ONCOLOGIC PERCUTANEOUS INTERVENTION: 2015 UPDATE

HANH VU NGHIEM, MD

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

ONCOLOGIC PERCUTANEOUS IMAGE GUIDED TUMOR ABLATION

Evolving, growing and increasingly accepted treatment option for patients with malignant disease of multiple organ systems in particular the liver, kidney, lung, bone and soft tissues.

Direct thermal or non-thermal destruction of cells and tissue in a known manner

Minimally invasive

Allows for reduced morbidity and mortality

Conservation of normal tissue of the organ

Low procedural cost

Safe and technically feasible

Combined therapy may result in improved survival (TACE, radiation therapy, chemotherapy)

EVALUATION AND MANAGEMENT OF PATIENTS

Consultation: H &P, benefits, risks, side effects, alternatives, realistic expectation, informed consent.

Outpatient procedure: usually same day discharge or 23 hour short stays especially following lung lesion ablation.

Anesthesia: GETA- General EndoTrachial Anesthesia or MAC- Monitored Anesthesia Care (ie moderate or deep sedation without intubation by anesthesia)

Imaging:

Pre-procedure imaging: recent high quality and full imaging essential to minimize complications and maximize therapeutic efficacy and for staging of the disease.

Immediate post procedure imaging: routinely done to assess for complications, and success/incomplete/failure of the initial ablation and the need for immediate re-ablation.

Post-procedure follow up imaging: Critical to measure success or failure of the procedure, need for repeat ablation, and assessment of interval tumor growth or metachronous tumor development.
There is no standardized post-ablation follow-up imaging algorithm. Proposed post-ablation imaging follow-up could include contrast-enhanced CT or MRI within 1–2 weeks after the procedure, early short-interval follow-up imaging at 1–3 months, surveillance imaging every 6 months for the second year, and annual imaging thereafter for at least 5 years from the ablation procedure. We use this protocol for liver ablation. For kidney ablation, our first post ablation imaging is 6 months, then yearly for 5 years. Findings worrisome for tumor recurrence include focal nodular enhancement greater than 10 HU or any qualitative level of MRI enhancement.

**ABLATION MODALITIES**

**THERMAL ABLATION:** Destruction of tumor tissue by increasing or decreasing the temperature to induce irreversible cellular injury

**HEAT BASED ABLATION:** Cellular damage caused by heat with target temperature higher than 55 degree Celsius to create coagulation necrosis

1- RADIOFREQUENCY ABLATION (RFA)
2- MICROWAVE (MWA)
3- HIGH INTENSITY FOCUSED ULTRASOUND (HIFU)

**COLD BASED OR CRYOABLATION:** The freezing process results in both intracellular and extracellular ice formation, both of which can lead to cellular death. Cryoablation achieves cell death at -20 to -40 degree Celsius.

**NON-THERMAL TISSUE ABLATION**

**IREVERSIBLE ELECTROPORATION (IRE):** Non-thermal form of tissue ablation using high-voltage electrical current to induce pores in the lipid bilayer of cell membrane, resulting in cell death.

**CHEMICAL ABLATION**

**PERCUTANEOUS ETHANOL INJECTION (PEI):** Injection of Ethanol into a tumor causes cellular dehydration, protein denaturation and ultimately cell death. Historically used for the treatment of HCC, and now has been largely replaced by thermal ablation techniques.

**TECHNICAL CONSIDERATION: CHOICE OF ABLATION DEVICE**

RFA, MWA and Cryo-ablation are most often used in current clinical practice and each has advantages and disadvantages that require careful consideration. Although IRE and HIFU have been described, these are not widely used in clinical practice and therefore will not be discussed here.

Regardless of the ablative device used, the post ablative goal is similar: to achieve a predictable and continuous lethal ablation volume with a tumor free margin of at least 5-10 mm.
### COMPARISON OF RADIOFREQUENCY ABLATION AND MICROWAVE ABLATION METHODS

<table>
<thead>
<tr>
<th>RFA</th>
<th>MWA</th>
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<tbody>
<tr>
<td>Alternating Electric Current</td>
<td>Oscillating Microwave Electromagnetic Energy</td>
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<tr>
<td>Grounding pads (risk of skin burn)</td>
<td>No grounding pads</td>
</tr>
<tr>
<td>Tissue charring, desiccation and water vapor increase impedance limiting electrical and thermal conductivity</td>
<td>Rapid and homogenous heating and ionic polarization</td>
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<tr>
<td>Lower intratumoral temperatures</td>
<td>Higher intratumoral temperatures</td>
</tr>
<tr>
<td>Limited ability to overcome local tissue effects as perfusion and ventilation</td>
<td>Microwave continues to heat through all biological tissues</td>
</tr>
<tr>
<td>Heat sink effect</td>
<td>Less susceptible to heat sink effect</td>
</tr>
<tr>
<td>Unpredictable ablation zone</td>
<td>More predictable ablation zone</td>
</tr>
<tr>
<td>Single lesion treatment</td>
<td>Simultaneous treatment of multiple lesions</td>
</tr>
<tr>
<td>More procedure time (12-30 min)</td>
<td>Shorter procedure time (2-8 min)</td>
</tr>
<tr>
<td>Less ablation volume (up to 5 cm)</td>
<td>Larger ablation volume (up to 8cm)</td>
</tr>
<tr>
<td>Surgical clips or pacemaker are contraindications</td>
<td>Surgical clips, pacemakers not a contraindication</td>
</tr>
<tr>
<td>Largest reported data and experiences</td>
<td>Relatively new with limited clinical data and experience</td>
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<tr>
<td>Technological developments to improve physical limitation: internal electrode cooling to limit charring; expandable, multi-tined or clustered electrodes to increase surface area and power delivery; rapid switching approaches allowing overlapping ablation zones; saline infused and high power generators.</td>
<td>Heterogeneous systems from different manufacturers with different performance characteristic (3rd generation system with both active antenna cooling and high-power generator recommended) (we use the AMICA MW system almost exclusively currently. It is a 3rd generation system)</td>
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</tbody>
</table>

Technological developments to improve the physical limitations of RFA have been done. However, these have also been reported to be associated with an increased risk of complications.

MWA system performance can vary widely so it is critical that the operators are familiar with the shapes and sizes of the ablation zones and the different time and power combinations with a particular system since the volume of the microwave ablation zones depends on the power used, antenna design, number and orientation of antenna and the microwave frequency.
Clinically, compared with RFA, MWA can produce hotter and larger ablation zones in multiple tissue types with fewer applicators to achieve predictable and reproducible post-ablation margins.

**CRYOABLATION METHOD**

Expanding ice ball (predictive of ablation zone) is well visualized at US, CT and MRI allowing more precise monitoring than with heat based method.

- True ablation zone (irreversible cell death) is 8-10 mm deep to edge of the ice ball
- Often less painful compared to heat ablation
- No grounding pads (no risk of skin burn)
- Several cryoprobes (Rule of thumb: # of probes needed = diameter of mass + 1) often required to treat most tumors due to small cryoprobe surface area which limits cooling
- Longer ablation times 30-40 minutes (freeze-thaw-freeze cycles)
- Potential bleeding complication requiring tract coagulation
  “Cryoshock”: systemic complication as a result of rapid release of cellular debris into systemic circulation

**CLINICAL CONSIDERATIONS**

Clinical decision in choosing the ablative device for individual patient should not be entirely a data driven process but importantly should also be based on:

1. Operator skill and expertise

2. Understanding and knowledge of:
   - Indications of the procedure
   - Physical properties of different ablation modalities
   - Systems used
   - Ability to accurately place the needles with US and CT guidance
   - The expected appearance of successful and unsuccessful ablations and complications at immediate post-procedural imaging
   - Ablation by heating mechanisms lowers the risk of hemorrhage as damaged blood vessels coagulate.

3. It is best to be familiar with and have available both a heat and cold based system.

**CLINICAL CONSIDERATIONS OF ORGAN SPECIFICS**

**KIDNEY**

Indications for ablation of renal tumor:

Although partial nephrectomy remains the reference standard for treatment of small renal masses, the guidelines of the American Urological Association support consideration of thermal ablative technique for patients with T1a disease (≤ 4cm), increased risk of multiple RCC tumors (e.g., von Hippel-Lindau syndrome), patients’ condition not suitable for surgery and solitary kidney.
Advantages of ablation therapy relative to surgery include:
- Reduced morbidity
- Better preservation of renal parenchymal volume which correlates with overall renal function
- Faster recovery time
- Shorter or no inpatient hospitalization
- Possibly the only option available to patients with serious comorbid conditions who are not surgical candidates
- Reduced healthcare cost

Clinical consideration for ablative therapy of renal tumor:

Awareness of bleeding risk associated with larger tumor size (increased bleeding risk with tumor >3cm) and tumor proximity to vital local structures is essential before ablation. Schmidt et al (AJR 2014; 202:894-903) suggests a practical algorithm for procedure planning called ABLATE (other considerations such as nephrometry score, and other systems, to predict success and complication rates are also available)
A: axial diameter of the tumor
B: bowel proximity
L: location within the kidney
A: adjacent to ureter
T: touching renal sinus fat
E: endophytic or exophytic position

Preventative measures such as retrograde pyeloperfusion and/or hydrodissection can be used and in fact, hydro dissection plays a much larger role in renal ablations than in hepatic ablations due to the relatively close proximity to the bowel, pancreas, adrenals and ureters.
Potential complication of nerve injury needs to be considered which can lead to post ablative neuralgia and paresthesia.

Renal tumors smaller than 3 cm can be ablated successfully with both heat based RFA/MWA and cryoablation. From a practical standpoint, MWA may be a good choice for exophytic tumors because of speed and the need for fewer applicators. However, central tumors and tumors adjacent to critical structures may benefit from the precision and relative sparing of the collecting system and ureter associated with cryoablation.

Outcome and complications:

Current literature suggests a technical success rates for patients with T1a tumors (4 cm or less) approaching 100% (ranges 88% to 100%). More than 95% of tumors under 3cm in diameter can be completely ablated. Reported complication rates range from 1%-7%. Long-term outcome data reveal metastasis-free survival rates of 88% to 99% five years after ablation.

A recent report by Thompson et al (European Urology Feb 2015, 252–259) from the Mayo Clinic Tumor Registry between 2000-2011 compares the outcome of partial nephrectomy (PN) and percutaneous ablation of 1424 patients with T1 renal masses shows a local recurrence free survival rates of 98% at 3 yrs. for all
three PN, RFA and Cryo for T1a (4cm or less) patients. The distant metastases-free survival rates at 3 yrs. for PN 99%, RFA 93% and Cryo 100%. (This paper actually states “if these results are validated, an update to clinical guidelines would be warranted implying that percutaneous ablation is comparable to partial nephrectomy in terms of outcomes and data to prove equivalent efficacy.)

The local recurrence free survival rates for T1b (> 4cm to 7cm) patients at 3 years for PN 96% and Cryo 97%. The distant metastases-free survival rates at 3 yrs. for PN 96% and for Cryo 92% with no statistical significant difference.

**LIVER**

The evolution of imaging and ablation devices has allowed for the increased utilization of percutaneous ablation as definitive and palliative treatment of primary and metastatic hepatic malignancies in non-surgical candidates due to comorbidities, and in patients who refuse resection or when there is a need to preserve liver function.

Heat is preferred for treating patients with HCC in liver cirrhosis because of increased bleeding risk and cryoshock associated with cryoablation. Cryoablation has not been widely used in the treatment of hepatic malignancies and in general has been used previously for larger lesion because of the ability to use multiple cryoprobes simultaneously. However, currently with the third generation microwave system, large confluent ablation zones can be achieved.

Percutaneous RFA or MWA is considered the optimal regional treatment of choice for focal unresectable HCC of early stage, but its use has been proposed for other clinical indications such as the reduction of tumor burden and as a bridge to transplantation.

The ablation success rate with RFA or MWA alone of small HCC lesions (up to 2-3 cm in diameter) reaches 90% with a local recurrence rate of 1% depending on tumor location. Treatment of larger tumor > 3cm with RFA or MWA alone is associated with high local recurrence rates. Combined local treatment with TACE followed by RFA or MWA is therefore recommended for tumors larger than 3cm diameter which results in fewer local failures and is well tolerated with few serious complications. RFA or MWA may also be used for four or more HCC nodules where applicable.

Overall, the published studies support the comparability of the two methods (RFA and MWA) in terms of survival, local recurrence and complications. Across the studies, the survival rates are reported within the range of 68%-100% at 1st year and 24%-78% at 4th year and local control rates range from 89%-95%.

The main contraindications to liver ablation therapy include: intravascular invasion, tumor location <1cm from the main biliary duct, severe bleeding diathesis, and decompensated ascites.

Major complications associate with heat based liver ablative therapy include liver failure, bleeding, infection, abscesses, intercostal nerve injury, organ injury, tumor lysis syndrome and pneumothorax. The rate of major complications is low 2.2 to 3.1%. The major complication rate for cryo-ablation is higher at 10.8%.

For secondary malignancies, most prefer to treat patients with five or fewer lesions with best results with tumors 3cm or smaller. In these patients with normal liver background, heat based therapy or cryotherapy
may be considered, but cryoablation is associated with increased risk of complications (bleeding, myoglobinemia, cryoshock, cracking of the liver)

**LUNG**

Percutaneous thermal ablation is best suited for high-risk non-surgical candidate patients with early stage lung cancers and small pulmonary metastases with favorable location without hilar, mediastinal or extrathoracic involvement. It has also been considered as a palliative treatment for tumor-related symptoms or chest recurrences within treatment fields.

Heat ablation, preferably MWA, should be the primary consideration in most cases due to speed, ability to obtain consistent and large ablation zone and ablate effectively in to normal lung for adequate ablative margins. Cryoablation may be considered in patients with large tumors, peripheral tumors close to the chest wall or with chest wall invasion, and more central tumors with large adjacent bronchi.

Important points to consider when performing RFA or MWA of the lungs:

A. Avoiding direct puncture of the peripheral tumor. An indirect approach that leaves an unablated tract of at least 2cm of aerated lung is desirable to avoid extension of ablation zone to the chest wall resulting in pain and potential skin burns.

B. The ablated lung becomes dehydrated with volume loss which may result in retraction of the antenna or electrode insertion site from the pleural surface with potentially causing persistent air leaks and bronchopleural fistulas.

C. Tract cautery should be avoided in the lung because of the risk for persistent air leak.

D. Caution not to over treat as this can be associated with increased complications

**Outcome and complications:**

The literature on pulmonary thermal ablations in early stage disease is heterogeneous due to diversity of study group and variations in duration of follow up as well as reporting standards.

Image guided percutaneous thermal ablation of lung cancer is generally safe and well tolerated. Most complications are treated conservatively or with minimal interventions. However, there are uncommon but serious complications such as massive pulmonary hemorrhage, bronchopleural fistula, and pulmonary artery pseudo aneurysm. A periprocedural mortality has been reported up to 1.4% of cases. Enough attention should be paid to patients with emphysema, sub pleural, or large target tumor.

The most common complication after percutaneous lung ablation is pneumothorax occurring in 11-52 % of cases with RFA although only 6-29% of patients require chest tube placement. Zheng et al (Ann Thorac Surg 2014; 98) documented a major complication rate after MWA of the lung of 20.6 %. Recently, Splatt et al (J Med Imaging Radiat Oncol 2015 Aug 4) reported a similar major complication rate of 20% after MWA of lung lesions with incidence of pneumothorax requiring chest tube placement of 12.9%. The authors concluded that MWA of pulmonary tumors carries moderate risk; nevertheless, the usually manageable complications should not deter from undertaking a potentially curative therapy for poor surgical candidates.

KS Lee and B R Pua. Alternative to surgery in early stage NSCLC-interventional radiologic approaches.
Complications following RFA

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence (%)</th>
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</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>6-12</td>
</tr>
<tr>
<td>Pneumothorax requiring chest tube</td>
<td>6-29</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>6-19</td>
</tr>
<tr>
<td>Bronchopleural fistula</td>
<td>0.6</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>3-9</td>
</tr>
<tr>
<td>Pulmonary hemorrhage</td>
<td>6-18</td>
</tr>
<tr>
<td>Pulmonary artery pseudoaneurysm</td>
<td>0.2</td>
</tr>
<tr>
<td>Reactive pneumonitis</td>
<td>0.4</td>
</tr>
<tr>
<td>Needle tract tumor seeding</td>
<td>0.3-0.7</td>
</tr>
<tr>
<td>Death</td>
<td>0.6</td>
</tr>
</tbody>
</table>

A M Splatt and K Steinke. Major complications of high-energy microwave ablation for percutaneous ct-guided treatment of lung malignancies: single-centre experience after 4 years (Queensland, Australia) with 70 ablations

J Med Imaging Radiat Oncol. 2015 aug 4. [epub ahead of print]

<table>
<thead>
<tr>
<th>Major complication</th>
<th>Our experience (%)</th>
<th>Other literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall rate of major complications</td>
<td>20</td>
<td>20.6%</td>
</tr>
<tr>
<td>Periprocedural mortality</td>
<td>1.4</td>
<td>0–0.5%</td>
</tr>
<tr>
<td>Pneumothorax requiring drain insertion</td>
<td>12.9</td>
<td>3.8–15.7%</td>
</tr>
<tr>
<td>Effusion requiring drain insertion</td>
<td>5.7</td>
<td>0–2.9%</td>
</tr>
<tr>
<td>Hemorrhage altering management</td>
<td>2.9</td>
<td>N/A for MWA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6–17.7% for RFA</td>
</tr>
<tr>
<td>Infection</td>
<td>2.9</td>
<td>0.9–3.4%</td>
</tr>
<tr>
<td>Mechanical failure</td>
<td>1.4</td>
<td>3.4%</td>
</tr>
<tr>
<td>Skin/chest wall burns</td>
<td>1.4</td>
<td>3%</td>
</tr>
<tr>
<td>Pleural seeding</td>
<td>1.4</td>
<td>N/A for MWA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.3–0.7% for RFA</td>
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