Interventional Management of NSCLC

Hiran C Fernando FRCS
Professor and Chief, Division Thoracic Surgery
Boston Medical Center
Comparison of MWA and RFA
Qiang Lu et al; AATS 2015

• 141 patients; 100 with NSCLC/ 41 with mets
• First comparative study of MWA and RFA for lung
• Randomized study
  – RFA 69; MWA 72
• Conclusions;
  – No difference in survival
  – MWA superior for local control for tumors >3cm
    • Size matters!
Thermal Ablative Therapies for NSCLC

- Radiofrequency ablation (RFA)
  - Most published data
- Microwave ablation (MWA)
- Irreversible Electroporation (IRE)
  - Direct Current; No published lung data
- Cryoablation (Cryo)
- Bronchoscopic Ablation (BsAb)
RFA system

- 3 components
  - An RFA generator
  - An active electrode
  - Dispersive electrodes (bovie pads)
- RF energy (alternating current) moves from the active->dispersive->active electrodes, resulting in frictional heating of tissue
- When temperature $>60^\circ$C, tissue dies
  - Most systems will heat around 90-100 $^\circ$C
Active electrode

RF generator

Patient return pads
(4 total; 2 on each thigh)
## RFA survival for Stage 1 NSCLC

<table>
<thead>
<tr>
<th>Author (n)</th>
<th>Median FU</th>
<th>Median Survival</th>
<th>1yr</th>
<th>2yr</th>
<th>5yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lanuti (31)</td>
<td>17m</td>
<td>30m</td>
<td>85%</td>
<td>78%</td>
<td>NR</td>
</tr>
<tr>
<td>Pennathur (13)</td>
<td>28m</td>
<td>Not reached</td>
<td>95%</td>
<td>68%</td>
<td>NR</td>
</tr>
<tr>
<td>Hiraki (50)</td>
<td>37m</td>
<td>67m</td>
<td>94%</td>
<td>86%</td>
<td>NR</td>
</tr>
<tr>
<td>Dupuy (75)</td>
<td>NR</td>
<td>29m</td>
<td>78%</td>
<td>57%</td>
<td>27%</td>
</tr>
</tbody>
</table>

NR = not recorded
Percutaneous Thermal Ablation for Stage IA Non-Small Cell Lung Cancer: Long-term Follow-Up

Chaitan K. Narsule¹, Divya Nair¹, Avneesh Gupta², Roy G. Oommen³, Michael I. Ebright⁴, Virginia R. Litle¹, Hiran C. Fernando¹

¹Division of Thoracic Surgery, Boston University School of Medicine, Boston, MA
²Department of Radiology, Boston University School of Medicine, Boston, MA
³The Thoracic Associates, Stoughton, MA.
⁴Division of Thoracic Surgery, Columbia University, New York, NY
BMC Results; Thermal Ablation
Stage I NSCLC

• 21 Lung tumors ≤ 3 cm in max diameter by CT scan of lungs
  – Median FEV1%=39%
  – Median DLCO%=37%

• 18 had RFA
• 3 had microwave

• Mediastinoscopy
  – Suspicious nodes by CT/PET

Presented; ISMICS 2014
BMC; Follow-Up after RFA (stage 1)

• Mean follow-up: 42 months

• Overall survival:
  – 2 years: 81%
  – 3 years: 52%

• Median survival: 39 months

• Local progression: 10 patients (47.6%)
  • Median time to local progression: 35m
  • 3 treated with SBRT
  • 3 retreated with ablation
Radiofrequency Ablation of Stage 1A NSCLC in Medically Inoperable Patients: Results from ACOSOG Z4033 (Alliance), an NCI Funded Multicenter Trial

Damian E. Dupuy¹, Hiran Fernando², Shauna Hillman³, Thomas Ng¹, Angelina D. Tan³, Jo-Anne Shepard⁴, William Rilling⁵, Kelvin Hong⁶, Joe B. Putnam⁷
Z4033; Study Design

- Single arm pilot trial
- 55 medically inoperable patients
- Histology confirmed NSCLC
Objectives

- **Primary Objective**
  - Two year survival

- **Secondary Objectives**
  - Establish procedure specific morbidity and mortality
  - Freedom from local recurrence* at 2-years
  - Freedom from distant recurrence at 2-years

*Local recurrence includes recurrence within the same lobe or hilum (N1 nodes) or progression at the ablated site after treatment effects have subsided*
## Results

Grade 3 AE’s possibly related to treatment (0-3 months)

<table>
<thead>
<tr>
<th>AE Type</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constitutional Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>Infection/Febrile Neutropenia</strong></td>
<td></td>
</tr>
<tr>
<td>Colitis, Infectious</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Infection – other, specify</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>Pulmonary</strong></td>
<td></td>
</tr>
<tr>
<td>Dyspnea (shortness of breath)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pneumonitis/pulmonary infiltrates</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>

- Grade 3 AE rate = 12%
- No Grade 4 or 5 AEs
- Two Grade 3 PTX requiring intervention
Overall Survival

N = 51
No. Event = 15
Survival Rate at 1 year: 86.3%
Survival Rate at 2 year: 69.8%
RTOG 0236; Overall Survival after SBRT

36 month overall survival = 56% (CI: 42-68%)

- Dead: 26
- Total: 55
- MST: 48.1 (95% CI): (29.6, not reached)

- Median survival is 48.1 months
Z4033; Local Recurrence

N=51
No. Event = 19
Local Recurrence Free Rate at 1 year: 68.9%
Local Recurrence Free Rate at 2 year: 59.8%
Z4033; Impact of Size on Outcomes

• Tumor size significantly (p=0.049) associated with overall survival at 2-years
  – <2cm; 78%
  – ≥2cm; 58.1%

• Tumor size; non-significant trend (p=0.406) for local progression free survival at 2-years
  – <2cm; 63.7%
  – ≥2cm; 56.1%
Microwave Ablation

- Several systems in USA, Europe;
  - Covidien (Evident), Microtherm-X, AveCure (915-MHz)
  - Covidien (Emprint) Certus 140, Acculis, (2.45GHz)
- Require multiple or single probe placements for similar ablation
- No trials comparing systems
  - Oncological outcomes
  - Safety
Microwave Ablation

Neuwave (2.45 GHz)

Covidien; Emprint (2.45 GHz)

BSD MicrothremX (915 MHz)
Differences Between MWA and RFA

• Higher frequencies have shorter wavelengths
• Amplitude
  – Applied voltage or current

<table>
<thead>
<tr>
<th></th>
<th>RF (470 kHz)</th>
<th>MW (915 MHz, 2.45GHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In AIR</td>
<td>0.64km</td>
<td>/ 30cm</td>
</tr>
<tr>
<td>In TISSUE</td>
<td>91m</td>
<td>~4-5cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>~7.6 cm in liver tumor</td>
</tr>
</tbody>
</table>
RF & MW Circuit Diagrams

- **RF**
  - Circuit pathway
  - Electrode passes current

- **MW**
  - No current flow through patient
  - Antenna radiation
Cryoablation

Cryohit (Galil Medical, Yokneam, Israel)  Cryocare (Endocare, Irvine, CA, USA)
Cryoablation

• 1.5, 1.7 and 2.4mm percutaneous probes
• Argon based systems
• Ice ball visible with CT, US, MRI
• Relatively painless during treatment
• Multiple applicators
## Stage I NSCLC; Results after Microwave & Cryoablation

<table>
<thead>
<tr>
<th>Author (n)</th>
<th>Modality Ablation</th>
<th>Median Follow-up</th>
<th>1-yr Overall Survival</th>
<th>2-yr Overall Survival</th>
<th>3-year Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wolf (50)</td>
<td>Microwave</td>
<td>10months</td>
<td>65%</td>
<td>55%</td>
<td>45%</td>
</tr>
<tr>
<td>Yang (47)</td>
<td>Microwave</td>
<td>30months</td>
<td>89%</td>
<td>63%</td>
<td>43%</td>
</tr>
<tr>
<td>Yamauchi (22)</td>
<td>Cryoablation</td>
<td>23months</td>
<td>N/A</td>
<td>88%</td>
<td>88%</td>
</tr>
<tr>
<td>Zemlyak (27)</td>
<td>Cryoablation</td>
<td>33months*</td>
<td>N/A</td>
<td>N/A</td>
<td>77%</td>
</tr>
</tbody>
</table>

N/A=not available

*median follow-up included patients treated with RFA and surgery
Bronchoscopic Ablation of peripheral tumors

• Next step in evolution therapies for NSCLC
• Potentially allow Dx and Rx-in same setting
• Lower risk of pneumothorax compared to percutaneous approaches
• However need improvements in
  – Navigation technology (accuracy of probe placement)
  – Available flexible ablation systems
## EN Bronchoscopy

<table>
<thead>
<tr>
<th></th>
<th>Number patients</th>
<th>Successful Diagnosis -</th>
<th>Pneumothorax rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamprecht (2012)</td>
<td>112</td>
<td>83.9%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Pearlstein (2012)</td>
<td>104</td>
<td>82% -true malignant</td>
<td>5.8%</td>
</tr>
<tr>
<td>Eberhardt (2007)</td>
<td>89</td>
<td>67%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>
Requirements for EN Bronchoscopy for Successful Ablation

• Need 100% accuracy of probe placement
  – unlike requirement for fiducial placement for SBRT
• Need to be sure about orientation of ablation probe to tumor to ensure optimal ablation achieved
  – Real-time CT scan confirmation of bronchoscopic probe
  – ? fiducial placement that could be tracked by ENB system
Bronchoscopic-guided MWA ablation
Ferguson J et al. Chest 2013:144;37A

• Animal study;
  • 4 ablations (different power/time settings)
  • 3 pigs
  • 12 ablations performed

• Neuwave 17 gauge antenna via bronchoscope
• Successful oval shaped ablations created (1.2-3.7cm in short axis) based on power used
Study 3 Different Bronchoscopic RFA catheters

• Ten patients cT1N0M0 had bronch ablation prior to planned resection
• 3 probe sizes – active tip (5mm, 8mm, 10mm)
• Bronch navigation with CT flouroscopy
• No complications (no PTX)
Internally cooled radiofrequency ablation (RFA) electrodes. The shaft (arrows) and tip of the electrode (arrowheads) are shown (A). The top electrode produced power output and measured the tip temperature and impedance. Three types of the tip were used: 5-mm cylindrical active tip (B); 8-mm active tip with four beads (C); and 10-mm active tip with five beads (D).
Comparison of area of RFA with the three different tips. The area of RFA lesion using an internally cooled electrode with the 10-mm tip with five beads was significantly larger than that using the electrode with a 5-mm cylindrical catheter tip. Values are means ± SEM; *P < .05. See Figure 1 legend for expansion of abbreviation.
Clinical Cases Bronchoscopy guided-RFA
Koizumi T et al; Case Reports on Oncol Med; 2013 ID 515160

• Two patients treated with bronchoscopy guided ablation only
• No recurrence at 4 and 3.5 years respectively
• 1 patient developed local recurrence and was treated with repeat bronchoscopy guided ablation
Conclusions; Thermal Ablation

- Good therapy for medically inoperable and high-risk operable patients
- Survival at two years as good as SBRT
- Thermal ablation technologies are evolving
  - Further studies comparing MWA systems and different technologies needed
- Approaches are also evolving
  - Bronchoscopic ablation may soon be feasible
Thank you!