Center for Computational Imaging and Personalized Diagnostics (CCIPD)

2014 Annual Report

Director: Anant Madabhushi, PhD
Professor,
Department of Biomedical Engineering
CCIPD Website: http://ccipd.case.edu
CCIPD in 2014

Wickenden Building
Dept. of Biomedical Engineering
Case Western Reserve University
2071 Martin Luther King Drive
Cleveland, Ohio 44106-7207

Center Space, Room 517

Faculty Offices, Room 523

Center Space, Room 525
Center Members
CCIPD Members

Center Director: Anant Madabhushi, PhD

**Research Faculty**
Satish Viswanath
Pallavi Tiwari

**Research Associates**
Mirabela Rusu    Mahdi Orooji
Haibo Wang     Andrew Janowczyk
Asha Singanamalli    George Lee
Jon Whitney    Rakesh Shiradkar

**Scientific Software Engineer**
Ahmad Algohary
Yu Zhou

**Graduate Students**
Shoshana Ginsburg
Sahir Ali
Prateek Prasanna
Gregory Penzias
Lin Li
Xiangxue Wang
Jacob Antunes

**Undergraduate Students**
Patrick Leo    Ania Gawlik
Nikita Agrawal  Jay Patel
Thomas Liao     Eaton Guo
Ross O’Hagan

**Administrative Staff**
Ann Tillet
Francisco Aguila

**Visiting Scientists**
Angel Cruz (Colombia)    Jun Xu (China)
Tao Wan (China)    Mehdi Alilou (Iran)
Center Members

Center Director

Anant Madabhushi, PhD

Research Faculty

Pallavi Tiwari, PhD

Satish Viswanath, PhD
Center Members

Research Scientists

Mirabela Rusu, PhD
Mahdi Orooji, PhD
Haibo Wang, PhD
Rakesh Shrikadkar, PhD
George Lee, PhD
Asha Singanamalli, MS
Andrew Janowczyk, PhD
Jon Whitney, PhD
Center Members

Graduate Students

Sahir Ali, MS
Shoshana Ginsburg, MS
Prateek Prasanna, MS
Xiangxue Wang, BS
Lin Li, BS
Jacob Antunes
Greg Penzias, BS
Center Members

Visiting Scientists

Angel Cruz, MS
Tao Wang, PhD
Jun Xu, PhD
Mehdi Alilou, PhD

Scientific Software Programmers

Ahmad Algohary, MS
Yu Zhou, MS

Administrative Staff

Ann Tillett, BS
Francisco Aguila, BS
Center Members

**Undergraduate Students**

Patrick Leo  
Ania Gawlik  
Jay Patel  

Thomas Liao  
Nikita Agrawal  
Eaton Guo  
Ross O’Hagan
Recent Alumni

George Lee, PhD, Research Associate, CCIPD

Ajay Basavanhally, PhD, Diagnostic Precision, Inc.

Andrew Janowczyk, PhD, Research Associate, CCIPD

Rachel Sparks, PhD, Post Doc at University College of London

Rob Toth, PhD, CEO, Toth Technology
Eileen Hwang, Cum Laude Award in SPIE Medical Imaging, 2014

Jacob Antunes, Reviewers Choice Award, SPIE Medical Imaging, 2014

Geert Litjens, 2nd place SPIE Medical Imaging Student Paper Award, 2014

Pallavi Tiwari, Cum Laude Award in SPIE Medical Imaging, 2014

Prateek Prasanna, Runner Up, Young Scientist Award, MICCAI, 2014
Conference Participation 2014

Left to Right: Larry Clarke, Director of the NCI Cancer Imaging Program, Navenka Dimitrova, Phillips Research, Dr. Madabhushi, CCIPD, and Dr. Tiwari, CCIPD: Radiomics Meeting, Houston, TX

Angel Roa-Cruz: SIPIAM in Cartagen, Colombia

Angel Roa-Cruz: SPIE in San Diego
Conference Participation 2014

Pallavi Tiwari: SPIE in San Diego, CA

Anant Madabhushi: SPIE in San Diego, CA

Mirabela Rusu: SPIE in San Diego, CA
Ibris, Inc
CCIPD Startup, showcased on Bioenterprise Wall
Summary of Accomplishments 2014

- **Center Members:** 32
  - Faculty: 3
  - Research Associates: 8
  - Graduate Students: 6
  - Undergraduate Students: 7

- **Theses (1):** 1 PhD
- **Books:** 1
- **Book Chapters:** 2
- **Peer-Reviewed Journal Papers:** 21
- **Peer-Reviewed Conference Papers:** 15
- **Peer Reviewed Abstracts:** 14

- **Issued Patents:** 2
- **Provisional Patents:** 1
- **Awarded Grants:** 6
- **Awarded Fellowships:** 2
- **Ongoing Projects:** 30

- **Invention Disclosures:** 8
- **Technologies Licensed:** 6
Peer Reviewed Publications for 2014

Summary

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Books</td>
<td>1</td>
</tr>
<tr>
<td>Book Chapters</td>
<td>2</td>
</tr>
<tr>
<td>Journal Papers</td>
<td>21</td>
</tr>
<tr>
<td>Conference Papers</td>
<td>11</td>
</tr>
<tr>
<td>Abstracts</td>
<td>8</td>
</tr>
</tbody>
</table>
Peer Reviewed Publications for 2014

Books


Book Chapters


Journal Papers

- Tiwari, P, Shabbar, D, Madabhushi, A, “Identifying MRI Markers Associated with Early Response following Laser Ablation for Neurological Disorders: Preliminary Findings”, PLOS One, Accepted.
Peer Reviewed Publications for 2014

Journal Papers (Contd.)

- Sparks, R, Bloch, N, Moses, D, Ponsky, L, Barratt, D, Feleppa, E, Madabhushi, A, “Multi-Attribute Probabilistic Prostate Elastic Registration (MAPPER): Application to Fusion of Ultrasound and Magnetic Resonance Imaging”, Medical Physics, Accepted pending minor changes.
Peer Reviewed Publications for 2014

Journal Papers (Contd.)

Peer Reviewed Publications for 2014

Journal Papers (Contd.)


Peer Reviewed Publications for 2014

Peer-reviewed Conference Papers


Peer Reviewed Publications for 2014

Peer-reviewed Conference Papers (Contd.)

Peer Reviewed Publications for 2014

Peer-reviewed Conference Papers (Contd.)

Peer Reviewed Publications for 2014

Peer-reviewed Abstracts


Peer-reviewed Abstracts (Contd.)

Invited Lectures

- “Computational Knowledge Fusion and sub-visual image features for personalizing medicine”, Department of Electrical and Computer Engineering, University of British Colombia, Vancouver, BC, Canada, December 1, 2014. (Anant Madabhushi)
- “Computational MRI analysis for treatment evaluation and survival prediction in brain tumors,” Imaging Seminar Series, Department of Biomedical Engineering, CWRU, November 25th, 2014. (Pallavi Tiwari)
- “Computational data convergence: Applications in diagnosis and prognosis of prostate cancer”, Department of Urology, Cleveland Clinic, Cleveland, OH, October 22nd, 2014. (Anant Madabhushi)
- “‘Radiomics’ risk score: Image based risk assessment for presence of recurrent tumor or radiation effects on MRI,” Grand rounds in Oncology, University Hospitals, Cleveland, October 15th, 2014. (Pallavi Tiwari)
Invited Lectures (Contd.)

- “Computational Imaging and mining sub-visual image features for personalized medicine: Use cases in breast, prostate, oropharyngeal and lung cancers”, Plenary Talk, 10th International Symposium on Medical Information Processing and Analysis, Cartagena, Colombia, Oct. 14th, 2014. (Anant Madabhushi)
- “Co-occurrence of Local Anisotropic Gradient Orientations (CoLlAGe): A domain-inspired descriptor to distinguish ‘similar appearing’ pathologies on imaging”, Workshop on Radiomics, MD Anderson, Texas, October 1st, 2014.
- “Computational convergence of imaging, pathology, and omics data: Use case in prostate cancer”, Workshop on Radiogenomics, MD Anderson Cancer Center, Houston, TX, September 29th, 2014. (Anant Madabhushi)
- “Multi-scale, sub-visual features for personalizing medicine”, Biomedical and Health Informatics Workshop, Case Western Reserve University, Cleveland, OH, September 16th, 2014. (Anant Madabhushi)
- “Radiology-pathology correlation: enriching imaging to enable disease signature discovery,” Imaging Hour, Case Western Reserve University, Cleveland, OH, September 9th, 2014 (Mirabela Rusu)
- “Computational Imaging and mining sub-visual image features for personalized medicine: Use cases in breast, prostate, oropharyngeal and lung cancers”, Case Comprehensive Cancer Center, Cleveland, OH, September 5th, 2014. (Anant Madabhushi)
- “Multi-scale Data Enrichment in Prostate Cancer: Diagnosis, Prognosis and Population Based Analytics,” International MRI Summer School, Iasi, Romania, August 5th, 2014. (Mirabela Rusu)
- “Computational Breast Imaging and mining sub-visual image features for personalized medicine”, Tata Memorial Hospital, Mumbai, India, July 24th, 2014. (Anant Madabhushi)
Invited Lectures (Contd.)

- “Computational Imaging and mining sub-visual image features for personalized medicine: Use cases in breast, prostate, oropharyngeal and lung cancers”, Tata Memorial Hospital, Mumbai, India, July 17th, 2014. (Anant Madabhushi)
- “Computational Imaging and mining sub-visual image features for personalized medicine”, General Electric, Bangalore, India, July 16th, 2014. (Anant Madabhushi)
- “Computational Imaging and mining sub-visual image features for personalized medicine”, Teleradiology Solutions, Bangalore, India, July 16th, 2014. (Anant Madabhushi)
- “Computational Imaging and the Personalized Image based Risk Score”, Case Comprehensive Cancer Center Retreat, Cleveland, OH, July 11th, 2014. (Anant Madabhushi)
- “3D Printing To Facilitate Prostate Cancer Diagnosis and Prognosis” Rapid, Detroit, MI, June 10th, 2014. (Mirabela Rusu)
- “Computer assisted diagnosis, prognosis, and treatment evaluation of prostate cancer from MRI and digital pathology”, Prostate Cancer Seminar Series, Cleveland Clinic, Cleveland, OH, May 15th, 2014. (Anant Madabhushi)
- “Preparing yourself for a career in non-academic environments?”, Graduate Student Senate Professional Development Conference, Case Western Reserve University, Cleveland, OH, May 2nd, 2014. (Anant Madabhushi)
- “Computational convergence of radiology and pathology data”, Joint workshop on Radiology-Pathology Fusion by Radiological Society of North America (RSNA) and American Society of Clinical Pathology (ASCP), Chicago, IL, April 22nd, 2014. (Anant Madabhushi)
Invited Lectures (Contd.)

- “Radiology-Pathology Convergence: Application to Biological Quantitation and Disease Characterization”, R25T Seminar Series, Memorial Sloan Kettering Institute Dept of Radiochemistry, New York, NY, April 18th, 2014. (Satish Viswanath)
- “Computational Imaging and Personalized Medicine”, Department of Thoracic Oncology, Cleveland Clinic, Cleveland, OH, April 16th, 2014. (Anant Madabhushi)
- “Computational pathology: Personalized Medicine and Enriching Radiology and molecular data”, Department of Rheumatology, Cleveland Clinic, Cleveland, OH, April 15th, 2014. (Anant Madabhushi)
- “Computational pathology: Squeezing the most out your pathology images”, Imaging Hour, Case Western Reserve University, Cleveland, OH, April 15th, 2014. (Anant Madabhushi)
- “Computational pathology: Squeezing the most out your pathology images”, University of Uppsala, Center for Medical Image Analysis, Uppsala, Sweden, April 10th, 2014. (Anant Madabhushi)
- “Computational Imaging and Big Data Convergence in Personalized Medicine”, Grand Rounds in Urology, University of Cincinnati, Cincinnati, OH, April 7th, 2014. (Anant Madabhushi)
- “Computer-extracted texture features on T2w MRI to predict biochemical recurrence following radiation therapy for prostate cancer” SPIE Medical Imaging, San Diego, CA, March 24th, 2014. (Mirabela Rusu)
- “Computational pathology: Image analysis for Big Pathology Data”, American Society for Clinical Pathology, Miami, FL, March 20th, 2014. (Anant Madabhushi)
- “A prostate MRI atlas of biochemical failures following radiotherapy,” SPIE Medical Imaging, San Diego, CA, March 18th, 2014. (Mirabela Rusu)
- “Computational Imaging and Big Data Convergence in Personalized Medicine of Prostate Cancers”, Grand Rounds in Department of Urology, Mount Sinai Medical Center, New York City, NY, March 5th, 2014. (Anant Madabhushi)
- “Computational Imaging and Big Data Convergence in Personalized Medicine”, Executive Council Meeting, Case Comprehensive Cancer Center, Cleveland, OH, February 27th, 2014. (Anant Madabhushi)
Invited Lectures (Contd.)

- “Quantitative Data Convergence: Applications to Personalized Medicine”, Department of Mathematics, Case Western Reserve University, Cleveland, OH, February 26th, 2014. (Anant Madabhushi)
- “Computational pathology: Personalized Medicine and Enriching Imaging”, Department of Epidemiology and Biostatistics, Case Western Reserve University, Cleveland, OH, February 20th, 2014. (Anant Madabhushi)
- “Image based risk score: Application to ER+ breast cancers”, Department of Biomedical Engineering Seminar Series, Case Western Reserve University, Cleveland, OH, February 10th, 2014. (Anant Madabhushi)
Patents

Issued Patents

- “System and Method for Accurate and Rapid Identification of Diseased Regions on Biological Images with Applications to Disease Diagnosis and Prognosis”, Anant Madabhushi, James Monaco, John E Tomaszewski, Michael D. Feldman, Ajay Basavanhally, United States Serial Number (USSN): 8,718,340.
- "System and Method for Automated Segmentation, Characterization, and Classification of possibly malignant Lesions and Stratification of Malignant tumors”, Anant Madabhushi, Shannon Agner, Mark Rosen, United States Serial Number (USSN): 8,774,479.

Provisional Patent Applications

- “Methodology for textural analysis of nodules on imaging to determine extent of invasion”

Invention Disclosures

- “Cascaded Ensemble of Convolutional Neural Networks and Handcrafted Features For Breast Cancer Diagnosis”, Case No. 2014-2572.
- “Histogram of Hosoya Index (HoH) features for Quantitative Histomorphometry”, Case No. 2014-2657
- “Co-Occurrence of Local Anisotropic Gradient Orientations (CoLIAGe)”, Case No. 2014-2655
- “Tumor+Adjacent Benign Signature (TABS) For Quantitative Histomorphometry”, Case No. 2014-2654
- “Methodology for creation of a differential atlas”, Case No. 2015-2775
- “Methodology for fusion of pathology and radiology data for disease characterization”, Case No. 2015-277
Awards and Accomplishments in 2014

Media Recognition

- “Undergraduate wins Research Choice Award at biomedical engineering conference”, The Daily, November 13th, 2014.

Awards and Accomplishments in 2014

Media Recognition (cont.)

- “Featured Faculty Member”, case.edu/faculty, October 30th, 2014.
- “Bioengineering’s Anant Madabhushi, team awarded patent relating to radiologic imaging of tumors”, Case School of Engineering, July 28th, 2014.
Awards and Accomplishments in 2014

Media Recognition (cont.)


- “Dr. Anant Madabhushi Awarded Phase II Coulter Grant on Brain Tumor”, The Daily, July 7th, 2014

- “Precision Medicine depends on big data”, Tech Page One, June 25th, 2014.

- “Biomedical engineering’s Anant Madabhushi and team awarded V Foundation Translational Research Grant”, The Daily, June 20th, 2014.

Awards and Accomplishments in 2014

Media Recognition (cont.)


- “Biomedical engineering’s Anant Madabhushi and team receive innovation research grant”, The Daily, April 25th, 2014.

- “vascuVis Inc., a wholly owned subsidiary of Elucid Bioimaging, has been awarded a two-year, $696,200 Small Business Innovation Research (SBIR) Phase II Grant from the National Science Foundation”, Press Release, March 31, 2014.

Awards and Accomplishments in 2014

Media Recognition (cont.)

- “HPV: Computerized Image Analysis May Distinguish Potentially Progressive Disease”, DermatologistsBlog.com


Professional/Editorial Activities in 2014

Chairing, Membership Program Committees of Conferences, Workshops, Special issues

- Session Chair, Cancer Imaging Track, 10th International Symposium on Medical Information Processing and Analysis, Cartagena, Colombia, Oct. 14th, 2014 (Anant Madabhushi).
- Program Committee Member, Ontology and Imaging Informatics, SUNY Buffalo, June 23rd, 2014 (Anant Madabhushi).
- Program Committee Member, 10th International Symposium on Medical Information Processing and Analysis, Cartagena, Colombia, Oct. 14-16, 2014 (Anant Madabhushi).
- Session Chair, Conference 9401: Digital Pathology, Keynote Session, International Society for Optics and Photonics (SPIE) Medical Imaging, Feb 18th, 2014, San Diego, CA (Anant Madabhushi).

Editorial Boards

- Associate Editor, IEEE International Symposium on Biomedical Imaging (ISBI) 2015 (Anant Madabhushi).
- Associate Editor, IEEE Journal of Translational Engineering in Health and Medicine, May 2014-Present (Anant Madabhushi).
New Grants Awarded in 2014

- Madabhushi, Anant (Co-I) 01/01/14 - 10/31/14
  V Foundation
  Use of PET and MR Imaging Biomarkers to Predict Response of Renal Cell Carcinoma to Tyrosine Kinase Inhibitor Therapy

- Madabhushi, Anant (Co-I) 01/01/14 - 12/31/15
  NSF
  Computer assisted prognosis of debilitating disease

- Madabhushi, Anant (PI) 06/01/14-05/30/15
  CTSC Coulter Annual Pilot Grant
  Computerized Histologic Image-based predictor of recurrence in breast cancers following treatment

- Madabhushi, Anant (PI) 09/01/14-08/31/16
  DOD CDMRP Lung Cancer Research Idea Development Award New Investigator (LC130463)
  Computer extracted CT features for distinguishing suspicious lung lesions with no, minimal, and significant invasion

- Tiwari, Pallavi (PI) 09/01/14 - 08/31/15
  Coulter Research Translational Partnership
  NeuroRadVision™: Image based risk score prediction of recurrent brain tumors (Phase 2)

- Madabhushi, Anant (PI) 09/01/14 - 8/30/16
  NIH 1R21CA179327-01A1
  Histologic image-based aggressiveness prediction in p16+ oropharyngeal carcinoma
Student Fellowships in 2014

- Patel, Jay (PI)  06/01/14-09/01/14
  SOURCE CAA 2014 Summer Research Scholar
  Case Western Reserve University
  Segmentation and Shape Based Feature Modeling for Treatment Evaluation of Glioblastoma Multiforme

- Penzias, Gregory (PI)  06/01/14-09/01/14
  SOURCE CAA 2014 Summer Research Scholar
  Case Western Reserve University
  Automatic Fusion of Prostate Histology, Multi-Parametric MRI, and PET for Improved Characterization of Prostate Cancer
Student, Post-doctoral Awards and Accomplishments

- Jacob Antunes, Reviewers Choice Award, Biomedical Engineering Society Department of Imaging and Optics Chair (5% of all submissions receive this commendation), 2014
- Jacob Antunes, Biomedical Engineering Society Scholarship for involvement in a professional integrity workshop focused on ethics of authorship, 2014
- Jacob Antunes, Case Western Reserve University Biomedical Engineering Society Executive Board Travel Award, 2014
- Jay Patel, SOURCE CAA Travel Award, Case Western Reserve University, 2014
- Prateek Prasanna, Runner Up, Young Scientist Award, Medical Image Computing and Computer Assisted Intervention Society (MICCAI), 2014
- Prateek Prasanna, Medical Image Computing and Computer Assisted Intervention Society (MICCAI) Travel Award, 2014
- Gregory Penzias, SOURCE CAA Summer Research Scholar, Case Western Reserve University, 2014
- Prateek Prasanna, Semi-finalist Launchnown Competition, 2014
- Jay Patel, SOURCE CAA Summer Research Scholar, Case Western Reserve University, 2014
- Eileen Hwuang, NSF Graduate Research Fellowship, 2014
- Eileen Hwuang, Cum Laude for Best Poster Presentation at the Image Processing Conference, International Society for optics and Photonics (SPIE) Medical Imaging, 2014
- Geert Litjens, Robert F. Wagner Best Student Paper Award, Runner up, International Society for optics and Photonics (SPIE) Medical Imaging, 2014
- Eileen Hwuang, SPIE Medical Imaging Student Grant, 2014
RESEARCH PORTFOLIO

METHODS
- IMAGE SEGMENTATION
- MACHINE LEARNING
- CO-REGISTRATION
- MULTIMODAL DATA FUSION

APPLICATION DOMAINS
- RADIOLOGY
- HISTOPATHOLOGY
- BIOINFORMATICS
- RADIATION ONCOLOGY

DISEASE SITES
- PROSTATE CANCER
- BREAST CANCER
- BRAIN TUMORS
- OROPHARYNGEAL CANCER
- LUNG CANCER
- COLORECTAL CANCER
IMAGE REGISTRATION AND SEGMENTATION
Biomechanical Model for Pre-, Post-Treatment Prostate Registration

- Model of prostate tissue properties (e.g. elasticity, compressibility)
- Physically-real deformations applied to prostate & internal zones
- Spatial alignment of pre-, post-treatment prostate volumes
- RMS error of alignment: 2.99 mm
- Traditional biomechanical model (not considering internal zones) RMS error: 5.07 mm

Spatially Aware Expectation-Maximization and Statistical Shape Model for Prostate Segmentation in Transrectal Ultrasound

- Orbital Boarder Model: New Statistical Shape Model for Prostate Segmentation in Transrectal Ultrasound Imagery

Preliminary Results

Multi-Attribute Probabilistic Prostate Elastic Registration (MAPPER)

Methods

1. Segment Prostate on MRI
2. Construct Model on TRUS
3. Align MRI Mask to TRUS Model

Results

Root Mean Squared Error (mm)

Histology - CT Fusion Facilitates the Characterization of Suspicious Lung Lesions with No, Minimal, and Significant Invasion on CT

Ground glass nodule histology-CT fusion; (a) 3D view of nodule with axial (blue) and oblique (red) cutting plane; (b) CT intensities (oblique cut); (c) CT intensities (axial cut); (d) H&E section corresponding to the oblique cut (b); invasion (black) and adenocarcinoma in situ + invasion (yellow); (e) the interactive alignment of histology and CT allows to map extent of invasion from histology onto CT; (f) CT-based textures will be included in a predictor

Rusu et. al. (Accepted Annual Meeting of the United States and Canadian Association of Pathology)
MACHINE LEARNING AND FEATURE ANALYSIS
Computerized Nuclear Shape Analysis of Prostate Biopsy Images Predict Favorable Outcome in Active Surveillance Patients

• Active surveillance (AS), an accepted monitoring program, may be offered for men with very low risk (VLR) CaP in lieu of immediate intervention to reduce unnecessary treatment and improve quality of life.
• Our objective is to identify computationally derived features from digitized biopsy core images which can predict favorable and unfavorable outcomes for VLR AS patients.

65 H&E stained biopsy core images (30 Favorable, 35 Unfavorable) obtained from 51 AS CaP patients

Nuclear shape features (AUC = 0.78)
Gleason Score (AUC = 0.60).

Figure 1: Combination of a nuclear shape-based feature (Std. Dev. Perimeter Ratio) and 2 nuclear orientation features (standard deviation tensor contrast energy, standard deviation tensor contrast variance) are able to separate out favorable and unfavorable outcomes in the prostate cancer active surveillance cohort.

Lee et al. Accepted for presentation at United States and Canadian Academy of Pathology (USCAP) 2015
Mitosis Detection in Breast Cancer Images by Combining Handcrafted and Convolutional Neural Network Features

**Goal:** To detect mitosis figures in high power fields of breast cancer tissues.

(a) Our mitosis detection framework detects nuclei candidates from a high-power field (HPF) using blue-rat color transformation as segmentation method and then each candidate is used to train and classify whether is a mitotic figure or not by a handcrafted based classifier and a feature learning classifier using a Convolutional Neural Network. When both classifiers disagree about the classification, other classifier combine both features, handcrafted and learned, to the final classification of these confounding cases. (b) Evaluation results show that our combined feature strategy outperform the performance of each feature independently and most of the previous baseline. (c) An example of mitosis detection in a HPF is presented with TP (green), FN(yellow) and FP(red).

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Method</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>Precision</th>
<th>Recall</th>
<th>F-measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scanner</td>
<td>HC+CNN</td>
<td>65</td>
<td>12</td>
<td>35</td>
<td>0.84</td>
<td>0.65</td>
<td>0.7345</td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>64</td>
<td>22</td>
<td>36</td>
<td>0.74</td>
<td>0.64</td>
<td>0.6864</td>
</tr>
<tr>
<td></td>
<td>CNN</td>
<td>53</td>
<td>32</td>
<td>47</td>
<td>0.63</td>
<td>0.53</td>
<td>0.5730</td>
</tr>
<tr>
<td></td>
<td>IDSIA13</td>
<td>70</td>
<td>9</td>
<td>30</td>
<td>0.89</td>
<td>0.70</td>
<td>0.7821</td>
</tr>
<tr>
<td></td>
<td>IPAL6</td>
<td>74</td>
<td>32</td>
<td>26</td>
<td>0.70</td>
<td>0.74</td>
<td>0.7184</td>
</tr>
<tr>
<td></td>
<td>SUTECH</td>
<td>72</td>
<td>31</td>
<td>28</td>
<td>0.70</td>
<td>0.72</td>
<td>0.7094</td>
</tr>
<tr>
<td></td>
<td>NEC12</td>
<td>59</td>
<td>20</td>
<td>41</td>
<td>0.75</td>
<td>0.59</td>
<td>0.6592</td>
</tr>
</tbody>
</table>

Assessment of Algorithms for Mitosis Detection in Breast Cancer Histopathology Images

**Goal**: To evaluate and compare different computational methods for mitosis detection.

(a) By taking a set of high-power fields (HPF), different methods for mitosis detection were evaluated in the AMIDA challenge 2013 (http://amida13.isi.uu.nl/). (b) Evaluation results show the best results for IDSIA and DTU algorithms outperforming the performance measures (Precision, Recall and F-measure) of others approaches. (c) Sumarize the performance measure of each approach in the final evaluation of the challenges where our approach (CCIPD/MINDLAB) occupied the 6th place but without significant statistical difference with the third one.

<table>
<thead>
<tr>
<th>Team name</th>
<th>Precision</th>
<th>Recall</th>
<th>F1-Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDSIA</td>
<td>0.610</td>
<td>0.612</td>
<td>0.611</td>
</tr>
<tr>
<td>DTU</td>
<td>0.427</td>
<td>0.555</td>
<td>0.483</td>
</tr>
<tr>
<td>SURREY</td>
<td>0.357</td>
<td>0.332</td>
<td>0.344</td>
</tr>
<tr>
<td>ISIK</td>
<td>0.306</td>
<td>0.351</td>
<td>0.327</td>
</tr>
<tr>
<td>PANASONIC</td>
<td>0.336</td>
<td>0.310</td>
<td>0.322</td>
</tr>
<tr>
<td>CCIPD/MINDLAB</td>
<td>0.353</td>
<td>0.291</td>
<td>0.319</td>
</tr>
<tr>
<td>WARWICK</td>
<td>0.171</td>
<td>0.552</td>
<td>0.261</td>
</tr>
<tr>
<td>POLYTECH/UCLAN</td>
<td>0.186</td>
<td>0.263</td>
<td>0.218</td>
</tr>
<tr>
<td>MINES</td>
<td>0.139</td>
<td>0.490</td>
<td>0.217</td>
</tr>
<tr>
<td>SHEFFIELD/SURREY</td>
<td>0.119</td>
<td>0.107</td>
<td>0.113</td>
</tr>
<tr>
<td>NTUST</td>
<td>0.011</td>
<td>0.685</td>
<td>0.022</td>
</tr>
</tbody>
</table>

Quantitative characterization of spatial heterogeneity using computerized methods

Textural analysis could identify subtle cues of invasion on CT that might not be visible

25% of positive nodules on baseline CT are Ground Glass or Semi-solid nodules

The extent of invasion is correlated with prognosis

Disease free survival at 5 years when resected:
- 100%: Minimally invasive
  - Adenocarcinoma in situ
  - Minimally Invasive Adenocarcinoma (≤ 5 mm invasion)
- 67-90%: Frank invasion
  - Invasive Adenocarcinoma (> 5 mm invasion)

Currently radiologists are unable to distinguish the level of invasion from in situ on CT

Orooji, M.; Rusu, M.; Rajiah, P.; Yang, M.; Jacono, F.; Gilkeson, R.; Linden, P.; Madabhushi, A.; “Computer Extracted Texture Features on CT Predict Level of Invasion in Ground Glass Non-Small Cell Lung Nodules”, Radiological Society of North America (RSNA), Chicago, IL.
Distinguishing Recurrent GBMs from Radiation Necrosis Using Co-occurrence of Localized Gradient Orientations (CoLLAGe)

Prasanna, Tiwari et al. SNO (2014)
Differential Expression of CoLlAGe Features for Different Molecular Subtypes of Breast Cancer

ER+

HER2+

Fibroadenoma

Evaluating stability and discriminability of graph features for digital pathology classification

Example of both local and global graphs built into a TMA image of OCSCC which was previously segmented by automatic thresholding into blue ratio colour space for nuclei detection. Cell Cluster Graphs (A and E), Voronoi Diagram (B and F), Delaunay Triangulation (C and G), and Minimum Spanning Tree (D and H). First row shows the graphs over TMA image (A-D) and second row details only the graphs (E-H). Notice that all graphs were built using the same nuclei segmentation method.

A Comparative evaluation of supervised and unsupervised representation learning approaches for anaplastic medulloblastoma differentiation

**Goal:** To evaluate and compare different methods of representation and deep learning for anaplastic medulloblastoma tumor differentiation.

(a) A representation learning framework is proposed to train and classify square tissue regions from medulloblastoma tumors. In order to evaluate which kind of representation learning, unsupervised or supervised, we evaluate the representation learning module by using different methods. Unsupervised feature learning methods used were: Sparse Auto-encoders (sAE), Topographic Independent Component Analysis Autoencoders (TICA), and Supervised feature learning method was: Convolutional Neural Network (CNN). All methods were trained and evaluated using the same experimental setup to classify between anaplastic and non-anaplastic tumor. (b) Evaluation results show how unsupervised feature learning method TICA obtained the best results for different configuration followed by a large supervised feature learning method of CNN. TICA has the advantage that introduce invariant properties of visual features that can be useful for this task. Interestingly, all representation learning methods, unsupervised and supervised, outperform the data-driven baseline methods based on bag of features (BOF).

<table>
<thead>
<tr>
<th>Method</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>$TICA_{F,8,P_1}$</td>
<td>0.97</td>
<td>0.88</td>
<td>0.96</td>
</tr>
<tr>
<td>$TICA_{F,8,P_1}$</td>
<td>0.92</td>
<td>0.86</td>
<td>0.95</td>
</tr>
<tr>
<td>$TICA_{F,16,P_1}$</td>
<td>0.91</td>
<td>0.86</td>
<td>0.94</td>
</tr>
<tr>
<td>$CNN_{F,8,P_1}$</td>
<td>0.90</td>
<td>0.89</td>
<td>0.90</td>
</tr>
<tr>
<td>$sAE_{F,8,P_1}$</td>
<td>0.90</td>
<td>0.87</td>
<td>0.92</td>
</tr>
<tr>
<td>$sAE_{F,8,P_2}$</td>
<td>0.89</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td>$CNN_{F,8, P_1}$</td>
<td>0.85</td>
<td>0.97</td>
<td>0.74</td>
</tr>
<tr>
<td>BOF + A2NMF (Haar)$^{13}$</td>
<td>0.87</td>
<td>0.86</td>
<td>0.87</td>
</tr>
<tr>
<td>BOF + A2NMF (Block)$^{13}$</td>
<td>0.78</td>
<td>0.89</td>
<td>0.67</td>
</tr>
<tr>
<td>BOF + K − NN (Haar)$^{12}$</td>
<td>0.80</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BOF + K − NN (MR8)$^{12}$</td>
<td>0.62</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

MULTI-MODAL DATA FUSION
Supervised Multi-View Canonical Correlation Analysis (sMVCCA): Integrating Histologic and Proteomic Features for Predicting Recurrent Prostate Cancer

- Our new data integration methodology, supervised Multi-view Canonical Correlation Analysis (sMVCCA), aims to integrate infinite views of high-dimensional data to provide more amenable data representations for disease classification.
- Additionally, we demonstrate sMVCCA using Spearman’s rank correlation which, unlike Pearson’s correlation, can account for non-linear correlations and outliers.

Lee et al. IEEE Trans Med Imaging (2014)
Group-Sparse Multi-modal Feature Selection for Prostate Cancer Prognosis

Characterizing Pulmonary Inflammation on in vivo MRI via 3D Histological Reconstruction and Fusion in a Mouse Model

Multi-modal fusion to characterize the appearance of lung inflammation in a mouse model: (a) 3D reconstructed histology shows the extent of inflammation in 3D; (b) fusion of 3D histology and in vivo MRI; (c) 3D inflammation is mapped from histology onto in vivo MRI; Gabor feature in (d) wild type control mouse, (e) SPDKO inflammation caring mouse; (f) within the inflammation region

Rusu et. al. (submitted), Medical Physics
Supervised Multiview CCA: Data Fusion Strategy

**Goal:** Fusion of multi-modal data to improve prediction of disease diagnosis and prognosis

---

**Early Diagnosis of Alzheimer’s Disease**

- **T1w MRI**
- **Plasma Proteomics**

---

**In vivo prediction of prostate cancer risk**

- **T2w MRI**
- **DCE MRI**

---

**Prediction of Prostate Cancer 5-year Biochemical Recurrence**

- **Histology**
- **Proteomics**

---

TREATMENT EVALUATION AND OUTCOME PREDICTION
Quantifying Temporal Changes in MRI to Evaluate Treatment Changes Post-LITT in Epilepsy Patients

Pre-treatment MRI

Follow-up ($t_1$)  Follow-up ($t_2$)  Follow-up ($t_3$)  Follow-up ($t_4$)

Tiwari et al, PlosOne (in press)
A Novel Pathology-Radiology Fusion Workflow for Predicting Treatment Response and Patient Outcome in Rectal Cancers

Correlate rectal surgical specimens with pre-operative MRI, identify imaging signatures for chemoradiation response and different treatment effects.

Viswanath et al, “A Novel Pathology-Radiology Fusion Workflow for Predicting Treatment Response and Patient Outcome in Rectal Cancers”, USCAP 2015 (accepted)
Identifying PET/MRI Parameters for Early Treatment Response in Renal Cell Carcinoma

- **Goal:** Identify quantitative PET/MRI parameters that reflect early response in metastatic RCC to tyrosine kinase inhibitor treatment
- Quantified SUV, ADC, and T2W sum average parameters appear to be reflective of early changes due to cytostatic drug treatment response

Quantitative Identification of MRI Features of Prostate Cancer Response Following Laser Ablation and Radical Prostatectomy

Co-registration of post-LITT MRI and histopathology

Co-registration of post- and pre-LITT MRI

MRI feature extraction

Co-registration of radiological and histopathological data can help determine differentially expressing features in pre- and post therapy MRI to assess laser-interstitial thermotherapy success in prostate cancer ablation.

Clustering to determine residual disease extent using differentially expressing features obtained in previous steps.

Determining changes in features from pre- to post-treatment MRI in ablated areas and residual disease.

Radiomic Markers on Treatment-Naïve MRI can Predict Survival in GBM Patients

Kaplan Meier (KM) survival curves for long and short-term survival GBM patients

Tiwari et al, SNO (2014)
COMPUTER AIDED DIAGNOSIS AND PROGNOSIS
Prostate Cancer Recurrence can be Predicted by Measuring Cell Graph and Nuclear Shape Parameters in the Benign Cancer-Adjacent Field of Surgical Specimens

• The 'field effect' describes the micro-environment around the site of the tumor which may lead to a progression of disease.

• Combined features extracted from images corresponding to tumor regions with that of images corresponding to benign adjacent regions to create a Tumor + Adjacent Benign Signature

Figure 1: Prostate TMA cores corresponding to (a)-(f) progressors and (g)-(l) non-progressor case studies. (a),(d),(g),(j) Automated segmentation detects nuclear boundaries and locations from cancerous and benign tissue cores. In addition to (b),(e),(h),(k) nuclear shape features which demonstrate differences in size and shape for cancerous cores, (c),(f),(i),(l) nuclear subgraphs from the benign cores are shown to demonstrate differences between progressor and non-progressor cases unseen across cancerous cores. Kaplan-Meier curves for (m) features extracted from tumor region, (n) Tumor + Adjacent Benign Signature (TABS) and (o) Gleason Sum + TABS.

Lee et al. Accepted for presentation at United States and Canadian Academy of Pathology (USCAP) 2015
Gland Orientation Patterns on ex vivo 7 Tesla MRI for Prostate Cancer Diagnosis

Overview: Disorder in orientation of visible glands on ex vivo 7T prostate MRI can predict cancer presence and are correlated with disorder in gland orientations on pathology.

(a) Co-registration of histology and (b) ex vivo 7T MRI; Co-occurring gland tensors of (b, f) benign and (c, g) tumor tissues on (b, c) pathology and (f, g) 7T MRI; Entropy of gland orientations as computed from (d) pathology and from (h) 7T MRI distinguish between benign and tumor tissues.

Multi-Parametric MRI for Prostate Cancer Localization

Purpose: To identify computer-extracted features from multi-parametric MRI that are useful for detecting and localizing prostate tumors in the central gland or peripheral zone of the prostate.

Identifying similar subgraph structures that are recurring across the population and their effect on overall tumor morphology remains unexplored.

Hosoya index (HI) (originally introduced for analysis of chemical bonds) is a measure of a bond (in this context nuclei connections in a graph)

In this work, we have leverage HI to measure structural similarities of graphs across the populations that are indicative of recurrence in breast cancer tissue images

Illustration of Hosoya Index calculation

\[
\begin{align*}
Z(\text{HOSOYA}) &= Z(\text{HI}) \times Z(\text{HO}) + Z(\text{HO})^2 \times Z(\text{HI}) \times Z(\text{HI})^2 \\
Z(\text{HOSOYA}) &= (4 \times 5) + (2^2 \times 1^2) \\
Z(\text{HOSOYA}) &= 20 + 4 = 24
\end{align*}
\]

Figure 1. Original BCa TMA representing tumor with (a) recurrent tumor (d) non-recurrent tumor. (b) and (e) represent the corresponding cell graphs and resulting hosoya signature in (c) and (f) respectively.

SOFTWARE
Figure 1: Pairs of digitized prostate histological quadrants are pre-processed by segmentation and rotation (a), then automatically stitched (b) by ensuring contiguity of edges. Two fiducial points are automatically marked on each of these stitches (b), then the full PWMHS is reconstructed using all eight pairs of fiducial points (c). PWMHS stitches are evaluated by automatically marking a fiducial at the midpoint of each edge (d), then computing the mean separation distance of the four pairs. AutoStitcher (e, f) appears to yield similar reconstructions compared to Histostitcher (g, h) images for real ex vivo prostate PWMHSs. Note that (e, f, g, h) resized to 5% of 2x resolution.
ProstaCAD Ver. 2

- Updated
- GUI Redesigned
- Based Image Processing Redesigned
- New Features Added
- A Generic Image Analysis Framework
HistoView is a graphical user interface for pathology image analysis and visualization.

- Separates the image into different channels, corresponding to the actual colors of the stain used.
- Binarizes the channel image by thresholding and visualizes thresholded result.
- Supports whole-slide images.
The Case Comprehensive Cancer Center and Department of Biomedical Engineering at Case Western Reserve University invites applications for a tenure-track faculty position in Cancer Imaging informatics at the level of Assistant or Associate Professor. Candidates should have a doctorate and post-doctoral research experience in computational imaging, imaging informatics, computer aided diagnosis of cancers or a closely related field, an outstanding record of research achievements, and ability to contribute to the departmental educational mission. The successful candidate will have a primary appointment in the highly nationally ranked Department of Biomedical Engineering in the School of Medicine and in the Case Comprehensive Cancer Center and will be associated with the nationally reputed and funded Case Center for Computational Imaging and Personalized Diagnostics and the Case Center for Imaging Research. Faculty in this position will be able to take advantage of the very collaborative milieu at Case Western Reserve University and will have the opportunity to build upon the existing CWRU strengths in biomedical image analysis, digital pathology, radio-genomics, data integration, companion diagnostics, and personalized medicine. Opportunities exist for interdisciplinary and integrative research applied to cancer diagnostics in radiology, pathology, radiation oncology, and biomedical engineering. Preference will be given to candidates with a record of national funding and strong interest in translational research.

Please send curriculum vitae, a list of three or more references, and a cover letter outlining your research interests electronically to: cancersearch@case.edu. Please include “Cancer Imaging Informatics Faculty Search” in the subject line.

In employment, as in education, Case Western Reserve University is committed to Equal Opportunity and Diversity. Women, veterans, members of underrepresented minority groups, and individuals with disabilities are encouraged to apply.
INTERESTED IN JOINING CCIPD?

We are always looking for enthusiastic and motivated graduate, undergraduate students, post-doctoral and research scientists.

If you think you would be a good fit for CCIPD, send over your complete CV and 3 representative publications to “anantm” @ “case.edu”

Follow us on Twitter: @CCIPD_Case