Steven Raman, MD, Director of Abdominal Imaging Fellowship at UCLA Health, discussed radio ablation as an alternative to surgical or pharmaceutical treatment for clear cell renal cell carcinoma (ccRCC). Since VHL is a very scan-based disease, he emphasizes the importance of having an expert reading the scans. One of his top interests is distinguishing benign from malignant kidney tumors by scan. While many specialists will say that this cannot be accomplished reliably, Dr. Raman argues that 80+% of the tumors can be characterized correctly because different tumors behave differently on the scan. Biopsies can be used to confirm the ~20% of tumors that cannot be confirmed by scan. By correctly characterizing tumors by scan, Dr. Raman can avoid over-treating benign tumors and begin treating malignant (cancerous) tumors even before they are small than 3 cm. Note: the “3 cm rule”—which states that surgery is only recommended for tumors larger than 3 cm—has been the consensus since the 1994 VHL International Medical Symposium.

Dr. Raman also prefers to avoid using surgery to treat the malignant tumors. Instead, he uses needles inserted into the skin without an incision to ablate or freeze the specific tumor. In some cases he can even avoid needles by using focused ultrasound. He shared a case study of one VHL patient under his care since 2004 who has responded very well to ablations. It was only in 2015 that his kidney function began suffering, and in September 2016 he was one month post-transplant. While these results cannot be guaranteed for all cases, Dr. Raman suggests that his use of ablation to treat kidney cancer holds promise for other VHL patients with ccRCC.
Thermal Ablation for Patients with vHL

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Outline

- Background on Renal Masses
- Imaging of Renal Masses
- Biopsy of Renal Masses
- Ablation of Renal Masses
- Imaging Guidance
- Performing Ablation
- Imaging after Ablation
- Efficacy

Disclosures

- Consultant:
  - Covidien, Endocare, Bayer
Background on Renal Masses

Renal Cell Carcinoma

U.S. Incidence of Renal Cortical Cancers

- In 2008, the ACS estimates
  - 57,000 cases of RCC in U.S.
  - 12,000 deaths from RCC
Renal Cell Carcinoma

- 125% increase in RCC in last 30 years due to increased use of imaging
- 70%: < 3 cm (T1a) & asymptomatic


Imaging of Renal Masses

Algorithm: Prior to 2000

- Incidental solid renal mass
- Surgery
- Active surveillance in patients with limited life expectancy or co-morbidities

Are all solid renal lesions cancers?

Frank et al. J Urol 2003
- > 2770 solid renal masses
- Benign lesions:
  - 25% < 3 cm
  - 30% < 2 cm
  - 44% < 1 cm
- Lipid poor AML
- Oncocytoma
- Tuncali et al. Radiology 2004: 10/27 lesions referred for ablation were lipid poor AML
Histology of Renal Cortical Cancers

- Renal Cortical Cancers malignant epithelial neoplasms derived from renal cortex
  - Clear cell carcinoma (70%)
  - Papillary carcinoma (15%)
  - Chromophobe carcinoma (5%)
  - Collecting duct carcinoma (<1%)
  - Unclassified

Can we Characterize Renal Masses?

- Yes!
- 80-90% of renal masses can be accurately characterized by a multiphasic CT or MRI
- The rest can be characterized by biopsy

UCLA Renal Cell Database (n=400)

CT Enhancement of RCC subtypes & Oncoctyoma

MR Imaging


Young, Pantuck, Raman
Radiology 2013
Lipid Poor AML

Biopsy of Renal Masses

Reasons to Biopsy

- Uncertain of diagnosis by imaging (20%)
- Confirm benign or malignant lesion
  - Benign: leave me alone
  - Malignant: observe, ablate or excise

Growth of Renal Masses

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>N lesions</th>
<th>Size at presentation, cm</th>
<th>Duration of follow-up, months</th>
<th>Growth rate, cm/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oda et al [16]</td>
<td>2013</td>
<td>10</td>
<td>2.47 (1.0–3.0)</td>
<td>20</td>
<td>0.15 (0.02–0.33)</td>
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<tr>
<td>Kato et al [17]</td>
<td>2004</td>
<td>18</td>
<td>1.38 (0.8–3.4)</td>
<td>27</td>
<td>0.47 (0.03–1.06)</td>
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<td>Volpe et al [18]</td>
<td>2004</td>
<td>22</td>
<td>2.8 (0.3–3.8)</td>
<td>32</td>
<td>0.1 (NA)</td>
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<td>Kassouf et al [19]</td>
<td>2013</td>
<td>26</td>
<td>2.37 (1.0–7.0)</td>
<td>32</td>
<td>0.08 (0.0–1.3)</td>
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<td>Bozkulak et al [19]</td>
<td>1996</td>
<td>80</td>
<td>1.73 (0.2–3.5)</td>
<td>39</td>
<td>0.47 (0.0–1.1)</td>
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<tr>
<td>Weidner et al [20]</td>
<td>2004</td>
<td>29</td>
<td>3.02 (0.4–3.5)</td>
<td>32</td>
<td>0.13 (NA)</td>
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<tr>
<td>Leib et al [21]</td>
<td>2004</td>
<td>26</td>
<td>3.3 (0.5–20.0)</td>
<td>20</td>
<td>0.2 (0.0–1.7)</td>
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<tr>
<td>Sadowy et al [1]</td>
<td>2004</td>
<td>22</td>
<td>4.03 (0.2–8.8)</td>
<td>20</td>
<td>0.2 (NA)</td>
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<tr>
<td>Fujimoto et al [10]</td>
<td>1995</td>
<td>6</td>
<td>2.47 (1.8–3.4)</td>
<td>29</td>
<td>0.47 (0.05–0.73)</td>
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<td>Czura et al [15]</td>
<td>1998</td>
<td>65</td>
<td>2.97 (1.0–17.0)</td>
<td>36</td>
<td>0.21 (0.01–0.46)</td>
</tr>
</tbody>
</table>

[16] meta-analysis 2006, 254, 2.62 (NA) 34, 0.28 (NA)

*Metrics: NA, not available. Reproduced with permission from Crizan et al. [22].
Reasons to Biopsy

- Biopsy is safe: 18-25 G needles
- Biopsy is effective
  - Histology, immunohistochem, genetics
  - Raman SIR 2012: 92% sensitivity for RCC diagnosis
- Neuzillet et al. J Urol 2004;17 (18 G needles)
  - 92% concordance for tumor type
  - 70% concordance for Fuhrman nuclear grade

Percutaneous Core Biopsy of RCC

- Core biopsy (19/20 G)
- FNA (22-25 G)

Biopsy

- Histological subtypes change
- Biological behavior may be governed by:
  - Subtype
  - Genetics
  - Gene rearrangements

Algorithm 2013

- Active surveillance in patients with limited life expectancy or co-morbidities
- Active surveillance until 3 cm with CT or MRI at 3-6 mos, 12 mos, and then yearly
Ablation of Renal Masses

1792


Monopolar Radiofrequency Ablation

Exposed Electrical Conductors

Primary Electrode

Ionic Agitation due to High Current Density

Return Electrode (Grounding Pad)

RF Generator 480kHz

Temperature and time effects on tissue

- 60°C – instantaneous cell death
- 50-52°C – irreversible cellular damage (4-6 minutes)
- 46°C – irreversible cellular damage at 60 minutes
- Thermal injury starts at 42-45°C – hyperthermia

Radiofrequency Ablation Systems

Percutaneous Microwave Ablation

Microwave Ablation

Heat generation in tissue:
- RF: Tissue = Joule heating
  - Amount of current delivered is based on the impedance of tissue
  - Less focused at electrode current density
- MW: Tissue = water rotation
  - Friction caused by movement of water molecules against each other
  - Mechanism of friction is different, but the source of heat is friction in both
Available MW Devices USA: 2015

NeuWave: 2.45GHz
Amica: 2.45 GHz
Microsulis: 2.45 GHz
Medwaves: 902-928 MHz
BSD Medical: 915 MHz
Covidien Emprint

Cryoablation
Gallil
Endocare
Irreversible Electroporation

Technique that increases the permeability of cell membranes by changing the transmembrane potential resulting in disruption of the cell membrane.

![Diagram of intact and disrupted cell membranes](Image Courtesy: Stephen Kee MD UCLA)

**Irreversible Electroporation (IRE)**

- **Mechanism:**
  - Train of high voltage (2-3 KV) micro-second DC pulses across two electrodes
  - Irreversible cellular membrane disruption

**Edd and Davulcu, 2007**

**IRE in clinical practice**

**Lee, Kee, et al. JVIR in press**
Lee et al, Radiology, 2010

Preservation of vessels and bile ducts and lack of IRE contour deformity

TUNEL stain: Apoptotic markers in IRE zone

Deodhar et al, Urology 2011 (77);754 - 760

Irreversible Electroporation

Imaging Guidance: Key Skill

- Function of skill and experience
- CT
- US
- MR
- US & CT
- US-CT/MR fusion
US Guidance

- Unparalleled precision

- Monitoring ablation is difficult

CT Guidance

MRI Guidance

US CT Fusion Guidance

Performing Ablation

Ablation is a Program

Ultrasound Fusion Guidance

Imaging

Follow up
Urology
Primary Care

IR
IR clinic
Imaging

Diagnosis

Therapy
Performing Ablation
• Patient and lesion selection is key
• Clinical Evaluation:
  – Comorbidities
  – Life expectancy
• Imaging Evaluation:
  – Is it benign
  – Is it accessible?
  – Is it safe
  – Do I need protective measures?

Renal Tumor Ablation: Patient Selection
• Patients with life expectancy > 5 years
• Patients with contraindications to surgery
• Patient with solitary or transplant kidneys
• Patients with prior surgical resections
• vHL patients with multiple tumors

Renal Tumor Ablation: Lesion Selection
• Malignancy
• Lesions < 3 cm
• Posterior or Peripheral lesions
• Lesions not adjacent to
  – UPJ
  – Colon
  – Duodenum
  – Jejunum

Renal Ablation
R.E.N.A.L. Score

Favorable Lesion: RENAL 4p

Renal Tumor Ablation: Favorable Lesions (RENAL 4p)
- Lesions < 3 cm
- Posterior, exophytic lesions
- > 1 cm from bowel and psoas muscle

Renal Tumor Ablation: More Difficult Lesions
- Lesions 3-5 cm
- Central Lesions
- Anterior and Medial lesions
- Posterior and medial lesions adjacent to ureter or UPJ
- RENAL 7-10
Less Favorable

Posterior RCC: Cryoablation
RENAL 4p

Posterior Chromophobe RCC: RFA of RENAL 4p

Posterior Papillary RCC: RFA

RENAL 4p
Avoid Potential Trouble

- GF nerve
- Ureter
- Duodenum

Protective Measures

- Hydrodissection: D5 water or saline
  - Moves colon, duodenum, bowel
  - Minimizes nerve injury
  - Avoids ureteral injury
- JJ Stent or Nephrostomy Pyeloperfusion
  - Minimizes collecting system/ureter injury
- Other: Air, CO₂, balloon

Anterior RCC: RFA 6h

Percutaneous RFA: Posterior RCC
RCC: Percutaneous Cryoablation

70 yo woman with cystic RCC

RFA: Cystic RCC

Ureteral Stent

RENAL 9x
Follow up

- Immediate
- 1 month
- Every three months for 1 year
- Then 6 months x 2
- Then yearly for 5 years

Imaging after Ablation

CT Surveillance post RFA

Courtesy Matt Callstrom, Mayo Clinic
Post RFA MR: RCC

Pre 3mo 6mo 1 yr

Cryoablation Follow up Imaging

Pre 1 mo post 1 year post 2 years post

Residual After Lap cryoablation

vHL Case Studies
Case 1: 30 yo patient with vHL

12/04 and 4/05

6/05

3/06

7/05 and 8/05
Inflammatory Tissue: 2006-7

3/06 (R)

4/06 (L)

5/06 (L)
Herrera 2/07 (L)

4/07 & 6/07

7/07

8/07 (Rs)
Slowly Growing Left Solid Mass

9/07 (Ls)

Venous Phase

10/07 (L)
Case 2: 2014
38 yo patient with vHL

Case 3: 2012
27 yo patient with vHL

Post Ablation Urinoma
### Efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th>Tumors</th>
<th>Lesion size</th>
<th>Technical Success</th>
<th>Overall Success</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gervais '05</td>
<td>100/85</td>
<td>3.2 cm</td>
<td>75%</td>
<td>90%</td>
<td>2.3 yr</td>
</tr>
<tr>
<td>Zagoria '07</td>
<td>125/104</td>
<td>2.7 cm</td>
<td>87%</td>
<td>93%</td>
<td>13.8 mo</td>
</tr>
<tr>
<td>Breen '07</td>
<td>105/97</td>
<td>3.2 cm</td>
<td>79%</td>
<td>90%</td>
<td>16.7 mo</td>
</tr>
<tr>
<td>Raman '14</td>
<td>142/100</td>
<td>2.5 cm</td>
<td>95%</td>
<td>93%</td>
<td>2 year</td>
</tr>
</tbody>
</table>
Renal Cell Carcinoma

5 yr Survival
Radical Nephrectomy: 80-95%
Partial Nephrectomy: 80-94%
Lap. Partial Nephrectomy: 89-100%

RFA Complications:
- Gervais 2005: 100 lesions/85 pts
  - 5 Hemorrhage
  - 2 ureteral injuries & 1 urine leak
  - 1 skin burn
- Breen 2007: 105 lesions/97 pts
  - 1 Hematuria
  - 1 Calyceal leak
  - 1 Ureteral stricture
  - 1 Pneumothorax
  - 1 Duodenal injury
- Zagoria 2007: 125 lesions/104 pts
  - 3 Perinephric hematoma
  - 1 Pneumothorax
- Raman 2011: 149 lesions/100 pts
  - 5 Perinephric hematoma
  - 1 ureteral stricture

Cryoablation Complications

Brown. JVIR 2007:18
Summary

- Incidence of small renal masses are increasing
  - Grow slowly
  - Can be characterized on CT/MRI
  - Can be safely and effectively biopsied

- Thermal Ablation techniques
  - Are susceptible to heat sink effects
  - Equivalent efficacy and complication

- Key Skill:
  - Imaging guidance/tip management

"Quæ medicamenta no sanant, ea ferrum sanat. Quæ ferrum non sanat, ea ignis sanat. Quæ verò ignis sanat, ea insanabilia existimare oportet."

The diseases which medicines cannot cure, excision cures: those which excision cannot cure, are cured by the cautery; but those which the cautery cannot cure, may be deemed incurable.”

Hippocrates
Aphorisms, 400 B.C.E.