Minimally Invasive Treatment of Focal Malignant Hepatic Neoplasms

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Agenda

I. Discussion of Malignant Hepatic Neoplasms
II. Conventional Rx of Hepatic Neoplasms
III. Minimally Invasive Treatments
IV. Presentation of our patient RFA
V. Future Directions of Minimally Invasive Rx
Malignant Hepatic Neoplasms

- primary carcinomas of the liver are relatively uncommon in N. America (0.5-2% of all cancers)

- in countries where viral hepatitis is endemic (Asia and sub-Saharan Africa), it is much more common (20-40% of all cancers)
Hepatic Malignancies (Cont.)

- metastatic involvement of the liver far exceeds the incidence of primary neoplasia (by 20X in the US);

  - the most common primary tumors producing hepatic metastases are those of the breast, lung and colon;

- primary and secondary malignant hepatic tumors are among the most common tumors worldwide;
Conventional Rx: Surgical Resection

• Surgical resection is the only potential curative Rx;

• For patients with hepatic metastases, surgical resection achieves >90% response rate and a 30-35% 5 year survival rate (Without resection, the 5 year survival is 1% with median survival of 9.6 months);

• Surgical resection is associated with significant risks of morbidity and mortality (2-10%);
Surgical Resection (Cont.)

• only a small fraction of patients with hepatic metastases are surgical candidates;

• patients with HCC are often cirrhotic, and the associated liver dysfunction and coagulopathies can make surgery impractical;

• Systemic chemotherapy and radiation therapy are ineffective treatment options (response rates 15-20%);
Minimally Invasive Treatments

Minimally invasive therapies include:

1. Chemoembolization
2. Intratumoral injection of compounds (ethanol)
3. Thermal techniques (RF-Radiofrequency ablation laser, cryo, microwave, High Intensity Focused Ultrasound - HIFU)
Chemoembolization

Mechanism

% Blood supply

- Hepatic A.
- Portal V.

Hepatic Mets
Hepatic Tissue
Mechanism Of Chemoembolization (Cont.)

- Embolization of the hepatic artery coupled with arterial delivery of chemotherapy induces necrosis in tumors while normal hepatic tissue remains intact;
Chemoembolization

Technique:

1. Diagnostic visceral angiography is performed;

2. Catheterization of right/left hepatic artery with subsequent chemoembolization to near stasis using Gelfoam, EtOH, Iodized Contrast and chemotherapy;

3. Pain control with intraarterial lidocaine and conscious sedation;
Chemoembolization (Cont.)

Results:

1. 60-80% response rate for primary and metastatic tumors;

2. survival rates of 70% (1 year), 40% (3 years), and 10% (5 years);
Chemoembolization (Cont.)

- This angiogram reveals a clustering of vessels that branch off of the left hepatic artery;

- This finding localizes the tumor (in this case a metastatic carcinoid) and helps direct therapy;

Image from Matthew Halpern, Gillian Lieberman, MD
Chemoembolization (Cont.)

- CT w/o contrast taken 24 hrs post chemoembolization Rx;
- Hyperintense region denotes deposition of chemoembolization materials (iodinated contrast) in the left hepatic lobe;
- No evidence of backflow to gallbladder or stomach;

Image from Matthew Halpern, Gillian Lieberman, MD
Intratumoral Injection

Ethanol Ablation:

- highly accepted worldwide because of simplicity, low cost and good clinical results;

- Mechanism: ethanol causes dehydration and necrosis of neoplastic cells as well as necrosis of feeding vessels with resulting thrombosis and tissue ischemia;
Ethanol Ablation (Cont.)

**Technique:** percutaneous injection of 1-8 ml ethanol under US guidance;

**Cost:** Needle, syringe, tubing, ethanol ($45);
# Ethanol Ablation

<table>
<thead>
<tr>
<th>TUMOR SIZE</th>
<th>RESPONSE RATE</th>
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<tbody>
<tr>
<td>HCC &lt; 5 cm</td>
<td>70-75%</td>
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<tr>
<td>HCC 5-8 cm</td>
<td>60%</td>
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</table>
Thermal Ablation Techniques

Cryoablation:

- First used to treat hepatic tumors in 1963;

- Mechanism: subfreezing temperatures delivered to tissues via cryoprobes containing circulating cryogen, with irreversible tissue destruction < –20 degrees C;
Cryoablation (Cont.)

**Technique:** open laparotomy (<10% laparascopic), in which 1-2 probes are placed in the lesions under US guidance and cryogenic material is circulated;

Image from Dodd et
### Cryoablation Results

<table>
<thead>
<tr>
<th>Percent Survival</th>
<th>Years after Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>90%</td>
<td>1</td>
</tr>
<tr>
<td>40%</td>
<td>3</td>
</tr>
<tr>
<td>20%</td>
<td>5</td>
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</table>
Laser Ablation

**Mechanism:** optical or near-infrared light will scatter within tissue, be converted to heat, and cause necrosis;

**Results:** 26% 5 year survival rate in patients with hepatic metastases from CRC;
Laser Ablation

- Needles inserted into high signal intensity tumors;
- Low signal intensity represents tumor necrosis;

- MR-guided laser ablation;
- Needles inserted into high signal intensity tumors;
Microwave Ablation

**Mechanism:** microwaves emitted from an electrode causes vibration/rotation of molecular dipoles (water) generating heat and subsequent thermal coagulation of target tissue;

Image from Dodd et
Microwave (Cont.)

Technique:
1. Percutaneous needle placed in tumor;
2. Performed under US guidance;
2. 60 seconds of microwaves per treatment;

Patient Outcomes:
1. Complete tumor necrosis at 3 months in 72%;
2. Survival rates were 83.1% (1 year), and 68.2% (2 years);
Radiofrequency Ablation

- **Mechanism:**
  1. Alternating electric current in the range of radiofrequency is directed to tumor tissue via needle electrodes;
  2. This causes local ionic agitation and frictional heat;
  3. Temperatures > 50 degrees C produces necrosis;

*Image from Dodd et al*
RF Technique (Cont.)

- outpatient procedure;
- local anesthetic + conscious sedation;
- US-guided placement of the electrode (although CT and MRI can be used as well);

Image from Dodd et
Electrode Placement

• The liver is ideal for percutaneous access;

(Subcut. Fat, intercostal muscles, Intercostal vein, artery and Electrode Image from Netter

Matthew Halpern Gillian Lieberman, MD
RF Ablation Results

Patient Outcomes:
1. trials suggest 52-67% ablation rates (1 year);
2. survival rates of 96% (1 year), 64% (3 years) and 40% (5 years);

Reported complications:
1. intrahepatic arterial hemorrhage
2. ablation of the diaphragm
3. tumor seeding along the needle tract;
RF Limitations

• increasing tip temperatures $\rightarrow$ vaporization/charring $\rightarrow$ impedance (no increased volume of coagulation);

• in monopolar RF coagulation diameter is limited by heat dispersion to 1.6 cm (6 minutes of tx);
Incorporating Coagulation

- **cooled-tip electrodes**—internal cooling of the probe using chilled perfusate → heating of tissues adjacent to the electrode is reduced, thereby preventing tissue boiling and allowing an increased diameter of coagulation;
Increased Coagulation with Internally Cooled Electrodes

From Goldberg et
## Summary Table

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<tr>
<th>Techniques</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>Chemoembo.</td>
<td>Rx Entire Liver</td>
<td>Individ. Tumors</td>
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<tr>
<td>Laser</td>
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<td>Microwave</td>
<td>Penetrates Scar</td>
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<td>RFA</td>
<td>Low Tox/Wide range</td>
<td>Recurrence rate elevated</td>
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<td>ETOH</td>
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<td>Cryoablation</td>
<td>Large Tumors</td>
<td>Laparotomy</td>
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Our Patient: A Good Candidate for RFA

- Mr. L is an 82 year old man s/p right colectomy for colorectal cancer;

- On routine follow up examination, he was noted to have elevated CEA, although he was otherwise asymptomatic;

- CT scan performed at an outside hospital revealed a 2x2 cm low attenuation lesion in the superior right liver lobe;
Clinical Case History (Cont.)

• FNA confirmed metastatic colorectal carcinoma;

• PMH: Bladder Ca (s/p cystectomy), prostate Ca (s/p prostatectomy), CVA (s/p L CEA);

• Given the patient’s advanced age, and hx of multiple medical problems, a decision was made to pursue RFA rather than surgical resection in order to decrease associated morbidity and mortality of treatment;
Pre-RF CT Scan (C-)

- A 3.2x2.1 cm region of hypoattenuation within the dome of the liver.

Image from Matthew Halpern, Gillian Lieberman, MD
US-Guided Electrode Placement

- US reveals the hypoechoic 3 cm mass;
US Guidance (Cont.)

- We can see the needle electrode longitudinally as it enters the tumor;
- A portion of the tumor mass is now hyperechoic secondary to microbubbles of gas that form in the heated tissue;

Image from Matthew Halpern
Gillian Lieberman, MD

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CT Fluroscopy during RFA

- CT fluroscopy is used concomitantly with US for electrode guidance;
- The electrode tip is visible within the tumor;
- The hypoattenuated region represents gas formation with necrosis;

Image from Matthew Halpern, Gillian Lieberman, MD
Post RF CT (C+)

- 15 minutes after RFA there is a 4x3 cm hypoattenuated mass in the right lobe;

- An enhancing hyperdense rim around the treatment zone suggests inflammation;

- Central parenchymal enhancement possibly suggests residual tumor;

Image from Matthew Halpern, Gillian Lieberman, MD
3 Month CT Follow-up

• Interval reduction in size of tumor in right superior hepatic lobe;

• There is no evidence of enhancement or hypervascularity surrounding the tumor;

Image from Matthew Halpern
Gillian Lieberman, MD
6 Month Follow-up CT (C+)

- There are regions of central and peripheral enhancement within the hypoattenuated liver lesion;
- There are also irregular medial and posterior borders;
- These findings probably represent tumor recurrence;
- No additional Rx was pursued at this time;
9 Month Follow-up CT (C+)

- Interval enlargement of right hepatic lesion;

- Central low attenuation with ill-defined peripheral area of slightly higher attenuation and irregular borders are highly suggestive of tumor

- Patient scheduled for repeat RFA Procedure;
Successful RFA

- Arterial phase C+ CT shows hypervascular hepatoma;

- CT fluroscopy shows an electrode centered in the

- Post RF C+ CT shows absence of parenchymal enhancement and inflammatory sclerotic rim;

- 6 month F/U C+ CT shows no enhancement and smooth tumor borders suggestive of successful treatment;

Image from Goldberg et
Future Directions for Thermal Ablative Therapies

1. Strategies that Decrease Tumor Tolerance to Heat;
   • Vascular occlusion/antiangiogenesis-factor Therapies;
   • Chemotherapy (Doxil)/radiation;

2. High-Intensity Focused US (HIFU)
   • Use of an acoustic lens to create a focused beam of energy;
   • Transcutaneous transmission;
References


Acknowledgements

I would like to thank Dr. Nahum Goldberg and Dr. Wayne Monsky for their help and advice in preparing this presentation.

Thanks also to Dr. Gillian Lieberman, Beverlee Turner, and Larry Barbaras and Ben Crandall staff at the BIDMC for all of their assistance and expertise.