Defining Disease Recurrence in Adjuvant Bladder Cancer Trials: From a Radiologist's Perspective

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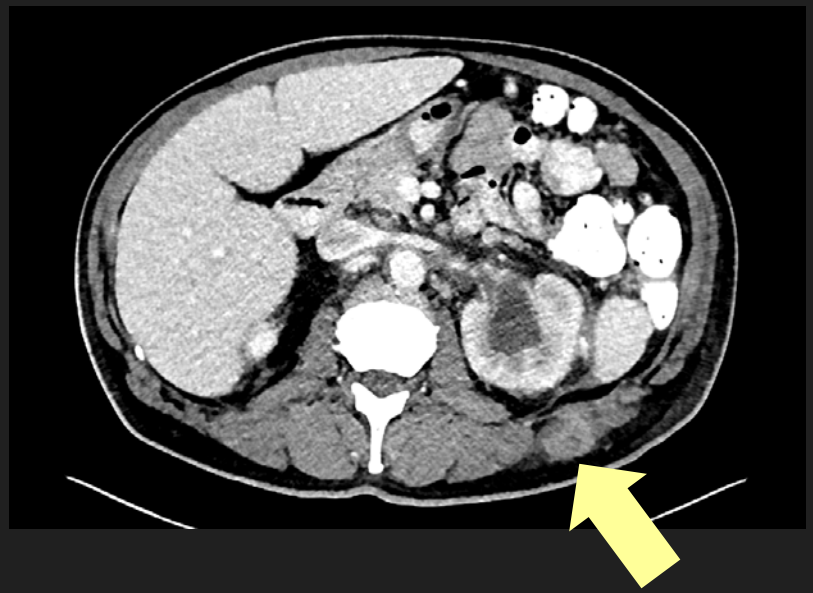
Baseline Imaging Examinations

- The aim of baseline examinations is to establish definitively the absence of disease on study entry.

- Recommend:
  - archiving previous imaging examinations—including reports—as extensively as conceivably possible to minimize equivocation of pre-existing lesions
  - methodical documentation of any potential inflammatory process, and consideration of delay of baseline until inflammation is resolved/minimized
  - consider the utility of acquiring FDG-PET acquiring at baseline only

Limitation of FDG-PET

- Renal excretion of FDG masks upper tract neoplastic lesions.



- However, FDG-PET bolsters detection of intra-abdominal/pelvic, lymph node, and bone metastasis.

Imaging Technique

Recommend:

- Standardization of *imaging acquisition technique* according to Radiologic Society of North America Quantitative Imaging Biomarkers Alliance guidelines (RSNA QIBA).

- Standardization of *imaging display technique* according what is representative of current practice standard.
- Eliminating chest radiographs from surveillance routine in favor of chest CT.

Proposed Definitions of Recurrence

• Given inherent morbidity of biopsy, consider that the pragmatic implication of any proposed categorization is equivalent to:

- unequivocal recurrence = biopsy warranted
- highly suspicious = biopsy warranted
- indeterminate = interval imaging surveillance sufficient

- Recurrence date is first recognition of the findings.

- If resorting to interval imaging surveillance of indeterminate or suspicious lesions which are prohibitively difficult to biopsy, recommend time intervals which are determined by rate of tumor growth.

Proposed Definitions of Recurrence

Site	Unequivocal Recurrence	Highly Suspicious Lesions	Indeterminate Lesions	Radiologic Considerations
Lymph Nodes	Lymph nodes ≥ 1.5 cm short axis, with confirmation of growth by at least 5 mm or appearance of new lesions on subsequent scans at least 4 weeks later	Lymph nodes <1.5 cm short axis that increase in size on subsequent imaging but remain less than 1.5 cm	Lymph nodes that are stable ≥ 1cm and <1.5cm short axis	Difficulty of imaging-guided biopsy of lymph nodes in different anatomic locations is variable
Lung	>3 non-calcified pulmonary nodules, all greater than 1 cm or new innumerable nodules of any size. For solitary pulmonary nodules, >2cm	Any number of nodules associated with thoracic adenopathy or not present at baseline	Any pulmonary nodules not meeting criteria for unequivocal recurrence or highly suspicious lesion	Atypical endobronchial and intraparenchymal cavitary pulmonary lesions have been reported, which should be excluded from this categorization

Proposed Definitions of Recurrence

Site	Unequivocal Recurrence	Highly Suspicious Lesions	Indeterminate Lesions	Radiologic Considerations
Bone	≥2 lesions of the bone on bone scan confirmed on CT or MRI. For solitary lesions, subsequent scan required to demonstrate growth or at least one new lesion at least 4 weeks apart	≥1 bone lesion with characteristic findings on imaging	Any bone lesion without characteristic findings or not meeting criteria for unequivocal recurrence or highly suspicious lesion	Consider incorporation of FDG-PET in these definitions
Liver	Abdominal CT or MRI demonstrating lesion that is ≥1 cm with confirmation of growth by at least 5 mm or appearance of one or more new lesions on subsequent scans at least 4 weeks later	Nodules < 10 mm in size that do not appear compatible with benign processes; lesions of any size not present on prior imaging	Any mass not meeting criteria for other 2 categories or that characteristically enhances compatible with benign processes	MRI is the preferred modality for liver lesion characterization. Consider standardization of image acquisition and image display for MRI.

Image-Guided Biopsy

- Given heterogeneity of operator skill and risk tolerance, recommend that every center participating in clinical trials routinely conferring with at least 2 interventionalists in concert to establish consensus.

Lymph node station	Typical difficulty level to biopsy
Supraclavicular	Low
Retrocrural	High
Para-aortic	Moderate
Pre-aortic	Moderate
Inter-aotocaval	High
Pre-caval	Moderate
Para-caval	Moderate
Retrocaval	High
External iliac-distal	Moderate
External iliac-proximal	Moderate
Internal iliac	Moderate
Obturator	Low to moderate
Presacral	Moderate

Image-Guided Biopsy

- Given variability of anatomic access and patient conditioning, when formulating definitions of disease recurrence, recommend anticipating the situation of a prohibitively difficult biopsy.

Organ	Typical difficulty level to biopsy	Radiologic considerations
Brain	N/A	N/A
Lung	Low to moderate	Morbidity of lung biopsy is substantially higher relative to other biopsies
Liver	Low to moderate	Difficulty level depends predominantly on anatomic location
Pelvis	Moderate to high	Difficulty level depends predominantly on anatomic location
Bone	Dependent on location	Difficulty level depends predominantly on anatomic location

Data Scalability

- In context of data compounding and continually improving analytic tools/techniques, clinical trials should anticipate changes in proposed definitions of imaging classifications.

- To maximize the scalability of imaging data, recommend methodically storing unprocessed imaging data for *post facto* analysis.

Questions and Comments