Current Challenges to AI in Cancer Imaging

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Artificial Intelligence in Cancer Imaging

• Promising roles of AI in cancer imaging
• Better quantitative assessment of
  o Tumor volume
  o Tumor margin definition
  o Tumor texture and internal heterogeneity
  o Tumor shape/morphology
  o Tumor compactness
  o Tumor necrosis
  o Tumor vasculature
Advantage of AI Approach in Cancer Imaging

- Objective measurement of tumor burden
- Reproducible
- Obtained in automated or semi-automated fashion
- Retrieved from routine clinical imaging
- Assess the entire tumor burden
  - unlike tissue sampling technique which are vulnerable to sampling bias
- Assess tumor burden at baseline and follow-up
  tuned to detect subtle changes of tumor behavior
Challenges to AI in Cancer Imaging

- Scarcity of annotated data
- **Non-standardization of image acquisition**
- Limited capacity to tackle one question
- Limited generalizability
Differences of Image Acquisition Effect on AI

- Multi-institutional cohort of ccRCC (TCGA & TCIA)
  - 138 pts → Discovery cohort
  - 55 pts → Validation cohort
- Outcome of interest:
  - develop an imaging biomarker capable of assessing tumor aggressiveness and patient’s survival
- Used unsupervised machine learning to classify tumors into two phenotypes in the discovery cohort
- These phenotypes were ultimately reproduced in the validation cohort
Heatmap of ccRCC AI-based Phenotypes
Visual Comparison of ccRCC AI-based Phenotypes

Phenotype 1

Phenotype 2
Clinical Implication of ccRCC
AI-based phenotype

• In comparison with AI-based ccRCC phenotype 2, phenotype 1 had higher
  – Stage
  – Grade
  – Percentage of tumor necrosis (central non-enhancing component)
AI-based ccRCC phenotypes Predict Tumor Recurrence

Days since diagnosis
Discovery Cohort, n=138

Days since diagnosis
Validation Cohort, n=55
AI-based ccRCC phenotypes Predict Cancer-specific Survival

Days since diagnosis
Discovery Cohort, n=138

Days since diagnosis
Validation Cohort, n=55
Conclusion

- AI-based ccRCC phenotypes at baseline CT scans can predict:
  - Tumor’s grade
  - Tumor’s stage
  - Risk of recurrence after resection
  - Cancer-specific survival
Before submission of the manuscript!

- Feature Collection:
  - 185 radiomic features
  - 1280 Deep learning features
  - 2 patient info
  - 5 CT scan parameters
  - totaling **1472 features**.
  - Feature ranking approaches → Feature forward selection
Re-visiting our results

<table>
<thead>
<tr>
<th>Patient's characteristics</th>
<th>Data distribution</th>
<th>Prediction Performance</th>
<th>Prediction Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Data</td>
<td>Discovery Cohort</td>
<td>Validation Cohort</td>
</tr>
<tr>
<td>Radiomic Cluster</td>
<td>Two Phenotypes</td>
<td>Cluster1 vs Cluster2</td>
<td>91 vs 102</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M1,MX vs M0</td>
<td>30 vs 163</td>
</tr>
<tr>
<td>Clinical Characteristics</td>
<td></td>
<td>CCA vs ccB</td>
<td>65 vs 73</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td>StageI vs StageII,III,IV</td>
<td>80 vs 58</td>
</tr>
<tr>
<td>tumor_status</td>
<td></td>
<td>tumor free vs tumor</td>
<td>139 vs 48</td>
</tr>
<tr>
<td>Survival</td>
<td></td>
<td>Alive vs Dead=36 vs 49</td>
<td>22 vs 30</td>
</tr>
<tr>
<td>Gene Mutation</td>
<td></td>
<td>BAP1 mut vs wt=15 vs 154</td>
<td>9 vs 110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>KDM5C mut vs wt=10 vs 159</td>
<td>8 vs 111</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PBRM1 mut vs wt=51 vs 118</td>
<td>35 vs 84</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SETD2 mut vs wt=15 vs 154</td>
<td>10 vs 109</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VHL mut vs wt=100 vs 69</td>
<td>74 vs 43</td>
</tr>
</tbody>
</table>
Further Exploration

- So we went back to the source of the data and tried to find what could explain the differences in the slice thickness.
Further Exploration

Discovery cohort

Validation cohort

Thin slice (1mm)

Thick slice (7.5mm)

Slice Thickness

Radiomic Phenotype 1

Radiomic Phenotype 2
Was there slice difference in CT images by institution?

- MSKCC
  - Thicker slices
  - Larger tumors with higher stages

- MD Anderson
  - Thinner slices
  - Smaller tumors with lower stages
Effect of CT Slice Thickness on Detection of Metastatic Lesions

Average Attenuation Difference (in Hounsfield units) Between Lesions and Surrounding Liver according to Confidence of Lesion Detection and Collimation

<table>
<thead>
<tr>
<th>Detection Confidence</th>
<th>2.5-mm Section Thickness</th>
<th>5.0-mm Section Thickness</th>
<th>7.5-mm Section Thickness</th>
<th>10.0-mm Section Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite</td>
<td>41.6</td>
<td>38.1</td>
<td>37.7</td>
<td>32.7</td>
</tr>
<tr>
<td>Probable</td>
<td>32.4</td>
<td>29.7</td>
<td>25.3</td>
<td>22.8</td>
</tr>
<tr>
<td>Total</td>
<td>38.0</td>
<td>34.5</td>
<td>30.4</td>
<td>27.0</td>
</tr>
</tbody>
</table>

Weg N., Radiology 1998
Number and size of lung, liver and lymph node lesions visible in images reconstructed at 15 and 7 mm

<table>
<thead>
<tr>
<th>Location; reconstruction interval; no. of lesions</th>
<th>Lung</th>
<th>Liver</th>
<th>Lymph nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean diameter</td>
<td>15 mm</td>
<td>7 mm</td>
<td>15 mm</td>
</tr>
<tr>
<td>&lt; 1.00 cm</td>
<td>49</td>
<td>88</td>
<td>29</td>
</tr>
<tr>
<td>1.00-1.49 cm</td>
<td>18</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>1.50-1.99 cm</td>
<td>11</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>2.00-2.99 cm</td>
<td>13</td>
<td>13</td>
<td>30</td>
</tr>
<tr>
<td>≥ 3.00 cm</td>
<td>4</td>
<td>4</td>
<td>14</td>
</tr>
</tbody>
</table>

Olson M., Journal de l’Association Canadienne des Radiologistes 1996
But, Thinner Slices are Not Always Better!

The images from A–G display the noise in the routine head CT protocol images at different slice thickness values of 0.6, 1, 2, 3, 4, 5, and 6 mm, respectively.
Solution to Slice Thickness Challenge in ccRCC Project – TCGA cohort

- Exclusion of radiomics and AI features that are affected by technical parameters
- Non-enhancing component of ccRCC was not affected by
  - Patient’s age or ECOG status
  - Scanner parameters
  - Institution where the scan was performed
Steps of ccRCC segmentations and estimation of NT component on CT scan of the abdomen before and after intravenous contrast.

A, Precontrast phase.
B, Postcontrast phase.
C, Postcontrast-precontrast subtraction.
D, Postcontrast-precontrast subtraction with automatic quantitation of NT

Green line delineating the non-enhancing tumor
Red line delineates the ccRCC margins.
Association of percent NT with cancer recurrence reflected - KM curves

Ahmed, et al. JCAT 2019
Association of percent NT with cancer-specific survival reflected - KM curves

Product-Limit Survival Estimates
With Number of Subjects at Risk and 95% Hall-Wellner Bands

Ahmed, et al. JCAT 2019
Association of percent NT with survival outcomes

TABLE 2. Multivariate Cox Regression Model Results Testing Association Between Percent of NT With Survival Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HR</th>
<th>95% Confidence Interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer recurrence</td>
<td>6.14</td>
<td>1.87–20.10</td>
<td>0.003</td>
</tr>
<tr>
<td>Cancer-specific mortality</td>
<td>3.00</td>
<td>1.05–8.58</td>
<td>0.040</td>
</tr>
</tbody>
</table>

Controlling for age at diagnosis and pathological staging

Ahmed, et al. JCAT 2019
Nonenhancing Component of Clear Cell Renal Cell Carcinoma on Computed Tomography Correlates With Tumor Necrosis and Stage and Serves as a Size-Independent Prognostic Biomarker

Firas S. Ahmed, MD, MPH,* Oguz Akin, MD,† Hiram Shaish, MD,* Lyndon Luk, MD,* Xiaotao Guo, PhD,* Hao Yang, MS,* Emily Zabor, MS,† Irina Ostrovnaya, PhD,† A. Ari Hakimi, MD,† Binsheng Zhao, DSc,* and Lawrence H. Schwartz, MD*
Other Technical Parameter

- Presence and absence of IV contrast
- Timing of IV contrast
Image Acquisition Guidelines
CT Contrast Administration
Image Acquisition Guidelines
CT Contrast Administration
Image Acquisition Guidelines
CT Contrast Administration
Quality Control Algorithm of the Contrast-Enhancement of CT-scan in AI studies
Impact of Variability in Portal Venous Phase Acquisition Timing in Tumor Density Measurement and Treatment Response Assessment: Metastatic Colorectal Cancer as a Paradigm
All patients had CT acquisition intended at PVP. However, we observed significant differences in the acquisition timing between (D) baseline (early) and (E) follow-up (optimal), even within the same patient.
PVP (portal venous phase) timing and region of interest (ROI) selection. Relative contrast enhancement of soft tissues at:

(A) Early PVP timing  
(B) Optimal PVP timing  
(C) Late PVP timing

ROIs were delineated in normal tissues (aorta, portal vein, inferior vena cava, liver, spleen, and kidney) as illustrated in the circles.
Computer-aided scoring output. Output in the form of isoprobability curves indicating the probability that PVP timing is optimal.
Image Acquisition Guidelines
Difference in Breath Hold
Image Acquisition Guidelines
CT Contrast Administration
Summary of Technical Parameter
Apart from IV contrast Enhancement & Timing

- CT scan
  - kVp
  - mAs
  - Pixel Spaceing
  - Reconstruction Algorithm
  - Scanner Manufacturer

- MRI
  - TE, TR
  - Image Matrix
  - FOV
  - Slice thickness & Slice gap
  - Magnet strength, coils, and manufacturer
Solutions

• Restrict data to homogenous sources
  – Limit the generalizability
  – Limit the power/sample size to build AI

• Account/adjust for technical parameters at
  – Machine learning algorithm building (transfer learning)
    • Example: Computer-Aided Scoring Algorithm of the Portal Venous Phase
  – Statistical analysis by including technical parameters in regression predictive models
Take Home messages

• AI algorithms are as good as the data you used to build it
  – It may apply well in the source environment (at your institution).
  – It may not reveal the same results at different institution

• Attention to technical parameters is important to build generalizable algorithms
  – Important with CT
  – Extremely important with MRI
Thanks for your attention

• Questions?