2019 Scientific Retreat

Friday, April 26, 2019
Discovery World Pavilion

PROSTATE CANCER
RADIO-PATHOMICS

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Associate Professor
Department of Radiology & Biomedical Engineering
Director, Quantitative Imaging Laboratory
Medical College of Wisconsin

Together, Taking on Cancer’s Toughest Challenges
OUTLINE

• Introduction to Prostate Radio-pathomics
• Data Integration Methods
  • Distortion and Slice Orientation
  • Alignment Software
• Research Studies
  • Radio-Pathomic Mapping in the prostate
  • Pathologist dependence
  • QIN Collaborative Research Project
• Conclusions and Future Goals
• **233,000 NEW cases per year** in the USA.
• **30,000 Men** will die in the US this year from prostate cancer.
• **1 in 7** men will be treated for prostate cancer in their lifetime.
• **Racial Disparity**

INTRODUCTION TO RADIO-PATHOMICS: DIAGNOSTIC TOOLS

Symptoms or PSA Screening

Radiology

- Non-Invasive
- Differential diagnosis: “Likely Clinically Significant”

Surgical Procedure or Biopsy

Need: Non-invasive Cost-Effective Diagnostics

- Invasive
- Expensive
- Diagnostic

Molecular Profiling

Pathology

- Invasive
- Diagnostic

Heat map from K. Yu et al Clin Cancer Res. 2004
“Images are more than pictures, they are data”

Gillies et al, Radiology 2015

R. Stoyanova et al. TCR 2016
INTRODUCTION TO RADIO-PATHOMICS: PATHOMICS

Lumen

Stroma

Epithelium

Gleason's Pattern Scale

1. Small, uniform glands.
2. More space (stroma) between glands.
3. Distinctly infiltration of cells from glands at margins.
4. Irregular masses of neoplastic cells with few glands.
5. Lack of or occasional glands, sheets of cells.

Well differentiated
Moderately differentiated
Poorly differentiated
Anaplastic

Picture Source: Fischer Scientific website
INTRODUCTION TO RADIO-PATHOMICS: PATHOMICS

Tissue Section

Whole Mount Histology

Graded Histology

Grading Key

HGPIN

G3

G4 Fused Glands

G4 Cribriform Glands

G5
INTRODUCTION TO RADIO-PATHOMICS: PATHOMICS

Lumen
Stroma
Epithelium
Gland
Segmentation

www.meyerinst.com
INTRODUCTION TO RADIO-PATHOMICS: PATHOMICS

Lumen
Stroma
Epithelium

Epithelium Thickness
Lumen Size
Epithelium Roundness
Lumen Ratio

Gland Segmentation
HOW DO WE GET EVERYTHING IN THE SAME SPACE?

Symptoms or PSA Screening

Radiology

- Non-Invasive
- Differential diagnosis: “Likely Clinically Significant”

Surgical Procedure or Biopsy

- Invasive
- Diagnostic

Molecular Profiling

- Expensive
- Diagnostic

Pathology

Need: Non-invasive Cost-Effective Diagnostics

Heat map from K. Yu et al Clin Cancer Res. 2004
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Data Integration: Step 1 Tissue Sectioning

T2 MRI

Prostate Mask

Resulting Prostate Slices

Whole Mount Prostate Slides

McGarry et al. International J. Rad. Onc. Biology Physics, 2018
Lutgen et al. Nature Machine Intelligence 2018
Hurrell et al. JMI 2018
Knowling et al. IEEE BHI 2019
ALIGNMENT SOFTWARE

LaViolette et al. Neurooncology 2014
McGarry et al. International J. Rad. Onc. Biology Physics, 2018
Hurrell et al. JMI 2018
ALIGNMENT SOFTWARE

McGarry et al. International J. Rad. Onc. Biology Physics, 2018
Hurrell et al. JMI 2018

Warped B/W H&E

Original H&E
ANNOTATION ALIGNMENT

Original H&E + Annotation

Warped Annotation

- Atrophy
- HGPIN
- Grade 3
- Grade 4fg
- Grade 4cr
- Grade 5

McGarry et al. International J. Rad. Onc. Biology Physics, 2018
Hurrell et al. JMI 2018

NIH
NATIONAL CANCER INSTITUTE
Informatics Technology for Cancer Research
Nonlinearly Warped Histology Segmentations

Original Segmentation

Warped Epithelium/Cell Segmentation

Warped Lumen Segmentation

Warped Stroma Segmentation

0% 100% Percent Segmentation
DATA INTEGRATION

MRI Values

\[
\begin{bmatrix}
ADC & DCE & T2 & \\
0.001 & 1.2 & 2.5 & \\
0.002 & 1.6 & 2.3 & \\
0.0012 & 1.5 & 2.8 & \\
\end{bmatrix}
\]

\[=\]

Histology Segmentation

\[
\begin{bmatrix}
\text{Lumen} & \text{Epith.} & \text{Stroma} & \\
.3 & .6 & .1 & \\
.4 & .4 & .2 & \\
.5 & .2 & .3 & \\
.4 & .4 & .2 & \\
.4 & .1 & .5 & \\
\end{bmatrix}
\]
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RADIO-PATHOMIC MAPPING

Patient Cohort (N = 39)

Cohort 1 (N = 10)  Cohort 2 (N = 10)  Test Cohort (N = 19)
# RADIO-PATHOMIC MAPPING: RESULTS

<table>
<thead>
<tr>
<th>T2</th>
<th>Expert Annotation</th>
<th>Model 1 Epithelium</th>
<th>Model 1 Lumen</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
</tr>
</tbody>
</table>

**Annotation Legend:**
- G4fg
- G4cg
- Atrophy
- G3
- HGPIN

---

**Graph:**
- **Lumen Density (%)**
- **Epithelium Density (%)**
- **Legend:**
  - Normal
  - Benign Atr.
  - HGPIN
  - Gleason 3
  - Gleason 4+

---

McGarry et al. International J. Rad. Onc. Biology Physics, 2018
### RADIO-PATHOMIC MAPPING: RESULTS

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<th>Model 2 Epithelium</th>
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</tr>
</thead>
<tbody>
<tr>
<td>True Positive</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
</tr>
<tr>
<td>True Negative</td>
<td><img src="image6.png" alt="Image" /></td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
</tr>
</tbody>
</table>

**Annotation Legend:**
- G4fg
- Atrophy
- G4cg
- G3
- HGPIN

0% - 90%
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<tbody>
<tr>
<td>True Positive</td>
<td><img src="" alt="Images" /></td>
<td><img src="" alt="Images" /></td>
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<td><img src="" alt="Images" /></td>
<td><img src="" alt="Images" /></td>
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<tr>
<td>True Negative</td>
<td><img src="" alt="Images" /></td>
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</table>

Annotation Legend:  
- **G4fg**  
- **G4cg**  
- **Atrophy**  
- **G3**  
- **HGPIN**  

![ROC Curves](attachment:roc_curves.png)

**Model 1**  
- ![Curve](attachment:curve1.png)

**Model 2**  
- ![Curve](attachment:curve2.png)
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ISSUES WITH THE "GOLD STANDARD"
PATHOLOGIST SPECIFIC RADIO-PATHOMIC MAPPING

Observer 1  Observer 2  Observer 3

Observer 4  Observer 5

Legend
- Atrophy
- HGPIN
- Gleason 3
- Gleason 4 FG
- Gleason 4 CG

ISMRM 2019, Montreal
### PATHOLOGIST SPECIFIC RADIO-PATHOMIC MAPPING

<table>
<thead>
<tr>
<th>Deep Annotation</th>
<th>T2</th>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Observer 3</th>
<th>Observer 4</th>
<th>Observer 5</th>
<th>Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>True Positive</strong></td>
<td><img src="image1" alt="Image of True Positive Annotation" /></td>
<td><img src="image2" alt="Image of True Positive Observer 1" /></td>
<td><img src="image3" alt="Image of True Positive Observer 2" /></td>
<td><img src="image4" alt="Image of True Positive Observer 3" /></td>
<td><img src="image5" alt="Image of True Positive Observer 4" /></td>
<td><img src="image6" alt="Image of True Positive Observer 5" /></td>
<td><img src="image7" alt="Image of True Positive Consensus" /></td>
</tr>
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</table>

- **High Grade**
- **Low Grade**
- **Benign Atrophy**

**Epithelium Density**
- 0
- 0.9

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<th>Observer 2</th>
<th>Observer 3</th>
<th>Observer 4</th>
<th>Observer 5</th>
<th>Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>True Negative</strong></td>
<td><img src="image8" alt="Image of True Negative Annotation" /></td>
<td><img src="image9" alt="Image of True Negative Observer 1" /></td>
<td><img src="image10" alt="Image of True Negative Observer 2" /></td>
<td><img src="image11" alt="Image of True Negative Observer 3" /></td>
<td><img src="image12" alt="Image of True Negative Observer 4" /></td>
<td><img src="image13" alt="Image of True Negative Observer 5" /></td>
<td><img src="image14" alt="Image of True Negative Consensus" /></td>
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Multi-site concordance of diffusion weighted imaging derived metrics, a comparison of fitting algorithms for differentiating whole-mount, pathologically confirmed, prostate cancer of differing Gleason patterns

Peter S LaViolette¹, Sean D McGarry², John D Bukowy³, Allison K Lowman⁴, Anjishnu Banerjee⁵, Dariya Malysarenko⁶, Tom Chenevert⁷, Yue Cao⁸,⁹, Andrey Fedorov⁸, Laura Bell⁹, C. Chad Quarles⁹, Melissa Prah¹⁰, Kathleen Schmainda¹, Stefanie Hectors², Bachir Taouli², Eve LoCastro⁹, Yousef Mazaheri⁴,¹⁰, Amrita Shukla-Dave⁹,¹⁰, Thomas Yankeelov¹¹, David A Hornuth II¹¹, Ananth J Madhuranthakam¹², Keith Hulsey¹², Kurt Li¹³, Wei Huang¹³, Kenneth Jacobsohn¹⁴, Mark Hohenwalter¹, Petar Duvcjak¹, Michael Griffin¹, William See¹⁴, Marja Nevalainen¹⁵, and Kenneth A Iczkowski¹⁵

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Project Overview:

- Distribute prostate DWI with 10 b-values on ~30 patients.
- Sites fit IVIM, kurtosis, bi-exponential, etc. to the dataset.
• Radio-Pathomics has the potential to bridge the gaps between diagnostic disciplines
• Radio-pathomic mapping is useful for predicting the underlying histological features non-invasively.
• Radio-Pathomics is helpful for validating imaging biomarkers of cancer
• This technology will be useful for targeted precision treatment in cancer patients
FUTURE WORK

- Improve annotations with deep learning
- Automate co-registration
- Clinical trial targeting radio-pathomic hot-spots with biopsy and/or radiation
- Further data integration software
- Parallel Brain Cancer Research
Acknowledgements

• Special Thanks to all those involved:
  • Participating Patients
  • LaViolette Lab
    • Sean McGarry
    • Allie Lowman
    • Alex Barrington
    • John Bukowy, PhD
    • Morgan Ford
    • James Davis
    • Sam Bobholz
    • Michael Brehler, PhD
    • Melissa Hollister
    • Sarah Hurrell

• PC-COE
  • Marja Nevalainen, MD, PhD
  • William See, MD

Funding: NIH/NCI: R01CA218144, R01CA218144-02S1, R21CA231892, American Brain Tumor Association, Advancing a Healthier Wisconsin, State of Wisconsin Tax Check off Program for Prostate Cancer Research, Novocure Inc. PC-COE Project Funds: Vince Mathews, MD

Radiology
  • Scott Rand MD PhD
  • Mark Hohenwalter, MD
  • Petar Duvnjak, MD
  • Michael Griffin, MD

Urology
  • Kenneth Jacobsohn, MD

NeuroOncology and Neurosurgery
  • Jennifer Connelly MD
  • Wade Mueller, MD

Pathology
  • Kenneth Iczkowski, MD
  • Craig Mackinnon, MD
  • Elizabeth Cochran, MD
  • Wei Huang, MD (UW)
  • Tatjana Antic, MD (UChic.)
  • Gladel Paner, MD (UChic.)

Biostatistics
  • Anjishnu Banerjee, PhD

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