NIST Medical Imaging Informatics Activities

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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
Collaborations

Buckler Biomedical Sciences LLC (BBMSC)

Cancer Statistics

2009 Estimated US Cancer Deaths*

- Lung & bronchus: 10% Men: 292,540
- Prostate: 9% Women: 268,800
- Colon & rectum: 9%
- Pancreas: 6%
- Leukemia: 4%
- Liver & intrahepatic bile duct: 4%
- Esophagus: 4%
- Uterine corpus: 3%
- Non-Hodgkin lymphoma: 3%
- Kidney & renal pelvis: 3%
- All other sites: 25%

*Other sites: 10% Men: 10%
*Other sites: 20% Women: 20%

Source: American Cancer Society, 2009.
BIOMARKERS

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
Medical Imaging

Improving Change Analysis in Lung Cancer

**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

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

<table>
<thead>
<tr>
<th>Complete</th>
<th>Partial</th>
<th>Progressive</th>
<th>Stable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disappear</td>
<td>30% decrease</td>
<td>20% increase</td>
<td>Small change</td>
</tr>
</tbody>
</table>

**NIST Biochange:**

**Improving Change Analysis in Lung Cancer**

**Target**: Late stage lung cancer patients

**Biochange '06 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:**
- 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

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.

Validating Biomarkers

Proposed Architecture and Design

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

<table>
<thead>
<tr>
<th>Technologies</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NBIA</td>
<td>Open source, federated grid-based image sharing</td>
</tr>
<tr>
<td>Algorithm Validation Toolkit</td>
<td>Analyzing annotation variability to validate medical</td>
</tr>
<tr>
<td></td>
<td>image processing algorithms</td>
</tr>
<tr>
<td>MIDAS</td>
<td>Open source, digital archiving system supporting</td>
</tr>
<tr>
<td></td>
<td>distributed processing</td>
</tr>
<tr>
<td>BatchMake</td>
<td>Cross platform batch processing tool for Big Data</td>
</tr>
</tbody>
</table>

Architecture

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

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

• 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
QIBA 1C Subgroup
Scanner Variability Study

- Scanning Protocols
- Experimental Design
  - Phantom Configuration

<table>
<thead>
<tr>
<th>Site</th>
<th>Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>UM SOM</td>
<td>Siemens</td>
</tr>
<tr>
<td>Duke</td>
<td>GE</td>
</tr>
<tr>
<td>UCLA</td>
<td>Phillips</td>
</tr>
<tr>
<td>Toshiba</td>
<td>Toshiba</td>
</tr>
<tr>
<td>NIST</td>
<td>Phillips</td>
</tr>
<tr>
<td>FDA</td>
<td>Siemens</td>
</tr>
</tbody>
</table>

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
Iterative Reconstruction
Collaboration: UMD School of Medicine, Duke, NIST

- Cadaver imaged with standard doses 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)

<table>
<thead>
<tr>
<th>Factor</th>
<th># Levels in CID</th>
<th># Levels in Population</th>
<th>Sample Setting</th>
<th>+ Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>X1 CT Dose</td>
<td>Continuous (0,standard)</td>
<td>2</td>
<td>1/2 Standard</td>
<td>Standard</td>
</tr>
<tr>
<td>X2 Image type</td>
<td>Discrete</td>
<td>2</td>
<td>2</td>
<td>Raw</td>
</tr>
<tr>
<td>X3 CT Vendor</td>
<td>Discrete</td>
<td>~5</td>
<td>2</td>
<td>Phillips</td>
</tr>
<tr>
<td>X4 Tissue Type</td>
<td>Discrete</td>
<td>~30</td>
<td>2</td>
<td>Soft</td>
</tr>
<tr>
<td>X5 “Patient” Type</td>
<td>Discrete</td>
<td>3</td>
<td>2</td>
<td>Phantom</td>
</tr>
</tbody>
</table>

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?”
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
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

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 illness 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”
Map Feature Vectors to Diagnosis

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

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