Liver Oncology Interventions

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DISCLOSURE

Consultant:
- Cook Medical Inc.
- Baylis Medical
- Terumo Interventional Systems
- Guerbet

Patents: Cook Medical Inc.
Liver Cancer

• Primary: Hepatocellular Ca
  Cholangiocarcinoma

• Secondary (metastasis):
  Colon
  Neuroendocrine tumors
  Pancreas
  Breast
Liver Cancer treatment goals

- Tumor control, ideally cure
- Increase patient survival
- Low complication rate
- $$ acceptable
- 2016 = Highest value treatment
Patient Selection in Liver Cancer

Treatment indication will dependent on:

- Lesion location (nodular, infiltrative)
- Number of lesions
- Hepatic profile (Liver enzymes, INR, T Bili, Albumin)
- Patient performance status
- Percentage of residual/cirrhotic liver
Liver Cancer – Treatment options

- Resection / Transplantation

- Endovascular: Chemoembolization, Radioembolization (Y-90 Infusion)

- Percutaneous: Ablations

- Systemic chemotherapy (I.V., oral, Intra-hepatic)

- Association of techniques (Chemoembol + RFA/MWA)
Types of Percutaneous Ablation

Chemical
- Alcohol

Heat
- RFA, MW, Laser
- HIFU (High-intensity US)

> Cell membrane permeability
- Irreversible Electroporation

Cold
- Cryoablation
Alcohol Ablation

• HCC is soft, cirrhotic liver is hard

• Helps in alcohol diffusion

• 22G needle, single /multiple holes
  – Volume = $\frac{4}{3}\pi (r+0.5)^3$
    • 2 cm - 12 ml
    • 3 cm - 32 ml
  – Limit to 20 ml per session
    • Pain
    • Systemic absorption
    • Multiples session in lesions > 2.5 cm
US guided HCC alcohol ablation
CT guided alcohol HCC ablation

HCC (AFP >1000)

Alcohol

3 m (AFP < 10)
RFA systems
F/U images post RFA Ablation (HCC)

Pre-RFA

Post-RFA
MW generators

NeuWave: 2.45GHz

BSD Medical: 915 MHz

Amica: 2.45 GHz

Medwaves: 902-928 MHz

Microsulis: 2.45 GHz
Differences in RFA vs MWA

Heat generation in tissue

RF
*Tissue – ionic agitation*

- Amount of current delivered is based on the impedance of tissue
- Ions focused at electrode / current density

MW
*Tissue – water rotation*

- Friction caused by movement of water molecules against each other
- Mechanism of friction is different, but the source of heat is friction in both
US vs CT = correlation with pathology

Immed post ablation

CE-CT: best correlation with path

Raman et al, AJR 2000
Up to 3 needles may be used simultaneously.
Ablation zone = 9.2 x 7.7 x 6.6 cm
Irreversible Electroporation

Electric pulses increase the permeability of the cell membrane what results in cell destruction.

Normal cell membrane  →  Electroporation  →  Ruptured membrane

Application of electric short pulses and high voltage current
Irreversible Electroporation

General anesthesia
Irreversible Electroporation
Irreversible Electroporation

Pre

Imediate

3 m post

8 m post

1 a post

Courtesia: G. Narayanan, Univ. de Miami
Tumor seeding in ablation?

- Cauterization: needle reposition or removal
- Shorter track, it is not always the best way
- Cauterization of track? Seeding = incidence ~ 0%

Drastically reduced neoplastic seeding related to radiofrequency ablation for hepatocellular carcinoma. AJG, 2014, 109, 774-776.
Image fusion US/CT/MRI
Endovascular Liver Ca Interventions

• Transarterial Chemoembolization (TACE)
  chemo + ischemia

• Transarterial Bland Embolization (TAE)
  only ischemia

• Transarterial Radioembolization (TARE)
  only radiation
Endovascular liver directed therapies
Hepatic TACE

- $\frac{3}{4}$ hepatic flow: portal vein
- Tu vascularization: > hepatic artery
- High local concentration of chemotherapy agent
- Lower systemic toxicity
- Preserve liver function
Hepatic TACE

INDICATIONS

• Nonresectable HCC
• HCC in transplantation list
• Multicentric HCC
• Metastatic lesions: Neuroendocrine, Breast, Colon
• Abdominal pain, mass effect (compression)
• In association with RFA/MWA
Angiographic catheters

Coaxial system
Embolic agents

- Gelfoam
- PVA (polyvinyl alcohol)
- Microspheres
Microesferas

Sem resposta inflamatória
Drug Eluting Beads (DEB)
Effective arterial blockage

Microspheres = better mechanical occlusion?
TACE technique
Colon mets = Irinotecan DEB

Pre

1 m F/U

3 m F/U

Tumor volume:
42.9 cc

Tumor volume:
57.8 cc

Tumor volume:
14.5 cc (-66%)
Cateterização superseletiva
Collateral tumor vascularization
Hepatic Chemoembolization

TREATAMENT PROTOCOL

• VIR Clinic + lab + image
  (Abdominal CT / MRI)

• TACE: 2-4 sessions, (average 3)

• Procedures every 4-5 weeks apart
Hepatic Chemoembolization

Post-TACE Syndrome (+/- 40%)

- Nausea, vomit
- Fever
- Abdominal pain and distension
- Flu-like symptoms (no appetite, no energy)
- Leukocytosis
Selective Internal Radiation Therapy (SIRT) Y90

Objectives:

- Selective delivery of high dose of radiation
- Treat primary and metastatic liver Ca
- Radioisotope Y-90 loaded in microspheres
- Flow directed therapy, minimal vessel target block
Radioembolization (TARE)

- Yttrium - 90
  - Pure beta energy emission
  - ½ life: 64.2 h
  - Tissue penetration: 2.5 - 11 mm
90Y-Microspheres

Glass
TheraSphere®
8 million spheres per dose
5-10 GBq/patient
FDA approved (HDE) for HCC

Resine
SIR-Spheres®
80 million spheres per dose
2-3 GBq/patient
FDA approved for Colo-retal mets
Hepatic pulmonary shunt?
Scan post $^{99m}$Tc MAA

Shunt = 26%

Acceptable: Shunt hepato-pulmonar < 20%

Shunt = 4.7%
Complications - Gastric ulcer
Colon cancer - 15 m post treatment
How can we improve outcomes?
Expanding the limits of Liver Ablation
HCC - Treatment options in 2014

- Resection / Transplant
- Chemoembolization (TACE), Radioembolization (TARE)
- Ablations: MW, RF, cryo, laser, electroporation, EtOH
- Combined techniques (TACE + RFA/MWA)
- Systemic chemotherapy

Year 2015: Which one is better to promote cell death? Ischemia, Chemotherapy, Radiation, Heat??
Rationale

Combined therapy in HCC

1. Better identification of the lesion border:
   - Precise needle placement
   - Risky locations, close to adjacent organs

2. Potentially:
   - Better long-term tumor control, better survival
   - Cure of lesions previously considered not curable (>3cm)
Reduction of tumor recurrence?

RFA only: ~15% residual disease

TACE+RFA: ~0%
2005 = our 1st Combined Therapy: TACE + RFA
TACE with Lipiodol first, better tumor visualization in non-contrast CT.
Correct identification of the HCC border
Precise RFA needle placement

1 cm ablative margin
Combined treatment in HCC
TACE and RFA

HCC lesions < 7 cm
Larger lesions, adjacent organs....
Combined treatment in HCC
TACE and RFA

Expanding the RFA indications

Protective techniques:
- large HCC
- small HCC but in risky areas

✓ Glucose hydrodissection
✓ Angioplasty balloon
✓ Chilled glucose infusion: gallbladder/bile ducts
✓ CO2 Pneumoperitoneum
HCC next to the colon, kidney
HCC next to the stomach
HCC next to the gallbladder
• 20 G needle
• Bile aspiration, same volume w/ chilled D5
• Chilled D5 infusion 10 ml/h
Needle positioning. How to avoid thermal injury?

Ablation zone beyond the needle tip?

= 6mm + 5/10 mm de margem
How to avoid diaphragmatic thermal lesion?
HCC next to the diaphragm
CT guided RFA under CO2 pneumoperitoneum

Veress needle
TACE with lipiodol
Endoscopic-guided Naso-biliary tube placement
Nasobiliary tube
Chilled D5 infusion in the bile duct
Case – TAE + RFA combined

- Male, 70 y
- ECOG: 1
- Colon Ca
- Metastasis in the liver
- Patient refused to have systemic chemotherapy or surgery
- Discussed Y-90 infusion
Flight Plan for Embolization Procedures

- Image fusion mapping + angiography
“Bulls eye” view

- View trajectory planning
- Real time track view
Needle ASSIST – Trackvision

- Entry-site position confirmation
Needle ASSIST – Trackvision

- View trajectory Planning
- Real time track view
Needle ASSIST – Trackvision

- View trajectory Planning
- Real time track view
Needle ASSIST – Trackvision

• Final trajectory check
FU images
Case – TACE + RFA combined

- Male, 68y
- ECOG: 1
- HCC
- Multiple TACEs in 2011
- Annual F/U: new HCC lesion
Early-stage HCC

104 Combination therapy vs 62 hepatectomy

Inclusion criteria:
- no previous treatment for HCC
- 3 or fewer tumors < 3 cm
- Single tumor < 5 cm
- Child-Pugh A
- No vascular invasion or extra-hepatic metastases

Primary Endpoint = global survival

Secundary endpoint = recurrence-free survival

Results:

- Global survival in 1, 3 and 5 yrs, similar:
  Combine therapy: 98%, 94%, 75% ($p = .87$)
  Hepatectomy: 97%, 93%, 81%

- Recurrence-free survival in 1, 3 and 5 yrs: comparable
  Combined therapy: 92%, 64%, 27% ($p = .70$)
  Hepatectomy: 99%, 69%, 26%
Comparative study: TACE/RFA vs Resection

• Resection: 40 ptes    TACE + RFA: 33 ptes
• Survival rate, lesions < 7 cm

• Survival               1-    3-  5-yrs
  TACE+RFA     97 %  77 %  56 %
  Surgery       81%  70 %  56 %

• No difference in survival (p=0.20)

Maluccio et al, JVIR 2005
Early HCC: TACE/RFA vs Resection
Child Pugh A, HCC < 5cm

Transcatheter arterial chemoembolization plus radiofrequency ablation therapy for early stage hepatocellular carcinoma: comparison with surgical resection.
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Abstract
BACKGROUND: Radiofrequency ablation (RFA) is becoming a well-known local therapy for hepatocellular carcinoma (HCC). Transcatheter arterial chemoembolization (TACE) is expected to enhance the effects of subsequent RFA by reducing arterial blood flow. However, the long-term efficacy of this combined therapy has not been elucidated. In this study, the survival rates of patients who received TACE combined with RFA (TACE + RFA) were compared with those of patients treated surgically.

METHODS: The study included consecutive patients who received TACE+RFA or surgical resection as the initial curative treatment for HCC between 2000 and 2005 at Tokai University Hospital. Inclusion criteria were a single HCC≤50 mm or up to 3 HCCs≤30 mm, presence of cirrhosis classified as Child-Pugh class A, no vascular invasion, and no extrahepatic metastasis.

RESULTS: Sixty-two patients (23 women, 39 men; aged 67.5±8.4 years [mean±standard deviation]) received TACE+RFA, and 55 patients (15 women, 40 men; aged 66.1±8.4 years) underwent surgical resection. Median follow-up periods were similar (50 months in the TACE+RFA group vs 49 months in the resection group). The probabilities of overall survival at 1, 3, and 5 years in the TACE+RFA group (100%, 94.8%, and 64.6%, respectively) were similar (P=0.788) to those in the resection group (92.5%, 82.7%, and 76.9%, respectively). Two major RFA-related complications were observed (1.5%).

CONCLUSIONS: RFA combined with TACE is an efficient and safe treatment that provides overall survival rates similar to those achieved with surgical resection.

5 y survival: 64%  No difference in survival p= 0.78
Personalized medicine

- 52 y, female
- Abdominal pain, ECOG 1
- Hepatitis C, normal AFP
- US Abdominal: large liver mass
Personalized medicine
Personalized medicine
Personalized medicine
Personalized medicine

- After 3 sessions of TACE
- Good performance status
- Preserved liver enzymes
Personalized medicine
Personalized medicine
Personalized medicine
Personalized medicine
Personalized medicine

- 56 y, male
- Abdominal pain, ECOG 1
- Hepatitis C, alcohol abuse
- AFP: 1,844
- Abdominal MRI: 7.2 cm HCC mass
Personalized medicine
Personalized medicine
Personalized medicine

- Be obsessive,
- Check: needle ablation zone length in relation to edge of the liver
- Check coronal and sagital images too
Personalized medicine

F/U @ 36 months
Conclusion

Liver Oncologic Interventions

- Safe, very cost-effective
- Increase patient survival
- Minimally invasive treatment
- Faster recovery
- Collaboration with clinical /surgical oncology
- Provide great value to patient care