Chemoembolization, Radioembolization and Focal Ablation in Oncology

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• No relevant financial relationships in the past twelve months by presenter or spouse/partner.

• The speaker will directly disclose the use of products for which are not labeled (e.g., off label use) or if the product is still investigational.
Interventional Oncology

- Concepts
- Tools
- Data
• 76 yo man with ETOH cirrhosis
• ECOG Grade 2
• Child-Pugh Score 6, Class A
• HCC in the Left Lobe of the Liver
Radioembolization, TACE, Microwave, IRE, Cryoablation, Tyrosine Kinase inhibitor, Partial Hepatectomy, Chemotherapy, Observation (BSC), Transplant, ETOH, RFA
## Treatment Options

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Local</th>
<th>Regional</th>
<th>Systemic</th>
</tr>
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## Interventional Radiology

### Treatment Options

#### Loco-regional

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Surgical Resection

- 1st line
- For those who are candidates
- Preserved liver function
- (Level IIA Evidence)
Surgical Resection

- Perioperative morbidity and mortality <5% in select patients.
- 5 year survival > 50%
- May be as high as 70% in patients with:
  - Early stage
  - Preserved liver function (Child-Pugh A)
Goal of Resection

- Negative surgical margins of 0.5 cm to 1cm (R0)
- Preservation of Liver Function

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<table>
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<tbody>
<tr>
<td>R0</td>
<td>Negative margins</td>
</tr>
<tr>
<td>R1</td>
<td>Microscopic residual tumor</td>
</tr>
<tr>
<td>R2</td>
<td>Gross residual tumor</td>
</tr>
</tbody>
</table>
Candidates for Surgical Resection

- Child-Pugh A (maybe B)
- Milan Criteria
  - Solitary tumor $\leq$ 5 cm
  - No more than 3 tumors $\leq$ 3 cm
- No vascular invasion
- No evidence of portal hypertension
- No major Comorbidities
- No Extrahepatic Metastases
Candidates for Surgical Resection

• Only 5 - 10% of HCC patients are resectable

1Llovet, JM. Current treatment Options for Gastroenterology. 2004;7:431-441
Transplant

- 4 year Overall Survival (OS): 85%
- Relapse Free Survival (RFS): 92%
Transplant

- Significant Heart, Lung, CNS, or other systemic disease
- Systemic infection
- Malignancy outside liver
- Active ETOH or Drug use
- Portal vein thrombosis
- Psychiatric
- Obesity
- Lack of sufficient social support
- Other severe comorbid conditions
Transplant

- Significant Heart, Lung, CNS, or other systemic disease
- Systemic infection
- Malignancy outside liver
- Active ETOH or Drug use
- Portal vein thrombosis
- Psychiatric
- Obesity
- Lack of sufficient social support
- Severe comorbid conditions
Transplant

- Patients on Transplant list: 114,436
- Waiting list for livers: 13,835

Organ Procurement and Transplant Network data as of July 2018
• 76 yo man with cirrhosis presented with mass in the Left Lobe of the Liver.

• ECOG Grade 2.

• Child-Pugh Score 6, Class A

• Evaluated by Transplant Team

• Evaluated by Hepatobiliary Surgeon
• 76 yo man with cirrhosis presented with mass in the Left Lobe of the Liver.

• ECOG Grade 2.

• Child-Pugh Score 6, Class A

• Evaluated by Transplant Team

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# Loco-regional Therapy

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<td>Non-Thermal</td>
<td>Transarterial Radioembolization (TARE)</td>
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Loco-regional Therapy

- Percutaneous Ablation (Local)
- Thermal
- Non-Thermal
Loco-regional Therapy

Percutaneous Ablation (Local)

Thermal
- RFA
- Microwave
- Cryoablation

Non-Thermal
Loco-regional Therapy

Percutaneous Ablation (Local)

Thermal
- RFA
- Microwave
- Cryoablation

Non-Thermal
- Ethanol Injection
- Irreversible Electroporation
Percutaneous Ethanol Injection

- Dehydrated 98% ethyl alcohol by volume (196 proof)
- Preferentially permeates softer tumor
- Effective, especially for tumors < 2cm in size
- Inexpensive
Percutaneous Ethanol Injection

- Effects of RF Ablation are more predictable

Level I evidence
Radiofrequency Ablation
RFA
Radiofrequency Ablation
RFA
Radiofrequency Ablation
RFA

100°C
RFA

- Goal is to achieve an ablation zone of 0.5 cm to 1 cm

- Randomized 180 patients
- Solitary HCC < 5 cm
- 71 Local Ablation
- 69 Surgical Resection

<table>
<thead>
<tr>
<th>Overall Survival</th>
<th>1 Year</th>
<th>2 Year</th>
<th>3 Year</th>
<th>4 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablation</td>
<td>95.8%</td>
<td>82.1%</td>
<td>71.4%</td>
<td>67.9%</td>
</tr>
<tr>
<td>Resection</td>
<td>93.3%</td>
<td>82.3%</td>
<td>73.4%</td>
<td>64%</td>
</tr>
</tbody>
</table>
RFA

• 5 Year OS in early stage HCC 50% - 64%
• Most favorable for tumors $\leq 3$cm
• For tumors $\leq 2$cm, 5 year OS 97%
RFA

• For small, solitary, early-stage HCC, RFA offers similar survival rates to surgical resection and may represent an equivalent alternative to surgical resection as 1st line treatment.

RFA

- Rates of successful ablation decrease as tumors exceed 3cm
- “Heat Sink” can decrease rate of complete tumor necrosis to < 50%
- Subcapsular Location increases risk of incomplete ablation and tumor progression
Microwave Ablation

- Similar to RFA
- Shifted on Electromagnetic Spectrum (2.45 GHz)
- Oscillation of water molecules
- Can reach 150 degrees Celsius
## Microwave Ablation

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Dissadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher Temperature</td>
<td>Not as much published research compared to RFA</td>
</tr>
<tr>
<td>(150°C vs. 100°C)</td>
<td></td>
</tr>
<tr>
<td>Not prone to “Heat Sink”</td>
<td></td>
</tr>
</tbody>
</table>
Cryoablation

- Thermal Ablation
- Cold instead of heat
Cryoablation

- Argon
- -40º C / F
Cryoablation

- Cause cell death by:
  - intracellular ice formation
  - cell dehydration
  - rupture of cell membrane

- 408 tumors
- 300 patients
- Mean Diameters 1.9cm to 15cm

- 185 tumors *completely* ablated
  - 1.9 cm to 7 cm with mean diameter of 5.6 cm
- 223 tumors *incompletely* ablated
  - 5 cm to 15 cm with mean diameter of 7.2 cm
OS of patients with 1 to 3 HCC < 3cm:

- 1 year: 91%
- 2 year: 85%
- 3 year: 65%
- 5 year: 54%


- Most common causes of death:
  - Variceal Bleeding: 36.3%
  - Liver Failure: 26.2%
  - Tumor recurrence and metastasis: 23.2%
Complications:

- Majority minor
- Severe in 19 (6.3%)
  - Hemorrhage
  - Intestinal fistula
  - Severe Liver Damage and Liver Failure

Cryoablation in Liver

- Relatively safe and effective
- Tumors < 5 cm
- Child-Pugh A (maybe B)
Irreversible Electroporation
Irreversible Electroporation

- Electrical current causes micro perforations “nanopores” through cell membrane
Irreversible Electroporation

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not susceptible to &quot;Heat Sink&quot;</td>
<td>Minimal data in clinical literature</td>
</tr>
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</table>
Percutaneous Ablation

- Very favorable response profile
- Should be considered for patients who are not candidates for surgical resection
- Ablation alone may be curative for lesions < 3cm
- Prolong survival for lesions 3 cm - 5 cm
• 75 years old man with incidental finding of a solid, enhancing, 2.2 cm, left kidney mass.
Renal Cell CA

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T1-T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0-1</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>T4</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
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## Renal Cell CA

<table>
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<th>Primary Tumor (T1)</th>
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<tr>
<td><strong>T1a</strong></td>
</tr>
<tr>
<td>&lt; 4cm</td>
</tr>
<tr>
<td><strong>T1b</strong></td>
</tr>
<tr>
<td>&gt;4cm but &lt;7cm</td>
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Renal Cell CA

- Stage T1a RCC (tumors <4cm) are curable
- Nephron Sparing Partial Nephrectomy replaced Radical Nephrectomy as Standard of Care
How does Thermal Ablation compare with Surgery?
Thermal Ablation

• T1 lesions (<7cm)
  • Similar distance recurrence free survival rates
  • Increased risk of local recurrence
    • (T1b: 4 - 7cm)
• American Urological Association: Thermal Ablation as alternative to surgery in high risk patients
Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis

- Talenfeld, et al., Annals of Internal Medicine, June 2018
- Population based SEER cancer registry data linked to Medicare claims
- 4310 patients
- Median follow up of 52 months
Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis

- 5-year RCC specific survival rate
  - 95% PA
  - 98% PN
  - 95% RN
Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis

• 5-year OS
  • 77% PA
  • 86% PN
  • 75% RN
Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis

• Non-neurological Complications at 30 days
  • 6% PA
  • 29% PN
  • 30% RN
Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis

- 10% of PN – Intraoperative conversion to RN
- 7% of PA – Additional PA within 1 year
Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis

- For selected patients with T1a RCC
  - Similar outcomes
  - Less Renal Insufficiency
  - Fewer complications
Cryoablation
Cryoablation
70 yo M with a history of lung cancer s/p surgical resection, now with new FDG avid right lung lesion; Patient wishes to not undergo additional surgery nor radiation

Pre-procedure PET; 1.2 x 1.1 cm nodule
Parenchymal hemorrhage from 20G core biopsy x2 and antenna placement; Single microwave antenna at 60W for 10 minutes
1 month post-ablation follow-up with no evidence of residual or recurrent disease
Lung Ablation

- Technical success 80% – 90%
- Best results lesions 2 – 3 cm
- 3,4,5 Year OS 97.7%, 72.9%, 55.7%

What about lesions > 5 cm?
What about lesions > 5 cm?

Or patients with > 3 lesions?
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Regional Therapy

• A region, such as a lobe or a segment of the liver, is targeted for drug delivery
  • Chemotherapy (TACE)
  • Radiation (TARE)
Conventional TransArterial ChemoEmbolization (TACE)

• Mixture of:
  • Chemotherapeutic Agents:
    • Doxorubicin
    • Cisplatin
  • Lipiodol or Ethiodol
Conventional TransArterial ChemoEmbolization (TACE)

- Administered directly into the artery which supplies the tumor or the segment of liver which contains the tumor.
Conventional TransArterial ChemoEmbolization (TACE)

- Recommended 1st line therapy in intermediate stage disease without
  - vascular invasion
  - distant metastases
Conventional TransArterial ChemoEmbolization (TACE)

• Based on 2 landmark prospective randomized trials demonstrating:
  • Improved survival compared with best supportive care
  • preserved liver function
    • (Level IA evidence)

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<th>1 Year</th>
<th>2 Year</th>
<th>3 Year</th>
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<tr>
<td>TACE</td>
<td>57%</td>
<td>31%</td>
<td>26%</td>
</tr>
<tr>
<td>BSC</td>
<td>32%</td>
<td>11%</td>
<td>3%</td>
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<th>1 Year</th>
<th>2 Year</th>
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<tr>
<td>TACE</td>
<td>75%</td>
<td>50%</td>
</tr>
<tr>
<td>BSC</td>
<td>63%</td>
<td>27%</td>
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Trial Stopped Early
DEB-TACE

- Drug Eluding Bead
- Doxorubicin (HCC)
- Irinotecan (Colon Mets)
Doxyrubicin DEB-TACE

- Prospective, randomized trial, demonstrating:
  - Similar efficacy as Conventional TACE
  - Higher Doxorubicin Concentration
  - Reduced liver toxicity
  - Reduced doxorubicin-related side effects

Trans-Arterial Radioembolization (TARE)
TransArterial Radioembolization (TARE)

- Glass (Therasphere™) or Resin (SirSpheres™) microspheres
- Yttrium-90
- Embolized into the hepatic artery branch which supplies the lobe or segment with tumor
Yttrium-90

- Beta decay to zirconium-90
- Half life 64 hours
- Average beta energy 0.9367 MeV
- Average tissue penetration 2.5mm
- Emitted electrons can interact with matter to cause Bremsstrahlung x-rays
Yttrium-90

- Low toxicity (well tolerated)
- Minimal PES (compared with TACE)
- Bridge to transplant
- Portal Vein Thrombosis
- Preserves liver vascularity
Calculate dose based on liver volume
Angiogram with 99mTc MAA
MAA Scan
Evaluate Lung-Shunt fraction
Treat
TransArterial RadioEmbolization (TARE)

- Alternative to TACE
- Safe in Portal Vein invasion
- Similar survival data to conventional TACE
- Significantly reduced toxicity compared to TACE
Sorafenib

- Tyrosine Kinase Inhibitor
- Survival advantage for *advanced metastatic* HCC
## Sorafenib Hepatocellular Carcinoma Assessment Randomized Protocol (SHARP)

<table>
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<tr>
<th></th>
<th>Median OS</th>
<th>Median TTP</th>
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<tr>
<td>Sorafenib</td>
<td>10.7 months</td>
<td>5.5 months</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.9 months</td>
<td>2.8 months</td>
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Sorafenib

- Recommended for patients with:
  - Metastatic Disease
  - Not candidate for local or regional therapy
  - Progression following loco-regional therapy

(Level I evidence)
Neuroendocrine Tumor

- 60 years old man
- Metastatic Carcinoid Tumor
- Carcinoid Syndrome
- on monthly Sandostatin
CRC Mets
CRC Mets

- Mainstay for **metastatic colon cancer** treatment is Systemic Therapy.
CRC Mets

- Mainstay for *metastatic colon cancer* treatment is Systemic Therapy.

*However...*
CRC Mets

- Surgical Resection
  - Isolated hepatic metastases
  - Limited in Number
  - No major vascular involvement
  - Increase 5-year survival from 40% to 60%
CRC Mets

- Patient who are not surgical candidates
- 5-year survival rates following RFA approach surgical resection
  - Tumors < 4cm
CRC Mets

- RFA added to systemic chemotherapy for unresectable CRC mets
  - increased median progression free survival by nearly 7 months (16.8 vs 9.9)
CRC Mets

• What about Regional Treatment for CRC Mets?
  • TACE/TARE?
Hepatic Intra-Arterial Injection of Drug-Eluting Bead, Irinotecan (DEBIRI) in Unresectable Colorectal Liver Mets Refractory to Systemic Chemotherapy: Results of Multi-Institutional Study

- Response rates of 66% at 6 months
- Overall survival 19 months
- Progression free survival 11 months

Hepatic Intra-Arterial Injection of Drug-Eluting Bead, Irinotecan (DEBIRI) in Unresectable Colorectal Liver Mets Refractory to Systemic Chemotherapy: Results of Multi-Institutional Study

- DEBIRI was safe and effective in treatment of metastatic colorectal cancer refractory to multiple lines of systemic therapy.

CRC Mets

- Randomized Phase III Trial of DEBIRI TACE v. FOLFIRI
  - Prolonged OS (22 months v. 15 months)
  - Progression Free Survival (7 months v. 4 months)
  - Extrahepatic Progression (13 months vs. 9 months)

Giammaria et al., Intra-arterial Infusion of Irinotecan-loaded Drug-eluting Beads (DEBIRI) versus Intravenous Therapy (FOLFIRI) for Hepatic Metastases from Colorectal Cancer: Final Results of a Phase III Study
CRC Mets TARE?

• Addition of Y-90 TARE to 2\textsuperscript{nd} and 3\textsuperscript{rd} line Systemic Chemotherapy

  • significantly prolonged TTP
    • 15.9 months v. 9.7 months
  • longer median survival
    • 29.4 months v 12.8 months
First Line Y90 for CRC?
First-line selective radiotherapy plus chemotherapy versus chemotherapy alone in patients with liver metastases from colorectal cancer (FOXFIRE, SIRFLOX, and FOXFIRE-Global): a combined analysis of three multicenter, randomized, phase 3 trials

FoxFire Combined

- SIRFLOX
- FOXFIRE
- FOXFIRE - Global
FoxFire Combined

- 1,103 Patients
- ITT
- Liver dominant +/- extrahepatic mets
FoxFire Combined

- mFOLFOX (+/- Bevacizumab)
- mFOLFOX (+/- Bevacizumab) + TARE
FoxFire Combined

HR 1.04 (95% CI 0.90–1.19); p=0.61

Overall survival (%)

Time from randomisation (months)

Number at risk (number censored)

FOLFOX 549 (0) 419 (29) 242 (43) 88 (87) 33 (115) 12 (130)
FOLFOX plus SIRT 554 (0) 417 (13) 247 (23) 91 (74) 35 (101) 17 (112)
FoxFire Combined

HR 0.51 (95% CI 0.43–0.62); p<0.0001
FoxFire Combined

- Objective (complete or partial) response
  - 400 / 554 (72%) – Folfox + SIRT
  - 346 / 529 (63%) – Folfox alone
  - P=0.001
FoxFire Combined

• Right sided primary Colon Cancer
  • FOLFOX + SIRT
    • Increased OS by 4.9 months
    • Decreased risk of death at any time point by 36%
      • P=0.007
CRC Mets to Liver

- Select patients can benefit
  - Local Ablation
  - Regional Treatment (TACE/TARE)
Conclusion

- Patient selection is key
- Interventional Radiologist has a lot to offer your oncology patients
- Make sure your IR is involved in MMC