How Should We Use CT for Screening?

Perry J. Pickhardt, MD
UW School of Medicine & Public Health
Overview

• *Intended* Screening with Body CT
  – Examples: CRC & lung cancer; coronary calcium scoring

• *Opportunistic* (Incidental) Screening
  – “Incidental” to the clinical indication for scanning
  – Examples: osteoporosis & “cardiometabolic” risks
  – Adding value to what we already do
  – Review our work at UW (& NIH) to date with Abdominal CT
Screening CT Colonography

- Currently the best test for CRC prevention & screening
  - Like invasive colonoscopy, highly effective for both advanced adenomas & cancer
  - The other non-invasive tests (FIT & mt-sDNA) lack prevention (miss large adenomas)
  - Despite these advantages, CTC is grossly underutilized
“Opportunistic Screening” at Abdominal CT

- CT scans are data rich beyond the clinical indication
  - Has led to widespread concern regarding “incidentalomas”

2010;7:754-773

Managing Incidental Findings on Abdominal CT: White Paper of the ACR Incidental Findings Committee

Lincoln L. Berland, MD, Stuart G. Silverman, MD, Richard M. Gore, MD, William W. Mayo-Smith, MD, Alec J. Megibow, MD, MPH, Judy Yee, MD, James A. Brink, MD, Mark E. Baker, MD, Michael P. Federle, MD, W. Dennis Foley, MD, Isaac R. Francis, MD, Brian R. Herts, MD, Gary M. Israel, MD, Glenn Krinsky, MD, Joel F. Platt, MD, William P. Shuman, MD, Andrew J. Taylor, MD
“Opportunistic Screening” at Abdominal CT

- CT scans are data rich beyond the clinical indication
  - Has led to widespread concern regarding “incidentalomas”
- But what about harnessing the “incidental” data for benefit?
  - Robust objective measures of body composition can be obtained
  - These CT biomarkers can be manual or automated
  - Requires no additional patient time or exposure
  - Effectively represents half-body or whole-body screening
  - ~75 million body CT scans performed each year in the U.S.
“Opportunistic Screening” at Abdominal CT

CT scans per 1000 inhabitants in 2016
“Opportunistic Screening” at Abdominal CT

Trends in Use of Medical Imaging in US Health Care Systems and in Ontario, Canada, 2000-2016

Abdomen imaging (CT only)

CT scans per 1000 inhabitants in 2016
“Opportunistic Screening” at Abdominal CT
“Opportunistic Screening” at Abdominal CT

- Extracolonic findings (ECFs) at CT colonography (CTC)
  - An early testing ground: net detriment or benefit?
“Opportunistic Screening” at Abdominal CT

- Extracolonic findings (ECFs) at CT colonography (CTC)
  - An early testing ground: net detriment or benefit?
Cardiometabolic screening opportunities
- Cardiovascular risk and metabolic syndrome
  - Abdominal aortic calcium scoring
  - Visceral (& subcutaneous) fat quantification
  - Muscle bulk & density for sarcopenia
  - Liver attenuation for hepatic steatosis
- Bone mineral density (BMD) for osteoporosis
- Can potentially be applied to any abdominal CT
BMD Screening for Osteoporosis
BMD Screening for Osteoporosis

• Femoral neck evaluation
BMD Screening for Osteoporosis

- L1 trabecular evaluation

Future Osteoporotic Fracture Risk Related to Lumbar Vertebral Trabecular Attenuation Measured at Routine Body CT

Scott J Lee, Peter M Graffy, Ryan D Zea, Timothy J Ziemlewicz, and Perry J Pickhardt

Department of Radiology and Department of Biostatistics and Medical Informatics, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA
BMD Screening for Osteoporosis

6 months later
Aortic Calcium Quantification & Scoring

N = 829 pts; mean f/u = 11.2 yrs

Agagston Score = 18,096

AoCa Quartiles for CV Events

FRS Quartiles for CV Events
Does Nonenhanced CT-based Quantification of Abdominal Aortic Calcification Outperform the Framingham Risk Score in Predicting Cardiovascular Events in Asymptomatic Adults?

Stacy D. O'Connor, MD, MPH • Peter M. Graffy, MPH • Ryan Zea, MS • Perry J. Pickhardt, MD
Visceral fat quantification in asymptomatic adults using abdominal CT: is it predictive of future cardiac events?

Eva M. Ryckman,1 Ronald M. Summers,2 Jiamin Liu,2 Alejandro Munoz del Rio,1 Perry J. Pickhardt1
Muscle Bulk & Density for Sarcopenia

Predicting Future Hip Fractures on Routine Abdominal CT Using Opportunistic Osteoporosis Screening Measures: A Matched Case-Control Study

Muscle Area ROC, Hip Fx

AUC=0.714
(0.656, 0.772)
Liver HU Assessment for Steatosis

Quantification of Liver Fat Content With Unenhanced MDCT: Phantom and Clinical Correlation With MRI Proton Density Fat Fraction

Natural History of Hepatic Steatosis: Observed Outcomes for Subsequent Liver and Cardiovascular Complications

Specificity of unenhanced CT for non-invasive diagnosis of hepatic steatosis: implications for the investigation of the natural history of incidental steatosis

Visceral Adiposity and Hepatic Steatosis at Abdominal CT: Association With the Metabolic Syndrome

Longitudinal Changes in Liver Fat Content in Asymptomatic Adults: Hepatic Attenuation on Unenhanced CT as an Imaging Biomarker for Steatosis

Opportunistic Screening for Hereditary Hemochromatosis With Unenhanced CT: Determination of an Optimal Liver Attenuation Threshold

Accuracy of Liver Fat Quantification With Advanced CT, MRI, and Ultrasound Techniques: Prospective Comparison With MR Spectroscopy

Quantification of hepatic and visceral fat by CT and MR imaging: relevance to the obesity epidemic, metabolic syndrome and NAFLD
Liver HU Assessment for Steatosis

Quantification of Liver Fat Content With Unenhanced MDCT: Phantom and Clinical Correlation With MRI Proton Density Fat Fraction

CT-HU vs. MRI-PDFF for Phantom and Human Cases

Unenhanced CT

MR-PDFF
Automated Assessment at Abdominal CT

- Computer-aided detection (CAD) at CTC
Automated CT Biomarkers for Predicting Future Cardiometabolic Events & Overall Survival: Methods
Methods

• Patient Cohort:
  – 9,305 generally healthy asymptomatic adults who underwent unenhanced CT for colonography screening
    • Mean age, 57.1 years; 5,194 women, 4,111 men
    • Initial CT scans performed over 12-year period (2004-2016)
  – Algorithmic EMR search for subsequent clinical outcomes
    • CV events (MI, CVA, CHF), fragility fracture, death, etc
    • Mean clinical follow-up interval = 7.9 years
Methods

• Patient Cohort:
  – Adverse clinical outcomes (after the time of CT):
    • Major CV Event in 1,569 (16.7%)
    • Fragility Fracture in 646 (6.9%)
    • Death in 549 (5.9%)
Methods

• Clinical Parameters:
  – Framingham Risk Score (FRS)
    • Validated multivariate algorithm combining age, sex, BP, cholesterol, lipids, and smoking for 10-year CV risk prediction
  – Fracture Risk Assessment Tool (FRAX)
    • Validated multivariate algorithm including age, sex, height, weight, smoking, previous fracture, and femoral neck T-score, for 10-year probability of osteoporotic fracture
  – Body Mass Index (BMI)
Methods

• Automated CT Biomarkers:

  - Fully-automated developed, trained, & tested algorithms
    • Deep learning segmentation followed by the specific task
Automated CT Biomarkers

- Preliminary work from fat measures:

Fully automated segmentation and quantification of visceral and subcutaneous fat at abdominal CT: application to a longitudinal adult screening cohort

2007 2017
Automated CT Biomarkers

- Preliminary work from BMD (L1 HU):
  - 99.8% success rate
Automated CT Biomarkers

- Preliminary work from muscle measures:
Automated CT Biomarkers

- Preliminary work from Ao Ca++:

![Automated segmentation and quantification of aortic calcification at abdominal CT: application of a deep learning-based algorithm to a longitudinal screening cohort](Abdominal Radiology)
Automated CT Biomarkers

- Preliminary work from liver HU:
Automated CT Biomarkers

• Final Biomarker Selection:
Automated CT Biomarkers

Final Biomarker Selection:

- A single automated CT parameter from each of the five abdominal components for predicting future events

1. V/S Fat Ratio at L1 level
2. Mean Muscle HU at L3 level
3. Agatston Ca++ score for L1-L4
4. Mean Volumetric Liver HU
5. Trabecular HU at L1 level
Automated CT Biomarkers

CT Scan Images From Original Screening Study

Automated CT Algorithms

- Visceral-to-Subcutaneous Fat Ratio at L1 level
- Muscle Density (HU) at L3 level
- Mean Volumetric Liver Density (HU)
- Aortic Calcium Score (Agatston) from L1-L4
- Vertebral Trabecular Density (HU) at L1

Longitudinal Follow-up for Adverse Clinical Outcomes
Automated CT Biomarkers for Predicting Future Cardiometabolic Events & Overall Survival: Results
<table>
<thead>
<tr>
<th>CT Biomarker</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=549)</td>
</tr>
<tr>
<td>AoCa (Ag)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>2471</td>
</tr>
<tr>
<td>Muscle HU</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>20.8</td>
</tr>
<tr>
<td>V/S Fat Ratio</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1.22</td>
</tr>
<tr>
<td>Liver HU</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>53.6</td>
</tr>
<tr>
<td>L1 HU</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>150.9</td>
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</table>
### Diagnostic Performance for Predicting Death

<table>
<thead>
<tr>
<th></th>
<th>2-year AUROC (n=7849)</th>
<th>5-year AUROC (n=6891)</th>
<th>10-year AUROC (n=4029)</th>
<th>Cox PH Model Concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRS</td>
<td>0.700</td>
<td>0.688</td>
<td>0.693</td>
<td>0.681</td>
</tr>
<tr>
<td>FRAX</td>
<td>0.653</td>
<td>0.653</td>
<td>0.664</td>
<td>0.657</td>
</tr>
<tr>
<td>BMI</td>
<td>0.546</td>
<td>0.499</td>
<td>0.533</td>
<td>0.520</td>
</tr>
<tr>
<td><strong>Automated CT Biomarkers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AoCa (Ag)</td>
<td>0.746</td>
<td><strong>0.743</strong></td>
<td>0.746</td>
<td>0.735</td>
</tr>
<tr>
<td>Muscle HU</td>
<td>0.736</td>
<td><strong>0.721</strong></td>
<td>0.717</td>
<td>0.700</td>
</tr>
<tr>
<td>V/S Fat Ratio</td>
<td>0.685</td>
<td>0.661</td>
<td>0.656</td>
<td>0.648</td>
</tr>
<tr>
<td>Liver HU</td>
<td>0.644</td>
<td>0.619</td>
<td>0.628</td>
<td>0.602</td>
</tr>
<tr>
<td>L1 HU</td>
<td>0.627</td>
<td>0.646</td>
<td>0.640</td>
<td>0.637</td>
</tr>
<tr>
<td><strong>Multivariate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AoCa + Muscle</td>
<td>0.780</td>
<td>0.768</td>
<td>0.768</td>
<td>0.772</td>
</tr>
<tr>
<td>AoCa + Muscle + Liver</td>
<td></td>
<td>0.811</td>
<td>0.782</td>
<td>0.777</td>
</tr>
<tr>
<td>AoCa + Muscle + Liver + V/S</td>
<td></td>
<td>0.817</td>
<td>0.789</td>
<td>0.780</td>
</tr>
</tbody>
</table>

**Muscle HU**

AUC = 0.721

(0.683 , 0.759)

**AoCa + Muscle + Liver**

Area under the curve: 0.811
Time-to-Event Plots by Quartile for Predicting Death:

- Liver HU
- AoCa
- Muscle HU
- BMI
- V/S Fat
- L1 HU
• **Time-to-Event Plots for Predicting** **Cardiovascular Events**

![Graphs showing cumulative incidence for various factors over months of follow-up](image)

- Liver HU
- AoCa
- Muscle HU
- BMI
- V/S Fat
- L1 HU
• **Time-to-Event Plots for Predicting **Cardiovascular Events:

Multivariate Cox Proportional Hazards Model

![Graph showing cumulative incidence over months of follow-up with different quartiles labeled Q1, Q2, Q3, and Q4.](image-url)
2005: Asymptomatic 57M CTC – “negative” (no polyps)
Clinical: FRS=5% (low), BMI=27.3
Risk of CV event within 2/5/10 years: 18%/35%/62%
Risk of Death within 2/5/10 years: 8%/21%/37%
2008: Acute MI
2017: Death
## Diagnostic Performance for Predicting Fragility Fractures

<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>FRAX</td>
<td><strong>0.722</strong></td>
<td>0.702</td>
<td>0.651</td>
<td>0.657</td>
</tr>
</tbody>
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### Automated CT Biomarkers

#### Univariate

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<tbody>
<tr>
<td>L1 HU</td>
<td><strong>0.715</strong></td>
<td>0.637</td>
<td>0.634</td>
<td>0.634</td>
</tr>
<tr>
<td>Muscle HU</td>
<td>0.647</td>
<td>0.640</td>
<td>0.623</td>
<td>0.606</td>
</tr>
<tr>
<td>V/S Fat Ratio</td>
<td>0.506</td>
<td>0.513</td>
<td>0.518</td>
<td>0.522</td>
</tr>
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#### Multivariate

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<tr>
<td>L1 + Muscle HU</td>
<td><strong>0.725</strong></td>
<td>0.697</td>
<td>0.663</td>
<td>0.652</td>
</tr>
</tbody>
</table>
• **Time-to-Event Plots for Predicting Fragility Fractures:**
59F CT 2017
FRAX(any) = 6.7%
FRAX(hip) = 0.5%
Auto Bone = 63 HU
Auto Muscle = -1.7 HU

3 months later
Future Directions

• Ultimate goal is prospective risk profiling in practice
• Make results available at time of initial CT interpretation
• Dashboard readout and automated structured reporting
• Serve as an opportunistic supplement to CT interpretation
• Could potentially apply to any CT, regardless of indication
• This approach can also apply to thoracic CT
Summary

• Body CT is frequently performed for a wide variety of clinical indications
• Robust additional data often goes unused in practice
• These simple yet relevant measures of body composition can be automated for rapid & objective assessment
• Performance equals or exceeds clinical prediction
• Adding value to services we already provide is critical
Thank You