Controversies in Surgical Management of Renal Cancer

Maurizio Brausi
Chairman Dept. of Urology Ausl Modena
Chairman ESOU (European Section Onco-Urology)
Surgical Controversies For RCC Treatment in 2014

- * Renal biopsy: actuarial role
- * Active Surveillance: is it safe?
- * Focal Therapy: which role?
- * Nephron sparing surgery: why, when, how?
- * Surgical Margins: impact on the patient outcome
The Role of Renal Biopsies in 2014

Maurizio Brausi
Renal Cell Carcinoma in 2014

- Incidental discovery of SRMs continues to increase due to the diffuse use of US and CT
  - More therapeutic options
  - Better understanding of natural history of SRMs
  - Risk of over treatment
- Significant progress in medical treatment of advanced RCC (targeted therapies)
- Increasing interest for clinical trials in RCC
RCC in 2014

- The concept that all solid renal masses are malignant and that surgery is the only option is no longer valid.
- However, RCC remains the only urological tumor where surgical treatment without histology is permitted
  - Not the case for medical treatment in metastatic RCC
# Multimodal Decision Table for Diagnosis and Management of SRMs

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Patient characteristics</th>
<th>Tumour characteristics</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>Age</td>
<td>Tumour size</td>
<td>NSS</td>
</tr>
<tr>
<td>CT Scan</td>
<td>Symptoms</td>
<td>Tumour location</td>
<td>OPN, LPN, RPN, Ablative therapies (Cryo, RFA)</td>
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<tr>
<td>MRI</td>
<td>ASA score</td>
<td>RENAL or PADUA Scores</td>
<td></td>
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<tr>
<td>US/CT guided biopsies</td>
<td>Renal function</td>
<td>Tumour histology</td>
<td>Observation</td>
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<tr>
<td></td>
<td>Comorbidity indexes</td>
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<td></td>
<td>Charlson</td>
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</table>

Patard et al., Cur Op Urol, 2009
KEY POINTS FOR SMALL RENAL MASSES MANAGEMENT

- 15-20% are benign
- 75-80% are malignant but
  - Most are good prognostic tumors
  - Usually, low stage, low grade tumors
- Competitive mortality
  - Risk of dying from cancer < 5%
  - Risk of dying from a non-cancer cause ≈ 20%
Role of Renal Biopsy in 2014

- Why should I biopsy a solid lesion?
- Answers:
  1. for a precise path diagnosis of indeterminate renal masses (future treatment plan)
  2. to select pts. with small renal masses (SRMs) for surveillance
  3. to obtain hystology before ablative treatment
  4. to select the most suitable form of targeted pharmacologic therapy in pts. with metastatic disease
Percutaneous Renal Biopsy

Long term results of prospective trials of active surveillance on biopsy proven tumors are awaited to further define the role of this approach in the management of renal tumors.
Technique: Coaxial
Quality Control of the Specimen
Risk of non diagnostic specimen

Specimen torn or less than 10 mm long

Immediate rebiopsy
Ø 3.7cm
ONCOCYTOMA
HE 200x
Renal Biopsy: Technique

- **Via**: Perc
- **Needle**: coaxial needle core 18 G or fine needle aspiration (FNA). No seeding of tumor cells
- **N of cores**: at least 2 of good quality, if not a third one indicated
- **Anesthesia**: local, along the needle tract (Lidocaine 2%)
Accuracy of renal tumor biopsy

Recent series
- **sensitivity**: 70-100%
- **specificity**: 100%
- **accuracy**: 90%

Volpe et al., J Urol 2007
Lane BR, J Urol 2008;179:20-7
### Rationale for Percutaneous Biopsy and Histologic Characterisation of Renal Tumours


<table>
<thead>
<tr>
<th>Study</th>
<th>No. of tumours biopsied</th>
<th>Image guidance</th>
<th>No. of significant complications (%)</th>
<th>No. of seeding (%)</th>
<th>No. of significant bleeding (%)</th>
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<tbody>
<tr>
<td>Neuzillet et al. [8]</td>
<td>88</td>
<td>CT</td>
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<tr>
<th>Study</th>
<th>No. of tumours biopsied</th>
<th>Diagnostic biopsies, %</th>
<th>Accuracy for malignancy, %</th>
<th>Accuracy for RCC subtyping, %</th>
<th>Accuracy for grading, %</th>
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<td>99.7</td>
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<td>63.5</td>
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The Use of PCB in practice, the french experience, Prospective NEPHRON Study

Prospective analysis of Renal Tumors Biopsy Accuracy


(Department of Urology, from Paris, Bordeaux, Lille, Strasbourg, Nancy, Nancy, Creteil, Toulouse, Clermont-Ferrand, Lyon, Angers, Tours, Limoges, Mulhouse, Castelnau, Limoges, Nancy, Rouen, Saint-Etienne, France)

RESULTS

- Frequencies of pre-operative RTB according to type of surgery:
  - 66 before PN (27.3%)
  - 65 before RN (5.7%)

- Mean tumor size: 4.0 (± 2.5) cm

- Tumor biopsy could be interpreted in 92.3% of cases.

- Results of the RTB according to type of surgery:

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<th>Pre-RN n=44</th>
<th>Pre-RN n=44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modern tumor size (cm)</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Conventional RFA</td>
<td>92.2%</td>
<td>92.2%</td>
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<tr>
<td>Renal tumors</td>
<td>1.7%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Clear Cell histology</td>
<td>83.3%</td>
<td>71.7%</td>
</tr>
<tr>
<td>Fuhrman Grade 3-4</td>
<td>40.0%</td>
<td>9.2%</td>
</tr>
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</table>

- Concordance between RTB and nephrectomy specimen (NS):

Comparison between RTB and NS available in 117 cases

<table>
<thead>
<tr>
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<th>RTB n=44</th>
<th>Nephrectomy specimen n=44</th>
<th>Kappa</th>
</tr>
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<tbody>
<tr>
<td>Renal tumors</td>
<td>3 (4.5%)</td>
<td>5 (15%)</td>
<td>0.716 (Good)</td>
</tr>
<tr>
<td>Clear cell carcinomas</td>
<td>21 (30.4%)</td>
<td>20 (30.4%)</td>
<td>0.88 (Excellent)</td>
</tr>
</tbody>
</table>
| Transitional cell carcinomas | 13 (15.5%) | 15 (21.5%)        | 0.48 (Interpret)
| Fuhrman Grade 3-4  | 24 (54.5%) | 21 (48%)             | 0.15 (Poor) |
| Tumor necrosis     | 22 (20.4%) | 22 (20.4%)             |       |

Pignot et al., AUA meeting, 2012
Renal Biopsy: Wider Indication....

- The indications to percutaneous renal biopsy has increased also because of the better quality of the pathological examination in the present era (97% accurate diagnosis) versus 10-15 years ago (40-50% accurate diagnosis).
- However not all the pathological centers have the same experience and training and this influences the urology attitude
- **Results:** cooperation with our pathology and/or a dedicated uro-pathologist is a need
Biopsy of Renal Masses: Need

We need better histological definition by percutaneous needle biopsy

- **Malignancy**
- **Grade**
Renal Biopsy: No Indication......

- “Renal biopsy is not necessary before surgical treatment in fit patients with a long life expectancy and a clearly suspicious contrast-enhancing renal mass at abdominal CT or MRI”

(Eau Guidelines 2013)
Controversy in Renal Biopsies
(Brausi Aiom-Siu 2014)

1. Old patients with co-morbidities taking anti-coagulant therapy: possible bleeding with chance of surgery for complications
2. Difficult puncture under US or CT for the tumor location (20% are not reachable)
3. The cores or renal tissue is not sufficient for a correct path diagnosis (20% of the cases)
4. Inter-infra observer variation in the diagnosis (10-15% cases)
5. Tissue difficult to interpret by pathologist (uncertain and requiring a second biopsy: 15%)
Indications for Renal Biopsies in Small Renal Masses (≤ 4cm)

Age ≤ 70
- No significant co morbidity
- Good life expectancy
- No surgical risk

Preferred option = surgery

Patient age > 70
- significant comorbidities
- Compromised renal function
- Poor life expectancy
- high surgical risk

PCB for confirming malignancy

Preferred options
- Active Surveillance
- Ablative Technique

(Adapted From Gill et al., NEJM, 2010 AFU Guidelines, 2010)
Case 1

- 55 yrs old man
- No medical past history
- Serum creatinine: 80µM/l
- MDRD GFR: 91ml/mn
- Solid enhancing mass, 3 cm
- Incidental diagnosis
- 70% exophytic

No PCB, PN->grade 2 clear cell RCC
Case 2

- 49 yrs old male patient
- Hypertension
- Incidental detection SRM, 3.5 cm
- Serum créatinine: 72 µM/l
- MDRD GFR: 141ml/min
- No PCB, Robotic PN: oncocytoma
Technically Challenging Case for PCB

- Solitary kidney

PCB and PN histology where concordant: Grade 2 clear cell RCC
• 45 ans yrs old male patient
• No medical past history
• Serum Creatinine: 80µM/l
• MDRD GFR: 98ml/mn
• Solid enhancing renal mass, 2.5 cm
• Incidental diagnosis
• Entirely endophytic
• Renal Score=10

- PCB and PN histology where concordant: papillary RCC
Case 3

- 76 yrs old man
- Medical past of coronary disease (1 stent, 4 yrs ago)
- BMI=28
- Creatinine: 110µM/l
- MDRD GFR: 45 ml/min
- Solid enhancing mass, 2 cm,
- 90% exophytic
- Estimated 10 yr survival (charlson):53%

PCB: papillary tumor
Proposition for ablative treatment (PN as an option)
Case 4

- 82 yrs old women
- Cerebral Vascular Accident
- Diabetes
- Overweight: BMI=35
- Serum Creatinine: 130µM/l
- MDRD GFR: 36 ml/min
- Solid enhancing mass, 3.5 m
- Asymptomatic
- Estimated 10 yr survival=0% (Charlson)

**PCB: grade II, clear cell RCC**

**Proposition for Active Surveillance**
Percutaneous Biopsies in Cystic Tumors

- Limited role: Bosniak IV tumors?
- Higher risk of biopsy failure
- False-negative results
- Potential spreading of tumour cells
- The combination of fine needle aspiration and PTB is still experimental

Volpe et Al. Eur Urol, 2012
DOWSTAGING ORGAN CONFINED TUMORS FOR ALLOWING NSS IN ELECTIVE CASES

Radical nephrectomy

Axitinib

\[ \leq T1b \]

Partial nephrectomy

\[ cT2a \]
Indications for PCB in locally advanced RCC

- The standard of care is upfront radical nephrectomy following CT imaging
- **Rare Indications for PCB**
  - Unresectable tumor
  - Patient not suitable for surgery
  - Neoadjuvant clinical trials
Indications for PCB in metastatic RCC

- The benefit of nephrectomy is not proven in the era of targeted therapies
  - Clinical trials are encouraged
- Poor prognosis patients (MSKCC or Heng classification)
- Patients at surgical risk
- Unresectable primary tumors
- Clinical trials
  - Carmena
  - Neorad
- Perspectives: rationalizing medical treatment based on
  - Histologic features
  - Molecular features
Other indications for PCB

- Renal lymphoma (suspicious)
- Other primary cancers with suspicious renal metastase
Contraindications for PCB

- Transitional Cell Carcinoma (Suspicious): T. spillage
- Angiomyolipoma: risk of bleeding
- Obesity + anticoagulant therapy and tumor location
- Relative contraindication: cystic tumor
Conclusions

1. Increasing Role of renal biopsy in SRMs
2. Limited role in Cystic Tumors
3. Limited role in locally advanced RCC
4. Key role in metastatic RCC
• Thank you !!!