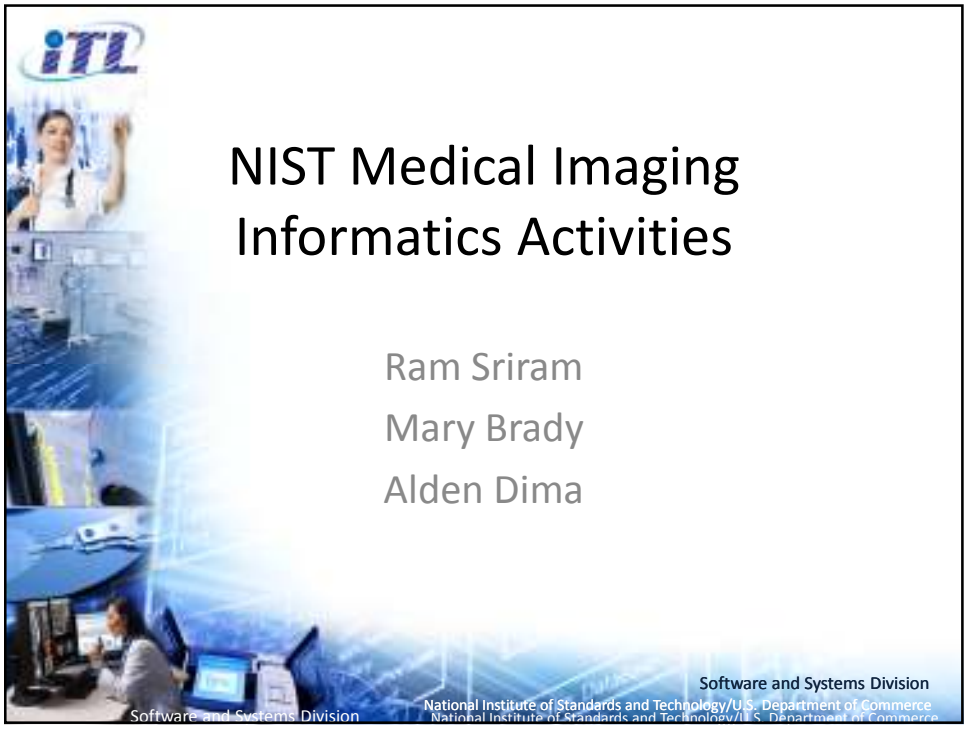
iTL
NIST Medical Imaging Informatics Activities
Ram Sriram
Mary Brady
Alden Dima
Software and Systems Division
National Institute of Standards and Technology/U.S. Department of Commerce
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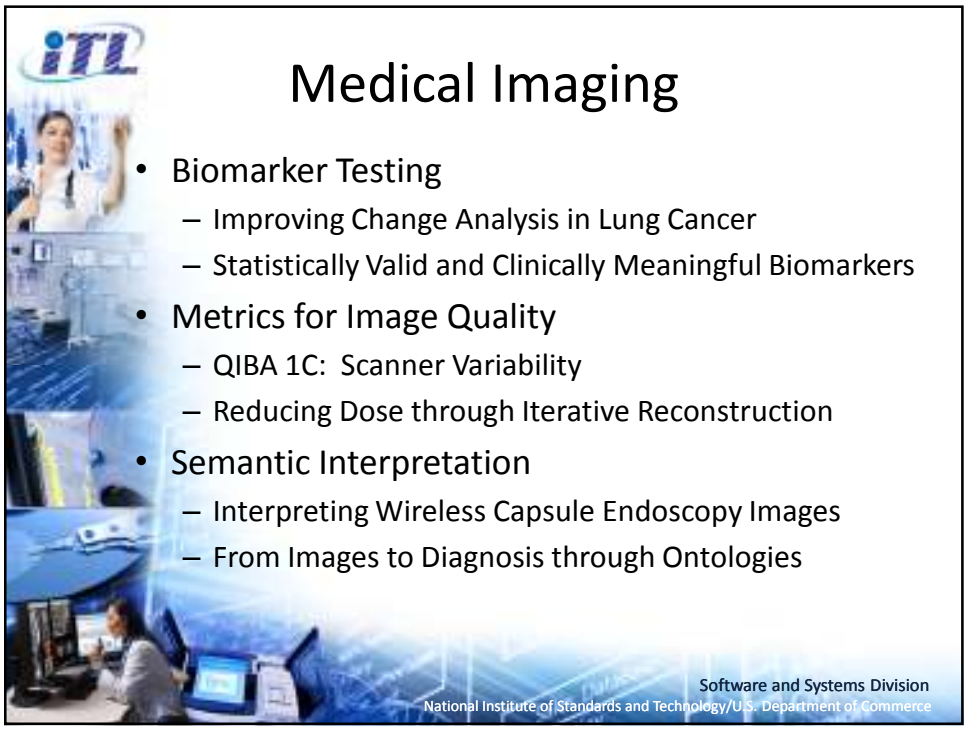
iTL
Medical Imaging
• Biomarker Testing
– Improving Change Analysis in Lung Cancer
– Statistically Valid and Clinically Meaningful Biomarkers
• Metrics for Image Quality
– QIBA 1C: Scanner Variability
– Reducing Dose through Iterative Reconstruction
• Semantic Interpretation
– Interpreting Wireless Capsule Endoscopy Images
– From Images to Diagnosis through Ontologies
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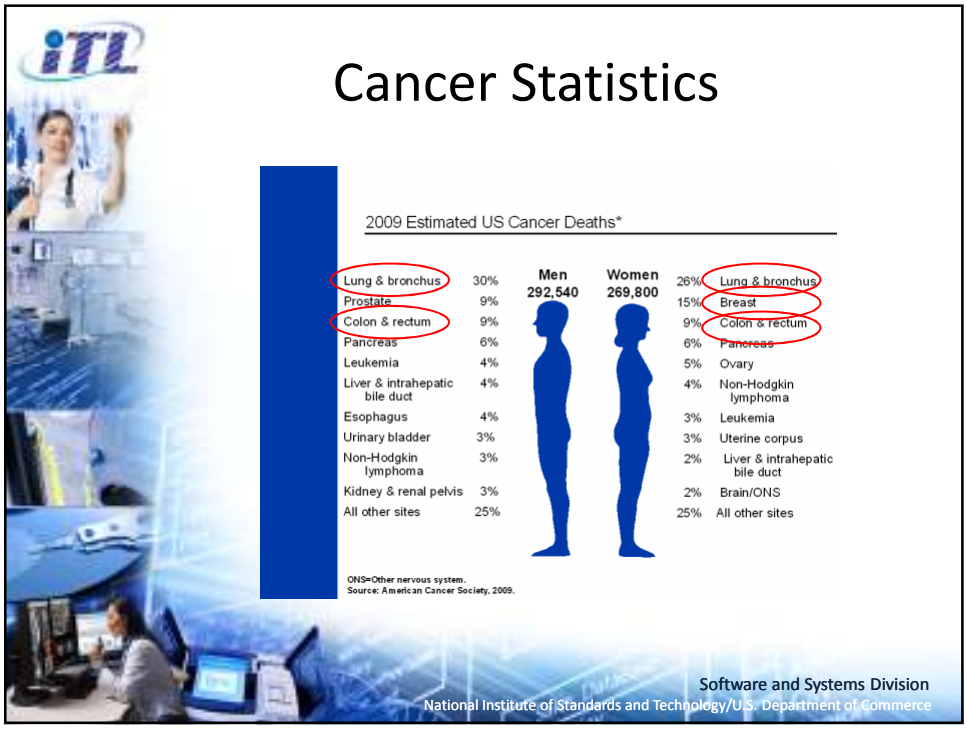
# Collaborations

Buckler Biomedical Sciences LLC (BBMSC)

# Cancer Statistics

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BIOMARKERS
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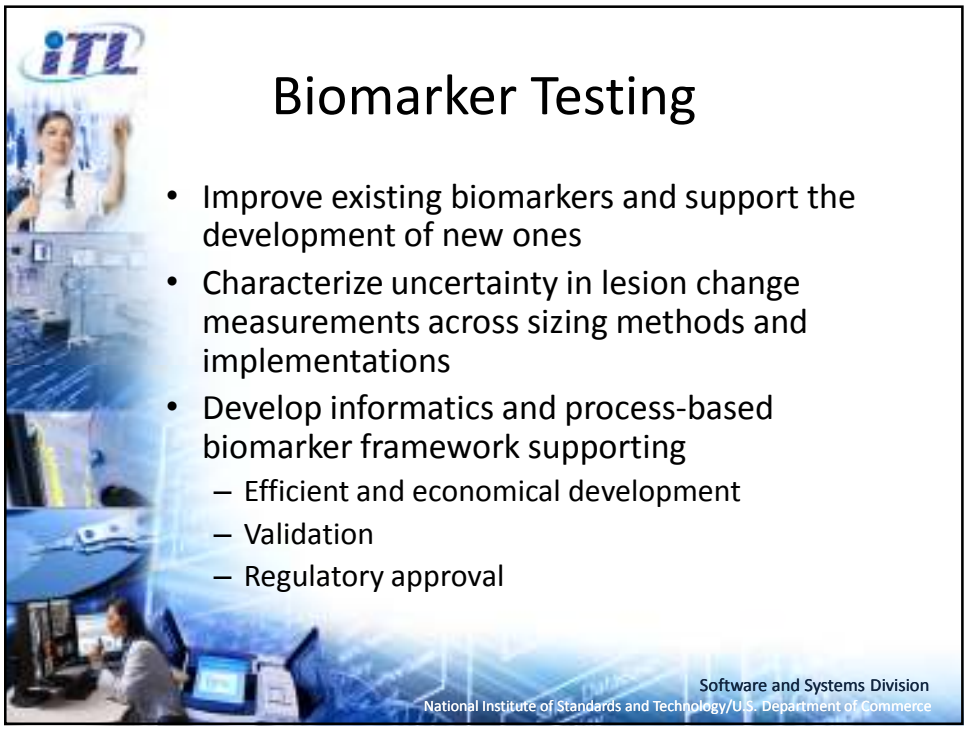
Biomarker Testing
• Improve existing biomarkers and support the development of new ones
• Characterize uncertainty in lesion change measurements across sizing methods and implementations
• Develop informatics and process-based biomarker framework supporting
– Efficient and economical development
– Validation
– Regulatory approval
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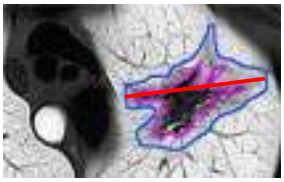
# Medical Imaging
## *Improving Change Analysis in Lung Cancer*



**RECIST :** ***Response Evaluation Criteria in Solid Tumors***

| Complete | Partial | Progressive | Stable |
|---|---|---|---|
| Disappear | 30% decrease | 20% increase | Small change |

**NIST Role**

- Provide a measurement infrastructure that enables quantifiable and reproducible measurements of tumors
- Develop reference material, measurements and metrics to compare sizing algorithms to ground truth

7

# NIST Biochange:
# Improving Change Analysis in Lung Cancer

***Target: Late stage lung cancer patients***

**Biochange '08 Pilot:**

- Thick-slice (5 mm) studies
- NCI's RIDER + FDA phantoms
- Radiologists (2) RECIST markup
- Retrospective analysis to obtain additional diameter and volume measurements

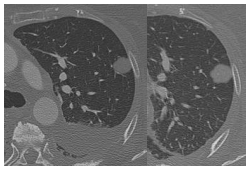
**Biochange Challenge:** NEW

- Thin-slice (1.25, 2.50 mm)
- 56 Clinical, *NCI RIDER*
- 16 Coffee Break, *NCI RIDER*
- 8 Computational Implants, *NIST Peskin*
- 16 Physical Phantoms, *NIST Levine*
- 7 institutions have declared they plan to participate & we're still recruiting

Ellipsoids
Physical Phantoms

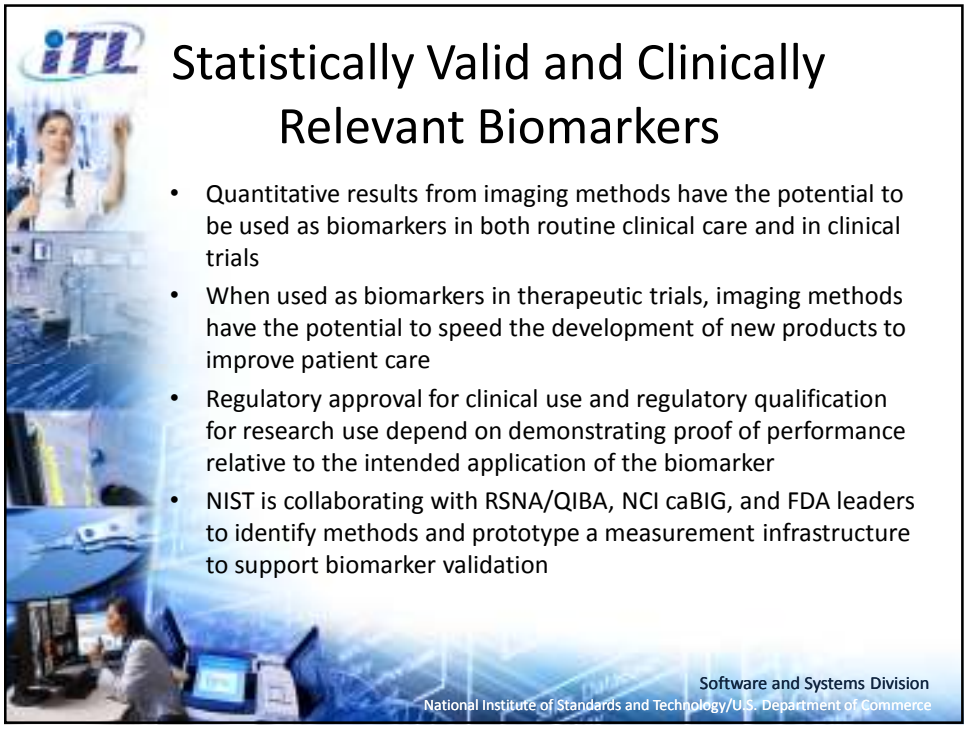
| | < 30% | 30–0% | 0–20 % | > 20% |
|---|---|---|---|---|
| Clinical | 8 | 24 | 16 | 8 |
| Coffee Break | 0 | 8 | 8 | 0 |
| Synthetic | | | 8 | |
| Ellipsoids | | | 8 | 8 |

**Biochange: 96 Lesion Pairs**



Synthetic
Computational Implants

http://www.nist.gov/itl/iad/dmg/biochangechallenge.cfm



# Statistically Valid and Clinically Relevant Biomarkers

- Quantitative results from imaging methods have the potential to be used as biomarkers in both routine clinical care and in clinical trials
- When used as biomarkers in therapeutic trials, imaging methods have the potential to speed the development of new products to improve patient care
- Regulatory approval for clinical use and regulatory qualification for research use depend on demonstrating proof of performance relative to the intended application of the biomarker
- NIST is collaborating with RSNA/QIBA, NCI caBIG, and FDA leaders to identify methods and prototype a measurement infrastructure to support biomarker validation

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# Validating Biomarkers Proposed Architecture and Design


***Goal***

- Validation assessment of quantitative imaging biomarker technical and clinical performance via high-throughput computing

# Technologies

| Technologies | Description |
|---|---|
| NBIA | Open source, federated grid-based image sharing |
| Algorithm Validation Toolkit | Analyzing annotation variability to validate medical image processing algorithms |
| MIDAS | Open source, digital archiving system supporting distributed processing |
| BatchMake | Cross platform batch processing tool for Big Data |



# Architecture

| Architectural Issue | Technical Approach |
|---|---|
| **Profile Editor** | MIDAS extended to support XML files created by QIBA |
| **Data Management** | NBIA is main resource for datasets; MIDAS serves as a proxy to avoid downloading large datasets during experiments |
| **Computation** | MIDAS as interface for workflows and grid of computing jobs |
| **Batch Processing** | Profile Editor provides workflow driving remote computing via MIDAS/BatchMake |
| **Validation Tools** | Integrate Algorithm Validation Toolkit with BatchMake |
| **Workflow Management** | MIDAS is workflow and data manager integrating input data and parameters, processing tools and validation results |
| **Validation Analysis** | Statistical analysis via R using interface between R and MIDAS; Extend MIDAS with dashboard for results |

# Progress to Date

- Define use model and requirements
  - Basic Story Board: Abstracted to facilitate translation to UML
  - Enterprise Use Case: The way most users think
  - System Use Cases: Specific mapping to technical solutions
- Define and build services
  - NBIA/MIDAS integration
  - IHE profile approach
- Apply services for proficiency testing with NIST as a neutral broker
  - NBIA / MIDAS integrated approach configured at NIST
  - Instantiating with QIBA 1C phantom images, NIST phantoms, and computational phantoms
  - Engaged in discussions with Pharma/QIBA/NIST Legal on hosting clinical trial data

http://www.kitware.com/NISTQuantitativeImaging/Wiki/index.php/Main_Page



# Contributors

- Investigators:
  - Buckler Biomedical Sciences LLC (BBMSC)
  - Kitware, Inc.
- In collaboration with:
  - Information Technology Laboratory of (ITL) of the National Institute of Standards and Technology (NIST)
  - Quantitative Imaging Biomarker Alliance (QIBA)
  - Imaging Workspace of caBIG
  - Stanford Center for Biomedical Informatics Research (BMIR)


METRICS FOR IMAGE QUALITY
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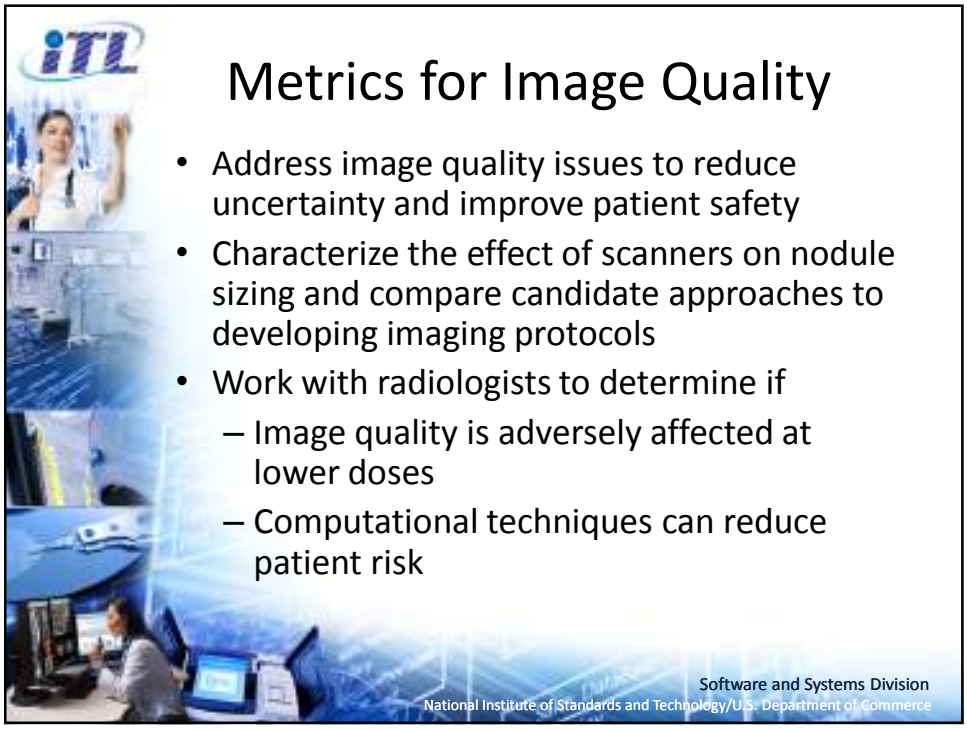
Metrics for Image Quality
• Address image quality issues to reduce uncertainty and improve patient safety
• Characterize the effect of scanners on nodule sizing and compare candidate approaches to developing imaging protocols
• Work with radiologists to determine if
– Image quality is adversely affected at lower doses
– Computational techniques can reduce patient risk
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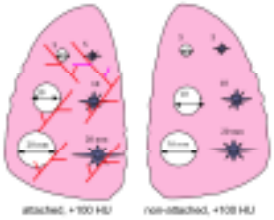
# QIBA 1C Subgroup
# Scanner Variability Study

Scanning Protocols



Experimental Design
Phantom Configuration

| Site | Device |
|---|---|
| UM SOM | Siemens |
| Duke | GE |
| UCLA | Phillips |
| Toshiba | Toshiba |
| NIST | Phillips |
| FDA | Siemens |

ACR Phantom

FDA Phantom

NIST Phantom

# QIBA 1C: Scanner Variability Study

- ACR phantom scanned at multiple sites
- Collaborated with medical physicists to converge on “equivalent” scanning protocols
- Designed study to address scanner variability using FDA and NIST phantoms
- Scanned phantoms across sites
- Ground truth to be provided by CoreLab
- In process of loading image sets into NBIA/MIDAS infrastructure for further analysis

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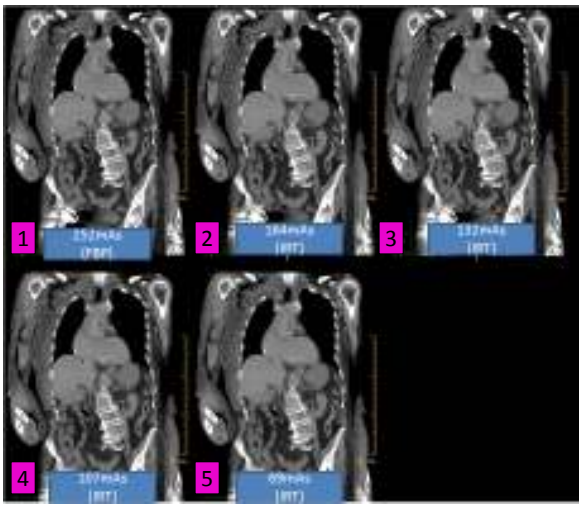
# Iterative Reconstruction

## Collaboration: UMD School of Medicine, Duke, NIST

- Cadaver imaged with standard does and filtered back projection with decreasing dose up to 73% reduction
- No significant difference in mean reader scores and quantitative measurements of image noise

*RSNA 2010*

- New study to evaluate iterative reconstruction techniques and compare against back projection




# Experimental Design

**UMd Medical Center CT Dosage & Iterative Reconstruction Alg. Study**

**Design 1 Factor List**

(siegeldex1factorlist.xls) (2/3/11)

| | Factor | C/D | # Levels in Population | # Levels in Sample | - Setting | + Setting |
|---|---|---|---|---|---|---|
| X1 | CT Dose | Continuous | (0,standard) | 2 | 1/2 Standard | Standard |
| X2 | Image type | Discrete | 2 | 2 | Raw | Image Recon |
| X3 | CT Vendor | Discrete | ~ 5 | 2 | Phillips | Siemens |
| X4 | Tissue Type | Discrete | ~30 | 2 | Soft | Hard |
| X5 | "Patient" Type | Discrete | 3 | 2 | Phantom | Cadaver |

The central practical question is: “Could the radiation output from the CT scanners across the country be reduced by a significant amount with no discernible degradation in the quality of the diagnostic image that the scanner produces?”

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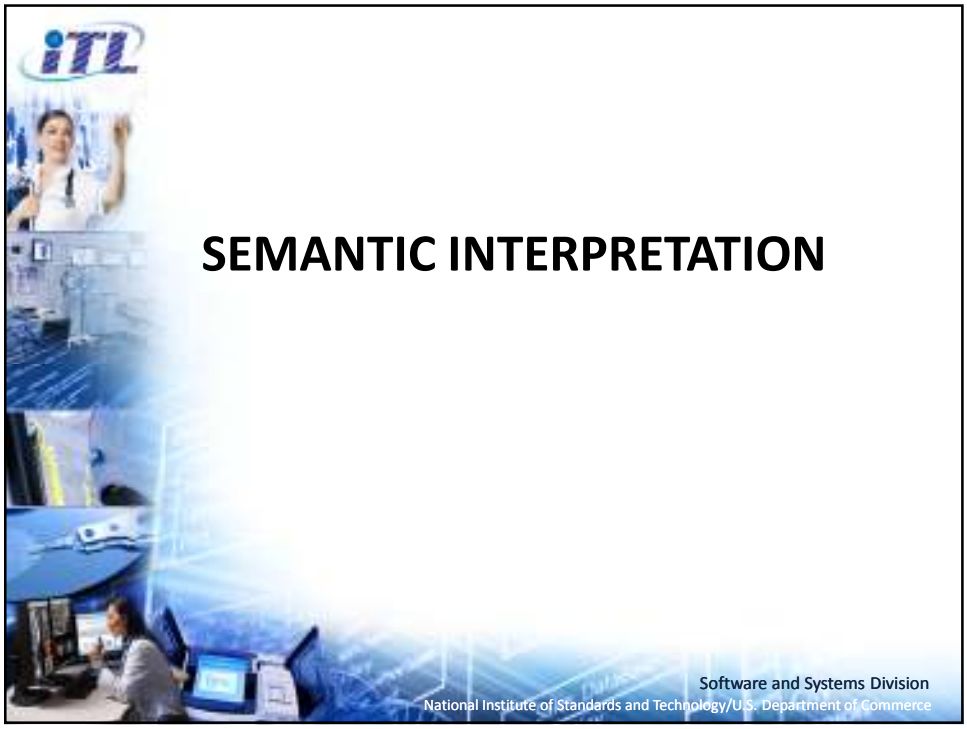
SEMANTIC INTERPRETATION
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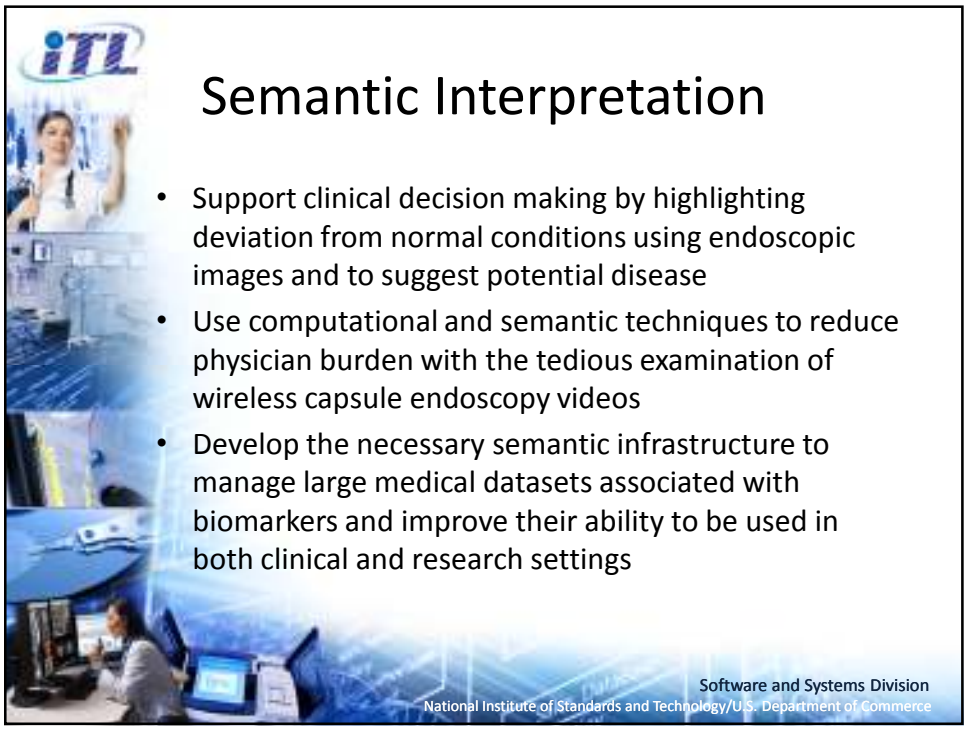
Semantic Interpretation
• Support clinical decision making by highlighting deviation from normal conditions using endoscopic images and to suggest potential disease
• Use computational and semantic techniques to reduce physician burden with the tedious examination of wireless capsule endoscopy videos
• Develop the necessary semantic infrastructure to manage large medical datasets associated with biomarkers and improve their ability to be used in both clinical and research settings
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# Interpreting Wireless Capsule Endoscopy Images

- WCE provides visual images of small bowel
- Searching for abnormalities is a time-consuming, tedious process
- Requires a high level of concentration
- Localization of the capsule is difficult and often inaccurate

Images: courtesy of GivenImaging

# From Images to Diagnosis: Using Disease Ontology to Support Clinical Decision Making

- Endoscopic video interpretation involves viewing the video and searching for tissue changes due to diseases such as bleeding, erosion, polyps and many more.
- Because of the huge amount of images to review, the investigation takes a significant amount of time.
- Advanced states of the lines usually give large lesions occurring on the large number of consequent images (video frames).
- In the early states of the illness a focal lesion might be present on only one or few video frames. It is very easy to miss such a lesion during ”manual investigation”

*Ram D. Sriram, Eswaran Subrahmanian (CMU), Marcin Kocielak (GR), Mala Ramaiah, MD (GR), Nageshwar Reddy, MD

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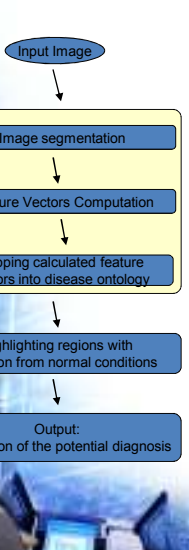
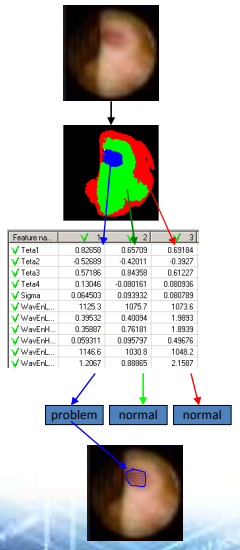
# Map Feature Vectors to Diagnosis




- Feature vectors are used to query disease ontology
- Lesion features are mapped to the appropriate disease

Suggested diagnosis: Ulcer...



# Summary

- Methodology for biomarker testing
  - Biochange Challenge
  - Biomarker Validation
- Studies to address image quality and improve patient safety
  - Scanner Variability - expect similar efforts in additional imaging modalities
  - Reduce patient dose by validating iterative reconstruction?
- Methods for semantic interpretation
  - New computational methods for identifying biomarkers in endoscopy images - extend to incorporate markers from radiology and pathology
  - Extend feature / ontology mapping to address issues in the broader biomedical community