Primary Liver Cancer

- 5th leading cause of cancer in the world
- Heterogeneous incidence
  - Low in America and Northern Europe
  - Intermediate in South Europe
  - High in Subsaharian Africa and Far East
- In the U.S. > 20,000 new cases in 2000
  - 75% increase since 1993
- Rising incidence of chronic hepatitis in U.S.
  - 1.2 million cases of hepatitis B
  - 3 million cases of hepatitis C
  - Predicted to equal levels in Japan within two decades

Hepatocellular Cancer in Cirrhotic Patients

Natural history of HCC (n=102)

- Median survival 17m
- # of deaths = 79 patients

References:
- NEJM 1999; 340:745
- PNAS 2002;99:15584-89
HCC Carcinogenic Sequence

- Dysplasia (size criteria)
- Dysplastic Nodule
- Regenerative Nodule
- Early HCC
- Solitary-encapsulated
- Multifocal/multinodular, Bilobar
- Diffusely Infiltrative/Invasive
- Neoplasia

3-50 months

Imaging of the Liver

OPTIONS
- Ultrasound
  - Contrast
- Computed Tomography
  - Multi Detector Technology
- Magnetic Resonance
  - Ultrafast Imaging
  - Diffusion Weighted
  - Eovist

GOALS
- Lesion characterization
- Lesion detection
- Staging for potential resection
- Assessment of therapeutic response

Hepatocellular Carcinoma

- Receives its blood supply from the hepatic artery and consists of abnormal hepatocytes arranged in a trabecular, sinusoidal pattern
- Expansive tumors: well differentiated and relatively slowly growing; usually well defined
- Invasive tumors: poorly differentiated with aggressive growth patterns; usually ill defined
- Invades vascular structures, more commonly the portal vein than the hepatic vein; arterioportal shunting is characteristic

HCC

Duplex Ultrasound

Left Hepatic Vein Tumor Involvement
**Portal Vein Thrombosis**

**Computed Tomography**

**Advances**
- Spiral
- Multidetector Spiral CT
- Major Advances
  - 3D Reformatting
  - CT Angiography

**HCC Characteristics on CT**
- Hyperdense enhancement during arterial phase
- Lesion become lower in density during later phase i.e. “Washout”

**Hepatocellular Carcinoma**

**Multiphasic CT-Scan**

- Example 1
- Example 2
**MR Imaging**

- Conventional Imaging
  - T1 (anatomy)
  - T2 (pathology)
  - Flow (MR angiography)

- Others
  - Fat (lesion characterization)
  - Metabolites (spectroscopy)
  - Tissue oxygen consumption (fMRI)
  - Diffusion & perfusion (ischemia, necrosis)
  - Temperature (monitoring therapy)

**Management of HCC**

- **Multidisciplinary:** Hepatologist, Oncologist, Diagnostic Radiologist, Interventional Radiologist and Surgeons

- **Supportive Care**

- **Palliative Therapies**
  - Transarterial embolization (TAE) or Chemoembolization (TACE)
  - Percutaneous Ablative Procedures
  - Hormonal treatments/Immunotherapy
  - Antiproliferative agents
  - Radiation Therapy: external and transarterial

- **Curative (Radical) Therapies**
  - Surgical resection (5-40%)
  - Liver Transplantation (CLT/LDLT)
  - Ablative procedures: Percutaneous ethanol injection (PEI) / Radiofrequency
Ablation Tools

- Chemical
  - ETOH
  - Acetic Acid
  - Chemotherapy
  - Experimental protocols
- Thermal
  - RF ablation
  - Cryoablation
  - Laser
  - Microwave

Percutaneous Ethanol Injection (PEI)

- Need to be able to locate the lesion
- Should be < 3cm

PEI 6 months later

Principles of Embolization Therapy

- Dual blood supply to liver facilitates preferential delivery of embolic/toxic agents to tumor “sparing” normal liver
- Access to hepatic artery allows for targeted regional therapy, minimal systemic effect
Patient Selection for TAE or TACE

- Unresectable disease
  - Multiple small tumors
  - Large >5 cm involving critical structures
- Liver only/dominant disease
- Adequate hepatic functional reserve
  Labs: T.bili< 2.0; Cr. < 1.5, Plts> 75
- Most are palliative procedures

Single Lesion Embolization

CT Scan

NON-CONTRAST  EARLY ARTERIAL

Celiac -- Scout

Tumor

Left HA

Selective

Left HA

Post-embolization

Left HA
Multiple / Bilobar Disease

Embolization Procedures
--Complications--

- Occlusion of vessels to non-target organs
  - Cystic artery → chemical cholecystitis
  - Right gastric artery → gastric or duodenal ulceration
  - GDA → Acute pancreatitis
  - Biliary Necrosis (dilated intrahepatic ducts)
- Catheter related vascular injuries
  - Hemorrhage
  - Dissections
  - Aneurysms
  - Puncture site hematoma
- Liver Abscess
- Liver Decompensation
- Post-Embolization Syndrome

Patient Selection for Thermal Ablations

- Non-operative potential --quality of life issues.
- Unresectable
  - Anatomy – often not good for RFA either
  - Extending limits of resection
- Tumor Characteristics: Size and Distribution
  - Number < 3
  - Size < 3 cm, < 5 cm
- Assuming perfect accuracy should be as good as resection
Thermal Ablation – Guidance

- Ultrasound
- Computed Tomography
- Magnetic Resonance Imaging

RFA/Microwave – Techniques

- Percutaneous: CT scan/US
  - General anesthesia not always necessary
  - Less trauma/pain/recovery
  - Some tumors not anatomically feasible
  - No operative staging
- Laparoscopic/Thoracoscopic
  - Minimally invasive surgery
  - Better staging
  - Able to move organs from heat source
- Open
  - Optimal staging
  - Optimal probe placement
  - Able to combine with resection

CT – Guidance

Laparoscopic Technique

Umbilical Vein
RFA/Microwave – Local failure

- Increasing size
- Tumor vascularity
- Proximity to vascular structures
- Surgical versus percutaneous technique

Preoperative MRI
Post-RFA MRI

6 months 14 months

Curative Therapies

- Surgical Resection
- Liver Transplantation
- Ablative Therapies

Two Problems

- Chronic Liver Disease & HCC
- Underlying cirrhosis limits aggressive treatments.
- Surgery remains the only chance for long-term survival.
- Majority of patients are not suitable for operation.

Hepatic Resection in Cirrhotic Livers: The Early View

“...Partial hepatectomy for tumors occurring in cirrhotic livers should not be done unless it is necessary to control hemorrhage.”

- Liver Tumor Survey-- 1974
- Mortality rate was 58% in cirrhotic patients (n =26).

Foster JM, Berman MM., Solid Liver Tumor, 1977; p. 62-104
Preoperative Assessment of Liver Function

<table>
<thead>
<tr>
<th>Test</th>
<th>Author</th>
<th>Contraindication for Resection</th>
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<tbody>
<tr>
<td>Child-Pugh</td>
<td>Franco</td>
<td>Score &gt; 8</td>
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<tr>
<td>Serum alanine</td>
<td>Noun</td>
<td>ALT &gt; twofold upper limit of norm</td>
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<tr>
<td>Indocyanine green</td>
<td>Lau</td>
<td>Retention rate at 15 minutes &gt; 15 %</td>
</tr>
<tr>
<td></td>
<td>Makuuchi</td>
<td>Retention rate at 15 minutes &gt; 10 %</td>
</tr>
<tr>
<td></td>
<td>Fan</td>
<td>Retention rate at 15 minutes &gt; 14 %</td>
</tr>
<tr>
<td></td>
<td>Wu</td>
<td>Retention rate at 15 minutes &gt; 10 %</td>
</tr>
<tr>
<td></td>
<td>Hasegawa</td>
<td>Retention rate at 15 minutes &gt; 10 %</td>
</tr>
<tr>
<td></td>
<td>Hemming</td>
<td>Clearance &lt; 5 mL/min/kg</td>
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<tr>
<td></td>
<td>Kanematsu</td>
<td>Retention rate at 15 minutes &gt; 20 %</td>
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<tr>
<td>Urea nitrogen synthesis</td>
<td>Paquet</td>
<td>&lt; 6 g/day</td>
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<tr>
<td>Portal Vein Pressure</td>
<td>Brux</td>
<td>HVPG &gt; 10 mm Hg</td>
</tr>
<tr>
<td>Lidocaine (MEGX) test</td>
<td>Ercolani</td>
<td>MEGX &lt; 25 ng/ml*</td>
</tr>
<tr>
<td></td>
<td>Grazi</td>
<td>MEGX &lt; 25 ng/ml*</td>
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</table>

*alone not considered an absolute contraindication to resection

Preoperative Interventions

- Prevention of Variceal Bleeding
  - Sclerotherapy
  - Transjugular intrahepatic portosystemic shunt (TIPS)

- Arterial Embolization
  - Diagnostic Angiogram
  - Reduces tumor bulk

- Sequential Arterial and Portal Embolization (*double vascular embolization*).

Right Hepatic Artery Embolization

Sequential Arterial and Portal Embolization

3 Weeks After Right Hepatic Arterial Embolization
Right Portal Vein Embolization
Sequential Arterial and Portal Embolization

Occluded PV

Occluded PV

Repeat Right & Left Hepatic Arterial Embolization

Recanalized Branch from Replaced RHA
Left HA Branches

CT Scan
6 weeks after PVE, 9 & 3 weeks after TACE
**General Operative Considerations**

- **Specific technical difficulties in the Cirrhotic:**
  - Parenchyma is hard.
  - Anatomic landmarks are distorted.
  - Tissue friability.
  - Tumors may be difficult to recognized from the surrounding cirrhotic liver.

*Yoshida Y, Ann of Surg 1989;209 (3):297-301*

- **Complete Staging:** Bone scan, CT-chest
- **Preserved Liver Function**
  - Childs A-- ONLY
- **Cardiopulmonary assessment** (> 65 yrs).
- **Open Resections are now rare:** Majority are done Laparoscopically, or Not at all.
- **When done open, we prefer a Makuuchi incision**
  - Full abdominal exploration.
  - Intraoperative ultrasound.

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Non-Anatomic Resections

Operation

Operative Management of Large HCC
--Anterior Approach--

Large HCC –Anterior Approach
Extended Resections

• Most patients are treated by multiple complementary ablative approaches
• The order depends on the pattern of disease
• Options include
  – Resection, RFA/microwave, TACE, and/or PEI
  – RFA/microwave then TACE
  – PEI then, TACE
Presentation CT Scan

Hepatic Arterial Embolization

Tumor Invading R Kidney

Venous Shunt

Right (posterior) HA

Venous Shunt

Right Renal Artery Embolization

Post Embolization Right posterior HA & Superior Pole Renal Artery
Repeat RHA (entire) Embolization

CT Scan Following TAE x 5
- Residual Tumor

CT Scan Following TAE x 6
- Enhancing tumor

Percutaneous Ultrasound Guided RFA of Residual Liver Tumor

Kidney
HCC

Pre RFA  Post RFA

Multiple Modality Approach

AFP levels

RFA

TAE

Post Laparoscopic Resection and RFA
Summary

- Therapy of liver tumors in patients with cirrhosis remains challenging.
- However, hepatic resection for HCC can be performed safely, provided a limited resection is anticipated.
- Resection should be considered the standard therapy for HCC.
- Inoperable patients can benefit from liver directed transarterial ablative therapies to halt tumor progression and to extend survival.

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