Memorial Sloan Kettering Cancer Center

Radiographic modalities and procedures, baseline and surveillance imaging, and the role of biopsy in determining recurrence

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Adjuvant clinical trials

- All patients should have all macroscopic disease fully resected
- Goal of treatment is to eliminate microscopic disease present in a proportion of patients
- Purpose of baseline imaging is to exclude patients with persistent/recurrent macroscopic disease at the time of enrollment
- Monitoring on trial to identify time of recurrence
  - Critical for disease-free endpoint

Radiologic followup

- Goals of radiologic followup
  - Detect upper tract tumors
  - Detect disease in most common sites of recurrence so therapy may be administered in a timely fashion
  - Urinary diversion related issues (e.g. hydronephrosis)
  - In trials, identify time of recurrence for study endpoints
- Little evidence for optimal followup schedule

Monitoring for upper tract recurrence

- Meta-analysis: prevalence of UTUC after RC was 0.75% to 6.4%
  - 38% of cancers detected on followup imaging
  - 62% based on symptoms
- Can occur beyond 2 years

Picozzi S, Ricci C, Gaeta M et al: Upper urinary tract recurrence following radical cystectomy for bladder cancer: a meta-analysis on 13,185 patients. J Urol 2012; **188: 2046.**

Role of novel imaging

- No data to support PET/CT over conventional imaging in the adjuvant setting
  - May help resolve equivocal findings
  - Particularly helpful for bone lesions
- Can this be used in the trial setting to adjudicate recurrences?

Clinical guidelines: AUA/ASCO/ASTRO/SUO vs NCCN

	AUA		NCCN
	pT2 or <ypT2N0	Yp>T2 or N+	Individualized followup
CT A/P	Every 6-12 months for 2-3 years	Every 3-6 months	3-6 months for 2 years, then annually to 5 years, and as indicated thereafter
Chest imaging	-	Annual CXR	CXR with CT chest f/u if concerning findings present on CXR
Upper tract imaging	Option for annual with CT or US to year 5		After 5 years, renal u/s annually
PET	Only if equivocal findings		Only if metastasis is suspected, in selected patients

Differences among ongoing adjuvant trials

- Schedules of imaging
  - Frequency varies beyond 2 years
- Definition of imaging recurrence is variable
  - RECIST 1.1 for lymph nodes
  - Any new lesion
  - Confirmatory scans if not amenable to biopsy
  - Not clearly specified
- Biopsy requirement
  - Only if equivocal
  - Mandatory unless not feasible
- New urothelial primary as DFS event

Indeterminate findings are a problem in this patient population

- Many patients are current and former smokers
- High incidence of indeterminate pulmonary nodules
- Minority of indeterminate pulmonary nodules represent metastatic disease
  - Recent data from FCCC indicates 92% of indeterminate pulmonary nodules were clinically benign after 2 years f/u

Cahn, et al. *Journal of Clinical Oncology* 35, no. 6_suppl (February 2017) 297-297

Problems with defining recurrence on adjuvant trials

- If not amenable to biopsy, what size cutoff do we use?
  - RECIST 1.1. not meant for adjuvant trials
  - Is PET an alternative? What SUV cutoff defines a positive lesion for recurrence? Can PET be used for bone lesions?
- If clinical factors are used (progressive increase in size), which is correct date?
  - First abnormal finding? Confirmatory scan?

Proposed definitions of recurrence based on organ site

Site	Residual Disease	Unequivocal Recurrence	Highly Suspicious Lesions	Indeterminate Lesions
Lymph Nodes	Local/regional LN ≥1.5 cm in short axis	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
Lung	N/A	>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

Proposed definitions of recurrence based on organ site

Site	Unequivocal Recurrence	Highly Suspicious Lesions	Indeterminate Lesions
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
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

Recurrence date is first recognition of the findings

Discussion questions

- Biopsy at relapse is not consistent in the community setting
  - Should be biopsy required?
  - Or just treat for metastases based on imaging
- If lesion is not biopsy-able non-invasively, should surgical excision be pursued?
  - Minimally invasive surgery has less morbidity than open surgery