Tips, Tricks and Pitfalls in Body Oncology CT

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Disclosures DS

• Research agreement
  – GE Health Care

• Advisory Board
  – Allena Pharmaceuticals

• Royalties
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Disclosures AG

- Siemens Speaker’s Bureau
- Consultant
  - Takeda Pharmaceuticals, Inc.
- Expert Witness
  - DOJ
  - Rice, Dolan, Kershaw
Learning Objectives

1. Review the Role of CT in Oncology
2. Discuss common pitfalls and limitations
3. Provide approaches with CT protocols
4. Introduce Recent Advances in CT
Cancer Statistics, 2016
Cancer Statistics, 2016

### Estimated Deaths

<table>
<thead>
<tr>
<th>Cause</th>
<th>Males</th>
<th>%</th>
<th>Females</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>85,920</td>
<td>27%</td>
<td>72,160</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>26,120</td>
<td>8%</td>
<td>40,450</td>
<td>14%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>26,020</td>
<td>8%</td>
<td>23,170</td>
<td>8%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>21,450</td>
<td>7%</td>
<td>20,330</td>
<td>7%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>16,260</td>
<td>6%</td>
<td>14,240</td>
<td>5%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>14,130</td>
<td>4%</td>
<td>10,470</td>
<td>4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>12,720</td>
<td>4%</td>
<td>10,270</td>
<td>4%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>11,820</td>
<td>4%</td>
<td>8,690</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>11,520</td>
<td>4%</td>
<td>8,630</td>
<td>3%</td>
</tr>
<tr>
<td>Brain &amp; other nervous system</td>
<td>9,440</td>
<td>3%</td>
<td>6,610</td>
<td>2%</td>
</tr>
<tr>
<td><strong>All Sites</strong></td>
<td>314,290</td>
<td>100%</td>
<td>261,400</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Top 5 culprits**

- Lung and Bronchus
- Prostate
- Colon and rectum
- Breast
- Pancreas

- ~46% cancer deaths
Pancreas Cancer Death Prediction-2025

Recorded and projected number of pancreatic and breast cancer deaths in the EU

- Pancreatic Cancer
- Breast Cancer

FAST FORECAST FOR 2025

1. Globally, more trips will be made using car sharing programs than privately owned cars.
2. 30% of corporate audits will be performed by artificial intelligence.
3. Norway bans new sales of gas-powered cars, giving preference to electric cars.
5. Prescription drugs can be brewed at home.
6. Electronic devices can be charged using Wi-Fi.
7. Blood test detecting any virus you have had becomes widespread.
8. Severe food allergies become treatable.
9. Male contraceptive pills become widely available.
10. Hepatitis C is eradicated.
11. Drone usage in agriculture is adopted globally.
12. U.S. military uses electricity to stimulate soldiers' brains, increase reaction times and improve attention spans.
13. New device diagnoses pancreatic cancer earlier and faster.
14. Robotic, mind-controlled prosthetics become widely available.
# Role of CT in Oncology

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Local staging</th>
<th>Metastasis staging</th>
<th>Re-staging</th>
<th>Screening</th>
<th>Sensitivity for staging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>77%</td>
</tr>
<tr>
<td>Prostate</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>78%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>65-91%</td>
</tr>
<tr>
<td>Breast</td>
<td>-</td>
<td>++</td>
<td>+++</td>
<td>-</td>
<td>80-85%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>No Screening</td>
<td>80-90%</td>
</tr>
</tbody>
</table>

Infact, NCCN even suggests optimal CT imaging protocols in its guidelines.
Management Algorithm

SUSPECTED PANCREATIC CANCER

IMAGING

Group 1
+METASTASES
Chemotherapy

Group 2
•NO METASTASES
•LADC/Borderline
Chemoradiation +/- IORT

Group 3
•NO METASTASES
•No/Abutment
Surgery

AASLD 2010 Guidelines for HCC Management

Liver nodule

< 1 cm
- Repeat US at 3 months
  - Growing/changing character
    - Investigate according to size
  - Stable

> 1 cm
- 4-phase MDCT/ dynamic contrast enhanced MRI
  - Arterial hypervascularity AND venous or delayed phase washout

Other contrast enhanced study (CT or MRI)
- Yes
  - Arterial hypervascularity AND venous or delayed phase washout
- No
  - Biopsy
Monitoring Response to Chemotherapy

Conventional method of monitoring treatment response is change in tumor size

**RECIST 1.0**
- 10 Target Lesions (>1-2 cm)
- 5 max in an organ
- Non-target lesions

**RECIST 1.1**
- 5 Target Lesions (>1 cm)
- 2 max in an organ
- Short-axis of LN>15 mm

Therasse P et al. JNCI 2000
Therasse P et al. EJC 2006
Eisenhauer EA et al. EJC 2009

RECIST = Response Evaluation Criteria in Solid Tumors
WHO = World Health Organization
Clinical Decisions from Quantitative Imaging

**Problem**

Measure = 7 ± 6

**Goal**

Measure = 7 ± 2

**Analysis**

Sources of Variance

Differences in:
- Patient Handling
- Acq. Protocols
- Reconstruction
- Segmentation

**Solution**

When all participating actors conform...

- Protocol Reqs
- Recon Reqs
- Resolution Reqs
- Noise Reqs
- Segment. Reqs
- Patient Prep & Operation Reqs
- Segment. Reqs
- Calibration Reqs

RSNA 2016
QIBA Process

**Academic Research**
- Select a Biomarker

**Clinical Trials & Clinical Practice**
- Coordinate Groundwork
- Draft Profile
- Publish Profile
- Validate Equipment & Sites

- **Apply selection criteria:** Translational, Transformational, Practical, …
- **Draft Initial Performance Claim**
- **Identify** significant sources of variance
- **Estimate** achievable repeatability and accuracy
- **Validate** underlying assumptions and mechanisms
- **Determine** details critical to specify in the Profile
- **Initiate** regulatory engagement

- **Document** the agreed parameters and procedures
- **Specify** details necessary to be robust in general use
- **Drive out** any impeding variance and complexity
- **Make** details stable, clear, implementable, testable

- **Make** Profile available to the community
- **Engage** with sites/trials adopting the Profile
- **Converge** practice; reduce gratuitous variation

- **Test** conformance with QIBA Profile specifications
- **Publish** validated products/sites
QIBA Biomarker Selection

- Dr. Dan Sullivan, founding chairman of QIBA, proposed 5 characteristics:
  - Translational — ready to move from research into clinical care
  - Transformational — considerable impact on public health
  - Feasible — good chance of success in a reasonable time frame
  - Practical — cost-effectively use existing resources where possible
  - Collaborative — existing interest across stakeholders

- QIBA's job is not exploration; QIBA's job is industrialization
- Make a biomarker robust, reliable and available
- Bring it “the last mile” into clinicians hands where it can help patients
- Too few biomarkers reach that point

_RSNA 2016_
**Claims:**

"95% probability that measured change -25% to +30% encompasses the true tumor volume change…"

**Requirements:**

**Actor Table**
- Acquisition Device
- Measurement Software
- Radiologist

**Activity Definitions**
- Product Validation
- Calibration / QA
- Patient Preparation
- Image Acquisition / Recon
- Post-Processing
- Analysis / Measurement

**Assessment Procedures:**
- Image Noise and Resolution
- Tumor Volume Change Variability
- Site Performance

**User View**

Will it do what I need?

What/who do I need involved?

What do I have to do to achieve the Claims? (requirement checklists: procedures, training, performance targets)

How will I be tested?

**Vendor View**

Why do you want me to do this?

Which of my products are affected?

What do I have to implement; (requirement checklists: features, capabilities, performance targets)

How will I be tested?

RSNA 2016
QIBA Claim Template

1. Type of Claim
   - X-sectional
   - Longitudinal

1a. Same measuring system at all time-points?
   - Yes
   - No

2. Characterize Bias
   - Negligible
   - Known
   - Unknown

3. Characterize wSD or wCV
   - Constant wSD
   - Constant wCV
   - Multiple wCVs

Scenario A: Constant wSD; negligible bias: Construct 95% CI from wSD
Scenario B: Constant wSD; bias known: Construct 95% CI from TDI and wSD
Scenario C: Constant wCV; negligible bias: Construct 95% CI from wCV
Scenario D: Constant wCV; bias known: Construct 95% CI from TDI and wCV
Scenario E: Multiple wCVs; negligible bias: Construct 95% CIs in multiple claims from different wCVs
Scenario F: Multiple wCVs; bias known: Construct 95% CIs in multiple claims from different TDIs
Scenario G: Constant wSD; negligible bias: Construct 95% CI from wSD & estimated RDC
Scenario H: Constant wCV; Construct 95% CI from wCV & estimated RC
Scenario I: Multiple wCVs; Negligible bias: Construct 95% CIs in multiple claims from different wCVs & estimated RDCs
Scenario J: Multiple wCVs; Negligible bias: Construct 95% CIs in multiple claims from different TDIs & estimated RDCs
Scenario K: Constant wCV; bias known: Construct 95% CI from TDI, wSD & estimated RDC
Scenario L: Constant wCV; Construct 95% CI from wCV & estimated RDC
Scenario M: Constant wSD; bias known: Construct 95% CI from TDI, wSD & estimated RDC
Scenario N: Constant wCV; bias known: Construct 95% CI from TDI, wCV & estimated RDC
Scenario O: Multiple wCVs; bias known: Construct 95% CIs in multiple claims from different TDIs & estimated RDCs
19 Profiles total (4 CT, 3 NM, 9 MR, 3 US)

Technically Confirmed Stage:
- FDG-PET/CT SUV as an Imaging Biomarker for Measuring Response to Cancer Therapy (v1.05)*

Publicly Reviewed (Consensus) Stage and Posted:
- CT Tumor Volume Change (v2.2) for tumor response*
- DCE-MRI Quantification (v1.0) for tumor response

In Public Comment and Consensus Development Stage:
- CT: Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening Quantification
- SPECT: Quantifying Dopamine Transporters with 123-Iodine labeled Ioflupane in Neurodegenerative Disease
- DW-MRI for tumor response

*Highlighted on Cancer Moonshot website
Single energy CT

Image of the scanned object is obtained based on the photon attenuation of its materials

• X-ray attenuation is different by different materials
• Clinical practice: Scanned bodies are composed of multiple materials
  • Material attenuation depends on the energy of the photon

Single X-ray source

• 70 to 140 kVp:
• 120 kVp (default)
• 100 kVp (arterial phase)
• Helical mode

Single sinogram

Lesion to background contrast
Role of Contrast Media
Oncology CT Protocol

- Oral and IV CM
- Reformats
- +/- 3D
Role of OCM: Luminal Vs. Extraluminal
Oral CM Protocols-Luminal and Extraluminal disease
OCM-Duodenum and Ampulla

Megibow et al. Radiology 2005;238:87-95
OCM Advised for Cancer Protocols

- Ovarian Ca
- GIT (Stomach, CRC, Bowel)
- Bile Duct
- Pancreas
- Melanoma
- Lung
- Breast
IV CM and Tissue Enhancement
Injection Rate and Scan Delay Timing is Critical

Contrast injection 300 mg I/ml @ 5cc/sec

Lesion “Washout”
Compared to liver parenchyma:
– Hypervascular on HAP
– Hypovascular on PVP/Equil

• Usually a “Ominous” finding: >90% specific

– HCC
– Mets: NET, RCC, melanoma
– Adenoma (HCA)

Delayed hypointensity (washout pattern) improves specificity
CTA-Pre-surgical planning
Optimized CM Injection Protocol
Abdomen CECT/CTA-Scan delay
Test Bolus (20 mL) or Auto Triggering

- **tCMT (100 HU)+8s**
  Arterial Mapping/ Assessment of hypervascular pancreatic lesions as neuroendocrine

- **tCMT (100 HU)+15s**
  Late arterial phase- Assessment of hypervascular liver lesions.

- **tCMT (100 HU)+25s**
  Pancreatic Phase- Assessment of hypovascular pancreatic lesions, degree of vascular encasement

- **tCMT (100 HU)+50s**
  Portal venous phase- Hypodense liver lesions, portal invasion, hepatic veins assessment / Assessment perivenous pancreatic tumor extension/CTE/Routine Abd

- **tCMT + 3-5 min**
  Delayed-Equilibrium phase –Lesion characterization Hemangioma/tumor (fill-in or wash out)

- **tCMT +10-15 min**
  Delayed post-equilibrium – Bladder Ca
  No longer needed for Cholangio
IV Contrast Injection Protocols

**Diagnostic CECT**
- 80-100 mL @ 2 mL/sec
- 100 mL @ 3 mL/sec 50-
- 65 mL @ 2 mL/sec
- 80-120 mL @ 3 mL/sec

**CTA**
- 85-100 mL @ 4 mL/sec Aorta (50 HU)
- 110 mL @ 4 mL/sec 22 delay
- > 250 lbs. @ 4 mL/sec 30 delay
- 90-110 mL @ 3.5-4 mL/sec Aorta (150 HU)

MDCT-16 and beyond

CT/CTA in Patients with Larger Body Habitus (BMI >45)

- Increased central blood volume
- Increase CM volume by 20 mL
- Increase scan delay by additional 5-8 sec
“For Oncology CT, Prioritize Image Quality”

<table>
<thead>
<tr>
<th>Dose</th>
<th>-30%</th>
<th>-50%</th>
<th>-70%</th>
</tr>
</thead>
</table>

- 90%
Controversy...

<table>
<thead>
<tr>
<th>Studies supporting increased CANCER risks from CT</th>
<th>Studies offering divergent views on the radiation risks from CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miglioretti DL, et al.. <em>JAMA Pediatr</em> 2013. <em>4 Million pediatric CTs are projected to cause 4870 future cancers.</em></td>
<td><em>Health Physics Society Website. Accessed 2013. Quantification of radiation risks should not be performed for individual doses &lt; 50-100 mSv as the risks are too small.</em></td>
</tr>
</tbody>
</table>
Risk of Radiation Induced Cancer in Young Adults from Body CT

• 21,945 young adults 18-35 had body CT for cancer and trauma between 2003-2007

• Risk of death from the morbidity of underlying disease is a magnitude higher than death from long term radiation induced cancer

• 95% of patients with cancer died within 5 years of presenting with diagnosis

Zondervan RL et al. Radiology 2015
<table>
<thead>
<tr>
<th>Activity</th>
<th>Risk of dying per 1000 people</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer (non-radiation induced)</td>
<td>228</td>
</tr>
<tr>
<td>Motor vehicle accident</td>
<td>12</td>
</tr>
<tr>
<td>Married to a smoker</td>
<td>10</td>
</tr>
<tr>
<td>US average radon level in home</td>
<td>3</td>
</tr>
<tr>
<td>Drowning</td>
<td>0.9</td>
</tr>
<tr>
<td>Abdomen CT</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Caution in LG-Lymphomas, Testicular Ca, Cystic Lesions, WDD-NET

Courtesy Amy Hara MD, Mayo Clinic, Scottsdale, AZ
Reducing Dose and Improving Lesion Conspicuity with Low kV CT

Stiller et al, Eur J Radiol. 2011
Perisinakis et al, Br J Radiol. 2011
Utsunomiya et al, Eur Radiol. 2010
Marin et al, Radiology. 2010
Hunsaker AR. AJR. 2010
Godoy MC. Eur J Radiol. 2010
Feuchter GM. Eur J Radiol. 2010
Sahani DV. AJR 2007
Iterative Reconstruction Techniques

- ASIR, GE Healthcare
- iDose$^4$, Philips Healthcare
- AIDR, Toshiba
- SAFIRE, Siemens Healthcare

ADMIRE, advanced modeled iterative reconstruction; AIDR, adaptive iterative dose reduction; ASIR, adaptive statistical iterative reconstruction; IMR, iterative model reconstruction; IRT, interstitial irradiation; MBIR, model-based iterative reconstruction; SAFIRE, sinogram affirmed iterative reconstruction.

CTDIvol: 6.1 6 mGy

120 kV

CTDIvol: 4.80 mGy

100 kV
## MDCT Oncology Protocol

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Arterial</th>
<th>Venous</th>
</tr>
</thead>
<tbody>
<tr>
<td>DC (mm)</td>
<td>64x0.625</td>
<td>64x0.625</td>
</tr>
<tr>
<td>Table feed mm/sec</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>Pitch</td>
<td>1-1.5</td>
<td></td>
</tr>
<tr>
<td>Slice arterial (mm)</td>
<td>2-3</td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>Coronal and Sag Recons 2-3</td>
<td>Coronal and Sag Recons 2-3</td>
</tr>
<tr>
<td>Delay Arterial</td>
<td>Bolus track /automated trigger</td>
<td></td>
</tr>
<tr>
<td>Delay Venous (sec)</td>
<td></td>
<td>65-70 sec</td>
</tr>
</tbody>
</table>
# Abdomen CTA Protocol

<table>
<thead>
<tr>
<th>Parameters</th>
<th>64-channel</th>
<th>16-channel</th>
</tr>
</thead>
<tbody>
<tr>
<td>DC (mm)</td>
<td>0.625</td>
<td>0.625</td>
</tr>
<tr>
<td>T-Speed (mm/sec)</td>
<td>39</td>
<td>18.75</td>
</tr>
<tr>
<td><strong>Slice arterial (mm)</strong></td>
<td>1.25</td>
<td>1.25</td>
</tr>
<tr>
<td><strong>Slice venous (mm)</strong></td>
<td>2.5-5</td>
<td>2.5-5</td>
</tr>
<tr>
<td><strong>Delay Arterial</strong></td>
<td>Bolus track /automated trigger Threshold 125-150 HU</td>
<td></td>
</tr>
<tr>
<td><strong>Delay Venous (sec)</strong></td>
<td>60 sec</td>
<td>60 sec</td>
</tr>
</tbody>
</table>
## Is Pelvic CT Required in Cancer Subjects?

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Reference</th>
<th>Patients</th>
<th>Pelvic Spread</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Ayhan et al. 2005 Curtin et al. 1994</td>
<td>154, 121</td>
<td>35 (23%), 31 (25%)</td>
</tr>
<tr>
<td>Lung</td>
<td>Sereno et al. 2013. Satoh et al. 2001</td>
<td>325, 1041</td>
<td>2.7-16%, 12 (&lt;1%)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Thomassen et al. 2013 Sadeghi et al. 2000</td>
<td>2924</td>
<td>265 (9%), 15.6%</td>
</tr>
</tbody>
</table>

Pelvic CT has low yield for staging- pancreas NET, Pancreas IPMN/MCN, HCC, Lung Ca, Mesothelioma, Thyroid Ca, Oral Ca..
Errors in Oncology CT

• Halo effect due to the presence of a more conspicuous lesion
• Lesions located in anatomic sites that may be commonly overlooked
• Improper CT window settings
• Lack of pertinent patient history
• Atypical manifestation of a disease process
• Misread the organ of origin of a lesion

A. Pinto, et al, Semin Ultrasound CT MRI 2012;33:275-9
Errors in CT - Distractors
Presence of a more conspicuous lesion

4-10% risk of PDAC in BD-IPMN

Yamaguchi K et al. Pancreatology 2002; 2:484-490
Yamaguchi K et al. Pancreas 2011; 40:571-580
Tanno S et al. Pancreas 2010; 39:36-40
Tanaka S et al. Radiology 2010; 254:965-972
Matsubara S et al. Pancreas 2012; 41:1241-1246
Errors in CT-Distractors
Presence of a more conspicuous lesion

BD-IPMN

Distinct PDAC

4%-10% of patients with BD-IPMN are found to have concurrent PDAC

**Incidental pancreatic cysts are associated with 3X increased risk of subsequent PDAC**

Yamaguchi K et al. Pancreatology 2002; 2:484-490
Yamaguchi K et al. Pancreas 2011; 40:571-580
Tanno S et al. Pancreas 2010; 39:36-40
Tanaka S et al. Radiology 2010; 254:965-972
Lesion located in anatomic sites that may be commonly overlooked

Tail of the pancreas

- Left lobe of liver extending beyond spleen
- Dome and Tip of Liver - Spleen
- Stomach and proximal small bowel
- Pelvic floor
- Abdomen wall, paraspinal and gluteal muscles
Isodense Lesions - Window Setting and Secondary Signs

Sensitivity up to 90% for detection
Accuracy 80%-90% for staging

CT Sensitivity for < 2cm lesions 58-62%

Duct “Cut off”: Ominous Sign

Gangi et al AJR 2002
Error in Reporting Terminologies

- **Abutment**
  - Tumor-vessel
  - \(< 180^\circ\)

- **Encasement**
  - Tumor-vessel
  - \(> 180^\circ\)

Pitfall in Local Staging with CT

Tumor extent vs inflammation
Soft tissue around vessel (>25%)
Lack of pertinent patient history
Role of chest CT
Small Lesion Detection CT Vs. MR

CT understages (>25% complete response @ CT macroscopic disease @ surgery)
Subtraction CT for Renal Mass Evaluation
<table>
<thead>
<tr>
<th></th>
<th><strong>WHO</strong></th>
<th><strong>RECIST</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of metric</strong></td>
<td>Bi-dimensional (CP)</td>
<td>Uni-dimensional</td>
</tr>
<tr>
<td></td>
<td>MAD X LPD</td>
<td>Total disappearance</td>
</tr>
<tr>
<td><strong>CR</strong> (Complete Response)</td>
<td>Total disappearance</td>
<td></td>
</tr>
<tr>
<td><strong>PR</strong> (Partial Response)</td>
<td>50% decrease</td>
<td>30% decrease</td>
</tr>
<tr>
<td><strong>PD</strong> (Progressive Disease)</td>
<td>25% increase New Lesion</td>
<td>20% increase New Lesion</td>
</tr>
<tr>
<td><strong>SD</strong> (Stable disease)</td>
<td>Neither PR or PD criteria met</td>
<td>Neither PR or PD criteria met</td>
</tr>
</tbody>
</table>
CT Image Biomarker

CT

Size

Volume

Density

Texture

Viability

How I Approach Oncology A+P CT
Evolving role of CT...

**Diagnosis**
- Detection
- Characterization
- Treatment plan

**Biomarker**
- Biomarker –
  - Response
  - Plaque characterization

**Safety**
- Contrast Media
  - Renal Insufficiency
- Radiation dose
  - Novel image processing techniques
Thank you...