# HCC - Ablative Treatment Current Recommendation

Dr Alankar Kumar Gupta

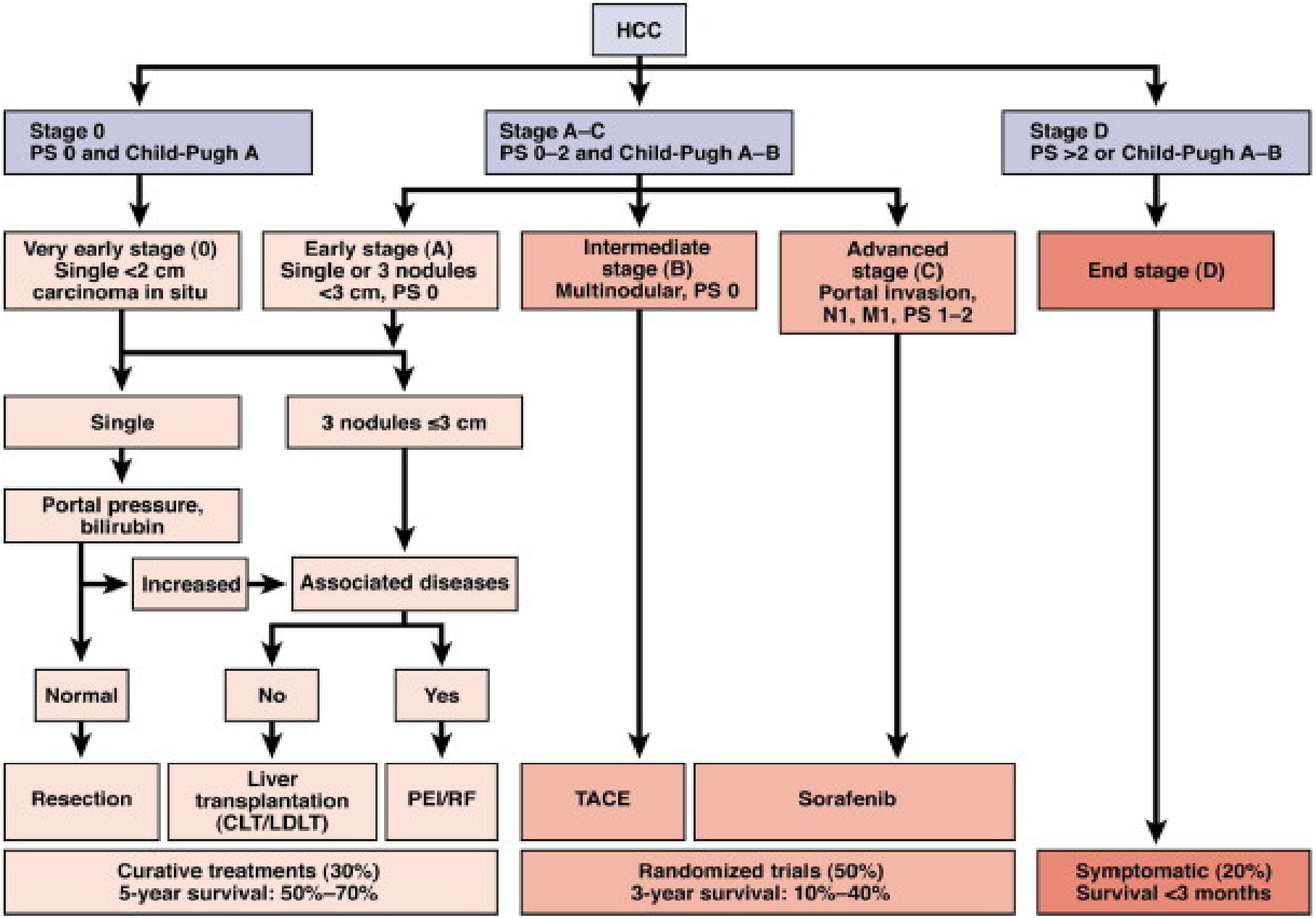
# TNM Staging

| | |
|---|---|
| **Tx** | Primary tumor cannot be assessed |
| **T0** | No evidence of primary tumor |
| **T1** | Solitary, ≤ 2 cm without vascular invasion |
| **T2** | Solitary, ≤2 cm, with vascular invasion; multiple, one lobe, ≤ 2 cm, without vascular invasion |
| **T3** | Solitary, > 2 cm, with vascular invasion; multiple, one lobe, ≤ 2 cm, with vascular invasion; multiple, one lobe, > 2 cm, with or without vascular invasion |
| **T4** | Multiple, > one lobe; invasion of major branch of portal or hepatic veins |
| **Nx** | Regional lymph nodes cannot be assessed |
| **N0** | No regional lymph node metastasis |
| **N1** | Regional lymph node metastasis |
| **M0** | Distant metastasis is absent |
| **M1** | Distant metastasis is present |

# Barcelona Clinic Liver Cancer

## BCLC STAGING SYSTEM[4]

| BCLC Stage | PS | Tumor Features | Liver Function | Treatment Options |
|---|---|---|---|---|
| A1 | 0 | Single <5 cm | No PH | Surgery, RFA |
| A2 | 0 | Single <5 cm | PH, normal bili | Surgery, RFA, transplant |
| A3 | 0 | Single <5 cm | PH, abnormal bili | RFA, transplant |
| A4 | 0 | 3 tumors <3 cm | Not applicable | Transplant, TACE |
| B | 0 | Large multinodular | CP A-B | TACE |
| C | 1-2 | Vascular invasion or metastases | CP A-B | sorafenib |
| D | 3-4 | Any | CP C | Supportive care |



# Percutaneous Ablation of Hepatocellular Carcinoma

- HCC is the fifth most common tumor throughout the world
- incidence is increasing worldwide because of the spread of infections caused by the hepatitis B and C viruses.
- Surveillance programs have been developed for patients with cirrhosis, and this approach is associated with annual HCC detection rates ranging from 3% to 8%
- Conventional approaches, such as systemic chemotherapy and radiation, have proved to be ineffective in HCC,
- Sorafenib may be associated with slightly improved survival in patients with advanced HCC

- Surgical resection can result in tumor eradication and improved survival in patients with small HCCs;
- Few patients are candidates for potentially curative resection, which comes with an 80% risk of recurrence
- Liver transplantation is the ideal approach for early HCC, but it is limited by age-related contraindications and a shortage of organs
- Percutaneous methods have been developed for the chemical or thermal ablation of HCC, and all have displayed satisfactory efficacy in terms of local tumor control.

# Pretreatment Studies and Patient Selection

- For HCC patients, treatment eligibility screening
  - routine laboratory tests,
  - abdominal ultrasonography (US)
  - contrast-enhanced US, spiral computed tomography (CT) or magnetic resonance imaging (MRI),
  - esophagogastroduodenoscopy

- Diagnosis of cirrhosis is generally based on histology or concordant laboratory and imaging findings.
- HCCs more than 2 cm in diameter can be reliably diagnosed on the basis of characteristic findings documented with at least two imaging modalities.
- One modality is sufficient if the patient also has an α-fetoprotein (AFP) level greater than 200 ng/mL.
- For HCC nodules less than 2 cm in diameter, diagnosis requires typical findings of two imaging techniques and AFP levels above 200 ng/mL. Otherwise, biopsy is mandatory

- The criteria most commonly used include
  - documented cirrhosis;
  - no more than three HCC nodules,
  - measuring no more than 3.0 to 3.5 cm each in diameter;
  - no neoplastic thrombosis of the portal or hepatic veins;
  - no evidence of extrahepatic metastases.

- Child-Turcotte-Pugh (CTP) system - patients with scores higher than B7 to B9 are usually considered unsuitable for ablation.

- Safe coagulation parameters—prothrombin time (PT) ratio of 50% or higher, international normalized ratio (INR) no higher than 1.7, and a platelet count of 50 to 70 x $10^9$/L or more—and no esophageal varices at a high risk for bleeding

- Metastatic tissue is more difficult to ablate than HCC tissue, so METs with diameters exceeding 2.5 to 3 cm are often considered ineligible for curative percutaneous ablation.

# Location of the tumor

- Laparoscopic or surgical approach is preferable
  - nodules located superficially in segments III, IV, or V of the liver;
  - on the subdiaphragmatic surface of the liver
  - exophytic nodules (surrounded by abdominal viscera) or those close to gallbladder

- Caution must be used when the tumor is situated close to a major bile duct, because damage to these structures can lead to biliary stricture or fistula

- For tumors located near a large hepatic blood vessel, risk of incomplete treatment and treatment failure is increased. Flow through these vessels can increase convectional heat loss near the tumor, thereby reducing the volume of the thermal lesion, and it can also result in more rapid clearance of the chemical ablative substances.

- It is often useful to devascularize these tumors before chemical or thermal ablation; this can be accomplished with selective transarterial embolization (TAE or balloon-catheter occlusion of the vessels supplying or draining the tumor

# Assessment of Local Tumor Control

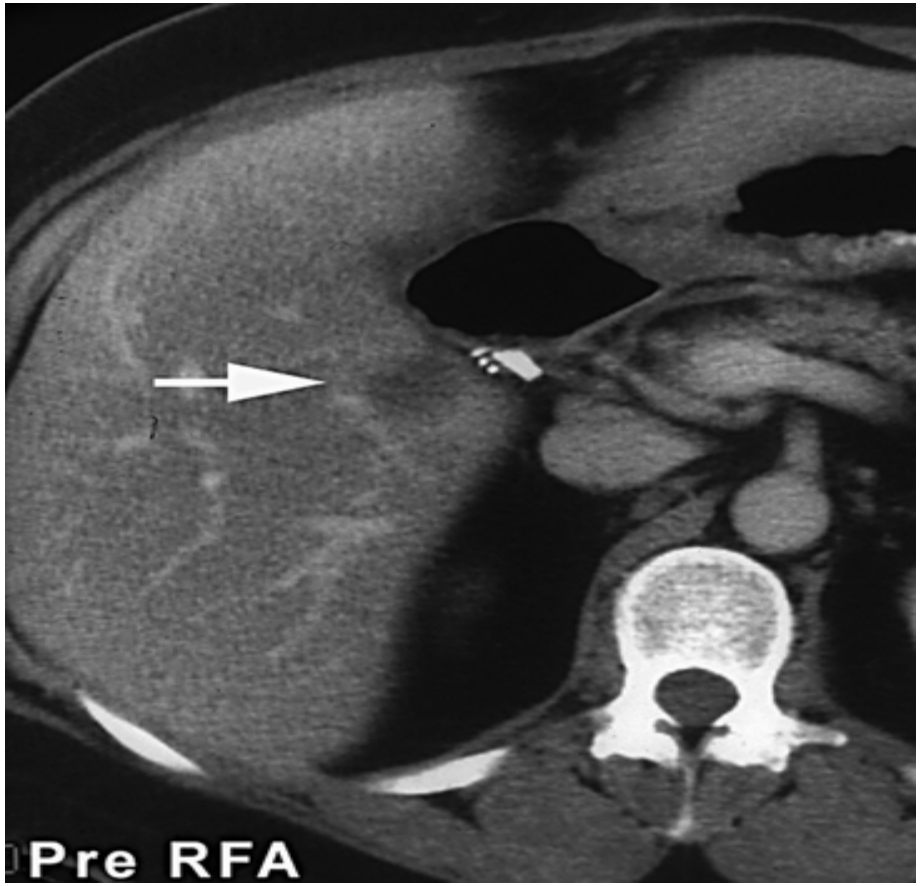
- Evaluation of local efficacy is based largely on evidence of complete tumor ablation that persists during the follow-up (lack of local recurrence).
- Shortly after the procedure, the necrotic area is surrounded by a halo of edematous, intensely hyperemic tissue.
- A few days later, this halo is replaced by an inflammatory halo, which persists for approximately 1 month.
- Thereafter, the mass of necrotic tissue shrinks and is replaced by fibrotic tissue .
- The location, size, and evolution of this ablation zone are assessed with radiologic imaging techniques.

# Evaluation of Immediate Treatment Response

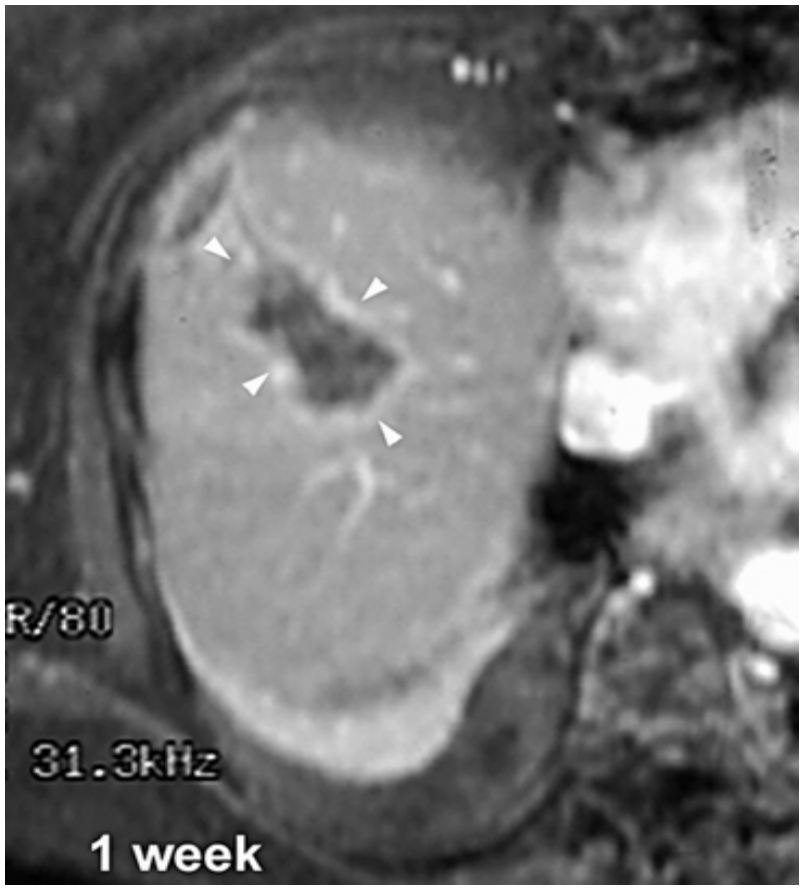
- The immediate response to any type of percutaneous ablation procedure is generally assessed with contrast-enhanced US (CEUS), enhanced spiral CT, or T2-weighted MRI—the gold standards for this purpose (Chen et al, 2007; Cioni et al, 2001).
- The presence at the ablation site of a well-defined, nonenhancing area as large or larger than the treated tumor itself is regarded as reliable evidence of a complete response, or complete radiologic necrosis.

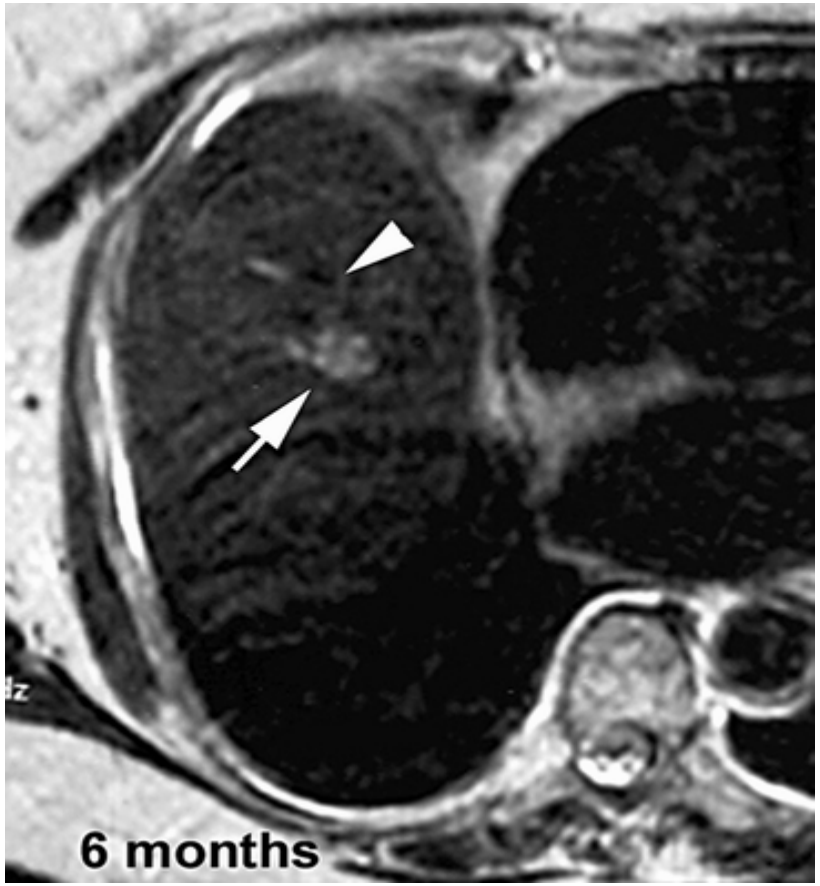
# Evaluation of Long-Term Results

- Abdominal US/CEUS studies and tumor marker assays are performed every 4 to 6 months, or even more frequently if needed.
- Local recurrence is diagnosed when enhancement reappears within the ablation zone or within 2 cm, 1 cm according to some authors, from its margins, or when there is histologic evidence of tumor viability in this area (Berber et al, 2005).
- If the ablation zone remains unenhanced but fails to shrink during follow-up, or when levels of tumor markers are elevated in the absence of other intrahepatic or extrahepatic lesions, focused US-guided biopsy of the ablation zone is indicated.
- Nonlocal recurrence comprises extrahepatic metastases and all new intrahepatic regrowth located more than 2 cm from the ablation zone.



# MRI





# Chemical Ablation

- The most widely used cytotoxic substance is
  - ethanol
  - acetic acid
  - sodium hydroxide is under evaluation
- Chemical ablation has been extensively used to treat HCCs. It has also been evaluated for the treatment of METs, but this experience was abandoned based on unsatisfactory results

# Percutaneous Ethanol Injection

- cytotoxic effects that include cytoplasmic dehydration and denaturation of cellular proteins.
- The endothelial cell necrosis and platelet aggregation it causes occlude tumor vessels and produce ischemic damage in the neoplastic tissue
- The final result is coagulative necrosis within the tissue around the site of injection.

# Technique

- OPD Basis
- overnight fast.
- The procedure is performed under real-time US monitoring. The ethanol is usually injected with a 20- to 22-gauge endhole needle (Chiba or Chiba-like) or a conical-tip needle with multiple sideholes

- The tip is positioned at the desired point in the HCC nodule with the aid of real-time US guidance, and the predetermined amount of ethanol is infused slowly into the tumor. After few seconds, the HCC nodule becomes completely hyperechoic.
- Light aspiration is applied during withdrawal to prevent excess ethanol from leaking into the peritoneum through the insertion tract. If all goes well, the patient is kept under observation for about 2 hours.

# Percutaneous Acetic Acid Injection

- it dissolves lipids and extracts collagen from various kinds of tissues
- advantages
  - more effective destruction of tumor septa and capsules.
  - smaller infusion volume

- The technique of PAI is quite similar to that of PEI. The infusion consists of a 50% solution of acetic acid and sterile water injected with the same technique and needles used for ethanol.
- volume of acetic acid needed to ablate a tumor nodule is roughly one third of ethanol

# Complications of Percutaneous Ethanol/Acetic Acid Injection

- The mortality rates ranging from 0% to 1.4%.
- Major complications  0% to 4.6%

- hemoperitoneum
- hemobilia
- subcapsular or intraparenchymal hematoma
- hepatic abscess
- cholangitis
- intestinal perforation
- hepatic venous thrombosis
- pneumothorax or pleural effusion
- hepatic infarction
- tumor seeding along the needle insertion tract.

# Complications Reported after PEI and PAI

| First Author, Year | Patients/Sessions | Mortality Rate, n (%) | COMPLICATIONS, N (%) | |
|---|---|---|---|---|
| | | | Major | Minor |
| Di Stasi, 1997 | 1066 P | 1 (0.09) | 15 (0.15) | 295 (27.7) |
| Livraghi, 1998 | 128 S | 1 (0.7) | 6 (4.6) | 24 (19) |
| Huo, 2003 | 62 P | 0 (0) | 0 (0) | 28 (45) |
| Sung, 2006 | 248 P | 0 (0) | 0 (0) | 2 (0.8) |
| Brunello, 2008 | 69 P | 1 (1.4) | 1 (1.4) | 10 (14.5) |
| Huo, 2003* | 63 P | 0 (0) | 0 (0) | 20 (32) |
| Fartoux, 2005* | 37 P | — | 0 (0) | 13 (35.1) |

# Local Tumor Control of Chemical Ablation

- The 2-year local HCC recurrence rates
  - 10% for nodules smaller than 2 cm in diameter
  - 18% for those between 2.1 and 3 cm
  - 30% for those larger than 3 cm (Ishii et al, 1996).

- In other studies, local recurrence rates ranged from 33% to 38% for HCCs smaller than 3 cm and from 43% to 68% for those exceeding 3 cm in diameter (Gaiani et al, 2003; Khan et al, 2000).

- Complete response rates observed after PAI seem to be similar to those obtained with PEI, but very few studies are available for comparison.

# Long-Term Results

- 5-year survival rates close to 50% after PEI for HCCs up to 3 cm in diameter in patients with cirrhosis.
- In a consecutive series of 685 patients with HCC nodules measuring 3 cm or less, initial treatment with PEI was reportedly associated with a cumulative 5-year survival rate of 49% (Shiina et al, 2009).
- The Seventeenth Nationwide Follow-up Survey conducted by the Liver Cancer Study Group of Japan revealed survival rates of 91.3%, 77.5%, 63%, 50.2%, and 39.4% at 1, 2, 3, 4, and 5 years, respectively, for 14,726 patients whose HCCs were treated with ethanol injection (Ikai et al, 2007).
- A randomized trial failed to detect any significant difference in survival between HCC patients treated with PEI or surgical resection (Huang et al, 2005)

- Randomized trials have also shown that radiofrequency ablation (RFA) is superior to all types of chemical ablation for small HCCs, and the difference involved treatment responses, local tumor control, and survival rates (Bouza et al, 2009; Lin et al, 2005; Orlando et al, 2009; Shiina et al, 2005).

- Thermal ablation techniques are now preferred over chemical ablation for treatment of HCC. The chemical approach is still the treatment of choice when thermal ablation cannot be performed safely, such as when tumors form adhesions to the gastrointestinal tract, or when tumors are located in difficult sites or close to a bile duct.

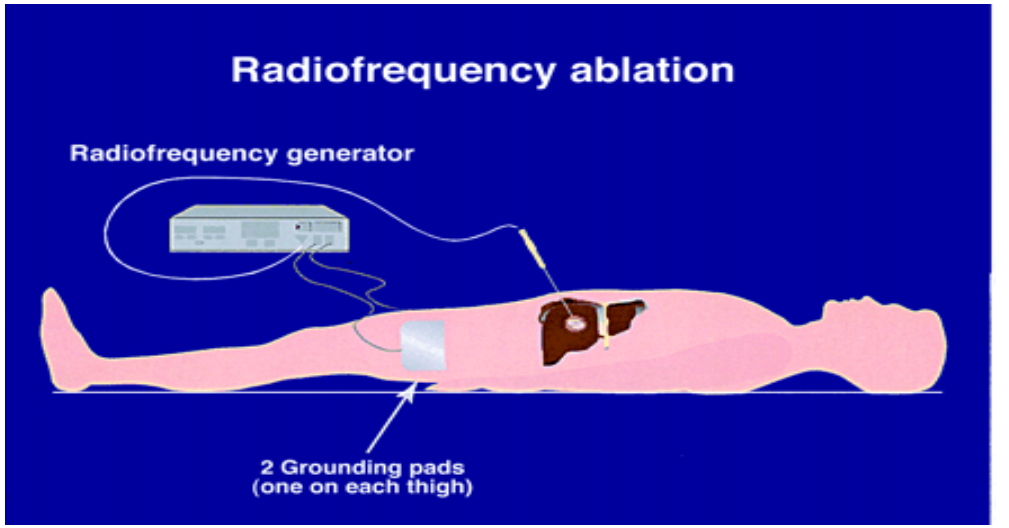
# Thermal Ablation

- Temperatures, those exceeding 45° C or less than −40° C, within the mass of tissue that has to be ablated.
- The temperature reached and the duration of exposure determine how rapidly cell death occurs.
- RFA is the thermal technique most widely used for HCCs and liver METs and the one supported by the largest body of published evidence.
- Microwave ablation (MWA) and laser thermal ablation (LTA) have also been used in these settings, but these experiences are more limited.
- Experiences with high-intensity focused ultrasound (HIFU) have been confined to experimental studies

# *Radiofrequency Ablation Liver*

**Basics of RFA:**

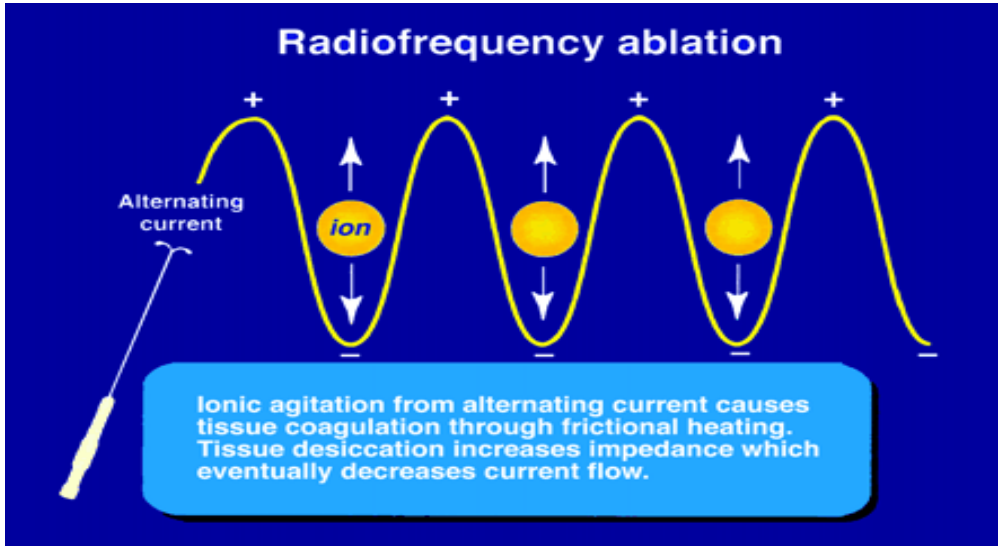
- RF energy is an alternating current with a frequency of 10-900 MHz. RF waves have long WL and as such are of a very low energy.



# *Radiofrequency Ablation Liver*

- **RF energy effect on body tissues:**
- When RF electric field is applied to the body, the interaction losses in moving ions and water molecules at a frequency of the electric field, creating conduction current.

- The friction and ionic agitation generate heat that is produced within the tissues near the electrode called “resistive heat”.

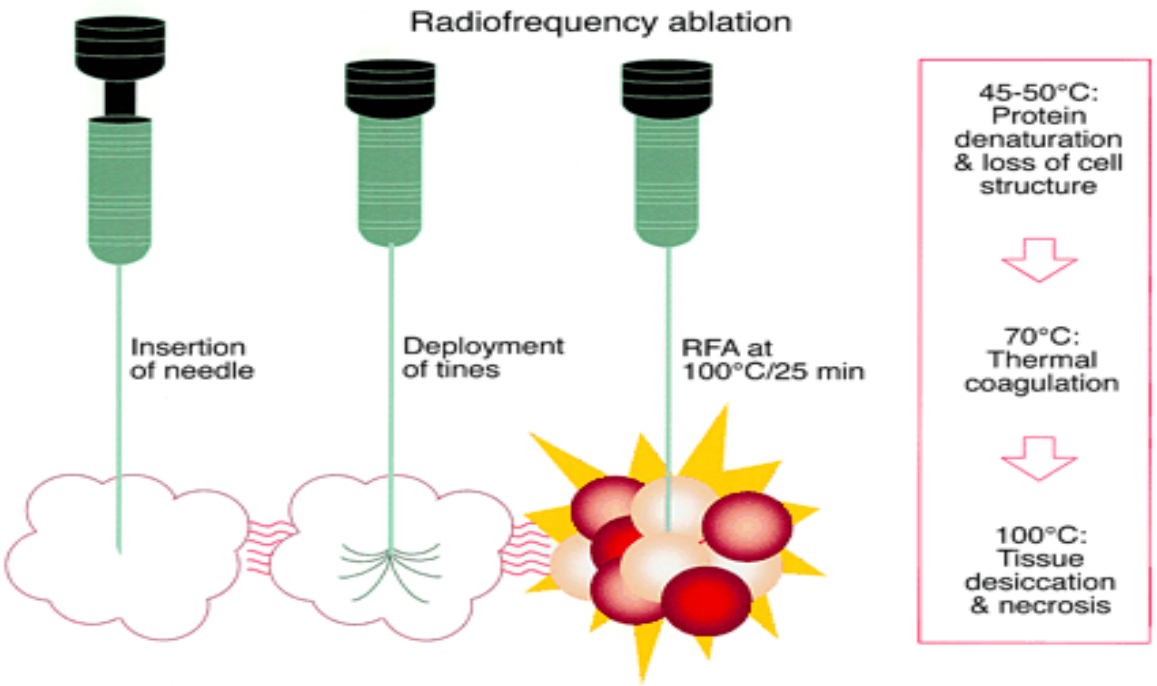


# *Radiofrequency Ablation Liver*

## Physical background

- **Induction of Coagulative necrosis:**
- The aim of tumour ablation therapy is to destroy the entire tumour by using heat to kill malignant cells and including 0.5-1 cm safety margin.

- The aim for RF ablation is achieving and maintaining a 50-100ºC-temperature range throughout the entire target volume.



# *Radiofrequency Ablation Liver*

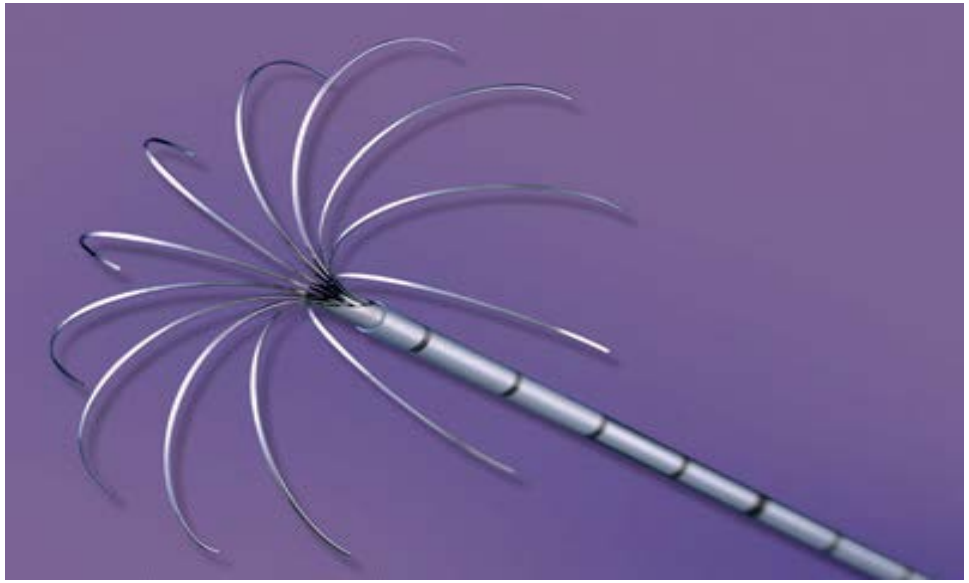
## Ablation system

- RF 2000 system ( RadioTherapeutics Corporation) which consists of:

1. RF generator with frequency of 460 kHz and an output of 100 W. It has a front panel for the power, time, and impedance.
2. LeVeen electrode (3.5 cm arrays) which is insulated cannula housing 10 expandable curved electrodes that, when deployed, assume the configuration of an umbrella.
3. Dispersive electrode pads.

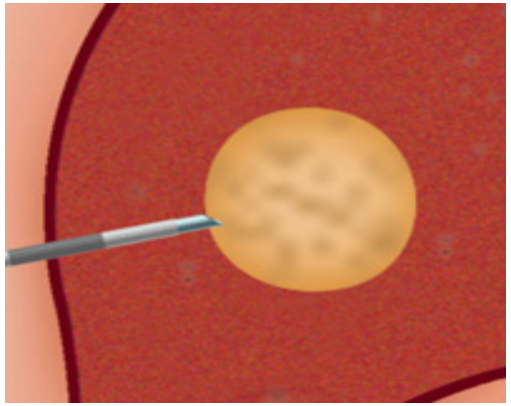
# *Radiofrequency Ablation Liver*

## Ablation system

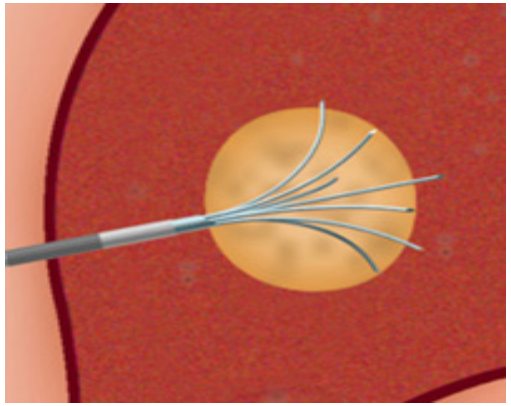



# Radiofrequency Ablation

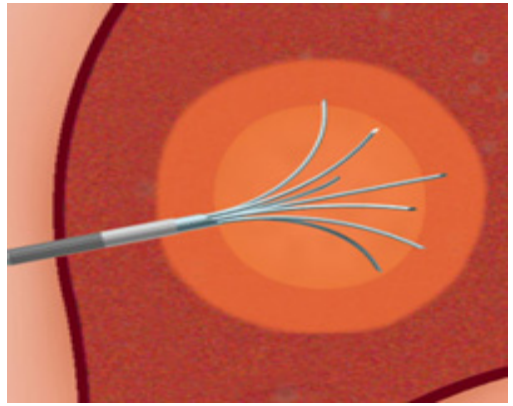
- High-frequency (460 kHz) alternating current flows from electrical probe through tissue to ground



Probe insertion

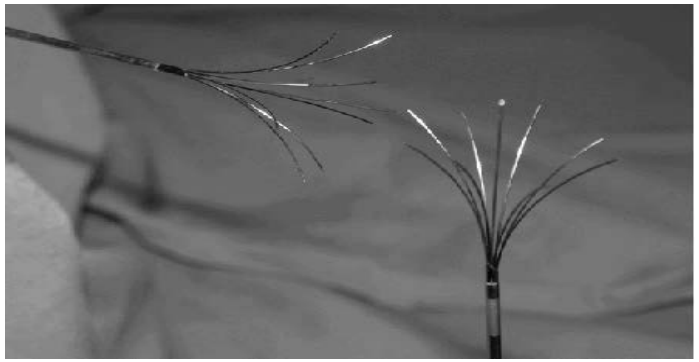


Extension of prongs

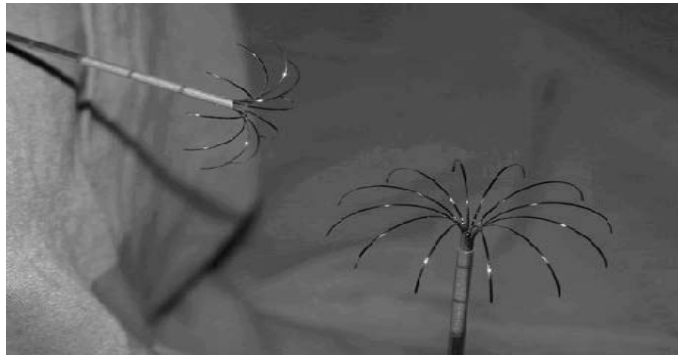


RF current application

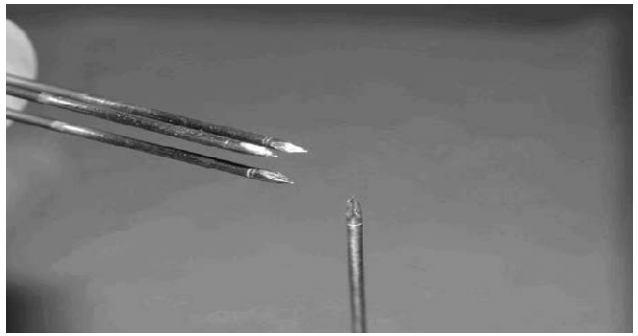
# Radiofrequency Ablation



9-prong “Starburst” probe, 5 cm diameter
(Rita Medical)



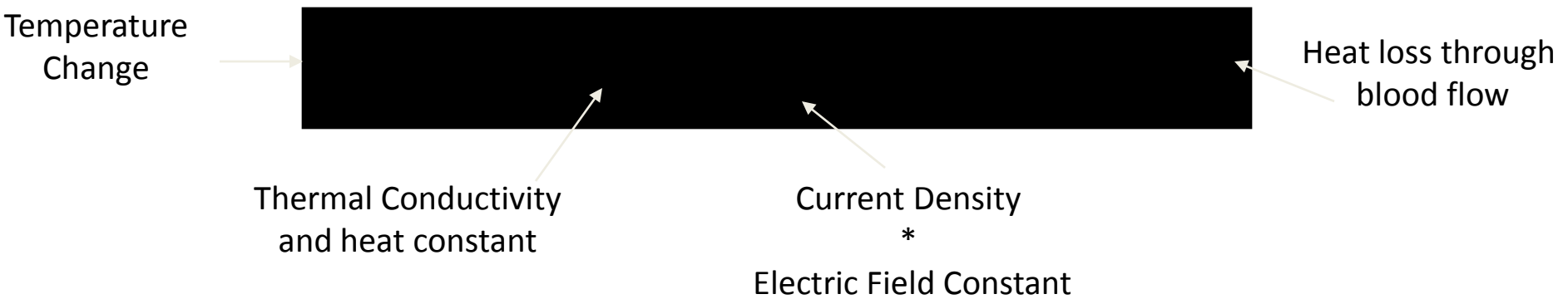
12-prong “Leveen” probe, 4 cm diameter
(Radiotherapeutics)



Cool-Tip probe (17-gauge needle)
(Radionics)

# Radiofrequency Ablation

- Bioheat Equation
  - Lesion ≈ (Energy Applied x Local Tissue Factors) – Energy Lost



# Radiofrequency Ablation

- The heat is the result of ionic and molecular friction, and it spreads into the surrounding tissues by a process of conduction.
- Permanent tissue destruction occurs at temperatures of 45° C or higher (Cosman et al, 1983; Organ, 1976).
- Temperatures ranging from 46° C to 60° C produce irreversible cellular damage only after relatively long periods of exposure.
- In contrast, temperatures between 60° C and 100° C cause almost instantaneous protein coagulation with irreversible damage to mitochondria and cytosolic cell enzymes.
- When temperatures exceed 100° C, tissue fluids undergo boiling, vaporization, and ultimately carbonization.

- monopolar mode produce thermal lesions with a maximum diameter of about 1.8
- second-generation RF electrodes produced thermal lesions with diameters as large as 3 cm,
- The expandable electrodes allow the delivery of larger amounts of RF energy, because rapid charring is less likely when the volume of tissue to be dehydrated is large.
- Cooled-tip electrodes achieve the same result by preventing temperatures rising above 100° C in tissues adjacent to the active surface of the electrode.

- Larger thermal lesions, those 4 cm or larger, have also been produced with multiple cooled electrodes combined in a cluster (Head & Dodd, 2004), cooled catheter electrodes, and expandable spiral electrodes (Rossi et al, 2006).

- RFA performed after balloon-catheter occlusion of the hepatic artery, the thermal lesions produced were large

- RFA was performed after embolization of the feeding arteries with gelatin sponge particles, the thermal lesions produced were larger than expected (Rossi et al, 2000).
- With this approach, in fact, HCC nodules more than 6 cm in diameter could be treated in a single RF session.

# *Radiofrequency Ablation Liver*

## Approaches

- **Percutaneous approach**, is the least invasive, with minimal morbidity, can be performed on an outpatient, requires only sedation, and can be repeated.
- **Laparoscopic approach,**
- **Open surgical approach,** has associated morbidity and mortality of an open procedure and general anaesthesia, and the technique is a one shot therapy.

- Patients undergoing RFA are hospitalized and treated after an overnight fast.
- A grounding pad is attached to the patient's back and connected to the RF generator to close the electrical circuit.
- A local anesthetic (1% lidocaine) is injected along the predefined electrode insertion line, from the skin to the peritoneum. The skin is nicked with a small lancet to facilitate insertion of the electrode, and the tip is then advanced into the HCC nodule under real-time US guidance. The RF generator is activated, and the predefined amount of energy is delivered for 8 to 12 minutes.
- On US, the nodule becomes hyperechoic with a posterior acoustic shadow (Rossi et al, 1996). The pull-back technique can be used to create multiple thermal lesions along the major electrode axis (Rossi et al, 2000).
- At the end of the procedure, the electrode is withdrawn, but the generator remains on during this phase; this way, the electrode tract itself also undergoes coagulation, which diminishes the risks of bleeding and tumor seeding.

- This technique can be used for HCCs up to 3.5 cm in diameter and for CRC liver METs with diameters of 2.5 cm or less.

- For larger tumors, other treatment strategies have been adopted. For HCC nodules whose diameters exceed 3.5 cm, RFA has been performed with a multiple-insertion technique (Livraghi et al, 2000), an expandable triple-spiral electrode (Rossi et al, 2006), clusters of cooled electrodes (Cheng et al, 2008), and combination of RFA with other techniques (Murakami et al, 2007).

- Larger volume of necrotic tissue can also be achieved by preablation embolization of the tumor with gelatin sponge particles.

# Complications

- RFA is a safe procedure with very low rates of death and major complications.
- Mortality rates ranged from 0% to 3.7%,
- major complication rates were reported in 0% to 22%.
- The complications described include abdominal hemorrhage, hepatic abscess, pleural effusion, hepatic infarction, bronchobiliary fistula, bile peritonitis, biloma, hemobilia, thrombosis of vessels in the hepatic venous system, skin burn, and perforation of the stomach, intestine, or diaphragm.
- the most frequent complication is therefore mild to moderate pain during the procedure that occurs in about 30% of all patients. The pain is easily managed with intravenous analgesia and disappears entirely shortly after the procedure.

| | | | COMPLICATIONS, N (%) | |
|---|---|---|---|---|
| First Author, Year | Patients/Sessions | Mortality Rate, n (%) | Major | Minor |
| Livraghi, 2000 | 114 P | 1 (0.8) | 1 (0.8) | 5 (4.4) |
| Bowles, 2001 | 99 S | 1 (1) | 7 (7) | 10 (10) |
| Mulier, 2002 | 3670 P | 20 (0.5) | 327 (8.9) | — |
| Livraghi, 2003b | 2320 P | 6 (0.3) | 50 (2.2) | 110 (4.7) |
| Mazzaferro, 2004 | 50 P | 0 (0) | 4 (8) | 10 (20) |
| Curley, 2004 | 608 P | 3 (0.5) | 33 (8.6)*<br>15 (2.4)† | — |
| Buscarini, 2004 | 166 P | 0 (0) | 7 (4.6) | 3 (1.9) |
| Tateishi, 2005 | 1000 S | 0 (0) | 40 (4) | 17 (1.7) |
| Giorgio, 2005 | 336 P | 1 (0.3) | 2 (0.6) | — |
| Khan, 2007 | 228 P | 0 (0) | 8 (5.4) | — |
| Chen, 2008 | 172 S | 0 (0) | 9 (5.2) | — |
| Brunello, 2008 | 70 P | 0 (0) | 2 (2.9) | 8 (11.4) |
| Livraghi, 2008 | 218 P | 0 (0) | 4 (1.8) | — |
| Kim, 2008 | 133 P | 2 (1.5) | 9 (6.8) | 8 (6) |
| Laspas, 2009 | 322 S | 0 (0) | 0 (0) | 9 (2.8) |
| Kong, 2009 | 255 P | 0 (0) | 35 (10) | — |

# Complications in Patients with Hepatocellular Carcinoma after 1921 Radiofrequency Ablation Sessions

| Complication | Number (%) |
|---|---|
| **Major** | |
| Hemoperitoneum | 6 (0.3) |
| Hemothorax requiring drainage | 2 (0.1) |
| Self-limiting hemobilia | 1 (0.05) |
| Subcutaneous seeding* | 2 (0.1) |
| Skin burn | 1 (0.05) |
| Total | 12 (0.6) |
| **Minor** | |
| Postoperative pain | 18 (0.9) |
| Self-limiting pleural effusion | 32 (1.6) |
| Transient worsening of liver function | 54 (2.8) |
| Low-grade fever | 76 (3.9) |
| Total | 180 (9.3) |

- A 12% seeding rate was reported by a Spanish group during their initial experience with RFA (Llovet et al, 2001).
- Seeding along the electrode tract is virtually impossible, if the electrode is activated before and during each withdrawal.
- When RFA is performed during or after TAE, other complications are also possible (Rossi et al, 2000).

- Some patients also display transient declines in liver function reflected by CTP scores, but these changes rarely last more than 2 weeks.

# Local Tumor Control

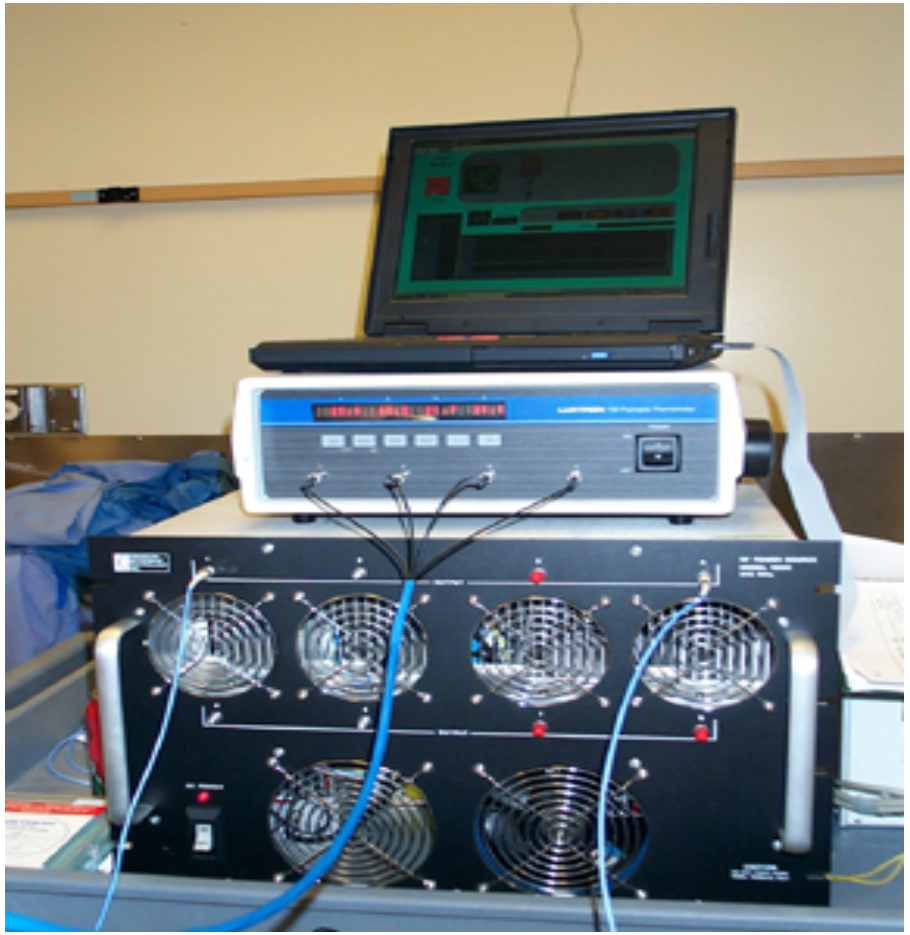
- More than 80% of HCCs measuring less than 3 cm are completely destroyed with a single RF electrode insertion (Mazzaferro et al, 2004).
- Complete response rates ranging from 95% to 98% have been documented in several studies
- the local recurrence rates range from 0 to 45%

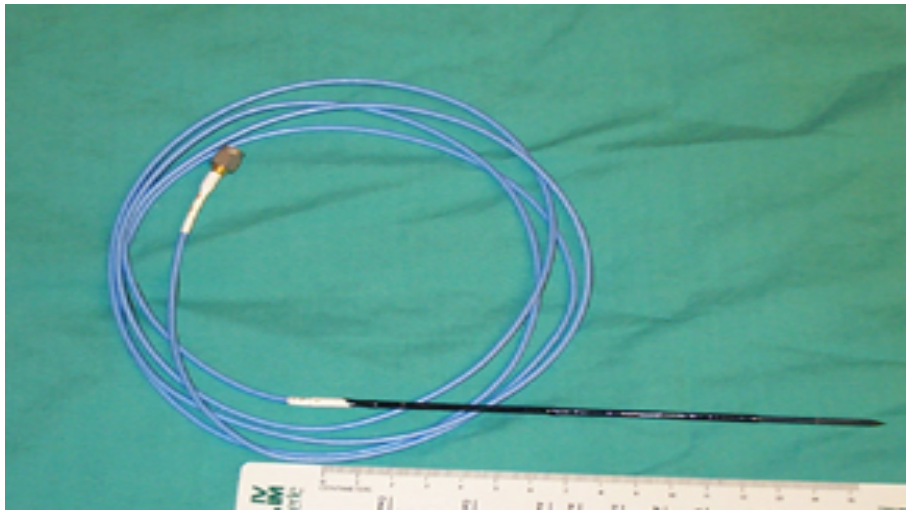
# Long-Term Results in Hepatocellular Carcinoma Patients

- Randomized controlled studies have demonstrated that RFA is superior to chemical ablation methods in terms of both local tumor control and survival (Bouza et al, 2009; Brunello et al, 2008; Orlando et al, 2009).
- These findings suggest that, when possible, RFA should be the first choice for nonsurgical ablation of HCCs.
- RFA was also directly compared with surgical resection in two randomized clinical trials, and neither revealed any significant differences between the local tumor control or survival rates associated with the two approaches (Chen et al, 2006; Lu et al, 2006).

- Recently, HCC nodules with diameters larger than 3 cm have been treated with a cluster of cooled RF needle electrodes and a multiple-insertion technique (Goldberg, 1998a).
- Complete responses were observed in 61% of the nodules up to 5.0 cm in diameter and in 24% of larger nodules.
- Better results have been obtained with more conventional RFA electrodes during gelatin-sponge occlusion of the hepatic artery flow
- RFA is now recognized as a potentially curative treatment for HCC nodules up to 3 cm in diameter, and some investigators maintain that it should be considered the treatment of choice for these cases (Choi et al, 2007; Livraghi et al, 2008; Shiina, 2009).

# Microwave Ablation System





- Vivant Medical
- 13g, 15cm dipole antenna
- 915MHz generator
- Fiberoptic temperature monitor

# Microwave Ablation

- The term *microwave* (MW) refers to electromagnetic radiation with frequencies ranging from 900 to 2450 MHz.
- MW radiation is emitted by the tip of a bipolar antenna electrode placed within the tissue.
- Microwaves cause rapid vibration and rotation of water molecules within the tissue, which immediately generates frictional heat that persists for the duration of energy delivery.

- Inpatient procedure after an overnight fast.
- General anesthesia or deep sedation is induced
- Thin (14- to 16-gauge) MW antenna is advanced directly into the tumor nodule under US guidance. The antenna is connected to the MW generator, which is activated to deliver 60 to 90 W of power.
- Delivery times vary from 2 to 30 minutes, depending on tumor size.
- In general, tumors less than 2 cm in diameter can be ablated with one or (more commonly) two electrode insertions; for larger tumors, multiple insertions are necessary. The same precautions described for RFA apply to MWA.
- The changes revealed by US consist of the appearance around the tip of the electrode of a hyperechoic area with a posterior acoustic shadow. This zone increases in size with exposure time and ultimately involves the entire tumor.
- The hyperechogenicity diminishes rapidly after the generator is switched off and disappears completely within 8 hours of the procedure.

# Complications

- The complications reported after MWA are quite similar to those listed above for RFA.

- Mortality ranged from 0% to 8.3%, and complication rates from 2.6% to 14% were reported.

# Complications Reported after Microwave Ablation

| First Author, Year | Patients/Sessions | Mortality Rate, n (%) | COMPLICATIONS, N (%) | |
|---|---|---|---|---|
| | | | Major | Minor |
| Shimada, 1998* | 42 P | — | 6 (14.2) | — |
| Shibata, 2000† | 14 P | 0 (0) | 2 (14) | — |
| Dong, 2003* | 234 P | 0 (0) | 0 (0) | 167 (71.36) |
| Aramaki, 2004* | 24 P | 2 (8.3) | — | — |
| Lu, 2005* | 49 P | 0 (0) | 4 (8.2) | — |
| Iannitti, 2007‡ | 87 P | 0 (0) | 14 (16) | — |
| Ohmoto, 2009* | 49 P | — | 6 (14) | 28 (56) |
| Zhang, 2008‡ | 160 P | 0 (0) | 23 (14) | — |
| Liang, 2009‡ | 3697 S | 0 (0) | 30 (2.6) | — |
| Martin, 2010‡ | 100 P | 0 (0) | 29 (29) | — |

# Local Tumor Control

- MWA can produce complete tumor necrosis.
- Histologic examination revealed no viable tumor in 180 (92.3%) of 192 treated HCC nodules that were biopsied after MWA and in 5 (90%) of 6 HCC nodules that were surgically resected after MWA (Seki et al, 1999).
- The local recurrence rates reported by several investigators after MWA of hepatic tumors ranged from 2% to 37%.

# Long-Term Results

- The overall survival rates 3 years after the procedure ranged from 50.5% to 90%, and at 5 years from 17% to 70%.
- The Fifteenth Nationwide Follow-up Survey conducted by the Liver Cancer Study Group of Japan found 1-, 2-, 3, and 5-year survival rates of 94.2%, 84%, 72.9%, and 44.1%, respectively, in 1751 patients whose HCC had been treated with MWA (Ikai et al, 2004).
- The effectiveness of MWA and that of RFA have also been compared in randomized trials (Ohmoto et al, 2009; Shibata et al, 2002). No statistically significant differences were observed between the two treatment methods in terms of local efficacy, but RFA tended to be associated with slightly better local recurrence and complication rates

- MWA is an effective method for the treatment of hepatic tumors.
- Its major limitation is the relatively small size of the thermal lesions it produces.
- To ablate most tumors, multiple overlapping lesions must be created; this requires multiple electrode insertions

# Laser Thermal Ablation

- Laser light, which has a wavelength of 800 to 1064 nm, is delivered to the tissue through the tip of a bare, flexible, quartz laser fiber (300 to 600 µm in diameter) where it is scattered, reflected, and absorbed to varying degrees, depending on its specific wavelength and the specific optical properties of the tissue.
- Area of thermal necrosis ranges from 1.0 to 1.5 cm in diameter (Germer et al, 1998).
- The relatively small volume of LTA thermal lesions limits the clinical applicability

- The use of sapphire-tipped laser fibers
- The use of interstitial fibers, quartz fibers with flat or cylindrical diffusers at the tip, reduces tissue carbonization and produces thermal lesions ranging from 2.3 to 5 cm in diameter (Khan, 2008).
- Cooled laser application sheaths, designed to reduce temperatures around the laser fiber tip, allow the use of higher power output without carbonization and produce larger thermal lesions (Vogl et al, 2002
- The beam-splitting multiple-fiber LTA device offers further improvement in thermal lesion size.
- Positioning the multiple fibers in the tumor nodule is a highly complex procedure that requires training and a great deal of practice

- LTA can be performed percutaneously, laparoscopically, or during open surgery.

- The percutaneous technique is identical to those described above for RFA and MWA, and US is the technique most commonly used to insert the Chiba or Chiba-like needle into the tumor.

- When the needle tip is in the correct position, the laser fiber is passed through the needle and advanced, until its tip lies about 1 cm beyond that of the needle. Laser energy is then delivered for 6 to 10 minutes.

- LTA can be performed under the guidance of MRI.

# Complications

- The complications reported after LTA are also quite similar to those observed after the other percutaneous methods of thermal ablation.
- Mortality ranged between 0% and 0.8%,
- Complication rates were between 0% and 2%.

# Complications Reported After Laser Thermal Ablation

| First Author, Year | Patients/Sessions | Mortality Rate, n (%) | COMPLICATIONS, N (%) | |
|---|---|---|---|---|
| | | | Major | Minor |
| Pacella, 2001* | 117 S | — | 0 (0) | 3 (2.6) |
| Vogl, 2002‡ | 2132 S | 3 (0.1) | 42 (2) | 967 (45.4) |
| Vogl, 2004† | 1555 S | 2 (0.2) | 29 (1.5) | |
| Christophi, 2004† | 80 P | 0 (0) | 13 (16) | |
| Pacella, 2006* | 148 P | 1 (0.7) | 1 (0.7) | — |
| Ferrari, 2007* | 81 P | 0 (0) | 0 (0) | — |
| Arienti, 2008* | 1004 S | 4 (0.8) | 15 (1.5) | 62 (6.2) |
| Pacella, 2009* | 432 P | 1 (0.2) | 7 (1.6) | 424 (98.1) |

# Local Tumor Control

- LTA has been shown to be effective in producing complete ablation of tumor nodules, and as expected the probability of success depends on the size of the tumor.
- Increasing size is associated with decreasing rates of complete ablation;
- all three major methods for thermal ablation can produce complete ablation in more than 90% of HCC nodules, as long as their diameters do not exceed 3 cm.
- local recurrence rates reported by several investigators vary widely after LTA of hepatic tumors, from 2% to 37% (Eichler et al, 2001).

# Local Recurrence and Survival After Laser Thermal Ablation

| | | | SURVIVAL (%) | | | | |
|---|---|---|---|---|---|---|---|
| First Author, Year | No. Patients | Local Recurrence | Median (mo) | 1 Year | 2 Years | 3 Years | 5 Years |
| Pacella, 2001† | 74 | 5 (6) | — | 99 | 95 | 68 | 15 |
| Eichler, 2001† | 39 | 1 (2.5) | 53 | — | — | — | — |
| Vogl, 2004‡ | 603 | 71 (18) | 46 | 86 | 64 | 49 | 33 |
| Christophi, 2004‡ | 80 | 26 (33) | 35 | — | — | 48.3 | 6.7 |
| Pacella, 2006† | 148 | 18 (15) | 39 | 89 | 75 | 52 | 27 |
| Ferrari, 2007† | 81 | 8 (10) | — | 88.6 | 70.4 | 56.6 | 22.9 |
| Pacella, 2009† | 432 | 67 (20)* | 47 | — | — | 61 | 34 |

# Long-Term Results

- The best results were those of Vogl and coworkers (2004), who reported 3- and 5-year survival rates of 49% and 33% after LTA treatment of liver
- LTA is an effective method for treating hepatic tumors,
- Two major limitations
  - First, the small size of the thermal lesions obtained with a single laser fiber reduces the applicability of the technique and necessitates multiple treatment sessions to ablate most tumors.
  - Second, the multiple-fiber technique is a much more complex procedure that requires a high degree of skill and experience. It also tends to produce irregularly shaped thermal lesions

# Cryoablation

- Cryoablation kills tumor cells by the induction of hypothermia
- Rapid cooling near the cryoprobe tip produces an ice ball. Water molecules are trapped within the cells and are transformed into ice crystals, which aggregate and cause cell death.
- needle-like cryoprobes 3 mm in caliber have been developed that can be used for percutaneous tumor ablation, which is generally performed under US guidance (Mala, 2006)

- General anesthesia is typically used, because the procedure lasts longer than 30 minutes.
- The tip of the cryoprobe is placed in the deepest part of the tumor under US guidance, and the freeze-thaw cycle begins.
- On US, the ice ball appears as an increasing hyperechoic rim with a posterior acoustic shadow.
- Multiple cryoprobes must be inserted to ablate tumors larger than 3 cm in diameter. In this way, ablation areas larger than 5 cm in diameter can be created (Bilchik et al, 2000).

# Complications

- Cryoablation is associated with a higher rate of complications than other thermal ablation techniques (Seifert & Morris, 1999).
- cracking of the liver parenchyma, resulting in hemorrhage.
- syndrome known as *cryoshock,* which involves pulmonary, renal, and coagulation abnormalities in a variety of combinations (Head & Dodd, 2004).
- Severe hypothermia
- mortality and complication rates range from 0% to 4% and from 1.5 % to 29%, respectively.

# Complications Reported After Cryoablation

| | | | COMPLICATIONS, N (%) | |
|---|---|---|---|---|
| First Author, Year | Patients/Sessions | Mortality Rate, n (%) | Major | Minor |
| Weaver, 1995† | 47 P | 2 (4) | 11 (23) | 47 (100) |
| Sarantou, 1998‡ | 335 P | 5 (1.5) | 16 (4.8) | |
| Seifert, 1999‡ | 2173 P | 33 (1.5) | 21 (1) | 77 (3.5) |
| Adam, 2002‡ | 31 P | 1 (3.2) | 9 (29) | |
| Mala, 2004† | 24 S | 0 (0) | 10 (42) | |
| Jungraithmay, 2005 | 19 P | 0 (0) | 4 (21) | 7 (36.9) |
| Xu, 2008† | 326 P | 0 (0) | 5 (1.5) | — |
| Zhou, 2009* | 124 P | 1 (0.8) | 29 (23.4) | — |

# Local Tumor Control

- Cryoablation can completely destroy hepatic tumors,
- Complete response rates, are lower than those reported for RFA or MWA.
- Local recurrence rates (6.4% to 58%) also seem to be higher than those observed after RFA.

# Local Recurrence and Survival After Cryoablation

| | | | SURVIVAL (%) | | | | |
|---|---|---|---|---|---|---|---|
| First Author, Year | No. Patients | Local Recurrence | Median (mo) | 1 Year | 2 Years | 3 Years | 5 Years |
| Weaver, 1995‡ | 140 | — | 22 | — | — | — | — |
| Seifert, 1999† | 116 | 38 (33) | 26 | — | 56 | — | — |
| Zhou, 1998* | 235 | — | — | 63 | — | 40 | 27 |
| Ruers, 2001† | 30 | 3 (9) | 32 | 76 | 61 | — | — |
| Sheen, 2002‡ | 57 | — | 22 | — | — | 14 | — |

# Long-Term Results

- RFA has surpassed cryoablation in terms of local tumor control (Adam et al, 2002).
- The major drawbacks of cryoablation are
  - the large caliber of the cryoprobes,
  - long exposure times required to ablate even small tumors.
- These aspects need to be substantially improved before cryoablation can compete with the other thermal ablation methods.

# Thank You