Patient Selection for Ablative Therapies

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Patient Selection for Ablative Therapy

Renal Cell Ca

- USA:
  - 30,000 new cases annually
  - >12,000 deaths

- RCC accounts for 3% of all adult malignancy

- 40% of patients will die from their cancer

- Incidence is increasing @ 2.5% per year
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**Nephrectomy**

**Partial Nephrectomy**
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Nephron Sparing Surgery

What has made this possible?

- Better quality Imaging
- 60% of tumours are incidental findings
- Often <4cm
- 4-15% risk of contra-lateral tumour
- Preservation of nephrons protects against hyperfiltration injury with better long term renal function
Patient Selection for Ablative Therapy

All patients need to undergo standard staging protocols

Role of Biopsy in Patients selected for Ablative Therapy

Surface rendering CT & Angiogram
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- Patient Issues:
  - CKD
  - Medical Co-morbidity

- Tumour Related Issues:
  - Size
  - Site
  - Complexity

- Technique
  - Percutaneous
  - Laparoscopic
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“Imperative”

- Solitary functioning kidney
- Compromised Renal Function
- Bilateral / Multifocal Disease eg VHL
- Synchronous tumours
- Significant medical co-morbidity
  - Need for agreed co-morbidity index
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Patient Dilemma

- unwilling or unable to undergo surgical tumour resection

- Potential for recurrent renal surgery due to a hereditary predisposition to develop multifocal RCC (von Hippel-Lindau disease and hereditary papillary RCC).
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Treatment Modalities:

- Heat:
  - Radio Frequency Ablation
  - HIFU
  - Microwave

- Cold:
  - Cryotherapy
Cortical renal tumors and exophytic lesions are often more readily ablated due to the presence of surrounding fat, which provides an insulating 'oven effect' during ablation, and the absence of a heat-sink effect seen with medullary lesions.

Ablation of cystic tumors can be challenging. The probe might need to be moved to different locations within the cystic tumor to ablate the solid components [Stone et al. 2007].
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Determine whether patients:

- suitable for a percutaneous approach vs laparoscopically.

- The optimal puncture for the percutaneous approach should be via a posterior or lateral approach

- with the patient in a semiprone or lateral decubitus position with coordinated breathing to help position the target lesion without injuring surrounding structures

  Stone et al. 2007.

- Consider general anesthesia with suspended respiration to improve targeting and outcomes

Patient Selection for Ablative Therapies

Nephrometry Scoring Systems

Current systems include:

- the R.E.N.A.L.,
- PADUA,
- C-index systems.
<table>
<thead>
<tr>
<th>(R)adius (maximal diameter in cm)</th>
<th>1pt</th>
<th>2pts</th>
<th>3 pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4</td>
<td>&gt;4 but &lt; 7</td>
<td>≥7</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>(E)xophytic/endophytic properties</th>
<th>≥50%</th>
<th>&lt;50%</th>
<th>Entirely endophytic</th>
</tr>
</thead>
</table>

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<thead>
<tr>
<th>(N)eartness of the tumor to the collecting system or sinus (mm)</th>
<th>≥7</th>
<th>&gt;4 but &lt; 7</th>
<th>≤4</th>
</tr>
</thead>
</table>

<table>
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<tr>
<th>(A)nterior/Posterior</th>
<th>No points given. Mass assigned a descriptor of a, p, or x</th>
</tr>
</thead>
</table>

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<thead>
<tr>
<th>(L)ocation relative to the polar lines*</th>
<th>Entirely above the upper or below the lower polar line</th>
<th>Lesion crosses polar line</th>
<th>&gt;50% of mass is across polar line (a) or mass crosses the axial renal midline (b) or mass is entirely between the polar lines (c)</th>
</tr>
</thead>
</table>

* suffix “h” assigned if the tumor touches the main renal artery or vein

Nephrometry is a novel scoring system that quantifies the salient anatomy of renal masses in order to provide a useful clinical tool for: (1) guiding management decisions and (2) more meaningful comparisons of reports in the urological literature.

Nephrometry score of 4 to 6 = low complexity  
Nephrometry score of 7 to
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Specific tumour features such as tumor size, depth, location, and proximity to the kidney vasculature and urinary collecting system can affect the difficulty/outcome of treatment.

PADUA classification and the R.E.N.A.L. nephrometry score to predict peri-operative complications of partial nephrectomy can be used to assess complications of ablative technologies.
Patient Selection for Ablative Therapies

- Percutaneous radiofrequency ablation of renal cancer. NICE interventional procedures guidance 353 (2010).

- Current evidence on the safety and efficacy of percutaneous radiofrequency ablation (RFA) for renal cancer in the short and medium term appears adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit, and provided that patients are followed up in the long term.

- Patient selection for percutaneous RFA for renal cancer should be carried out by a urological cancer multidisciplinary team.

- NICE encourages data collection to provide information about the outcomes of this procedure in the long term. Further research should compare the long-term outcomes of RFA with those of other treatments for renal cancer.
Current evidence suggests that cryotherapy for renal cancer ablates tumour tissue and that its safety is adequate.

However, the evidence about its effect on long-term local control and survival is not yet adequate to support the use of this procedure without special arrangements for consent and for audit or research.

Clinicians wishing to undertake cryotherapy for renal cancer should ensure that patients understand the uncertainties about its effect on quality of life and long-term survival, and provide them with clear written information.

The procedure should only be offered after assessment by a specialist multidisciplinary team, which should include a urologist, an oncologist and an interventional radiologist.

Controlled studies into the long-term clinical outcomes will be useful. Clinicians are encouraged to collect long-term data and should enter all patients with renal cancer treated with cryotherapy into the British Association of Urological Surgeons Cancer Registry (www.baus.org.uk).

- Meta-analysis from 47 studies: 1375 renal tumours
  - 600 Cryo
  - 775 RFA

- The cryoablation procedures were predominantly surgical whereas RFA procedures were predominantly percutaneous

- 91% (43/47) of studies were included in regression analysis: Higher incidence of local tumour progression was found to be significantly associated with RFA treatment on univariate analysis (p = 0.001) and on multivariate regression analysis (p = 0.003).

- Mean follow up 18.7 mths
Repeat ablations were required in significantly fewer patients treated with cryotherapy than radiofrequency ablation (RFA) (1% [8/600] vs 8% [66/775], p < 0.0001).1

The review reported that significantly less patients treated with cryotherapy had local tumour progression (defined as radiographic or pathological evidence of residual disease after initial treatment, regardless of time to recurrence) than those treated with RFA over a mean follow-up of 18.7 months (5% [31/600] vs 12% [100/775], p < 0.0001).

Less patients treated with cryotherapy had progression to metastatic disease but this was not significant (1.0% [6/600] vs 2.5% [19/775], p = 0.06).1

Kunkle DA & Uzzo R Cancer 2008
The non-randomised study of 101 patients reported intraoperative complications occurred in 3% (1/36) of patients treated with cryotherapy and 14% (5/36) treated with LPN and postoperative complications occurred in 14% (5/36) treated with cryotherapy, 58% (21/36) treated with LPN and 7% (2/29) treated with RFA.

The non-randomised comparative study of 93 patients reported no difference in intraoperative (p = 0.25) and postoperative (p = 0.56) complications between those treated with percutaneous cryotherapy, laparoscopic cryotherapy and percutaneous RFA.

Haemorrhage requiring transfusion occurred in 28% (5/20) of patients treated with laparoscopic cryotherapy compared with 11% (2/18) treated with percutaneous cryotherapy in a non-randomised study of 37 patients.

10% (2/20) of patients treated with laparoscopic cryotherapy in a non-randomised study of 66 patients (20 treated with laparoscopic cryotherapy); and in 2% (3/123) and 11% (4/37) in 2 case series of 123 and 37 patients, respectively.
## Patient Selection for Ablation Therapies

### Table 3. Complications of ablative modalities

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Modality</th>
<th>No. patients</th>
<th>Major</th>
<th>Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson et al.</td>
<td>2004</td>
<td>PCA/LC</td>
<td>139</td>
<td>Significant hemorrhage (1), open conversion (1)</td>
<td>Probe site pain or paresthesia (10), UTI (2), postoperative pneumonia (1), minor hemorrhage (1), elevated serum creatinine (1), wound infection (1)</td>
</tr>
<tr>
<td>Hegarty et al.</td>
<td>2006</td>
<td>LCA</td>
<td>164</td>
<td>AMI (1), CHF (1), hemotorax (1)</td>
<td>Urine leak (1), blood transfusion (4), pneumothorax (1)</td>
</tr>
<tr>
<td>Hegarty et al.</td>
<td>2006</td>
<td>PRFA</td>
<td>72</td>
<td>None reported</td>
<td>Perirenal hematoma (3), retroperitoneal hematoma (2), perirenal abscess (2), upper pole hydrocalicosis (1)</td>
</tr>
<tr>
<td>Laguna et al.</td>
<td>2009</td>
<td>LCA</td>
<td>144</td>
<td>Conversion (4), AMI (1), Death × AMI (1), wound dehiscence (1)</td>
<td>Skin burn (2), UTI (5), flank pain (1), perirenal hematoma (3), ileus (7), pneumonia (1), atrial fibrillation (1), wound infection (1)</td>
</tr>
<tr>
<td>Badger et al.</td>
<td>2009</td>
<td>LCA</td>
<td>27</td>
<td>Stroke (1)&quot;, postoperative dialysis (1)&quot;</td>
<td>Atrial fibrillation (2), respiratory distress (1), pulmonary edema (1), retroperitoneal hematoma (1)</td>
</tr>
<tr>
<td>Varkarakis et al.</td>
<td>2005</td>
<td>PRFA</td>
<td>46</td>
<td>Death due to aspiration pneumonia (1)</td>
<td>Perirenal hematoma (14), neuromuscular laxity of the flank wall (1), liver hematoma (1)</td>
</tr>
<tr>
<td>Rouviere et al.</td>
<td>2006</td>
<td>Intraoperative RFA/PRFA</td>
<td>22</td>
<td>Urine leak (3)</td>
<td>Chronic pain at the ablated site (1),</td>
</tr>
<tr>
<td>Hacker et al.</td>
<td>2006</td>
<td>PHIFU</td>
<td>19</td>
<td>None reported</td>
<td>Grade III skin burn (2)</td>
</tr>
</tbody>
</table>

Masaki Kimura, Shiro Baba, Thomas J Polascik
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- RFA & Medial Tumours:
  - The ureters, surrounding bowel, and nerves (genitofemoral and ilioinguinal) are at risk for thermal injury operator needs to be aware.
  - Hydrodissection with a nonelectrolyte solution such as dextrose 5% in water (D5W) [Laeseke et al. 2005] has been described to try to protect adjacent structures and minimise risk for complications such as bowel perforation [Chen et al. 2006].
  - However, hydrodissection may result in dissipation or resorption, and therefore repeated injections in the proper plane of dissection may be required to maintain adjacent organ displacement, away from the probe.
Zagoria et al 2007: Renal Radiofrequency Ablation

- Overall: 93% (116/125) Primary: 87.2% (109/125)

- Oncological Efficacy:
  - Size: <3.7 cm Complete ablation
  - for each 1cm increase in tumour size:
    - Tumour free survival decreased by a factor of 2.19

- Site: Tumours in medial half had a marginally worse Disease Free Survival than lateral tumours

- Tumour Type: No influence relating to exophytic, central, parenchymal or mixed or cephalocaudal location in the kidney

*Am J Roentgenol 2007; 189(2): 429-436*
EAU Guidelines: Conclusions

Radiofrequency and cryoablation are the only minimally invasive approaches for the treatment of small renal tumours with medium follow-up data.

Although the oncological efficacy is not yet known, currently available data strongly suggest that cryoablation, when performed laparoscopically, results in fewer re-treatments and improved local tumour control compared with RFA.

For both RFA and cryoablation, recurrence rates are higher than with nephron-sparing surgery.
Patient Selection for Ablative Therapies

- **EAU Guidance:**

- **Recommendations:**
  - Patients with small tumours and/or significant co-morbidity who are unfit for surgery should be considered for an ablative approach for example, cryotherapy and radiofrequency ablation.
  
  - Pre-treatment biopsy has to be carried out as standard.
  
  - Other image-guided percutaneous and minimally invasive techniques, such as microwave ablation, laser ablation and high-intensity focused ultrasound ablation, are still experimental in character.
  
  - The experience obtained with radiofrequency ablation and cryoablation should be considered when using these related techniques.
Both RFA and Cryoablation have a role in renal tumour ablation.

Success appears to be a function of:
- Patient Selection
- Tumour Characteristics
- the technique used.

Proper patient selection needs to be based on an understanding of the mechanisms by which they work and the principles of delivery.

Cryoablation failures may be related to improperly performed freeze–thaw cycles.

RFA failures maybe related to improper selection of patients:
- larger tumor sizes,
- tumors nearer large blood vessels, rapid heating causing tissue charring and therefore more thermal insulation,
- non-uniform heating of the tumor.

Appropriate real-time thermal monitoring of tissues is extremely important while performing a RFA in order to ensure uniform heating.