Advances of Thermal Ablation

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INTERVENTIONAL RADIOLOGY
CME AND WORKSHOP - 2017

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Disclaimer

- Nothing to disclose

Goals of Minimally Invasive Thermal Ablation:

- Primary goal: eradicate all viable malignant cells within target volume
- 0.5–1.0-cm ablative margin of seemingly normal tissue.
- Sparing normal surrounding tissues (accuracy).
- Larger tumors (>/=3 cm) - multiple overlapping ablations

Image-guided minimally invasive ablative therapies.

- Thermal
  - Hyperthermic Ablation.
  - Cryoablation
- Nonthermal
  - Chemical ablation
  - Irreversible electroporation
  - Ultrasonic Ablation.

Thermal Ablation Therapies:

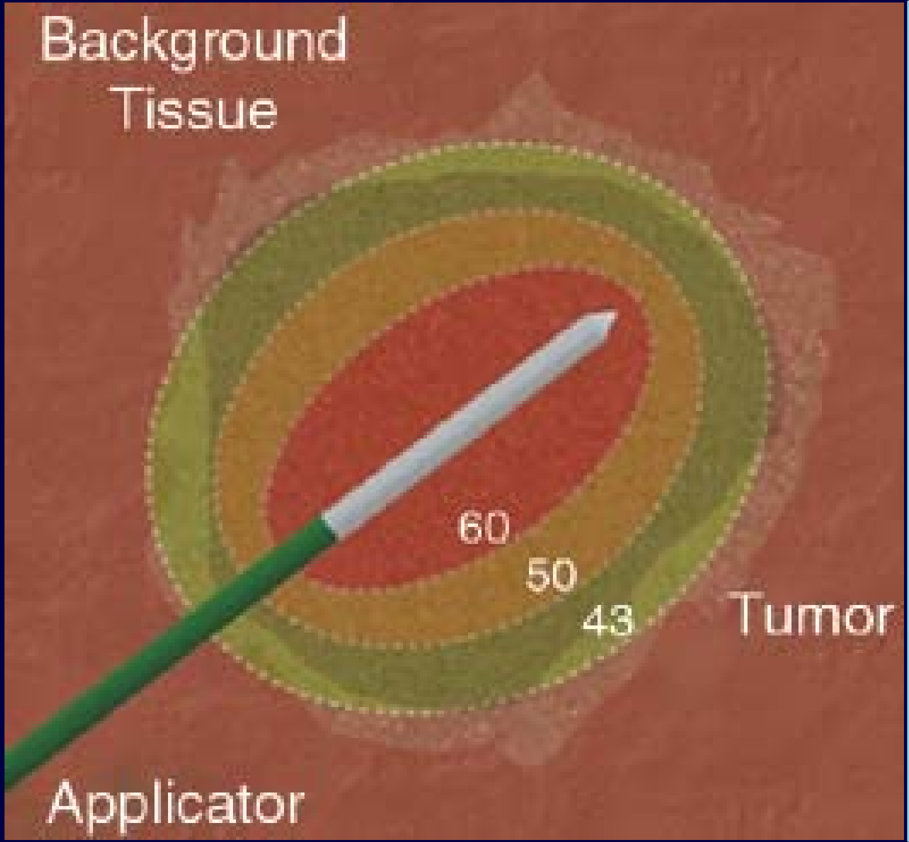
- Entire tumor and an ablative margin be subjected to cytotoxic temperatures
- Strategies developed to increase the amount of coagulation necrosis
  - Increasing energy deposition,
  - Modulating tissue characteristics,
  - Modifying tissue blood flow.

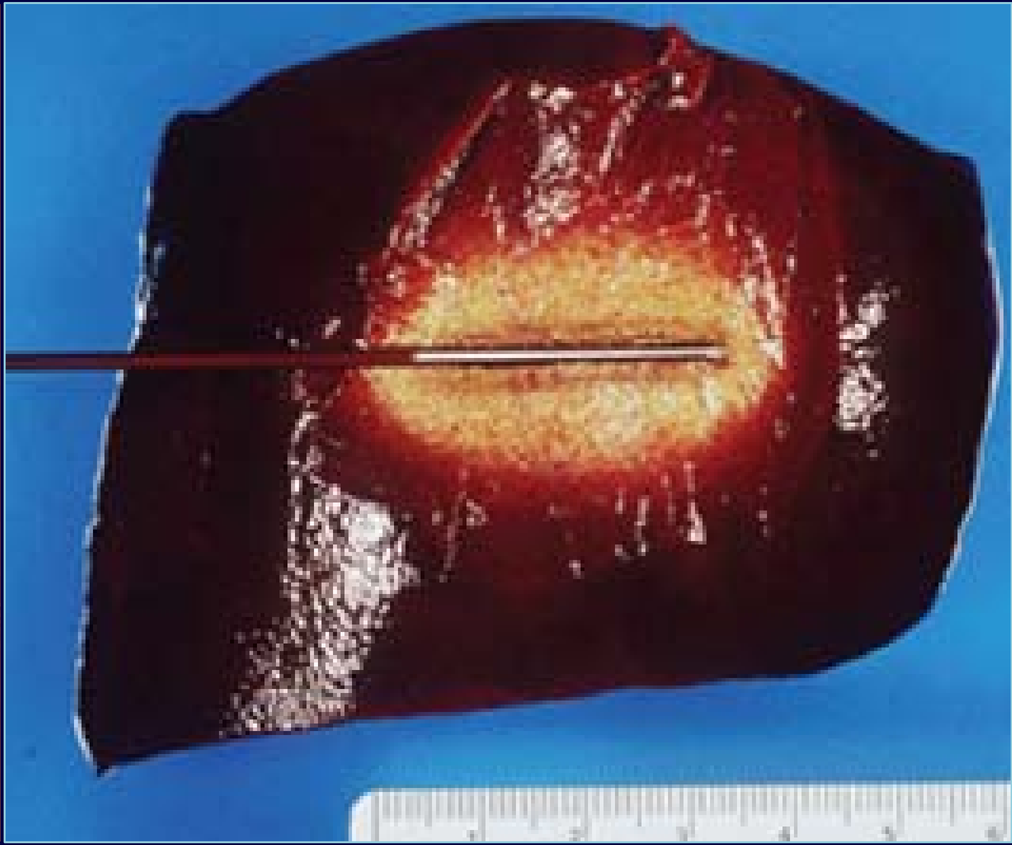
Hyperthermic Ablation:

- Thermal ablation of focal tumors uses high-temperature tissue heating (>50^{0}C) surrounding applicators placed at the center of a tumor.
- Irreversible cellular injury : 46^{0}C for 60 minutes, and more rapidly at higher temperatures
- Optimal temperatures for ablation : 50^{0}C to 100^{0}C.

Hyperthermic Ablation:

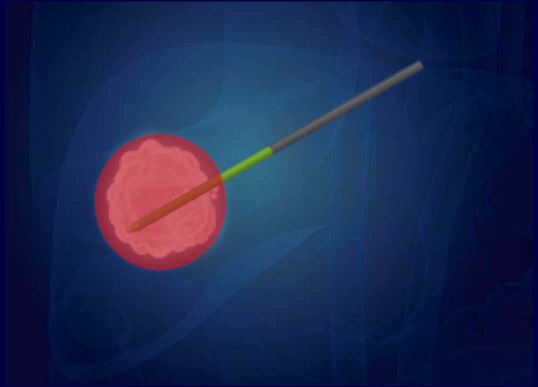
- Classic findings of coagulative necrosis - several days later.
  - Implications: early posttreatment percutaneous biopsy and standard histopathologic interpretation may not be a reliable measure of adequate ablation.
- Critical temperature : Maximum temperatures at the edge of the ablation zone
  - 30^0C to 77 ^{0}C for normal tissues
  - 41^0C to 64^0C for tumor models.
- Thermal dose required to induce cell death - varies in different tissues


Background
Tissue
60
50
43
Tumor
Applicator



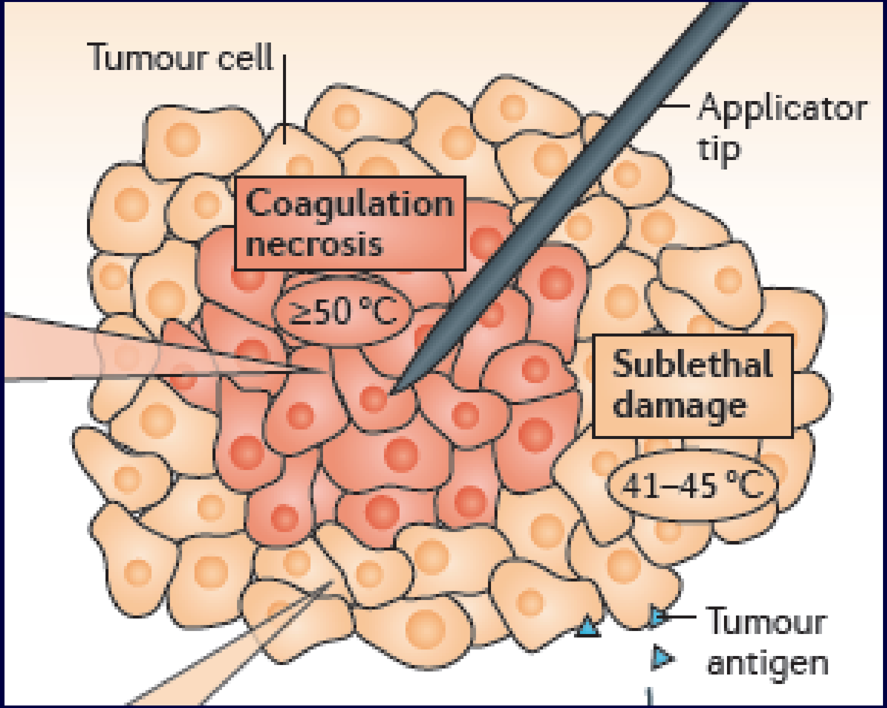
Radiofrequency ablation (RFA): Principle

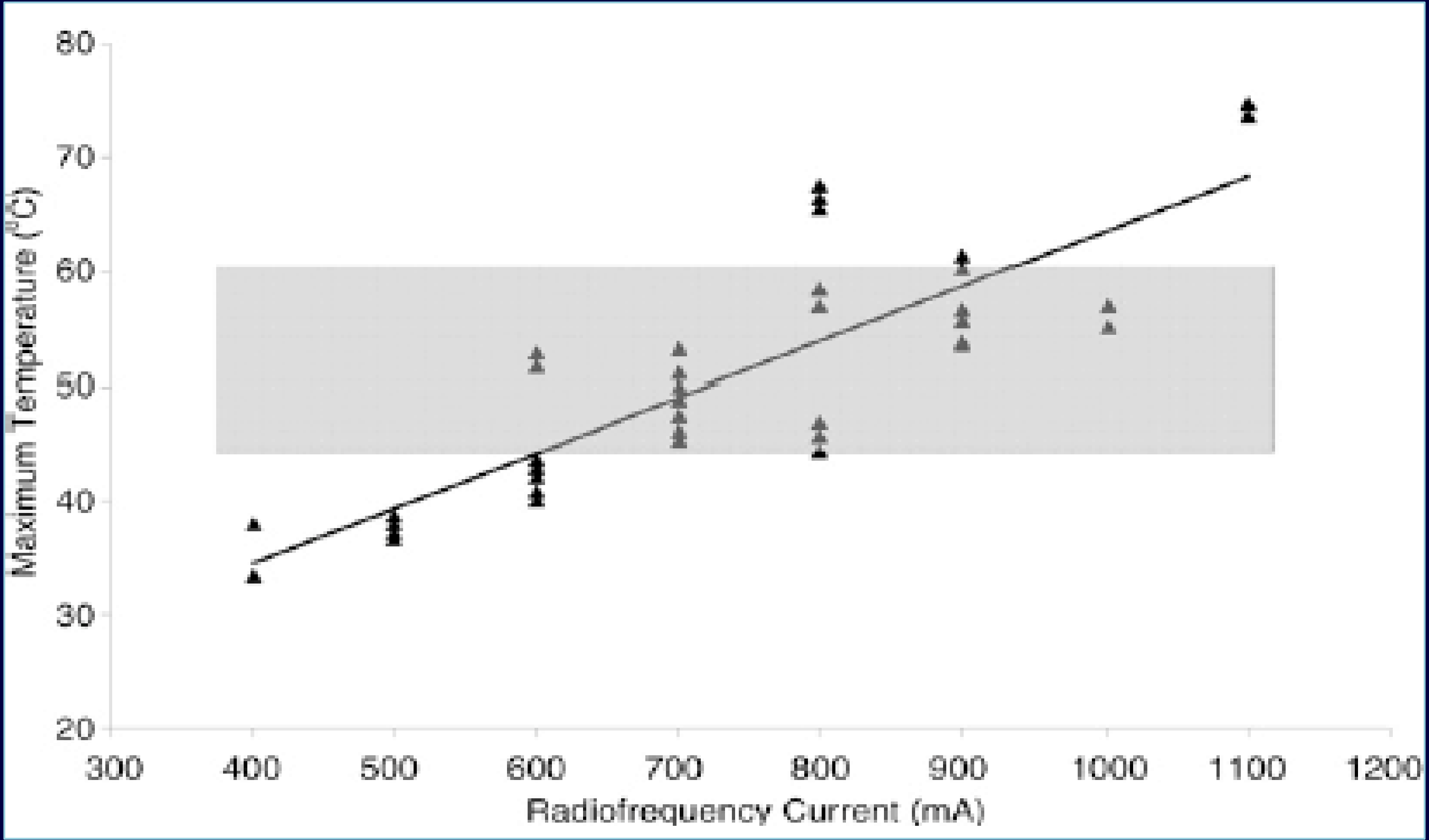
- RFA causes coagulation necrosis of tumor tissue
- By applying temperatures of 60–90°C.
- Resulting protein denaturation is irreversible.
- Thermal energy also cauterize tumor-vessels
- To ensure complete tumor ablation
  - the entire   tumor volume plus a 5–6 mm wide safety margin to be heated
  - up to a temperature of 60°C



Radiofrequency ablation (RFA): Principle

- Temperatures exceeding 50°C
  - Chromosomal alterations
  - Protein denaturation
  - Damaging cellular membranes
  - Damaging transport proteins
- General consensus has held that temperatures should reach 50–60°C





80
70
60
50
40
30
20
Maximum Temperature (°C)
300
400
500
600
700
800
900
1000
1100
1200
Radiofrequency Current (mA)

RF Ablation

- Electrical circuit : generator – cabling – electrodes - tissue(resistive element).
- Joule effect – leads to heat generation.
- Ablative heating - tissue dehydration and water vaporization - sudden increases in impedance - inhibit current flow from a generator.
- Methods to decrease circuit impedance & augment RF current flow:
  - expanding the electrode surface area
  - Pulsing the input power
  - Injections of saline.

RF Ablation

Electrodes:

- Monopolar mode: Most RF ablation systems
- Two different types of electrodes:
  - Interstitial electrodes - delivers energy to the tumor, creating localized heating.
  - Dispersive electrodes (ground pads) on the skin surface - disperse energy over a large surface area to reduce thermal injury to the skin.
- Monopolar electrode designs include both
  - straight insulated needles with an exposed metallic tip and
  - multitined electrodes.

RF Ablation

- Internally cooled electrodes - use a single needle, in which fluid is circulated inside the electrode's active tip, and temperatures at the electrode-tissue interface are reduced.
  - Lower temperatures - inhibit charring - allows increased power deposition – clinically relevant ablations.
  - smaller caliber applicator (17 gauge, 1.5-mm diameter)

RF Ablation

Electrodes with multiple tines - aim to distribute energy spatially.

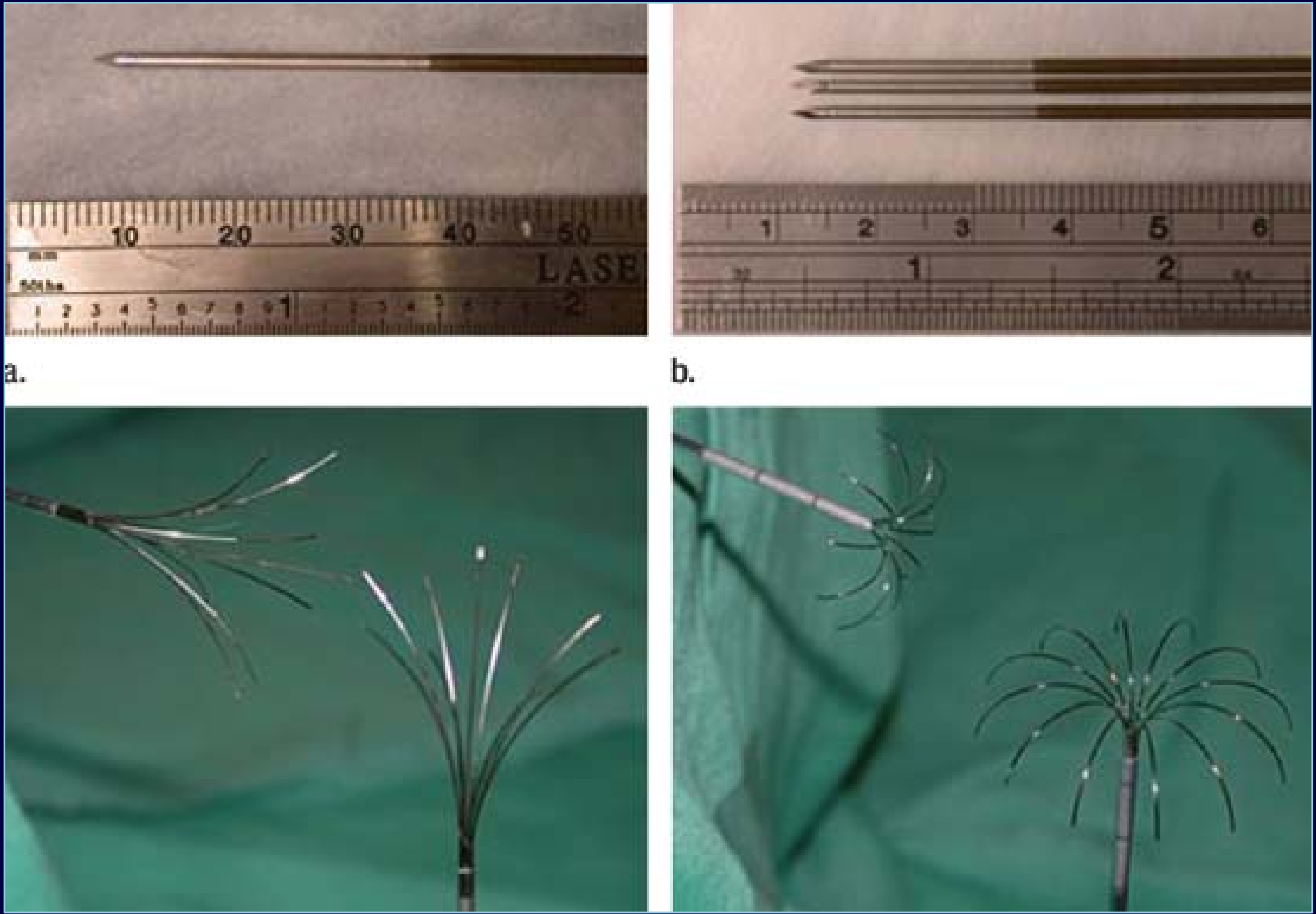
1) Nondeployable multitined electrode –

- Three single 17-gauge electrodes - spaced 5 mm apart triangular configuration
- Limited puncture area
- Zones of ablation - over 3 cm in diameter in normal liver in 12 minutes with a 200-W generator.

2) Deployable multitined electrode - deploy several smaller electrodes from a single needle shaft –

- Star-shaped arrays - 14-gauge (2.1-mm diameter) needle in arrays of 4, 9, or 12 tines.
- Umbrella-shaped arrays – 10 tines and a 13-gauge needle.

zones of ablation - ~3–4 cm in diameter.


a.
b.
LASE

RF Ablation

- Bipolar systems - current oscillates between two interstitial electrodes without the need for a ground pad.
  - Restricts current flow primarily to the area between the electrodes
  - Protects from perfusion-mediated cooling
  - Faster more focal heating.
  - Saline infusion to increase energy delivery between the electrodes.
- Multipolar operation – switch between pairs of bipolar electrodes situated on individual needles.

RF Ablation

Generator and ground pads:

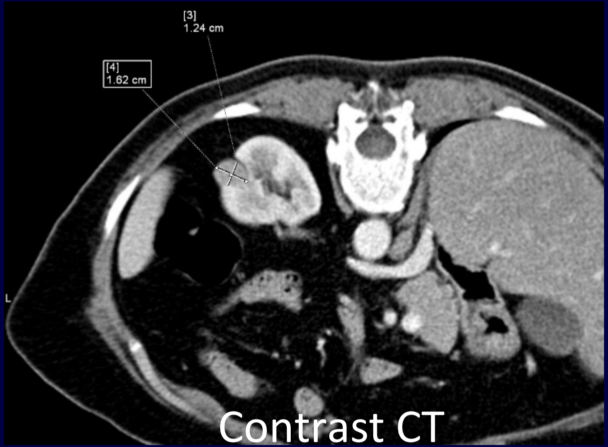
- Generators - 150 to 250 W (Lower in areas of high background impedance, lung)
- Higher-power designs - currently under development.
- feedback and control system:
  - Impedance-based and
  - Electrode temperature–based controls.

RF Ablation

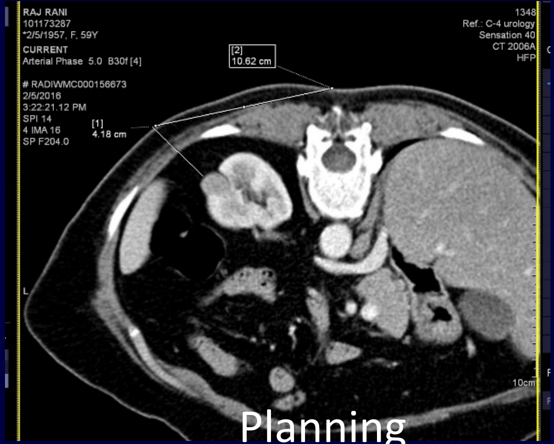
- Ground pad used - provide a large dissipative surface for electrical current flow through the skin.
- Skin burns can result from uneven placement or insufficient number of pads.
- Strategies to prevent ground pad burns
  – Monitoring temperature and impedance through each pad,
  – Cooling the pad,
  – Optimized pad designs,
  – Switching between pads to reduce heating.

RFA of Renal Mass

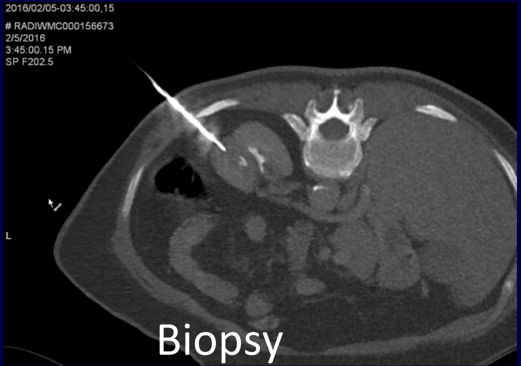
Case : H/o right nephrectomy, SRM in left kidney



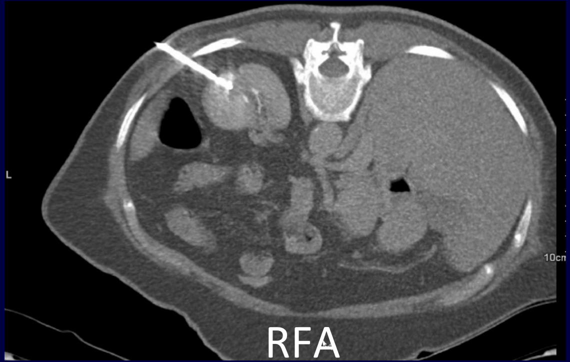
Contrast CT



Planning



Biopsy



RFA

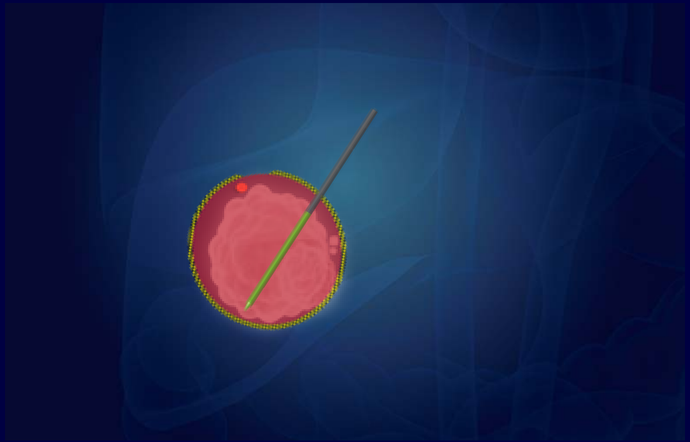
Post RFA

End point of RFA

- Duration of RFA : 5–20 min
- Success of RFA ablation depends on impedance of target tissue.
- Impedance rise reflects the dehydration of the ablated tissue.
- Once the impedance threshold is reached, the ablation process is repeated
- This is to ensure complete coagulation necrosis of the tumor

Microwave Ablation

- Microwave - electromagnetic energy in the 300 MHz to 300 GHz range
- Dielectric hysteresis (rotating dipoles) - Microwave heating
- Advantages :
  - Microwaves readily penetrate through biologic materials.
  - Can be continually applied to produce extremely high (~150 ‘C) temperatures.
  - Do not require ground pads.
  - Multiple antennas can be operated simultaneously.



Microwave Ablation

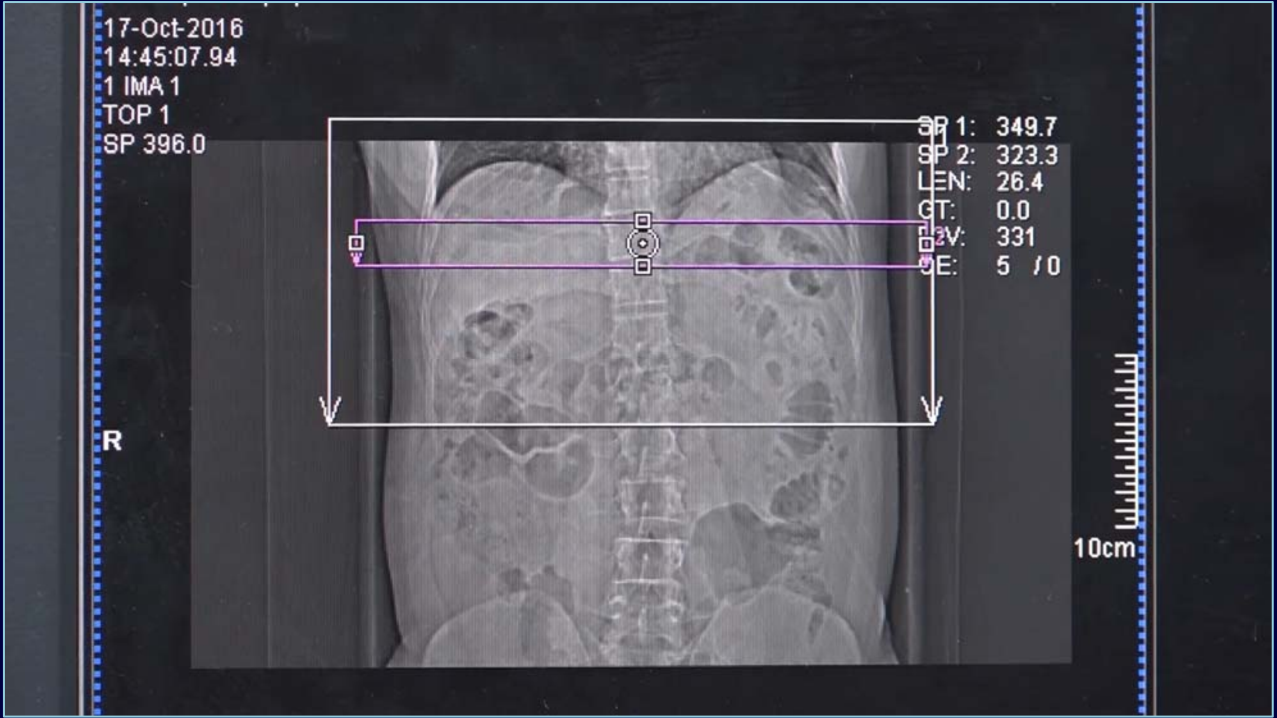
Disadvantages:

- Inherently more difficult to distribute.
- higher microwave powers can lead to unintended injuries to other tissues, such as the skin.
  - Adding a cooling jacket around the antenna can reduce cable heating and skin burns.

Microwave antenna

Microwave ablation

Microwave ablation of Liver Metastasis



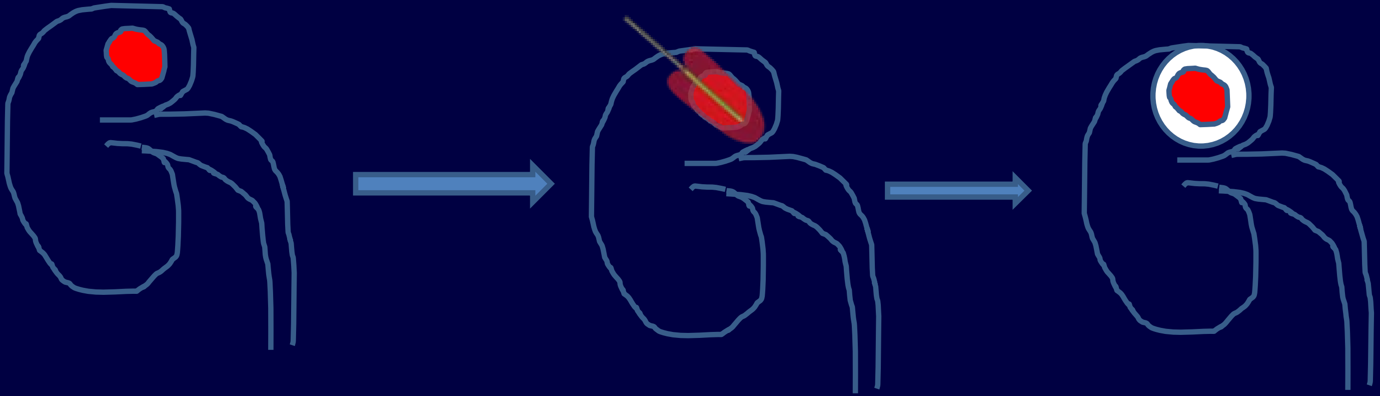
Microwave ablation of Renal Mass

Cryoablation

- Common clinically treated tumors include focal primary renal tumors and palliative treatment of osseous metastases.
- Joule-Thomson–based systems:
- Joule-Thomson effect: describes the change in temperature of a gas resulting from expansion or compression of that gas.
  - Argon cools during expansion; helium warms.
  - Used to create unique freeze and thaw cycles - Current cryoablation systems.

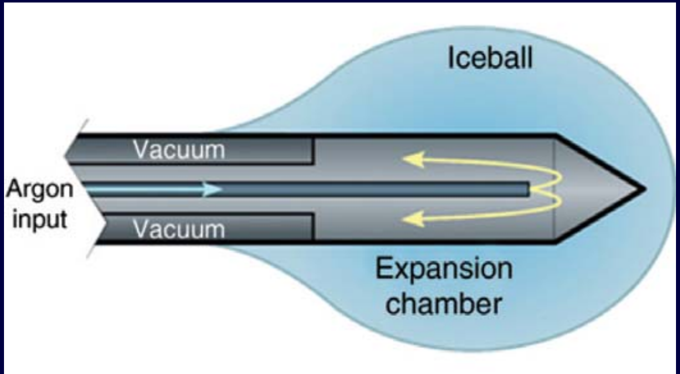
Cryoablation (CA) : Principle

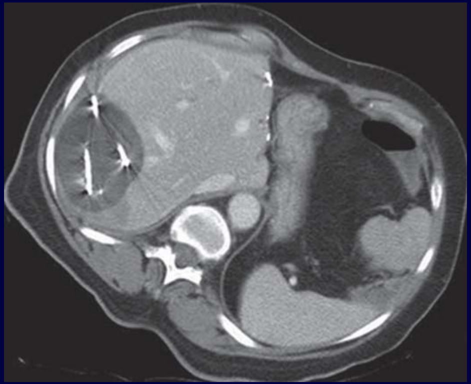
- Cryoprobe is inserted into the tumor under CT/US guidance
- Lowering the temperature of the adjacent tissue by means of helium or argon down to −40 to −60°C.
- Repeated freeze-thaw cycles ultimately result in the destruction of cell organelles and membranes
- The created intracellular ice crystals cause irreversible hydropic cell damage
- Cycle: 10-min freezing phase → 8-min active thawing phase → 10-min re-freezing phase.



Cryoablation

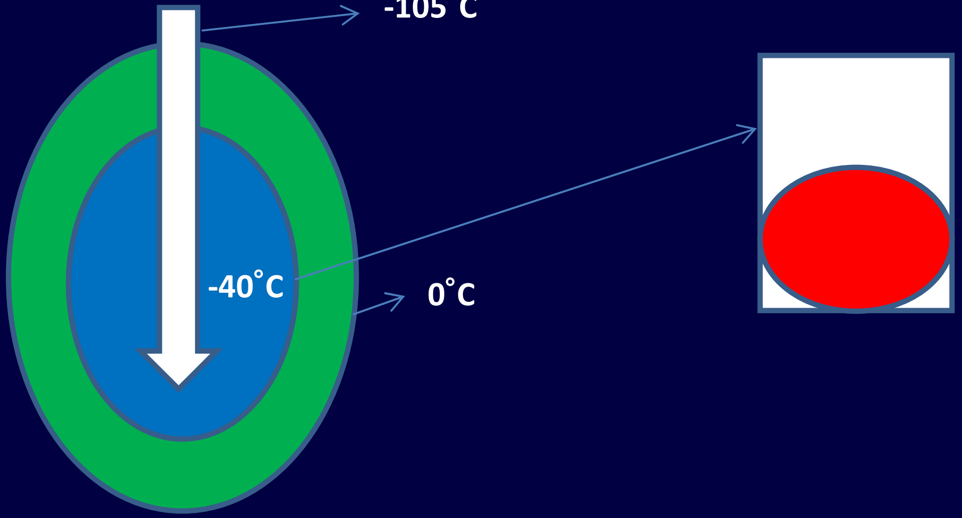
- Gas expansion occurs in a small chamber inside the distal end of the cryoprobe to create
  - heat sink during freeze cycles and
  - heat source during thaw cycles





Cryoablation (CA) : Principle

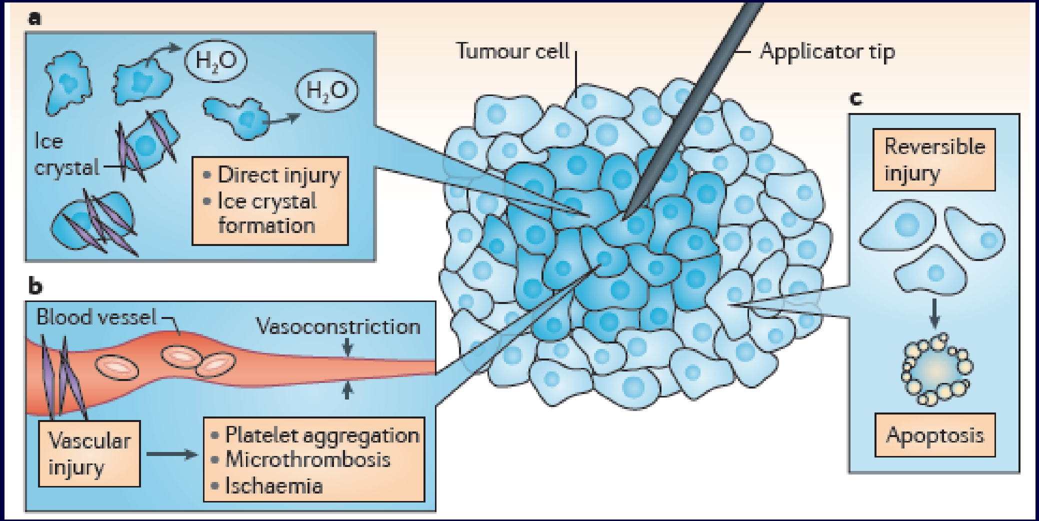
- Ice Ball with central probe



To guarantee the ablation, iceball is generally carried 5 to 10 mm beyond the edge of the tumor when viewed under real-time imaging

Mechanism of Tissue Destruction in CA

- CA cellular injury - classified as
  - cellular
  - vascular
  - immunologic



Cryoablation

- Newer system under development uses nitrogen near its critical point to provide lethal cooling.
  - more efficacious than Joule-Thomson–based systems.
- Advantages:
  - Smaller cryoprobes
  - Larger zones of ablation.

Laser Ablation

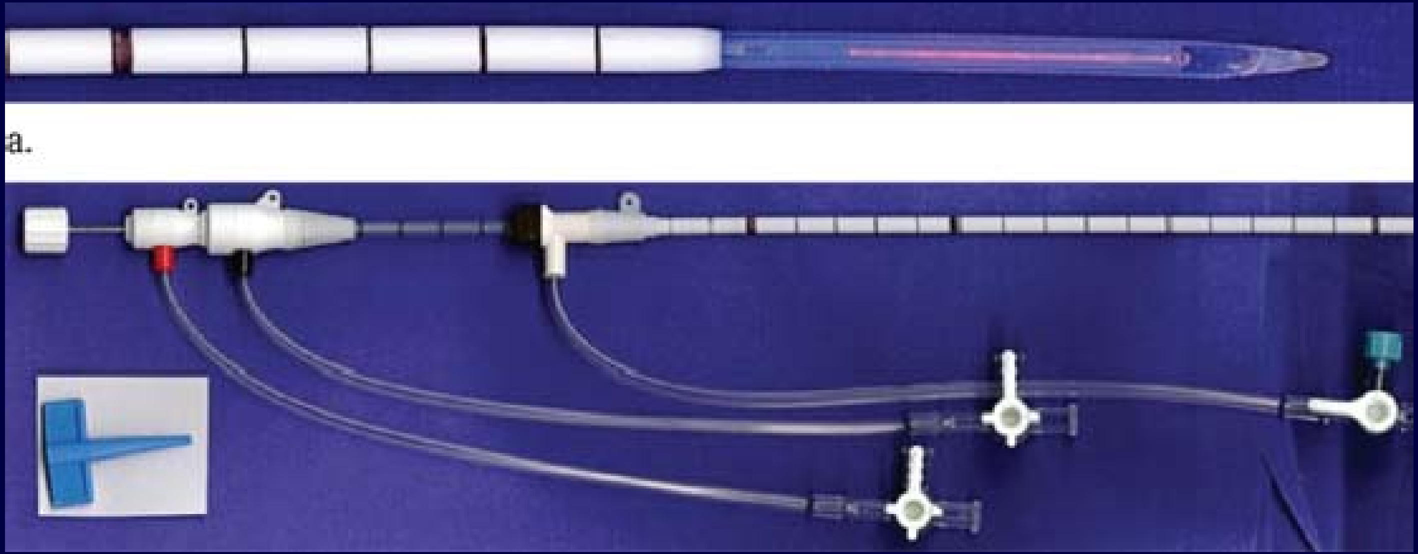
- Lasers induce electromagnetic heating to elevate tissue temperatures to lethal levels
- Advantage:
  - Eliminate image artifacts on CT and MR images. Thus, reasonable to perform MR temperature mapping : prostate
  - It may be coupled through optical fibers, which are inherently magnetic resonance (MR) imaging compatible.
  - The lack of metal in the power distribution chain and
  - Relatively small diameter of most applicators effectively.
- Efficient and precise energy source for tissue heating.

Laser Ablation

Limitations:

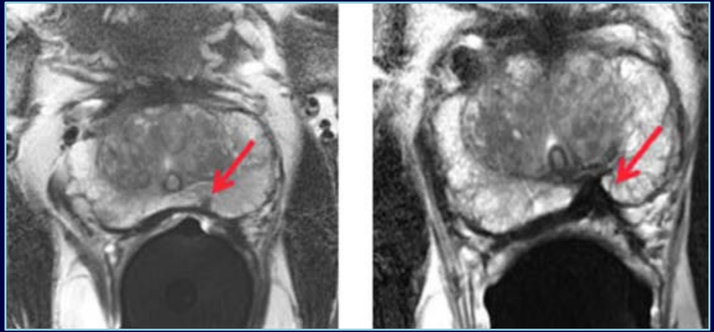
•Limited energy penetration and create smaller ablation zones (1–2-cm diameter).

•Does not penetrate through charred or desiccated tissues.



Laser Ablation

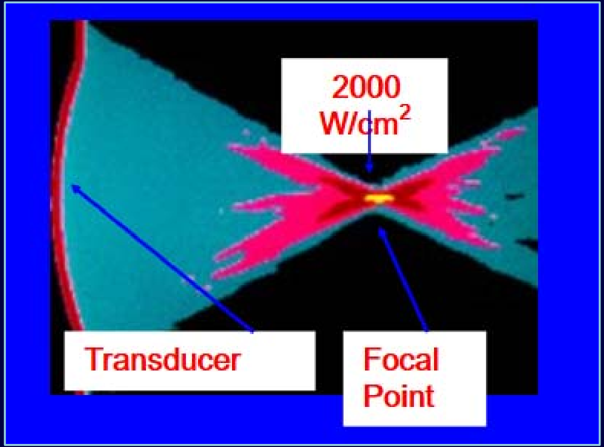
- Prostate cancer
- 980 Diode LASER
- Inbore Magnet guidance



Ref: University of Chicago website

High-intensity Focused Ultrasound (HIFU)

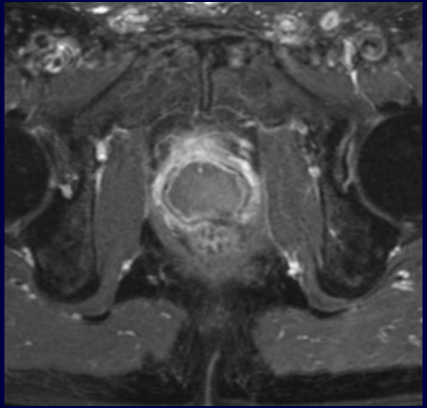
- Based on focused concentration of high-intensity US waves.
- At focal point, HIFU causes rapid increase in temperature 90^{0C}
- Soft tissue undergo cellular necrosis
- No need to puncture the tumor
- No risk of hemorrhage and tumor spillage

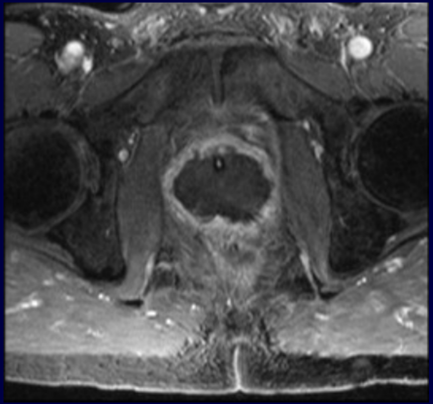


High-intensity Focused Ultrasound (HIFU)

HIFU is ideal for

- localized prostate cancer
- PSA <10
- Gleason </= 7
- Prostate volume </=50cc



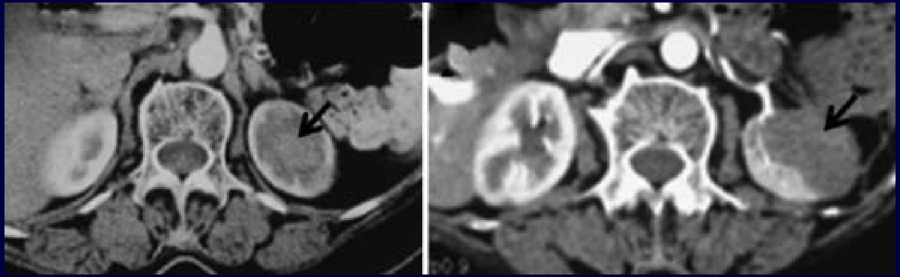


Complications of Thermal Ablation

- Post-ablation syndrome (myalgia, fever, nausea <48 h) (22%)
- Self-limiting hematuria (20%)
- Temporary cloudiness of urine
- Self-limiting perirenal hematom
- Perirenal hematoma requiring t
- Ureteral stenosis (1.5%)
- Skin Burns (<2%)

Follow up after Thermal Ablation

- Short-term follow-up : after 3 m to identify any residual tumor
- Long-term follow-up : after 6 m and then yearly intervals
- Follow-up imaging
  - CECT
  - CES
  - CEMRI
- Look for progressively increase in size of mass
- Recurrence should be distinguished from a small ribbon of scar tissue which delimits the outer ablation margin



Pre RFA   Post RFA

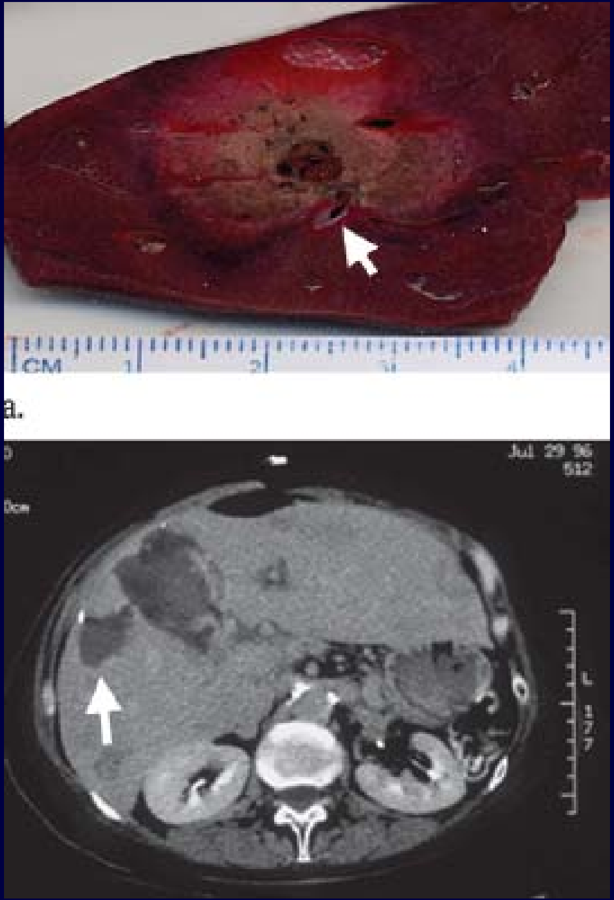
* Das CJ et al. Indian J Urol. 2015;31(3):202-8. Image-guided urological interventions: What the urologists must know.

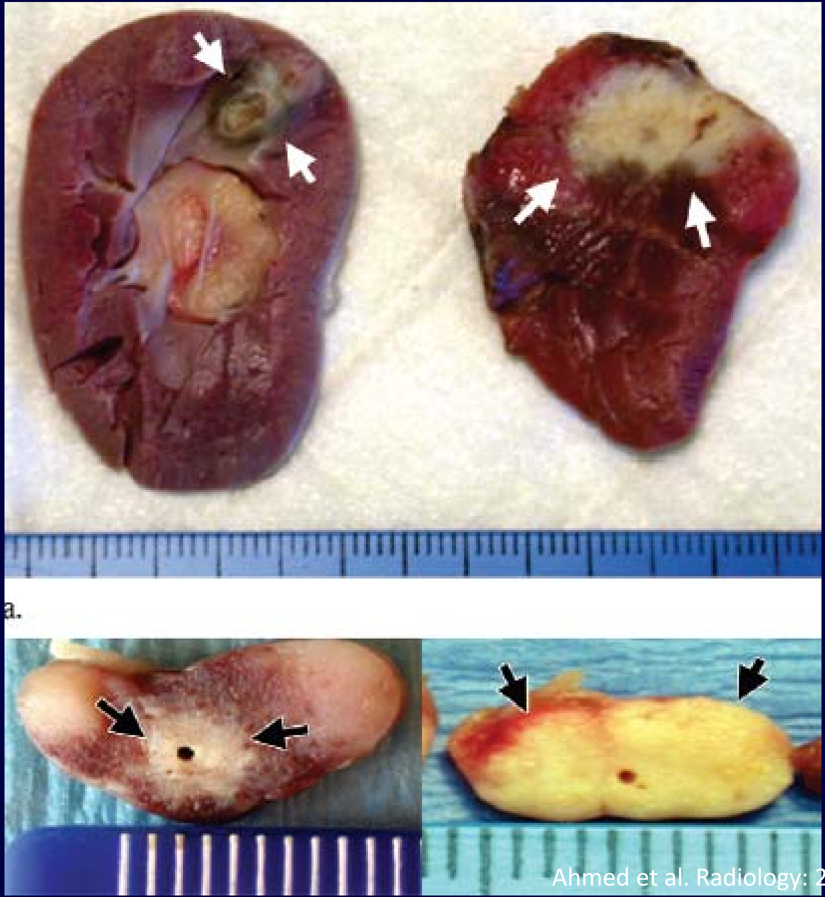
Current and Future Research

Modulating Tissue Characteristics:

- Tissue perfusion - foremost factor limiting thermal ablation.
- Larger diameter blood vessels (especially > 3 mm) act as heat sinks
- Zone of coagulation increases when blood flow reduces.
  - Arterial embolization techniques (eg, balloons, coils, particles, or lipiodol agents).
  - Intraarterial and systemic pharmacologic agents, such as halothane and arsenic trioxide
  - Antiangiogenic therapies: sorafenib

Effect of blood flow on RF ablation size





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Electrical conductivity

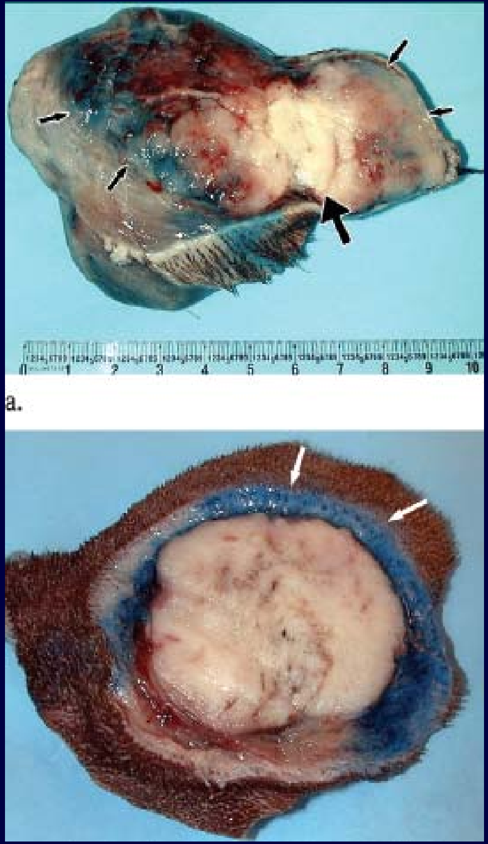
- Thermal conductivity –
- Effects of varying tumor and surrounding tissue thermal conductivity on effective heat transmission during RF ablation
  - Poor tumor thermal conductivity - limits heat transmission centrifugally away from the electrode.
  - Increased thermal conductivity (in cystic lesions) - heat dissipation - incomplete and heterogeneous tumor heating.

Electrical conductivity

- Oven effect - increased heating efficacy for HCC surrounded by cirrhotic liver.
- Tissue and tumor thermal conductivities - useful to predict ablation outcome in varying clinical settings
  - Exophytic renal cell carcinomas surrounded by perirenal fat.
  - Lung tumors surrounded by aerated normal parenchyma.
  - Osseous metastases surrounded by cortical bone.

Electrical conductivity

- Altering the electrical environment immediately around the RF electrode with ionic agents prior to or during RF ablation.
  - Increases coagulation volume.
  - Saline infusion.
- Hydrodissection: Nonionic fluids used to protect tissues adjacent to the ablation zone (eg, diaphragm or bowel) from thermal injury.
  - 5% dextrose



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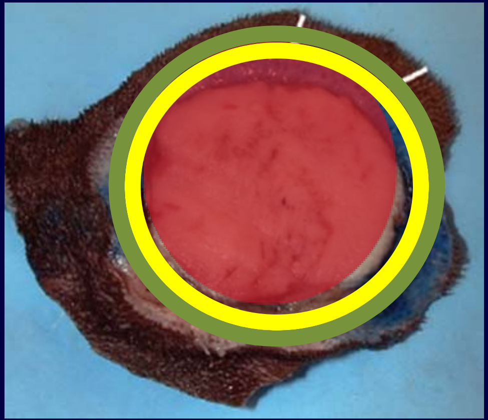
Computer Modeling in Understanding Tissue Heating Patterns

- Computer models to simulate ablation of focal tumors
- It can predict tissue heating patterns
- More realistic and clinically relevant simulation.
- Improve RF predictability
- 3D printing

Combining Percutaneous Ablation with Other Therapies

- Target tumors can be conceptually divided into three zones:
  - central area, predominantly treated by thermal ablation, that undergoes heat-induced coagulation necrosis
  - peripheral rim that undergoes reversible changes from sublethal hyperthermia
  - surrounding tumor or normal tissue : unaffected by focal ablation



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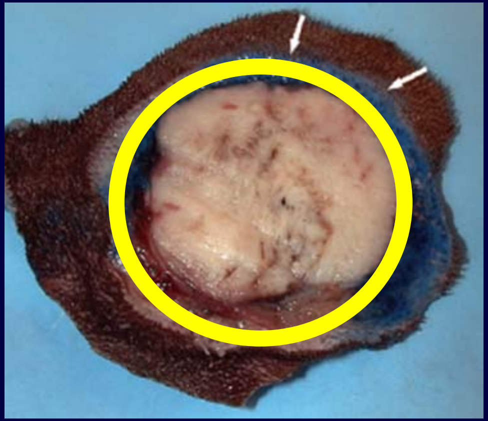
Combining Percutaneous Ablation with Other Therapies

- Strategy to increase the completeness of tumor destruction
- Goal - to increase tumor destruction within the sizable peripheral zone of sublethal temperatures
- Tumor death can be enhanced by combining thermal therapy with adjuvant chemotherapy or radiosensitizers



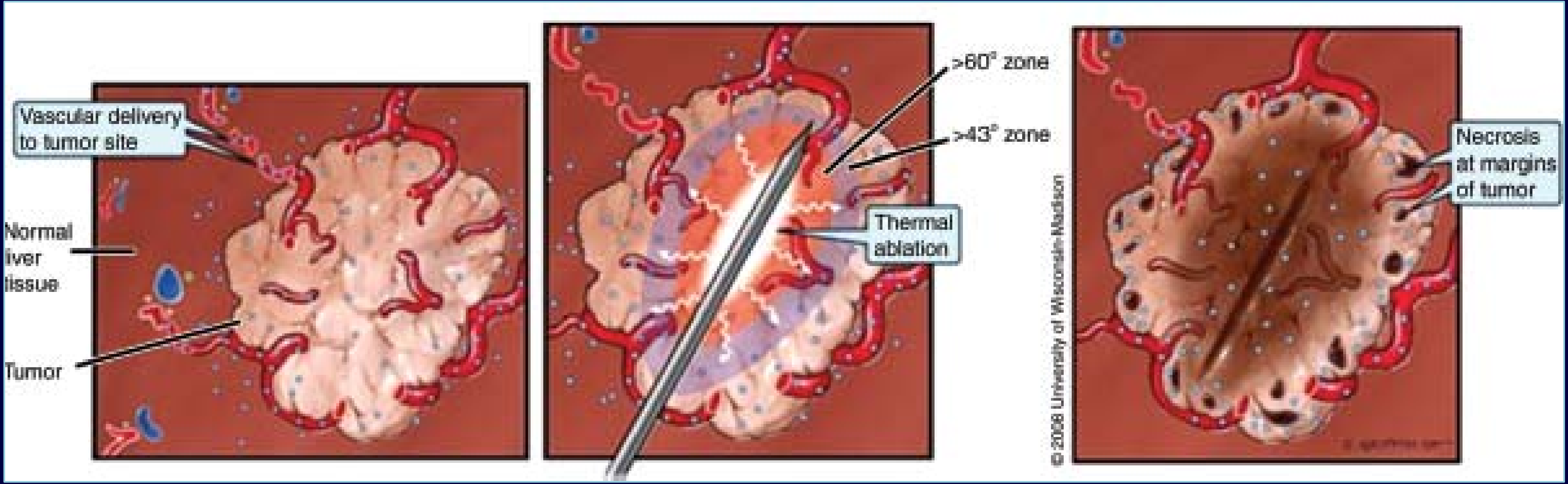
Thermal ablation with chemotherapy

- Chemotherapy - free or contained within liposomes
- Effects occur preferentially in peripheral zone of hyperemia
- Treatment effect extended to encompass peritumoral liver
- Enabled the destruction of the difficult 0.5–1.0-cm ablative margin

Thermal ablation with chemotherapy

- Underlying mechanisms- multifactorial
- Improved intratumoral drug delivery- owing to
  - increased circulation time
  - increased drug release with thermosensitive liposome types
  - vascular effects of sublethal hyperthermia in peripheral treatment zone
- Combined cytotoxic effects of the chemotherapy and heat increase apoptosis
- Heat-related cytotoxic effects of the liposome itself.

Combining thermal Therapy with targeted drug delivery



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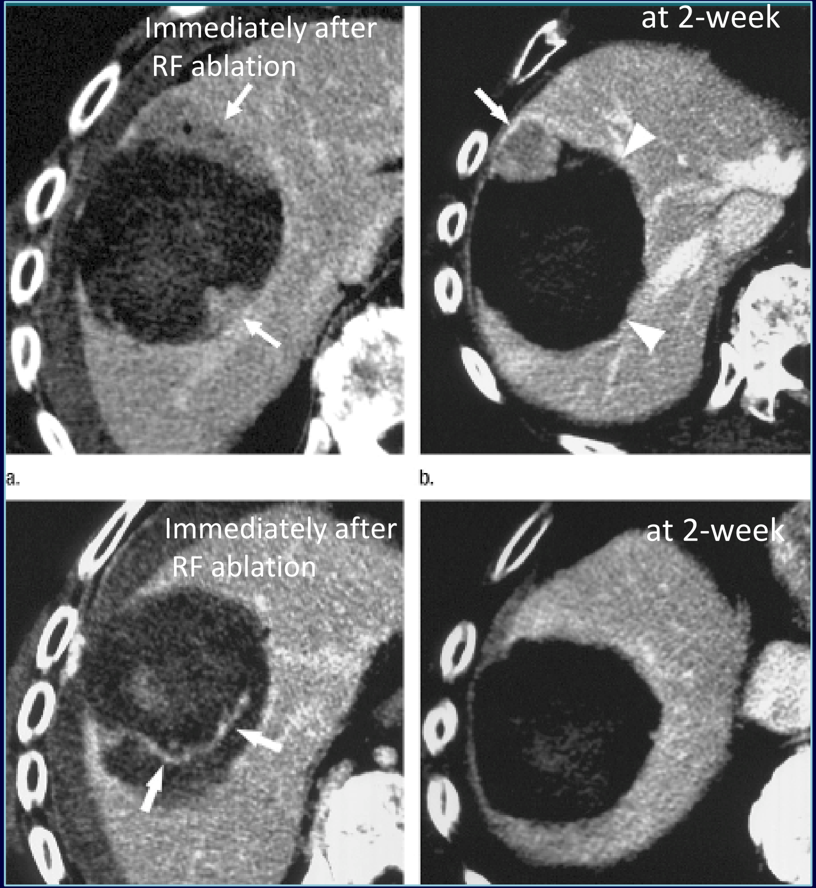
Thermal ablation with chemotherapy

Combined RF ablation and liposomal doxorubicin in an 82-year-old man with an 8.2-cm vascular hepatoma.



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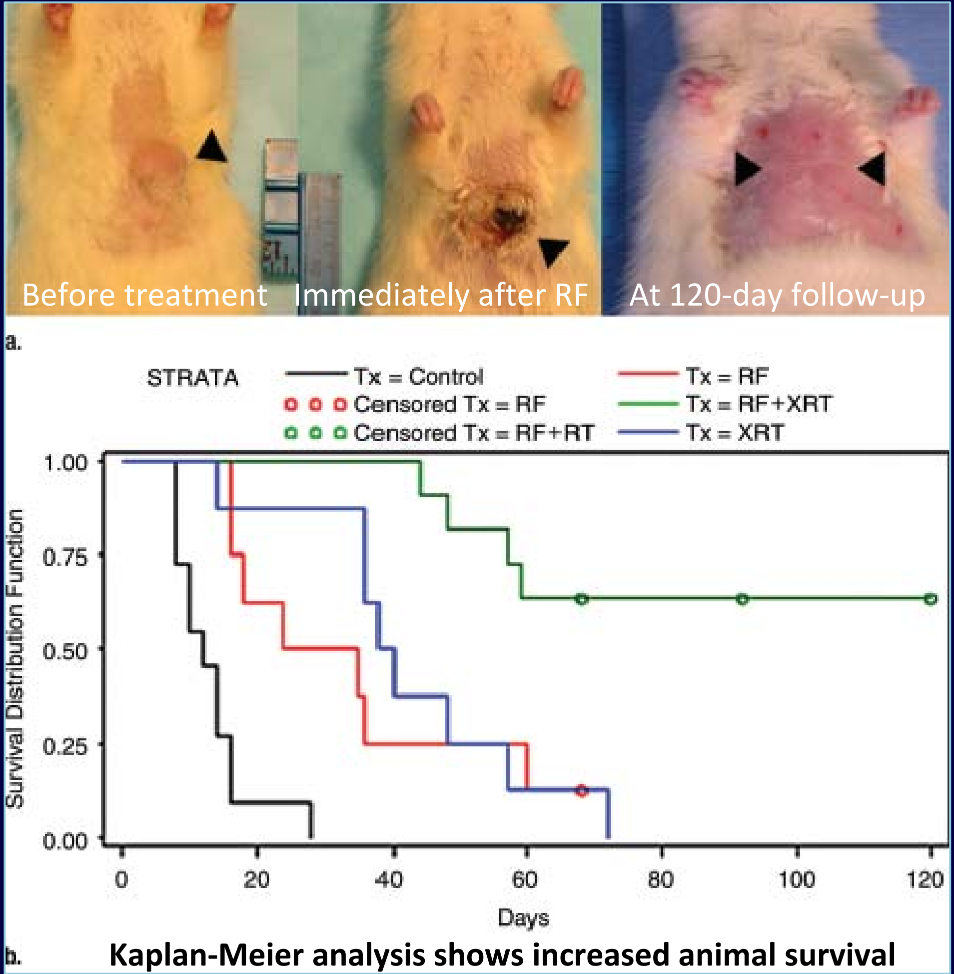
Thermal ablation with Radiation therapy

- Increased tumor destruction by combining external beam radiation therapy and low-temperature hyperthermia.
- Mechanism:
  - Sensitization of the tumor to subsequent radiation- owing to increased oxygenation from hyperthermia induced increased blood flow.
  - Radiation-induced inhibition of repair and recovery and increased free radical formation.
  - Increase in oxidative and nitrosative stress.
- research needed to identify the optimal temperature for ablation, the optimal radiation dose, and the most effective method of administering radiation therapy.

Thermal ablation with Radiation therapy



Kaplan-Meier analysis shows increased animal survival

Combining RF ablation with external beam radiation for treatment of subcutaneously implanted rat breast tumor.

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Conclusion

- **Minimally invasive percutaneous ablation has been well recognized as an important tool in the treatment of focal malignancies**

- Equipment and technologic modifications that have been developed to further improve clinical success of this therapy

- **Challenge: To optimize these devices for improved energy delivery to specific organ systems or tumor types to improve predictive abilities**

- To develop combination therapies to further improve the clinical effectiveness of minimally invasive thermal ablation

THANK YOU