Imaging for MIBC Trials: A Radiologist's Perspective

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Disclosures and Disclaimers

- No financial disclosures
- The content of this presentation is the responsibility of the presenter and does not necessarily represent the official views of the National Institutes of Health

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Objectives

- Review the recommendations from the panel for defining radiographic eligibility for adjuvant clinical trials in MIBC
- Review the recommendations from the panel for defining disease recurrence during an adjuvant clinical trial for MIBC
- Discuss potential future roles for imaging in the care of patients with MIBC

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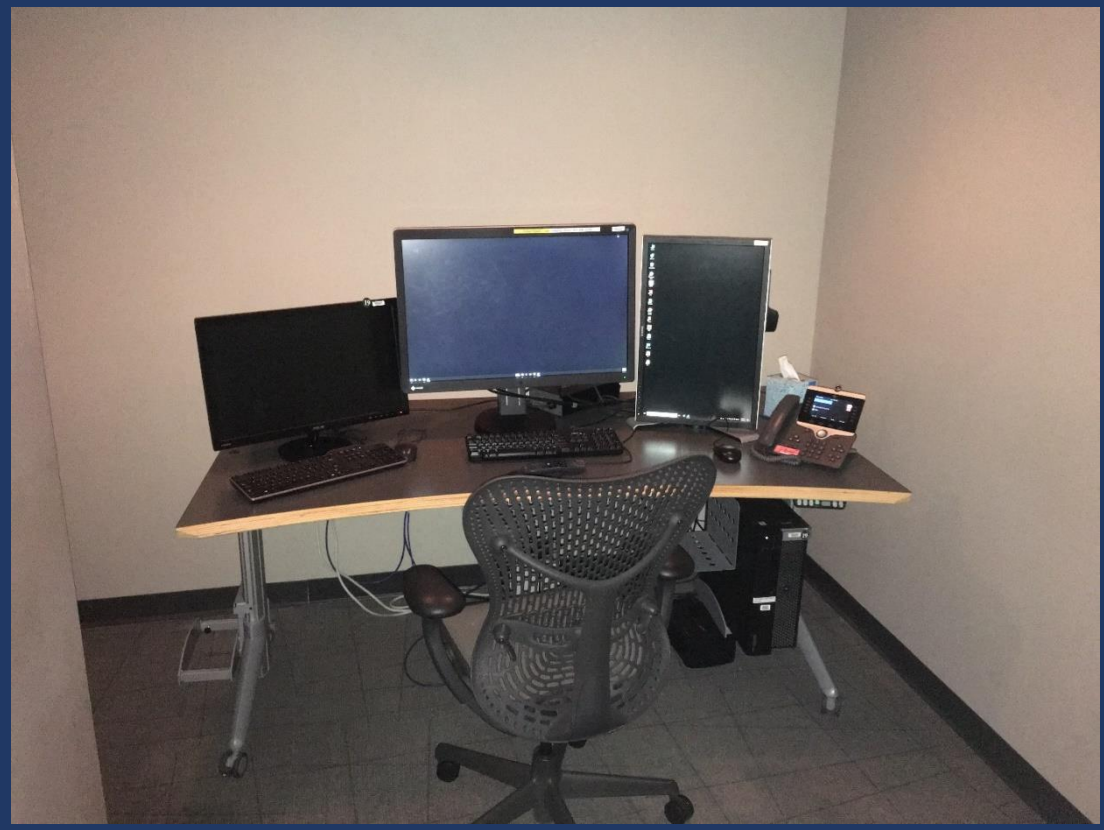
Facts about Radiologists: The Good

- We are there to help
- Most of us are smart
- We have lots of training
- Our technology is constantly improving making our images amazing
- We are an independent voice objectively describing what we see
- We are trained in radiologic pathology



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Facts about Radiologists: The Bad

- Our technology is constantly changing, making much of our research outdated or obsolete
- We are not pathologists, so we describe what we see but often can't be sure
  - Clinical correlation anyone?

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We are not all the same!

- Radiologist A: very sensitive
  - Over callers
  - “I don’t want to miss anything so I will call that 7 mm LN a possible metastasis and recommend follow-up”
- Radiologist B: favors specificity over sensitivity
  - Under callers
  - “That 1.4 cm lymph node is probably just reactive, let’s give the patient a chance to declare themselves”

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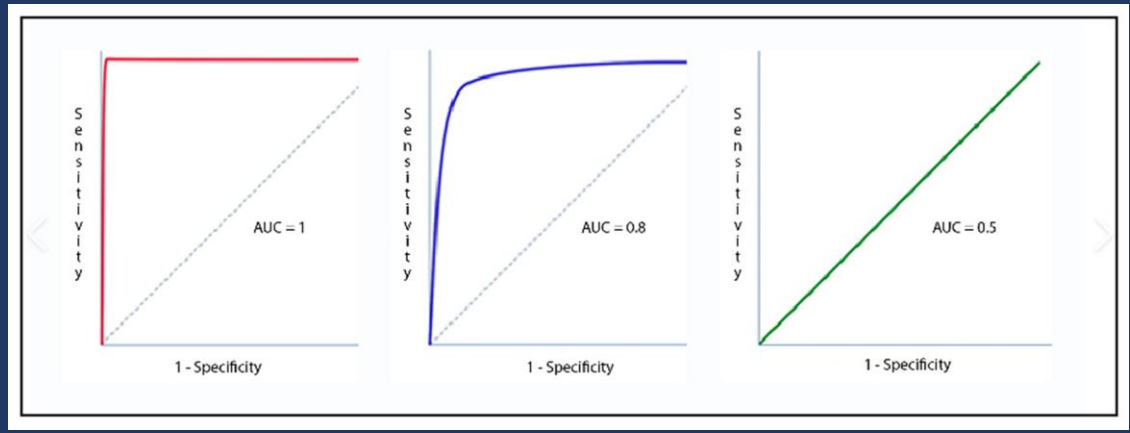
- Radiologist C: follows standard teaching, uses best available data
  - “I use 1 cm short axis as my cut-off for LN metastases given its balance of sensitivity and specificity”

Helping Radiologist C

- Participating in interdisciplinary discussions, such as the FDA/NCI panel, gives Radiologist C a fighting chance by making standards available
- But as we move to a discussion of the standards that the panel suggests, please keep in mind that choice of standards affects the sensitivity and specificity of our imaging examinations



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https://www.cienciasinseso.com/en/category/epidemiology/

ROC curve

- Lymph node:
  - Short axis > 0.5 cm: high sensitivity, low specificity
  - Short axis > 1.5 cm: low sensitivity, high specificity
  - Short axis ≥ 1 cm: good balance of sensitivity and specificity
- Lack of data on exact sensitivity and specificity numbers for lymph nodes by cancer type and nodal stations

Objective 1: Defining Radiographic Eligibility

- Indication: MIBC. Evaluate prior to clinical trial enrollment
- Goal: Show that this patient has no evidence of disease (NED) prior to enrolling in an adjuvant trial

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General Radiology Practices

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What test to order?

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What test to order?

- CT of the chest, abdomen and pelvis with IV contrast within 4 weeks prior to trial enrollment
- Why?
  - Widely available
  - Technique can be standardized
  - Able to demonstrate the common manifestations of recurrent or metastatic MIBC

Eur J Radiol. 2017;97:119-130.
Urology. 1980;16(2):142-144.
Cancer Imaging. 2003;3(2):96-100.

How should the test be done?

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How should the test be done?

- Trials should adhere to imaging acquisition, display and radiologic interpretation technique as advised by the Quantitative Imaging Biomarker Alliance (QIBA)
- Why?
  - Affects rate of lesion detection
  - Affects size measurements

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Radiology. 2003;226(1):231-234.
Radiology. 2005;234(3):934-939.

What about MRI and PET-CT?

- Although data show that MRI and PET-CT offer high specificity or negative predictive value, the differences are not substantial when compared directly to CT
- MRI and PET remain problem solving tools

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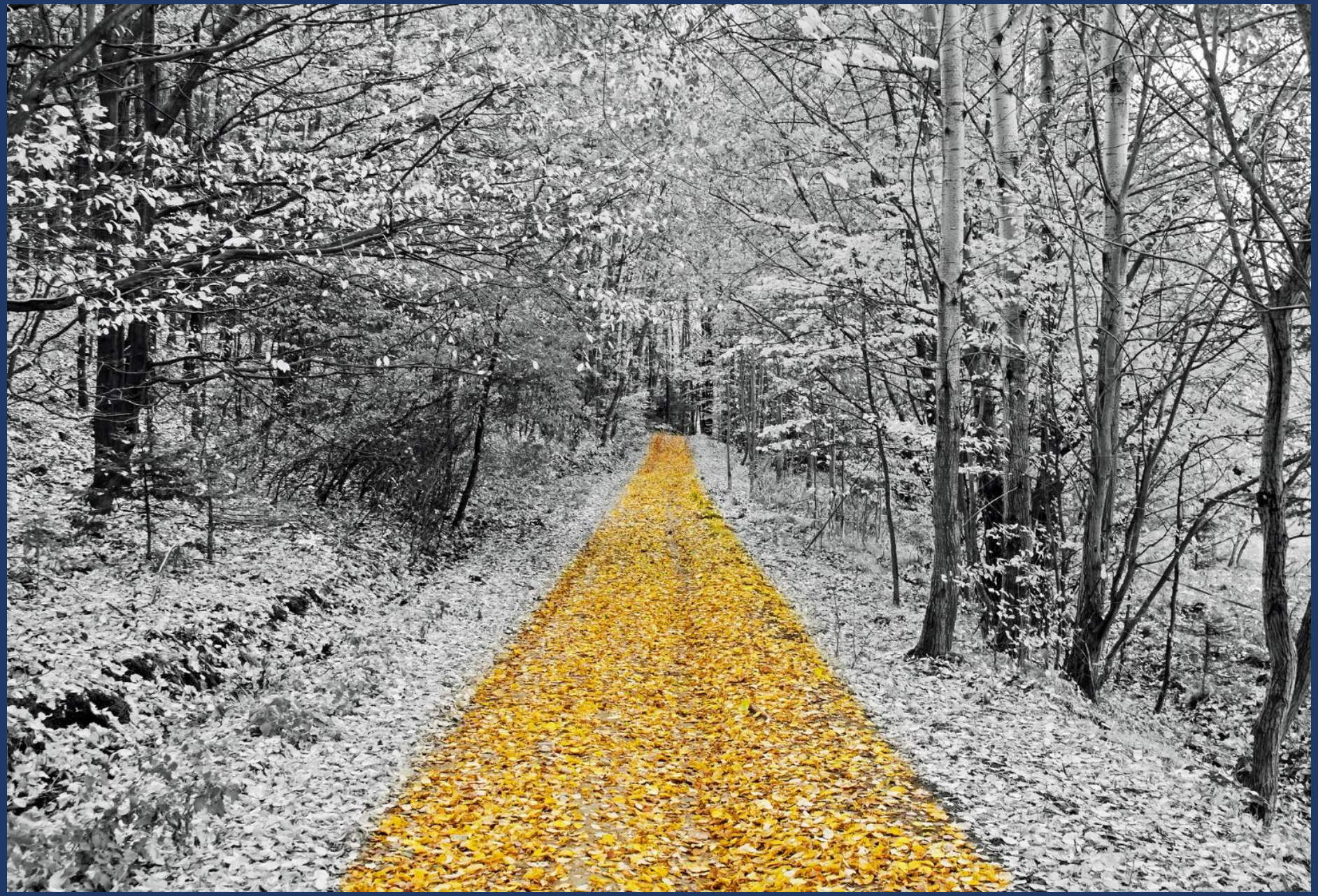
Curr Opin Urol. 2011;21(5):393-397.



Old Gold

- All prior relevant imaging examinations should be systematically archived
- Why?
  - Useful in clarifying equivocal findings at enrollment
    - 1.2 cm lung nodule
    - 2.1 cm hypodense liver lesion
    - 1.1 cm sclerotic bone lesion

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Interpretation Recommendations

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General Recommendation 1

- If there is an indeterminate lesion without prior studies available, the lesion should be considered benign if it is < 1 cm
  - 1 cm represent general consensus in radiology practice as to what is reasonably sensitive and specific for malignancy
  - 1 cm is the size needed to accurately characterize the density of a lesion at CT

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Eur J Radiol. 2017;97:119-130.
Radiology. 2010.;254(1):31-46.

General Recommendation 2

- An indeterminate lesion ≥ 1 cm should be regarded as suspicious for malignancy and should be further evaluated prior to trial enrollment
- Options for further evaluation include:
  - Customized radiologic work-up
  - Repeat CT imaging after an appropriate follow-up interval
  - Biopsy

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Site Specific Examples

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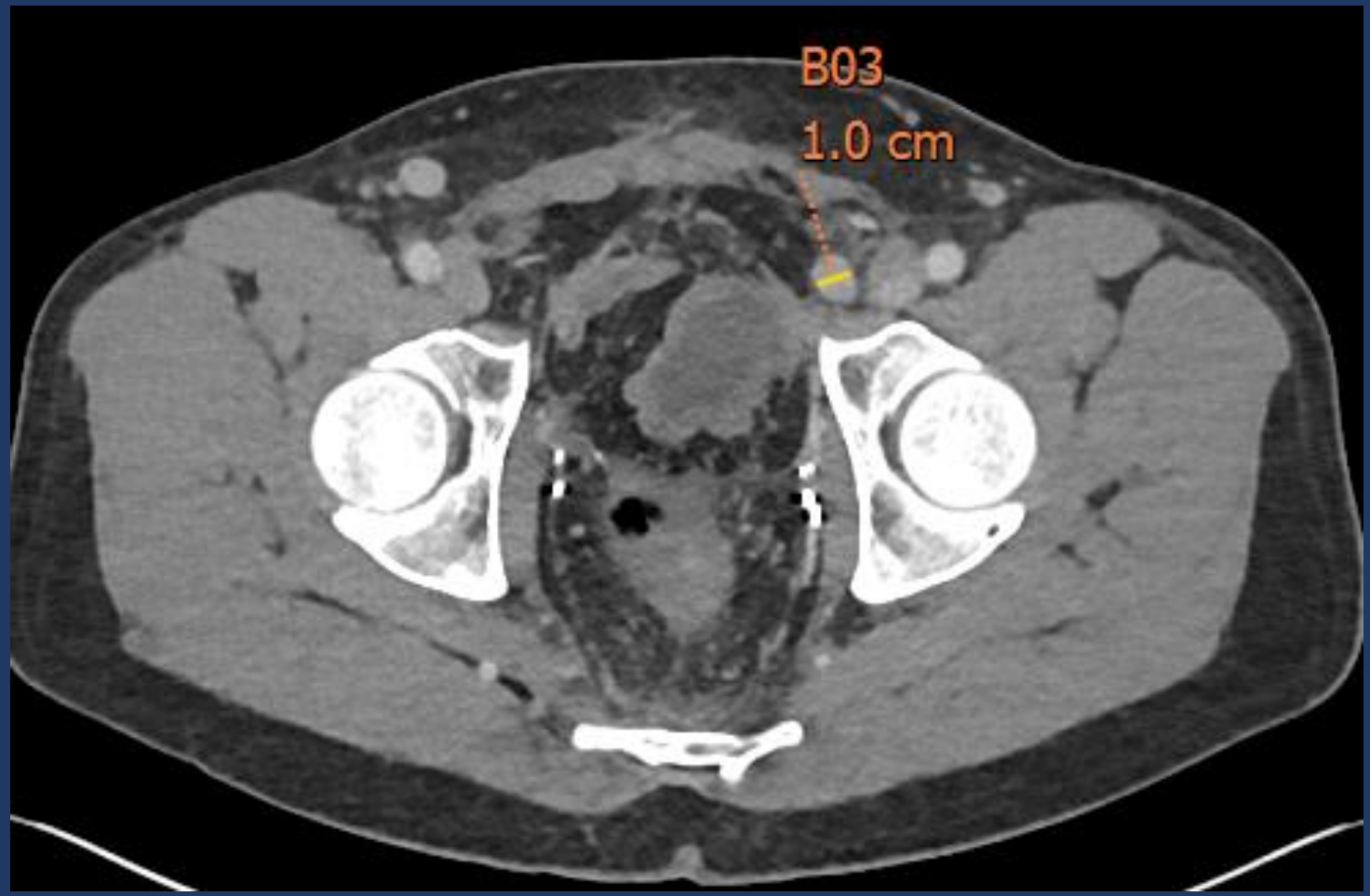
Case 1: Lymph node



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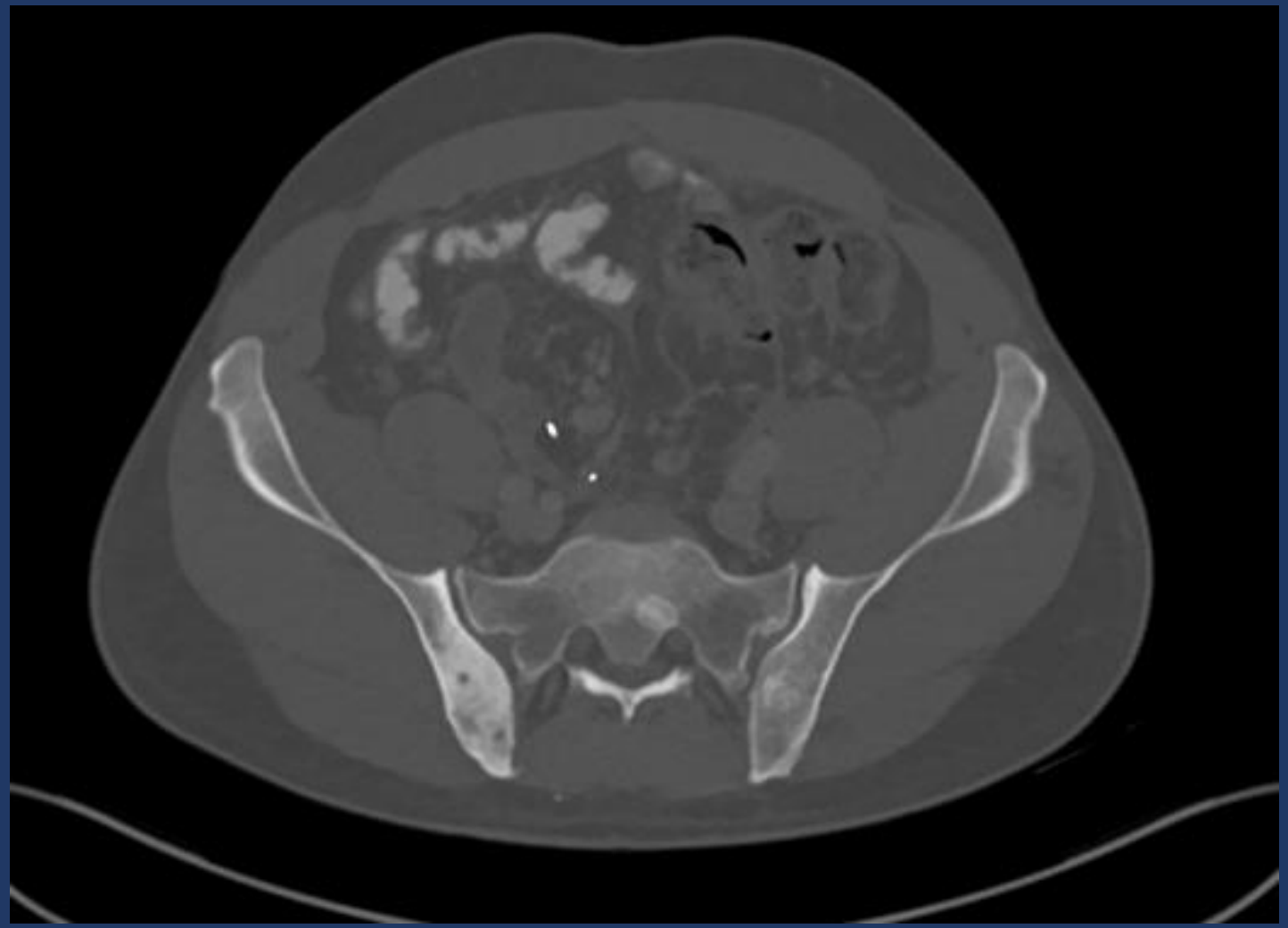
Lymph Nodes Recommendation

- Customized radiologic work-up, follow-up imaging or biopsy:

≥ 1 cm in short axis

Case 2: Bone lesions



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Bone Lesion Recommendation

- Customized radiologic work-up, follow-up imaging or biopsy if:

≥ 1 cm in long axis

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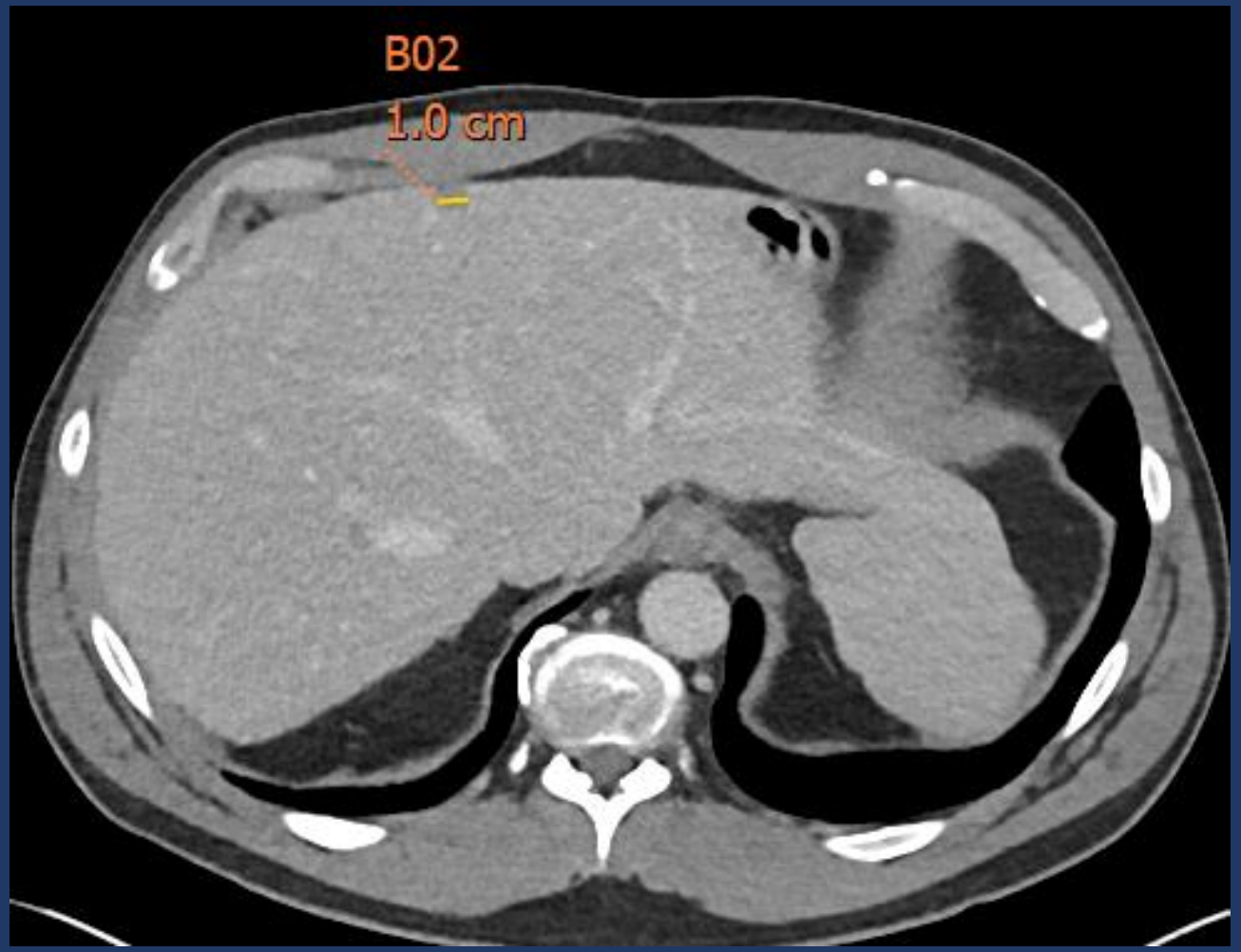
Case 3: Liver Lesion



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Liver Lesion Recommendation

- Customized radiologic work-up, follow-up imaging or biopsy if:

≥ 1 cm in long axis

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Objective 2: Defining Disease Recurrence

- Indication: MIBC. Adjuvant trial surveillance
- Goal: Determine if there has or has not been disease progression while on trial using imaging

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Uniform Model for Defining Recurrence

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Uniform Model for Defining Recurrent MIBC

- New lesion ≥ 1 cm that was absent on initial imaging
  - Short axis for LN
  - Long axis for all other lesions

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Uniform Model for Defining Recurrent MIBC

- New lesion ≥ 1 cm that was absent on initial imaging
  - Short axis for LN
  - Long axis for all other lesions
- Pre-existing lesion:
  - If < 1 cm on previous exam, demonstrating > 50% growth on 2 consecutive exams with ≥ 5 mm absolute increase
  - If ≥ 1 cm on previous exam, demonstrating > 50% growth on a single exam

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Uniform Model for Defining Recurrent MIBC

- New lesion ≥ 1 cm that was absent on initial imaging
  - Short axis for LN
  - Long axis for all other lesions
- Pre-existing lesion:
  - If < 1 cm on previous exam, demonstrating > 50% growth on 2 consecutive exams with ≥ 5 mm absolute increase
  - If ≥ 1 cm on previous exam, demonstrating > 50% growth on a single exam
- Multifocal lesions measuring <1 cm demonstrating geographic distribution or radiologic/metabolic features pathognomic for metastatic disease

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Site Specific Example

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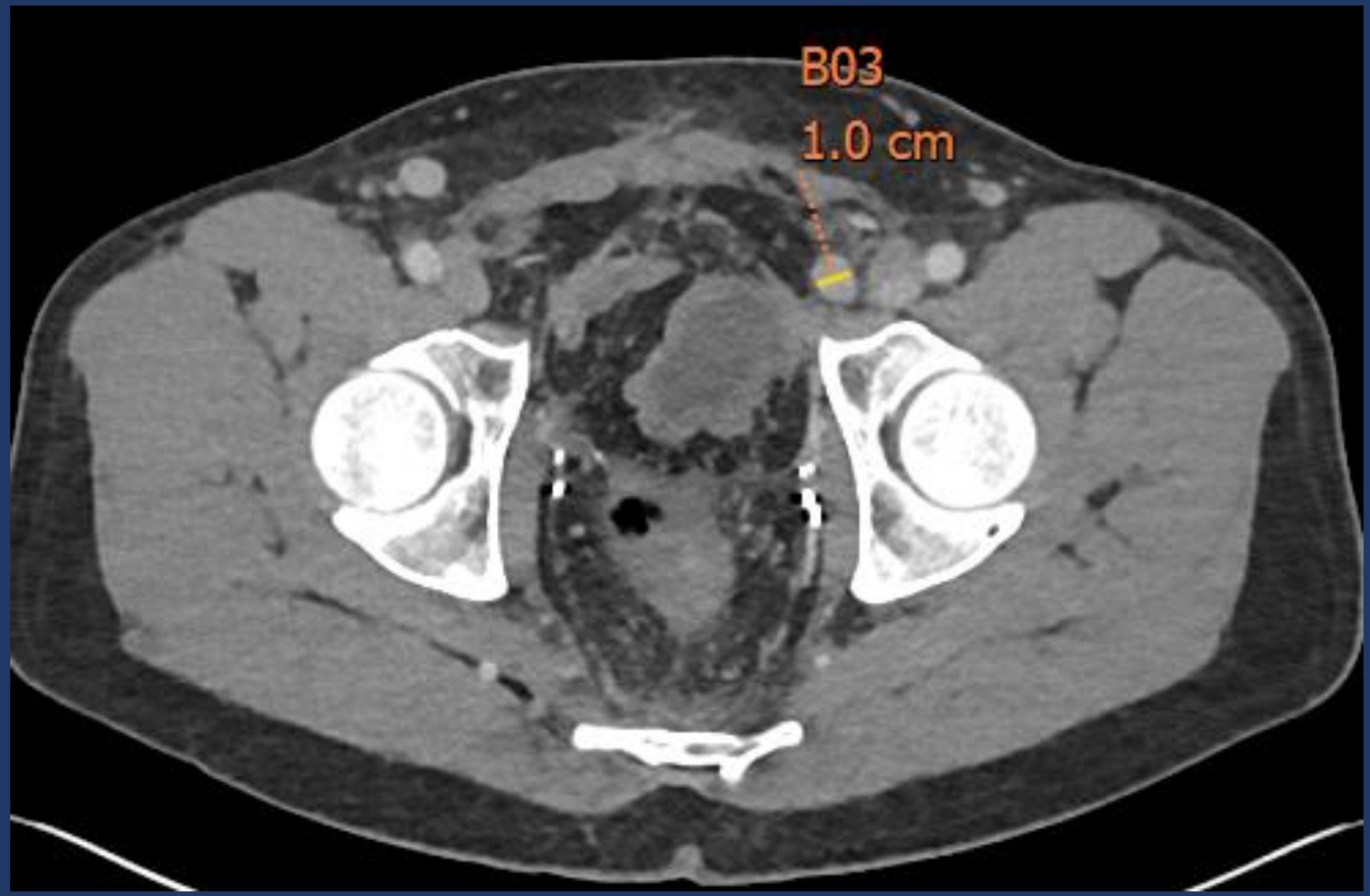
Case 1: Lymph node



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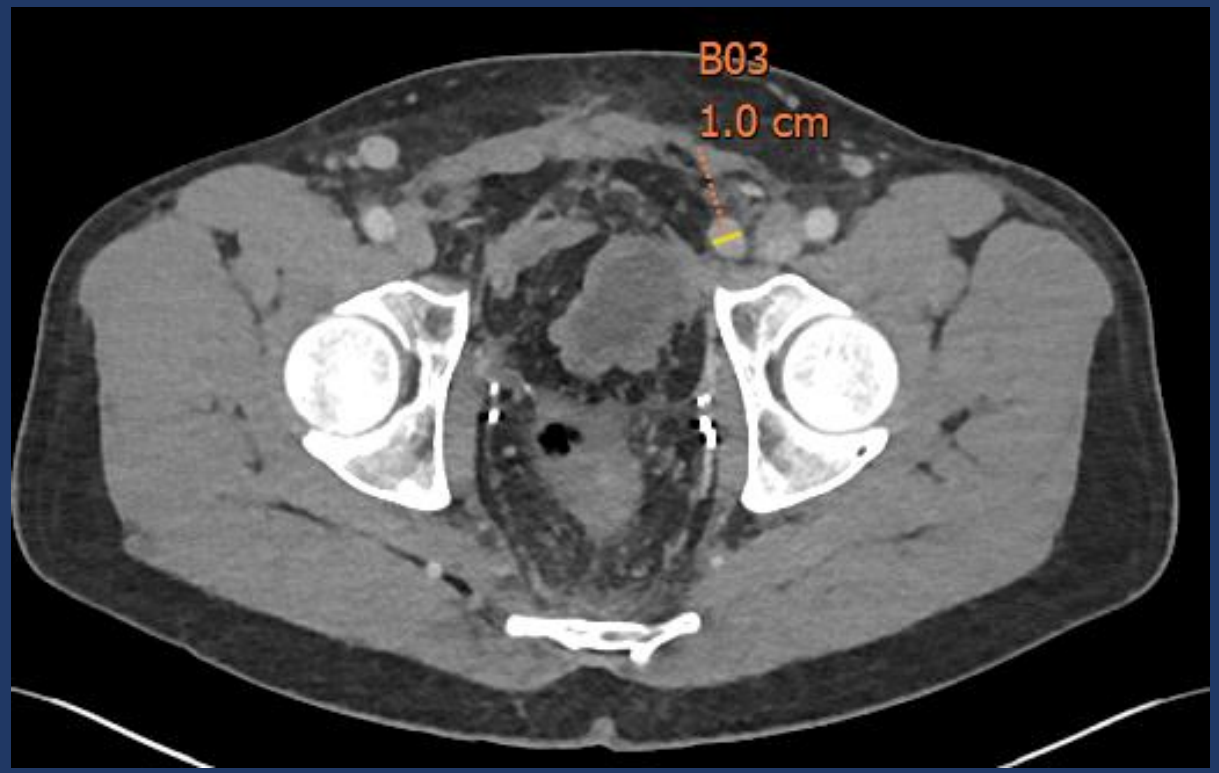
Case 1: Lymph node



- If new, then it is considered recurrent disease

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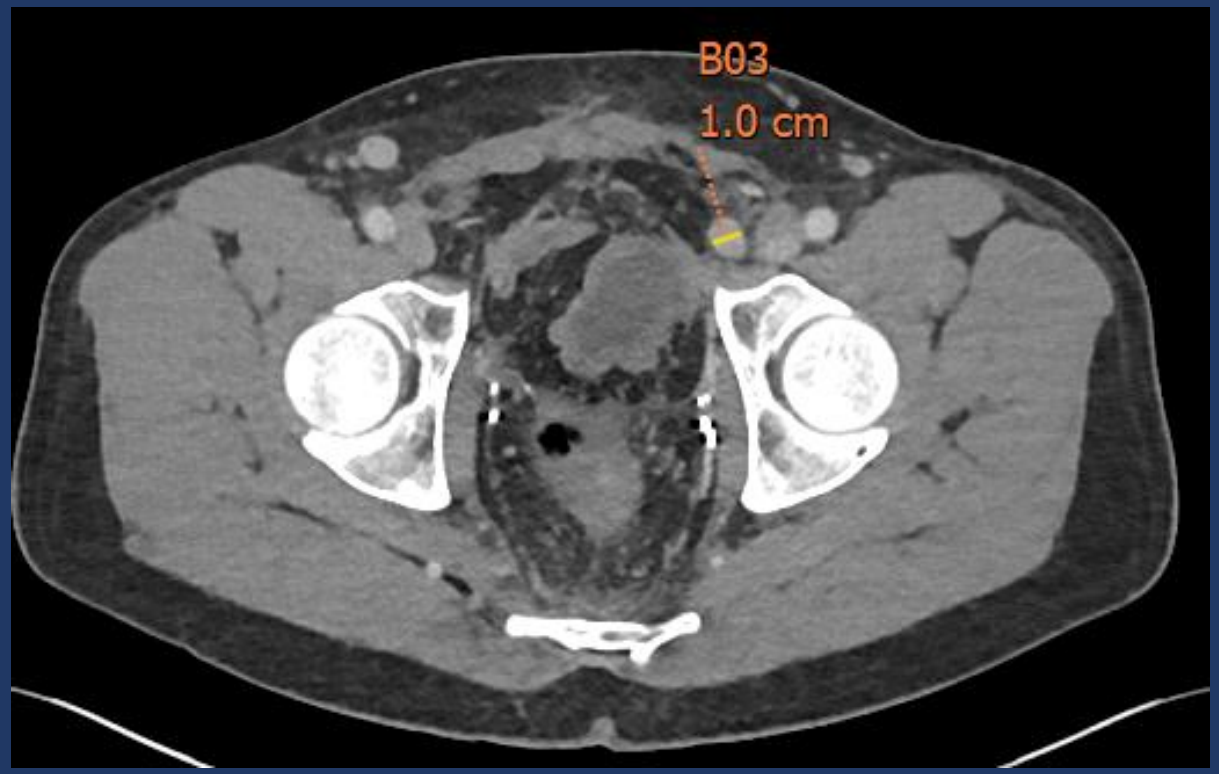
Case 1: Lymph node



- If pre-existing lesion, but negative for metastatic disease on customized radiologic work-up, follow-up CT or biopsy: would require >50% growth in short axis on 1 or 2 exams depending on the size on the eligibility CT

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Defining Date of Recurrence

- To backdate or not?
  - Backdating: using the date when a lesion was initially visible on imaging
    - More temporally accurate but introduces inconsistency
  - Not backdating: using the date when a lesion meets a pre-specified size criteria
    - More consistent but less temporally accurate

Defining Date of Recurrence

- We suggest that findings should not be backdated

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Future Radiologic Contributions

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The future

- Computer revolution
  - Radiogenomics
  - Artificial intelligence
  - Big data and deep learning
- Optimization of current techniques
  - DWI
  - DCE imaging
  - Lymphotropic nanoparticle enhanced MRI (superparamagnetic iron oxide)
- Novel imaging agents
  - ^{64}Cu-TP3805 PET-CT (VPAC receptors)

Thank you

Questions?

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