FDA-NCI Public Workshop: Defining Disease Recurrence and Harmonizing Conduct in Adjuvant Kidney Cancer Trials;

Medical Imaging

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Medical imaging in diagnosis and surveillance of renal cancer

• CT is the most commonly used Imaging modality
• MRI
• PET, PET-CT, PET-MR
• Interventional Radiology
  • Ultrasound
  • Plain x-ray
  } Limited role
What to do when recurrence is suspected on an adjuvant renal study?

- Organ involved: Lung, Bone Lymph Node, Liver, Adrenal, Brain, ...?
- Imaging plan depends on availability of imaging modalities and Interventional Radiology
- **Type of primary** renal cancer
  - Eg: HLRCC lesions are very aggressive and highly metastatic, frequently metastasizing even while under 1 cm in diameter
- For this presentation, we consider the most common RCC cell type: clear cell
Four approach dealing with indeterminate lesions in follow up imaging

1. When to just continue the routine follow up?
2. Biopsy by IR (consider risk and benefit)
3. Shorter imaging interval based on tumor type and grading: When?
4. When we must consider additional Imaging to confirm diagnosis such as PET, PET-CT, PET-MR, MRI?
IR biopsy

• For disease recurrence or progression, biopsy is needed when possible
• We need to consider limitations and contraindications of biopsy considering organ involved and clinical setting and size of the lesion
New Finding in Routine Imaging

Non-specific Findings:
Eg: Lung CT Ground Glass Opacity

- Shorter Imaging follow up
  - Correlate with tumor markers
  - Improve
  - Progress
  - Routine follow up

Suspicious for Metastasis:
Liver lesion or Lung nodule

- Biopsy is possible
  - Biopsy is possible
  - Biopsy is not possible

Positive Biopsy for metastasis

Negative Biopsy for metastasis

Alternate Imaging;
PET, MRI

Supporting Metastasis
Equivocal
Negative

Remove the patient
Sites

Most common sites of metastatic RCC. Graph shows the frequency of metastatic RCC by anatomic site. Note that the percentage of lung metastases is over twice the percentage of nodal metastases.

Radiographics. October 2013, Volume 33, Issue 6
Lung

- The most common site
- Usually multiple nodules
- Less commonly can be single large:
- RCC is cause of cotton ball >5m

Case courtesy of Dr Ian Bickle, Radiopaedia.org, rID: 46000
Size in Lung Mets

• **Sub-centimeter Pulmonary Nodules are not associated with Disease Progression in Patients with Renal Cell Carcinoma**

• Conclusions—In the current study, no evidence suggested IPNs <1cm were associated with RCC progression,
Bone Metastasis

• Expansile lytic lesions,
• Most commonly located in the axial skeleton; usually the vertebral bodies are involved more often than the pedicles
• Lytic lesions are usually extremely destructive and may be associated with an enhancing soft tissue component
• Solitary bone metastases are rare
Lymph node metastases are the third most common group of metastatic RCC lesions

• Size criteria:
  • In RECIST we consider 1.5cm in short axis for Lymph Node to be considered as Target. Note: 10-14 mm can be a non-target.
  • In Cheson and Lugano Criteria we consider 15 mm in long axis for LN to be a target.
  • In general 10 mm in short axis is considered the upper limit for normal nodes

• Size-independent criteria
  • Loss of fatty hilum
  • Focal necrosis or cystic change
  • Inhomogeneous Enhancement
LN

Normal Node hilar fat

12 mm in Short axis

Enhancement
Inhomogeneous texture
LN summary

- If ≥15 mm, it is considered abnormal: do Biopsy
- 10-14 mm is abnormal if it is growing since the past, enhancing, loss of hilar fat, cystic change, necrotic component
- <10 mm follow up if stable
Liver Metastasis

- Include an arterial phase in CT protocol especially with Clear Cell type.
- Lesions >10 mm need biopsy especially inhomogeneous enhancement.
- Lesion <10 mm, need follow up MRI with DWI.
Brain Metastasis

• Up to 90% of patients that develop brain metastases have concurrent disseminated metastatic disease in other locations.

• Brain metastasis from RCC usually manifests as a solitary lesion with a hemispheric location, (unlike metastases from other tumors such as those from lung cancer, breast cancer, or melanoma that usually appear as multiple lesions.)

• The hypervascularity of the metastatic lesions may lead to spontaneous bleeding. Intratumoral hemorrhage was seen in 46% of all patients with brain metastases from RCC [Urology. 1996;47:187–93.]

• High frequency of intracerebral hemorrhage in metastatic renal carcinoma patients with brain metastases treated with tyrosine kinase inhibitors (European Urology 53 (2008) 376–381)
Brain Mets: RCC

Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 23200
PET

• A meta-analysis reported an overall sensitivity and specificity for FDG-PET in identifying extrarenal lesions as 79% and 90%, respectively [Cancer Imaging 2012; 12:464–74.].

• However, most of the studies included in the analysis were of PET without CT. A multimodality approach might achieve higher sensitivity and specificity.

• Hybrid PET-CT increase the Sensitivity and specificity to 91% and 88% respectively.
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<tr>
<th>Author</th>
<th>Year</th>
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<th>Study type</th>
<th>Instrument</th>
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Acc = accuracy; NPV = negative predictive value; PET = positron emission tomography; PPV = positive predictive value; std = standard.
Summary

- Lung: Small nodules <1cm can be benign even multiple, watch closely
- Lung nodule >10 mm, consider biopsy
- Lymph node ≥1cm in short axis is suspicious especially if hilar fat is lost or there is cystic and heterogeneous texture.
- Liver: Small lesion in Liver CT: Consider MRI with DWI, Do biopsy when MRI is positive
- Adrenal: Small lesion in CT: Consider MRI with DWI
- Multiple small Lung and liver lesions, highly suspicious even if the lesions are <10mm
- New data supporting role of PET in extra-renal RCC spread
- For other soft tissue lesions, MRI with contrast including DWI is helpful
- Consider biopsy when possible
- Tumor Board discussion in borderline cases
New Lung abnormality in Routine CT Scan

Non-specific Findings:
   Eg: Lung CT Ground Glass Opacity

Nodule
   <1cm
   ≥1cm

Biopsy is possible
   Biopsy is not possible
   Consider Biopsy
   Alternate Imaging; PET

Biopsy is possible
   Negative Biopsy
   Positive Biopsy
   Routine follow up
   Routine follow up

Biopsy is not possible
   Remove the patient
   Alternate Imaging; PET

Tumor Board Discussion
   Supporting Metastasis
   Equivocal
   Negative

Stable
   Resolve
   Progress

<1cm
   ≥1cm
Bone

New Bone Lesion in Routine CT Scan or MRI

NaF PET

Negative

Shorter Imaging follow up
Correlate with tumor markers

Stable

Resemble

Progress

Positive

Biopsy is possible

Biopsy is not possible

Alternate Imaging; MRI+DWI,

Supporting
Metastasis

Negative or Equivocal

Routine follow up

Remove the patient

Consider Biopsy

Biopsy is possible

Positive Biopsy

Negative Biopsy
New Enlarging Lymph Node in Routine CT Scan or MRI

- <1cm in short Axis, Normal fat in hilum
  - Shorter Imaging follow up
  - Correlate with tumor markers
  - Stable
  - Resolve
  - Progress

- ≥1cm in short Axis, Lost Hilar Fat
  - Consider Biopsy
  - Biopsy is possible
  - Biopsy is not possible
  - Alternate Imaging; MRI+DWI, PET
  - Supporting Metastasis
  - Equivocal
  - Negative

- Routine follow up
- Remove the patient
New Liver abnormality in Routine CT Scan

Small Lesion <1cm no enhancement
- Biopsy is possible
  - Positive Biopsy: Improve
  - Negative Biopsy: Routine follow up

Biopsy is not possible
- Remove the patient

Nodule ≥1 cm or Enhancing
- Consider Biopsy
  - Biopsy is possible
    - Positive Biopsy: MRI with DWI (Supporting Metastasis), PET (Positive), Routine follow up
    - Negative Biopsy: Routine follow up
  - Biopsy is not possible
    - MRI with DWI (Equivocal, Negative), PET (Negative)

Shorter Imaging follow up
- Correlate with LFT & tumor markers
  - Improve
  - Progress

Routine follow up
New Finding in CNS Imaging

Non-specific Findings:
Eg: Small T2 Hyperintensity, no enhancement or edema

Typical Intraaxial Metastasis:
Enhancing Lesion, Edema

Atypical Intraaxial Lesion:
Small Enhancing Lesion, No edema

Biopsy is possible
Biopsy not possible

Shorter Imaging follow up

Biopsy is possible
Negative Biopsy
Positive Biopsy

Routine follow up

Extraaxial Metastasis:
Leptomeningeal

CSF analysis

Negative
Positive

Improve
Stable
Progress
Remove the patient
Thank you