Low-Dose CT: Clinical Studies & the Radiologist Perspective

RD-ASiR
RD-MBIR
SD-FBP

RD=0.35 mSv (80% dose reduction)

Perry J. Pickhardt, MD
UW School of Medicine & Public Health
Low-Dose CT: Clinical Overview

• Is there any real clinical benefit to dose reduction?
• Given the perceived risk, ALARA applies
• Dose reduction targets should be indication specific and should not degrade performance
• Neither subjective nor objective measures of “image quality” necessarily equate with diagnostic accuracy in clinical practice
• Dose optimization is an iterative process
Risks of Low-dose Radiation

- HPS Position Statement:
  - 2010: “Below 50-100 mSv, risks of health effects are either too small to be observed or are nonexistent”
  - 2016: “Below levels of about 100 mSv above background from all sources combined, the observed radiation effects in people are not statistically different from zero”

- Experience with radiation workers, airline pilots, TB patients, radon levels, etc:
  - No increase in cancer rates from low-level exposures

- Is the “linear no-threshold” (LNT) theory valid?
Death from Breast Cancer in TB Patients Treated with Pneumothorax (n = 25,007)

Miller AB et. al. Mortality from Breast Cancer after Irradiation NEJM 1989; 321:1285-1289
Death from Breast Cancer in TB Patients Treated with Pneumothorax (n = 25,007)

Miller AB et. al. Mortality from Breast Cancer after Irradiation NEJM 1989;321:1285-1289
Proposition: Radiation hormesis should be elevated to a position of scientific respectability

Cancer Incidence

Induction of radiation damage

Subjecting Radiologic Imaging to the Linear No-Threshold Hypothesis: A Non Sequitur of Non-Trivial Proportion

Jeffry A. Siegel¹, Charles W. Pennington², and Bill Sacks³
Radiation Exposure from CT

- 2007 review article
  - >3200 citations per WoS; >5500 per Google Scholar
- ~100 million scans performed each year in the U.S.
- CT is one of the greatest advances in medicine
- Are we a victim of our own success?
Radiation Exposure from CT

“.... a reasonable estimate of excess lifetime cancers would be in the hundreds of thousands. According to our calculations, unless we change our current practices, 3 to 5 percent of all future cancers may result from exposure to medical imaging.”
Dose Reduction at CT

• Prudent given perception of risk → ALARA
• Ongoing interaction between radiologists, physicists, and technologists (& referring docs)
• Beyond subjective & objective measures of image quality, we must maintain diagnostic performance (and confidence)
• Need to take patient population and specific study indication into consideration
Methods for Reducing Dose at CT

- Limit to clinically indicated studies
- Consider alternative imaging tests (US or MR)
- Limit scan coverage
- Tube current modulation
- Decrease kV setting
- Beam-shaping filters
- Z-axis collimators
- View in thicker slices
- Iterative reconstruction algorithms
Clinical Studies Employing IR

• Simple literature search yields >10,000 articles
• Mix of technical and clinical papers
• Of the clinical papers:
  – The vast majority report on dose reduction and various improvements (subjective and/or objective) in image quality, noise, etc, but very few:
    – 1) Compare standard & low dose from same exam
    – 2) Report on diagnostic performance and confidence
      • At AJR, I won’t consider low-dose papers w/out this
UW Ultra-Low-Dose Body CT Trial

• Prospective trial (NIH NCI R01-CA169331)
  – Principal Investigators: Chen & Pickhardt

• IRB approved (recruitment ongoing)
  – Signed informed patient consent obtained
  – >200 patient studies performed to date

• Studies performed GE Discovery CT750 HD
UW Ultra-Low-Dose Body CT Trial

- **Basic protocol:**
  - “Ultra-low-dose” series obtained immediately after routine clinical series
  - Target dose reduction: 60-90% (indication specific)
  - Goal is to validate ultra-low-dose CT for clinical use

- **Multiple sub-cohorts:**
  - Unenhanced CT for urolithiasis
  - Unenhanced CT colonography
  - Contrast-enhanced CT (PV phase)
  - Low-contrast liver lesion detection in oncology pts
  - NHL surveillance

Goal: sub-mSv
Abdominal CT With Model-Based Iterative Reconstruction (MBIR): Initial Results of a Prospective Trial Comparing Ultralow-Dose With Standard-Dose Imaging

Mean Image Noise (SD of mean HU)

RD-FBP
RD-ASiR
RD-PICCS
RD-MBIR
SD-FBP

Mean Dose Reduction = 74%

p < 0.001
Abdominal CT With Model-Based Iterative Reconstruction (MBIR): Initial Results of a Prospective Trial Comparing Ultralow-Dose With Standard-Dose Imaging

Cumulative Lesion Detection (Pooled)

- RD-FBP
- RD-ASiR
- RD-PICCS
- RD-MBIR
- SD-FBP

p < 0.05
Abdominal CT With Model-Based Iterative Reconstruction (MBIR): Initial Results of a Prospective Trial Comparing Ultralow-Dose With Standard-Dose Imaging

IV-contrast CT
SD = 19.7 mSv
RD = 2.3 mSV
88% dose reduction
Unenhanced CT
SD = 1.7 mSv
LD = 0.35 mSv
79% dose reduction
Reduced Image Noise at Low-Dose Multidetector CT of the Abdomen with Prior Image Constrained Compressed Sensing Algorithm

Prospective evaluation of prior image constrained compressed sensing (PICCS) algorithm in abdominal CT: a comparison of reduced dose with standard dose imaging

Meghan G. Lubner,1 Perry J. Pickhardt,1 David H. Kim,1 Jie Tang,2 Alejandro Munoz del Rio,1 Guang-Hong Chen1,2

Prospective Trial of the Detection of Urolithiasis on Ultralow Dose (Sub mSv) Noncontrast Computerized Tomography: Direct Comparison against Routine Low Dose Reference Standard

B. Dustin Pooler, Meghan G. Lubner,* David H. Kim,† Eva M. Ryckman, Sri Sivalingam, Jie Tang, Stephen Y. Nakada, Guang-Hong Chen and Perry J. Pickhardt‡

From the Departments of Radiology (BDP, MGL, DHH, EMR, GHC, PJP), Urology (SS, SYN) and Medical Physics (JT, GHC), University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

Sub-milliSievert (sub-mSv) CT colonography: a prospective comparison of image quality and polyp conspicuity at reduced-dose versus standard-dose imaging

Meghan G. Lubner • B. Dustin Pooler • Douglas R. Kitchin • Jie Tang • Ke Li • David H. Kim • Alejandro Munoz del Rio • Guang-Hong Chen • Perry J. Pickhardt

Ultra-low (FBP)

Effective Dose = 0.3 mSv

Ultra-low (PICCS)

Effective Dose = 2.7 mSv

Standard (FBP)

Sub-milliSievert (sub-mm S) comparison of imaging at reduced-dose versus

Meghan G. Lubner • B. Dustin
Douglas R. Kitchin • Jie Tang
Alejandro Munoz del Rio • Gary Perry J. Pickhardt

Radiology
Prospective Trial of the Detection of Urolithiasis on Ultralow Dose (Sub mSv) Noncontrast Computerized Tomography: Direct Comparison against Routine Low Dose Reference Standard

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Total Prospective Stone Detection (Pooled)

LD FBP
LD ASiR
LD PICCS
LD MBIR
SD FBP

p < 0.05
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SD = 8.0 mSv
LD = 1.3 mSv
84% dose reduction
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SD = 8.0 mSv
LD = 1.3 mSv
84% dose reduction
Lymphoma Surveillance

Goal: 90% dose reduction; Chest <1 mSv; A/P ~1 mSv
Lymphoma Surveillance

Standard

Low-Dose

Goal: 90% dose reduction; Chest <1 mSv; A/P ~1 mSv
# Lymphoma Surveillance

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All Studies
Low-contrast Lesion Detection

- A more challenging but critical CT task
Low-contrast Lesion Detection

• A more challenging but critical CT task
Low-contrast Liver Lesion Detection

- Patient cohort:
  - 70 adults with non-liver primary malignancy
  - Mean age, 59.4 ± 12.8 yrs; 31 men, 39 women
  - Mean BMI, 27.7 ± 5.2 kg/m²
Low-contrast Liver Lesion Detection

Patient cohort:
- Primary tumors:
  - Colorectal (n=18), Pancreatic (n=14), Neuroendocrine (n=9), Breast (n=9), Lung (n=4), Esophagus (n=3), GIST (n=3), Other (n=10)
Low-contrast Liver Lesion Detection

**Patient cohort:**
- SD CT A/P with IV contrast in PVP for metastatic survey
  - Followed by RD scan in same breath hold (60-70% reduction)
  - SD-FBP compared with RD-FBP, RD-ASiR, RD-MBIR (Veo)
  - Transverse (axial) and coronal reconstructions

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**European Radiology**

*Prospective Evaluation of Reduced Dose Computed Tomography for the Detection of Low-Contrast Liver Lesions: Direct Comparison with Concurrent Standard Dose Imaging*

B. Dustin Pooler\textsuperscript{1} · Meghan G. Lubner\textsuperscript{1} · David H. Kim\textsuperscript{1} · Oliver T. Chen\textsuperscript{1} · Ke Li\textsuperscript{1,2} · Guang-Hong Chen\textsuperscript{1,2} · Perry J. Pickhardt\textsuperscript{1,3}
Low-contrast Liver Lesion Detection

• **CT interpretation:**
  – All series randomized and reviewed in isolation
    • SD and RD series
    • >1 week washout between sessions
  – 3 readers blinded to all clinical data (& other CT’s)
    • Radiology attending, fellow, and resident
  – Size, location, density recorded for all lesions ≥4 mm
    • 5 most concerning lesions recorded
  – Diagnostic performance per-lesion and per-patient
Low-contrast Liver Lesion Detection

- CT interpretation:
  - 5-point score for likelihood of malignancy
    - 1 = definitely benign
    - 2 = likely benign
    - 3 = indeterminate
    - 4 = likely malignant
    - 5 = definitely malignant
  - 3-point score for diagnostic confidence
    - 1 = low confidence
    - 2 = moderate confidence
    - 3 = high confidence
Low-contrast Liver Lesion Detection

• **Reference standard (ground truth):**
  - All series reviewed in concert with relevant prior and subsequent imaging (CT, MR, PET/CT, etc) and clinical data by 2 abdominal radiologists
    - Mean of 5.3 CT scans over 2.1 years prior to index study
    - Mean of 4.3 CT scans over 1.6 years following index study
  - Each liver lesion classified

• **Mean effective dose:**
  - Standard dose series = 5.8 ± 4.0 mSv
  - Reduced dose series = 2.0 ± 1.4 mSv
  - Mean dose reduction = 64%
## Low-contrast Liver Lesion Detection

<table>
<thead>
<tr>
<th></th>
<th>SD-FBP</th>
<th>RD-FBP</th>
<th>RD-ASIR</th>
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<tr>
<td><strong>Sensitivity</strong></td>
<td>0.91 [0.84-0.99]</td>
<td>0.79 [0.68-0.90]</td>
<td>0.84 [0.75-0.94]</td>
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<tr>
<td><strong>Specificity</strong></td>
<td>0.78 [0.71-0.84]</td>
<td>0.75 [0.68-0.82]</td>
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<td>0.68 [0.61-0.75]</td>
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<tr>
<td><strong>PPV</strong></td>
<td>0.60 [0.50-0.71]</td>
<td>0.54 [0.43-0.65]</td>
<td>0.56 [0.45-0.66]</td>
<td>0.49 [0.40-0.59]</td>
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<tr>
<td><strong>NPV</strong></td>
<td>0.96 [0.93-0.99]</td>
<td>0.91 [0.85-0.95]</td>
<td>0.93 [0.88-0.97]</td>
<td>0.92 [0.87-0.97]</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td>0.81 [0.76-0.87]</td>
<td>0.76 [0.70-0.82]</td>
<td>0.78 [0.72-0.83]</td>
<td>0.72 [0.66-0.78]</td>
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## Low-contrast Liver Lesion Detection

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<td>54%</td>
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<td><strong>Accuracy</strong></td>
<td>81%</td>
<td>76%</td>
<td>78%</td>
<td>72%</td>
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</table>
Low-contrast Liver Lesion Detection

Per-Patient Performance by Reconstruction Algorithm (with 95% CI)

- Sensitivity
- Specificity
- PPV
- NPV
- Accuracy

Legend:
- SD-FBP
- RD-FBP
- RD-ASIR
- RD-MBIR
## Low-contrast Liver Lesion Detection

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<tr>
<td><strong>True Positive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Malignant</td>
<td>2.89</td>
<td>2.77</td>
<td>2.79</td>
<td>2.87</td>
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<tr>
<td><strong>p</strong></td>
<td>0.016</td>
<td>0.038</td>
<td>0.596</td>
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<tr>
<td>Benign</td>
<td>2.96</td>
<td>2.96</td>
<td>2.95</td>
<td>2.91</td>
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<tr>
<td><strong>p</strong></td>
<td>0.922</td>
<td>0.711</td>
<td>0.215</td>
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<tr>
<td><strong>False Positive</strong></td>
<td>2.43</td>
<td>1.64</td>
<td>2.00</td>
<td>1.69</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td>0.009</td>
<td>0.141</td>
<td>0.001</td>
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<tr>
<td><strong>False Negative</strong></td>
<td>3.00</td>
<td>2.33</td>
<td>2.50</td>
<td>3.00</td>
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<tr>
<td><strong>p</strong></td>
<td>0.495</td>
<td>0.423</td>
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<tr>
<td><strong>True Negative</strong></td>
<td>2.70</td>
<td>1.98</td>
<td>1.98</td>
<td>1.62</td>
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<tr>
<td><strong>p</strong></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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Low-contrast Liver Lesion Detection

False Negative at RD
Low-contrast Liver Lesion Detection

False Positive at RD-MBIR
Clinical Dose Initiatives at UW

- “Master Protocol” concept
  - Partnership with GE Healthcare
  - Clinically-validated and dose-optimized protocols
Clinical Dose Initiatives at UW

- Auto-QA system
Conclusions

• Aggressive dose reduction at CT is achievable
  – Especially for certain tasks (CTC, urolithiasis, NHL f/u)
  – Sub-mSv scanning possible

• Caution warranted for low-contrast lesion search
  – Diagnostic performance can fall off rapidly at low dose

• Critical to tailor dose reduction goals to both the clinical task and the patient cohort
  – ALARA concept remains a central tenet
  – Critical to maintain diagnostic ability as treatment decisions greatly outweigh the unproven theoretical harm related to low-level radiation
  – Iterative QA can effectively inform CT protocols