

# THE ROLE OF INTERVENTIONAL RADIOLOGY IN THE DIAGNOSIS AND TREATMENT OF SOLID TUMORS

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**Center for Interventional Oncology**

**Radiology & Imaging Sciences**

**National Institutes of Health**

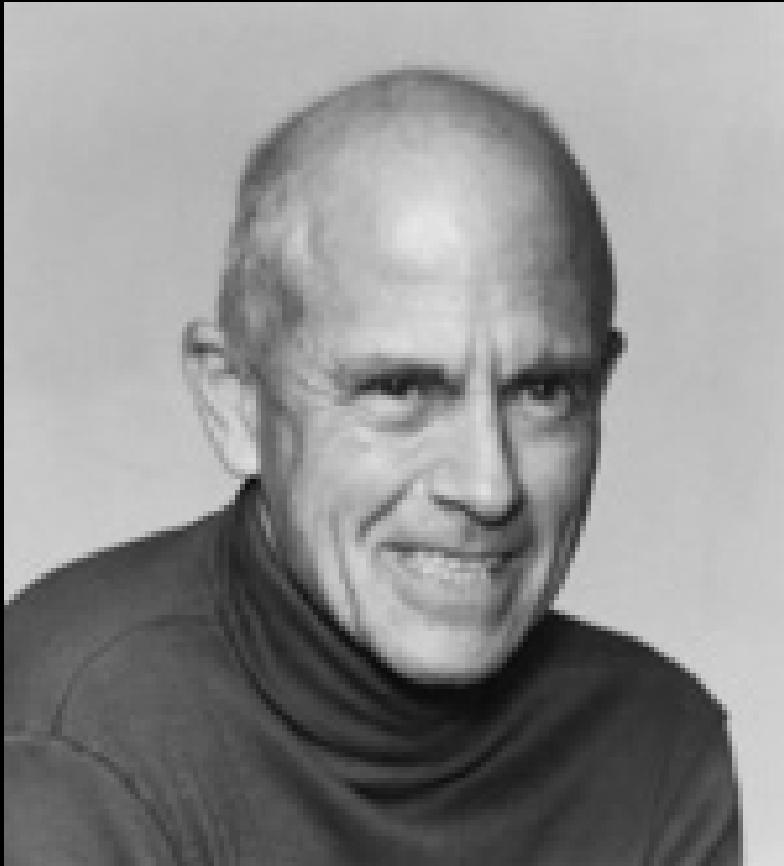
# OBJECTIVES

- Using Case Studies and Imaging examples:
  - 1) Discuss the role interventional (IR) procedures to aid in diagnosing malignancy
  - 2) Current and emerging techniques employed in IR to cure and palliate solid tumor malignancies will be explored
    - ❖ Within 1 and 2 will be a discussion of research in the field of IR
    - ❖ Q+A

# WHAT IS INTERVENTIONAL RADIOLOGY?

- Considered once a subspecialty of Diagnostic Radiology
- Now its own discipline, it serves to offer minimally invasive procedures using state-of-the-art modern medical advances that often replace open surgery (Society of Interventional Radiology)

# CHARLES T. DOTTER M.D. (1920-1985)



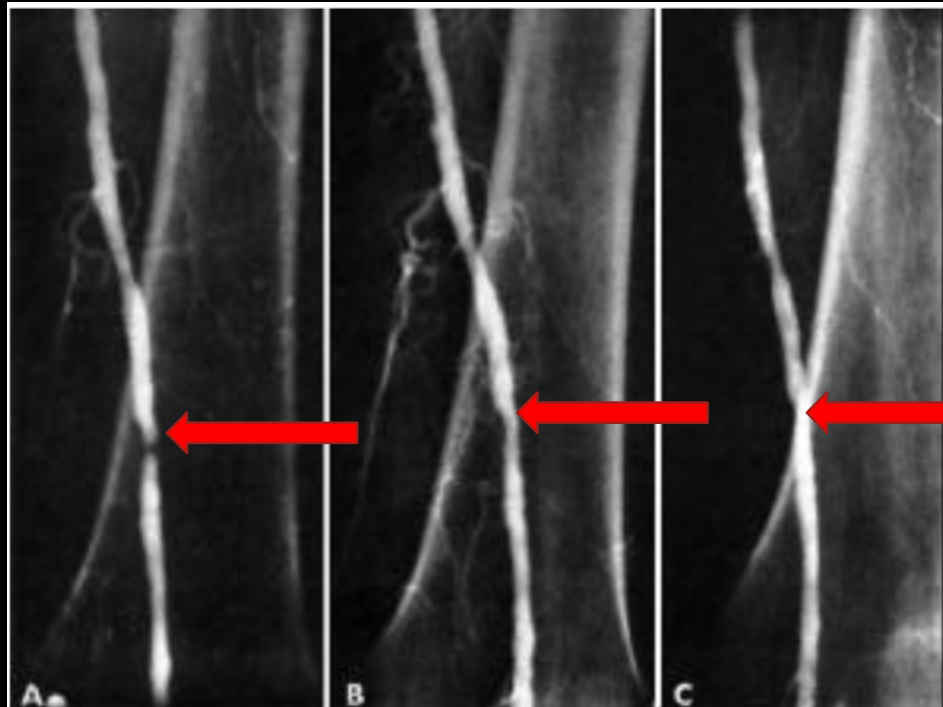
If a plumber can do it to pipes, we can do it to blood vessels.”

Charles T. Dotter M.D.

- Father of Interventional Radiologist
- Pioneer in the Field of Minimally Invasive Procedures (Catheterization)
- Developed Continuous X-Ray Angio-Cardiography
- Performed First Angioplasty (PTCA) Procedure in 1964.

# THE ROOTS OF INTERVENTIONAL RADIOLOGY

- Treated the first patient with catheter assisted vascular dilation



# THE “DO NOT FIX” CONSULT

University of Oregon Medical School  
Hospitals & Clinics  
**ANGIO** SURGERY  
64 Bldg. MH R. 2N 8th

**Radiology Consultation**

Please complete in full. One examination per request. Examination is based on the available clinical information. Date of last x-ray examination at the U. of O. Med. Center 3/9/64  
Initial exam

Unit No. 18-28-16  
Name BOURNE, HARRY  
Birthdate 11/22/99

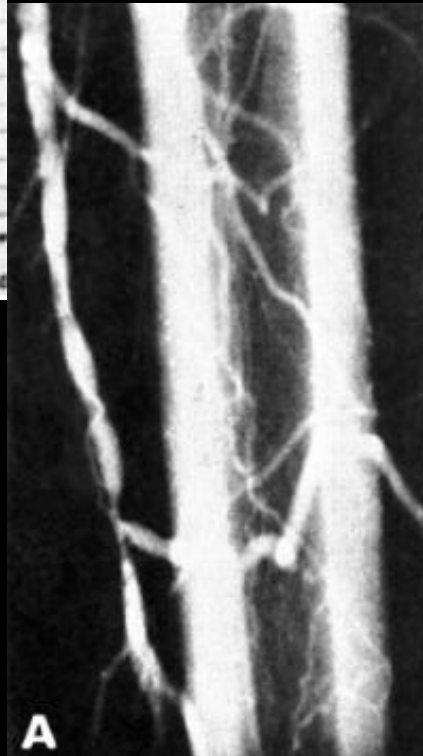
Anatomical part to be examined: Left femoral arteriogram  
Special orders: for all distal exams.  
Pertinent Clinical Data: Arteriosclerosis, Adductor hiatus occlusion, etc.

Clinical Diagnosis: Arteriosclerosis  
Specific Information Desired: VISUALIZE BUT DO NOT TRY TO FIX !!!

What Special Precautions are Needed: TRY TO FIX !!!

Bed to X-Ray     Emergency  
 Bedside         Wet Reading

Your signature on this request indicates your approval of the use of procedure and drugs appropriate to the examination.  
Service: SURGERY G Van Eldon M.D.



# THE DO NOT FIX PATIENT SCALES MOUNT HOOD WITH DR. DOTTER 1965



1950

- HIGH SPEED RADIOGRAPHY
- SELDINGER TECHNIQUE
- PERCUTANEOUS TRANSLUMINAL VASCULAR TECHNIQUES

1960

- ALLIANCE WITH BILL COOK DEVELOPED NUMEROUS CATHETERS AND GUIDE WIRES
- PERCUTANEOUS ANGIOPLASTY
- CORONARY ANGIOGRAM – MELVIN JUDKINS

1970

- FIRST EMBOLIZATION FOR GI BLEEDING
- FIRST BALLOON PERIPHERAL ANGIOPLASTY-- ANDREAS GRUENTZIG
- FIRST CORONARY ANGIOPLASTY-- ANDREAS GRUENTZIG
- TRANSHEPATIC EMBOLIZATION

# Timeline of discovery



1980's

- Intracoronary stents
- over-the-wire coaxial balloon systems introduced,
- brachial guiding catheters &
- steerable guide wires are developed

Golden Age

1990's-  
Present

2000

- DRUG ELUTING STENTS
- DRUG ELUTING BEADS
- RADIOPAQUE BEAD
- NAVIGATION PLATFORMS
- CONTINUED EFFORTS TO MODIFY AND PERFECT CATHETERS, STENTS, BASKETS, AND PROCEDURES

# Timeline of discovery

# INTERVENTIONAL RADIOLOGY IS...

## Less Invasive

- **8 out of 10 procedures use skin incisions smaller than 5 mm.**

## Safer

**9 out of 10 procedures use only local anaesthetic, sometimes with sedation.**

**Up to 8 out of 10 patients go home the same day**

## Cost Effective

- uterine fibroid embolization is 50% less than a hysterectomy
  - [www.sir.org](http://www.sir.org)
- solid renal masses, percutaneous cryoablation is associated with 40% lower hospital charges (mean, \$14175 vs \$23618) and a shorter hospital stay than laparoscopic cryoablation

– Vanketasen, 2011

# WHAT KIND OF THINGS CAN BE DONE?

- Treatment of vascular problems
- angiogram; angioplasty +/- stenting
- Biopsies to define cancer, infection or inflammation
- Drainage of fluid collections
- abscesses, kidneys or bile ducts/gallbladder
- Embolization (blockage) of arteries
- Treatment of infertility
- Insertion of feeding tubes
- Treatment of liver , kidney, pancreatic, and bone tumors

Center for Interventional Oncology IR is...  
Cutting edge research without the scalpel

If we knew what it was we were doing, it  
would not be called research, would it?

-Albert Einstein

NIH—marriage between  
development of imaging  
techniques and  
treatment tools  
Software development

- Chemistry
- Bioengineering
- Partnerships with  
public and private  
sector



# ROLE OF IR IN MANAGEMENT OF SOLID TUMORS

1. Supportive procedures for the oncology patient
2. Determination of disease
3. Facilitation of definitive surgical treatment
4. Treatment of non-surgical candidates

# IR ROLE : DIAGNOSIS

- Radiology Tools:
  - Cone beam CT—serial x-rays combined with fluoroscopy
  - Ultrasound
  - FD20 (fluoroscopy)
  - Traditional CT
  - Needle guidance systems
  - Catheters

# IR SUITE, CBCT, US, FLUORO

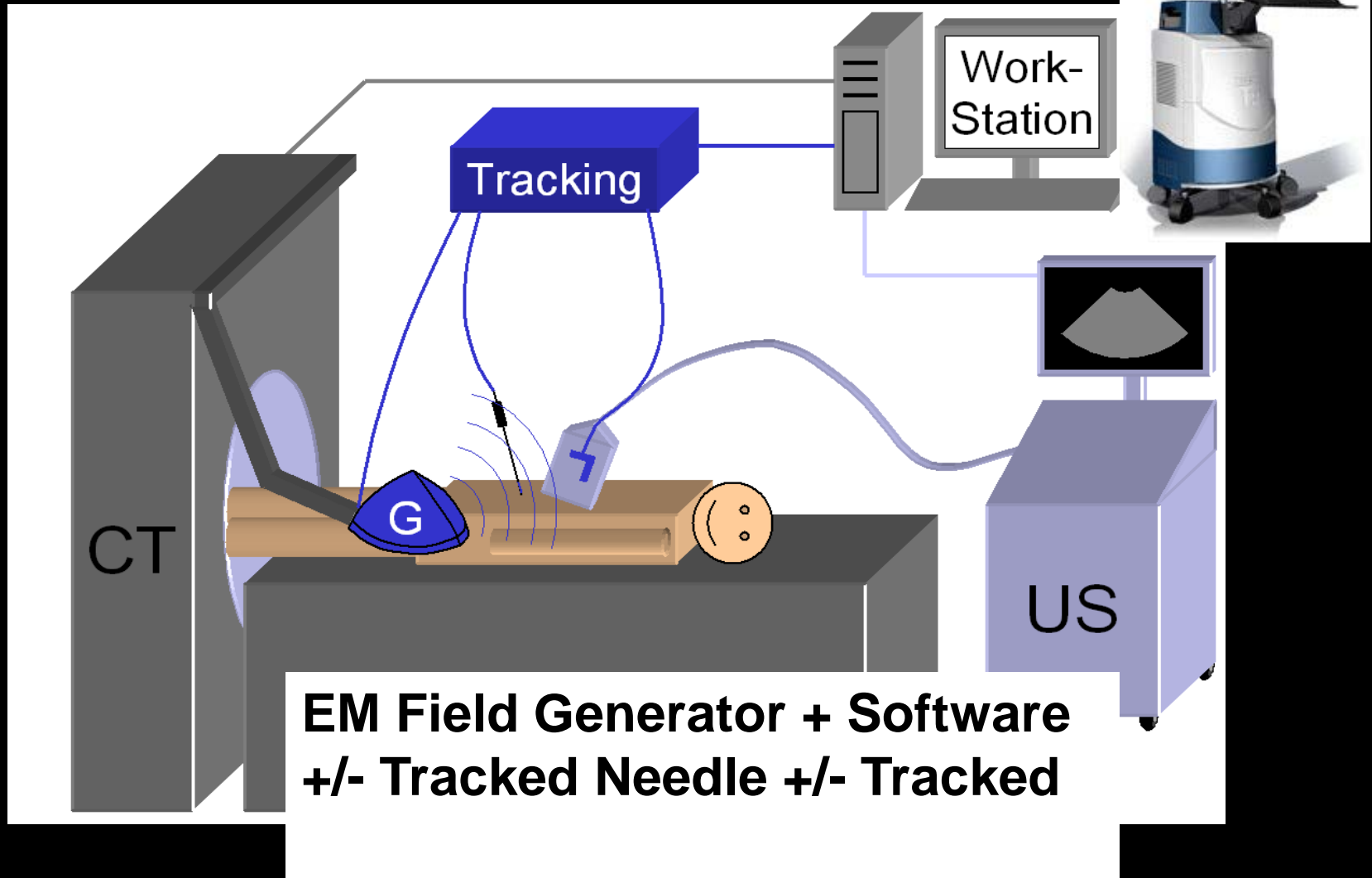


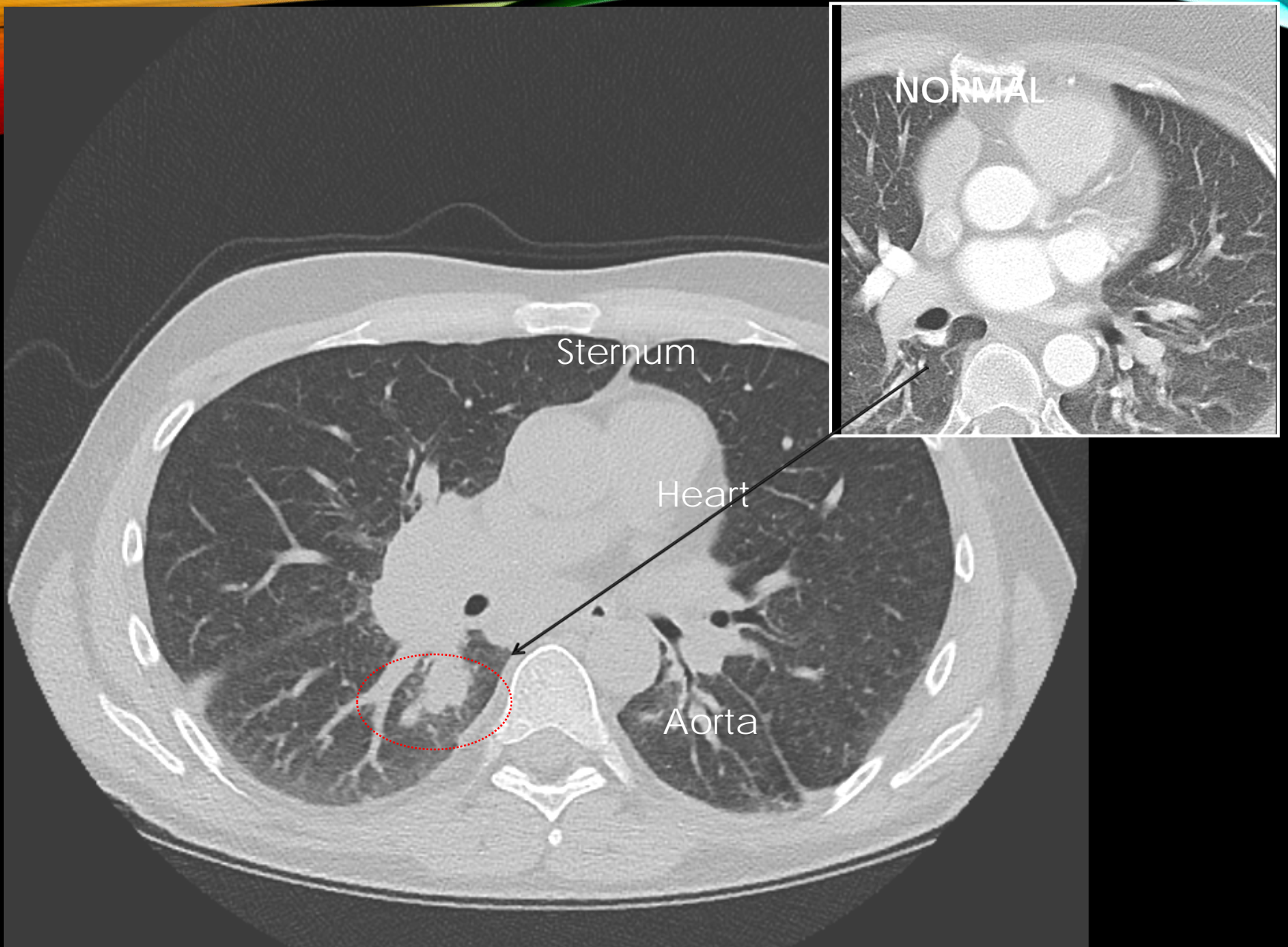
# LUNG MASS

- 32 y.o. with rare immune deficiency
- Presents with mass in his RLL
- Team wants to get a diagnosis vs. empiric treatment as patient is asymptomatic
- Infection (Viral, bacterial, fungal) vs. Malignancy?

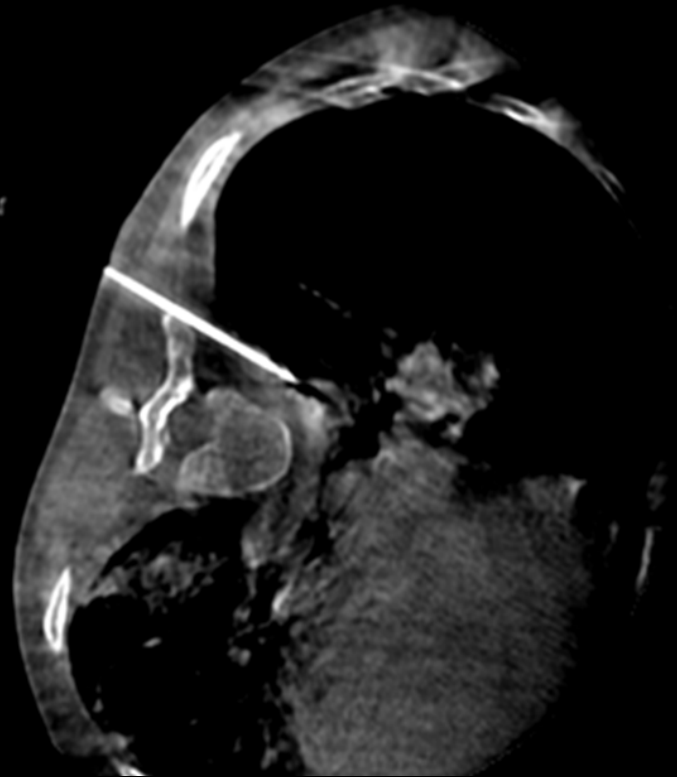
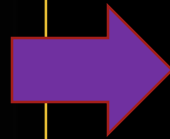
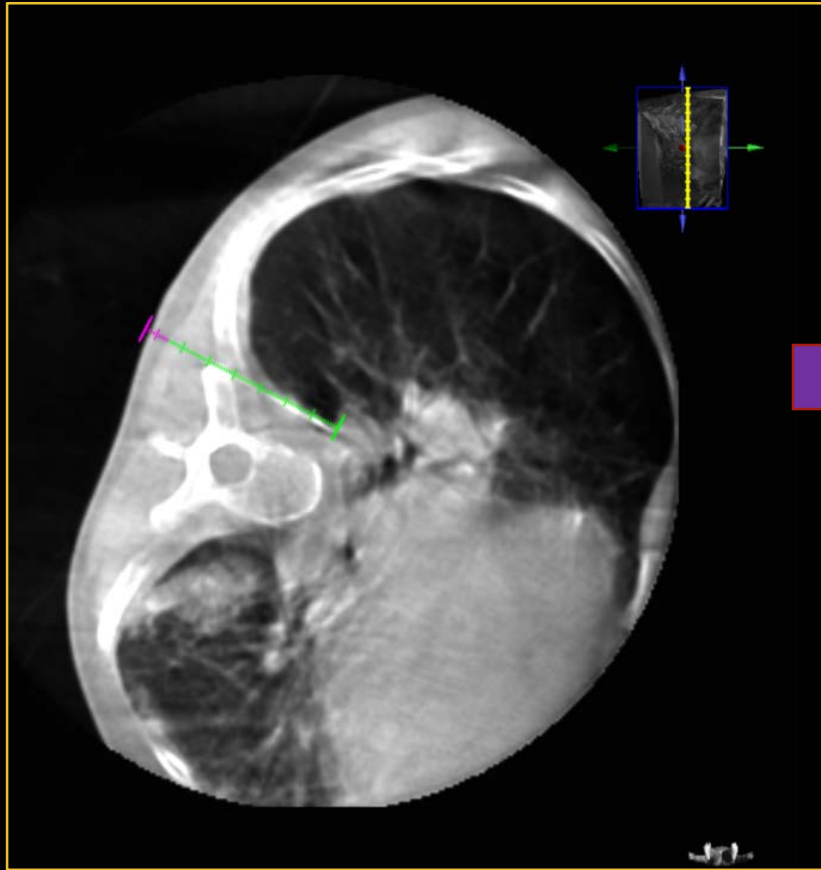


# EQUIPMENT



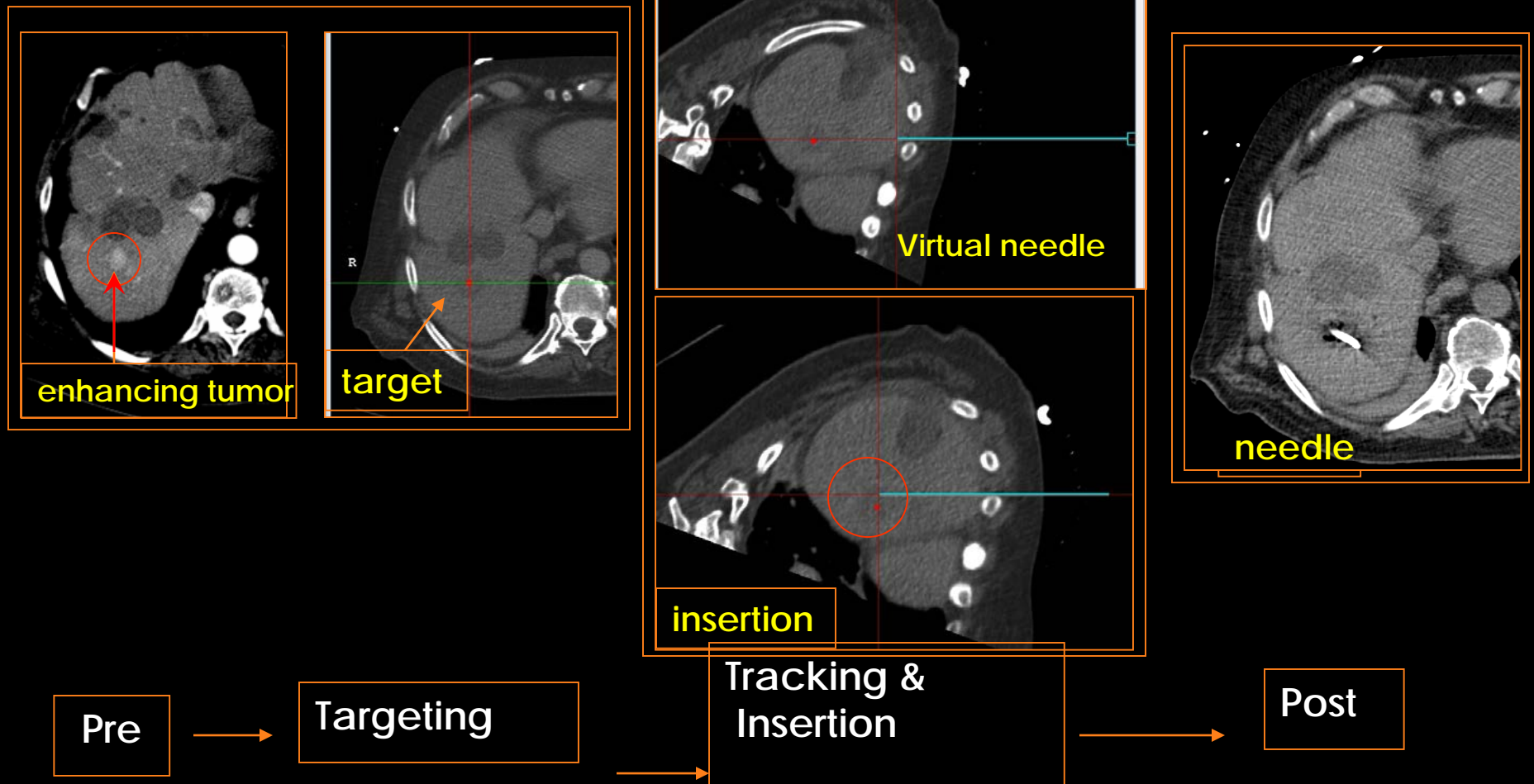


# PLANNING EXECUTION

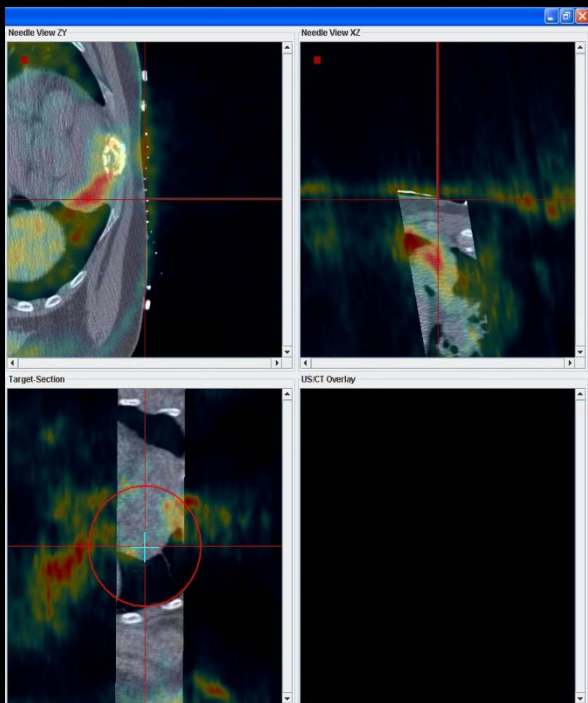
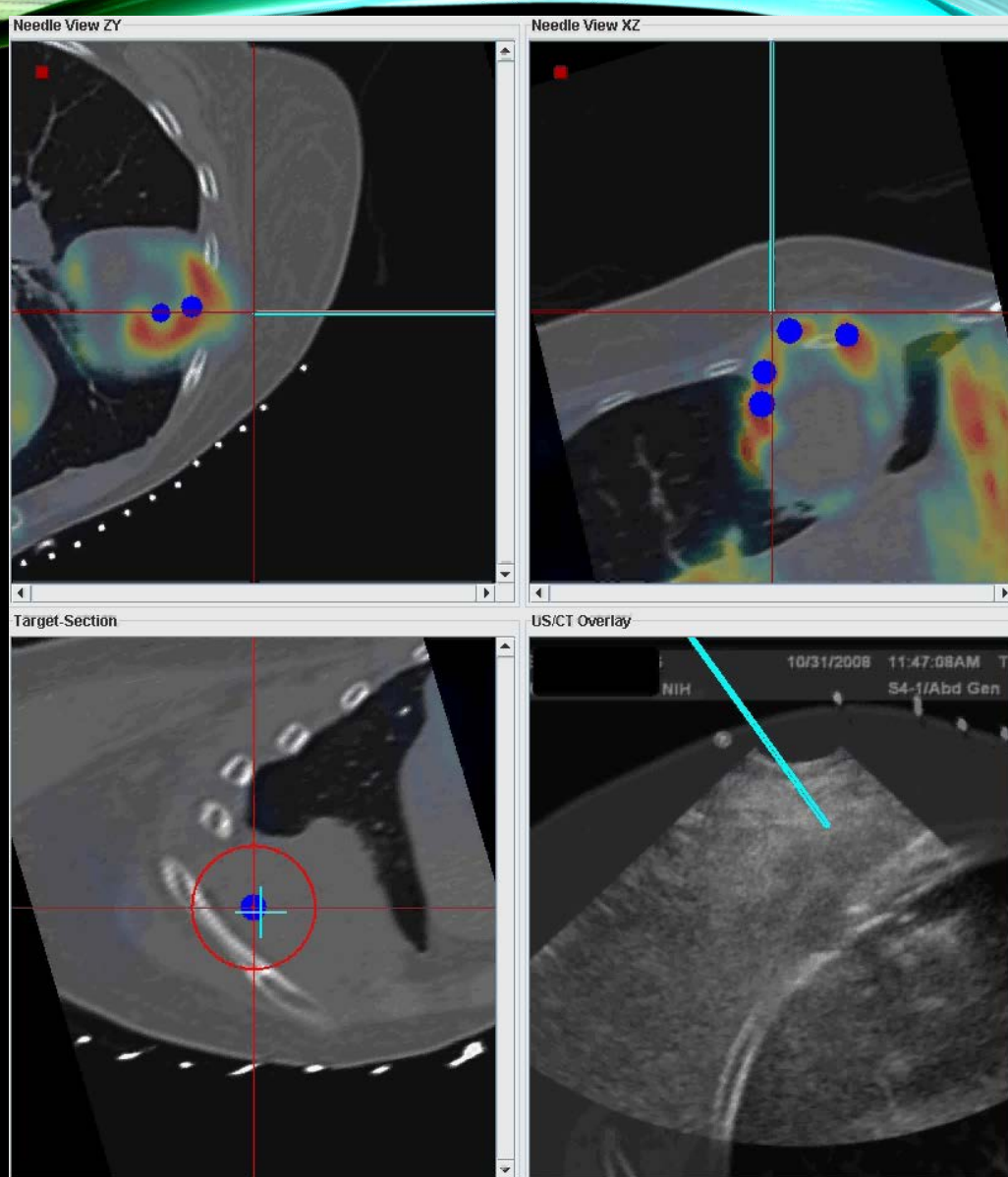


# Targeting a Hidden Tumor:

arterial phase enhancing HCC



# PET GUIDED BIOPSY: METABOLIC INTERVENTIONS



31 of 36 PET-guided biopsies diagnostic

Radiology 2011;260:848-56  
J Vasc Interv Radiol. 2011;22:515-24

# HEPATOCELLULAR CARCINOMA

- US in 2017
- Predicted
- About 40,710 new cases (29,200 in men and 11,510 in women) will be diagnosed
- About 28,920 people (19,610 men and 9,310 women) will die of these cancers
- Liver cancer incidence has more than tripled since 1980.
- Liver cancer death rates have increased by almost 3% per year since 2000.
- Liver cancer is seen more often in men than in women.
- Worldwide (American Cancer Society: Cancer Statistics)

# RISK FACTORS FOR HCC

## Rare inherited disorders:

- Tyrosine deficiency
- Alpha1-antitrypsin deficiency
- Porphyria cutanea tarda
- Glycogen storage diseases
- Wilson disease

Toxins: Flavotoxins, Arsenic, Tobacco,

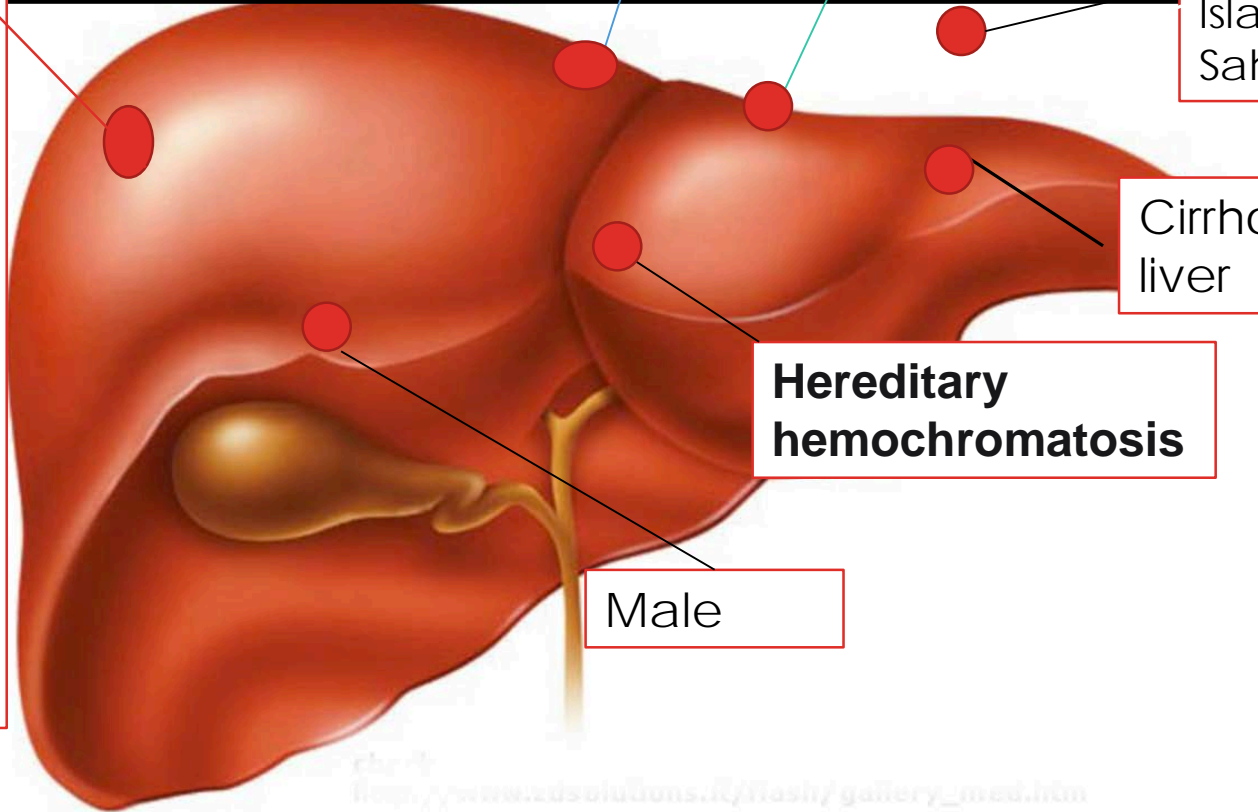
Hepatitis B,

Ethnicity: Asian, Pacific Islander, Sub-Saharan

Cirrhosis/Fatty liver

**Hereditary hemochromatosis**

Male



[http://www.xdsolutions.it/flash/gallery\\_med.htm](http://www.xdsolutions.it/flash/gallery_med.htm)

# TREATMENT OF HCC

HCC confirmed

- Multidisciplinary Evaluation
- H+P
- Hepatitis Panel
- Bilirubin, transaminases, alk phos, LDH
- PT /INR, albumin, protein, BUN, Cr
- CBC, platelets
- AFP
- Chest imaging
- Bone scan as indicated

Potentially resectable or transplantable, operable by performance status

or comorbidity  
Metastatic disease

Inoperable by performance status or comorbidity, local disease only

Unresectable

IR



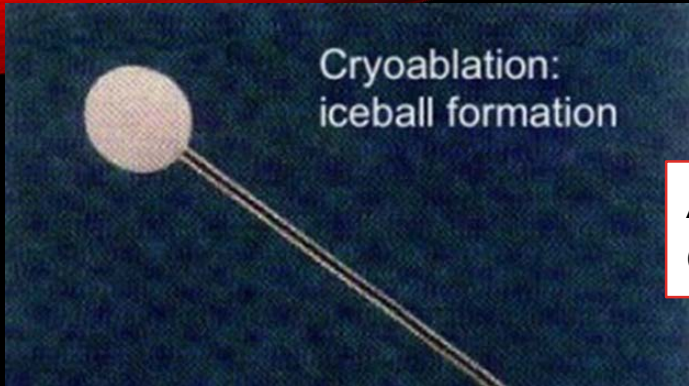
# CHILD PUGH SCORING

- Class A = 5-6 points; Class B = 7 -9 points; Class C = 10-15 points

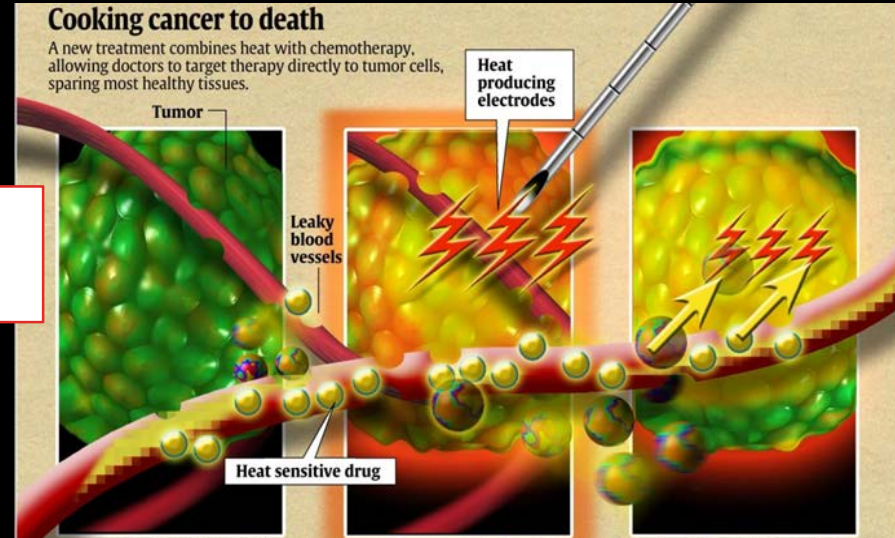
Points

Clinical/biochem.	1	2	3
Encephalopathy (grade)	None	1-2	3-4
Ascites	None	Slight	moderate
Albumin	>3.5	2.8-3.5	>2.8
Prothrombin time (sec)	1-4	4-6	>6
Bilirubin	1-2	2-3	>3
--Primary biliary cirrhosis	1-4	4-10	>10

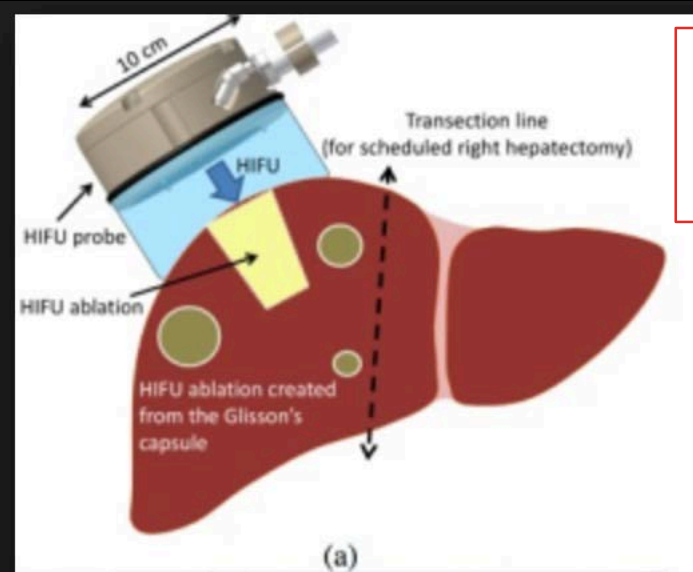
# IR OPTIONS FOR TREATING HCC



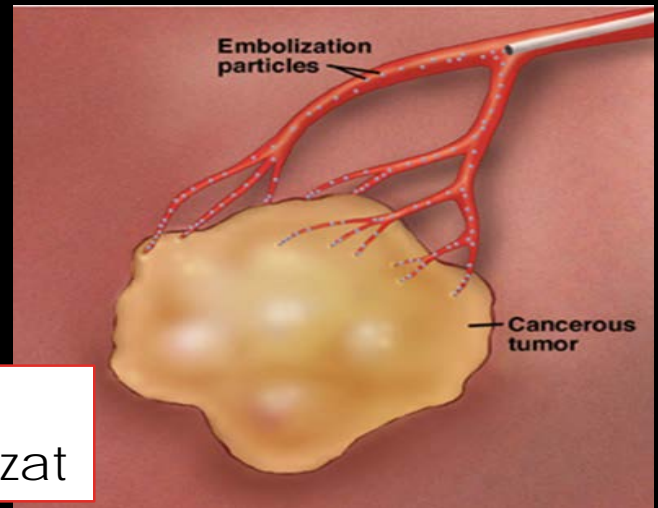
Ablation  
Cold or Hot



High Intensity  
Focused  
Ultrasound



Transarterial  
Chemoembolizat



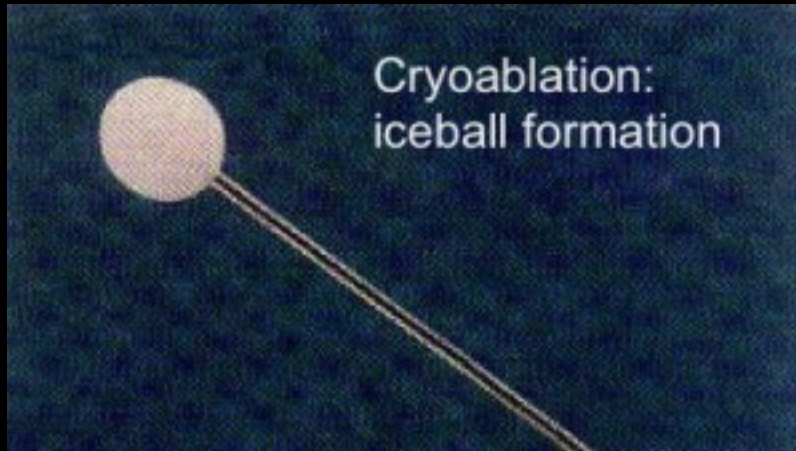
**“As a general rule, complete necrosis occurs almost instantaneously at temperatures below  $-40^{\circ}\text{C}$  or in excess of  $60^{\circ}\text{C}$  for most cell type ”**

Brace, C. (2011) **Thermal Tumor Ablation in Clinical Use**. *IEEE Pulse*. 2011 ; 2(5): 28–38. doi:10.1109/MPUL.2011.942603.



# ABLATION AND TRANSARTERIAL EMBOLIZATION

# CRYOABLATION



- Percutaneous
- Cryoablation probe (s) introduced into tumor  
And cooled to  $-40^{\circ}\text{C}$  for 10 minutes, thawed  
and then re-cooled
- Tumor tissue death r/t
  - Coagulative necrosis

# CRYOABLATION

- Target Organs
  - Liver
  - Kidney
  - Lung
  - Soft tissue
  - Bone
- PROS:
  - Ice ball
  - Immune eliciting
- CONS
  - Cryo-shock
  - Immune mediated

# RADIOFREQUENCY ABLATION

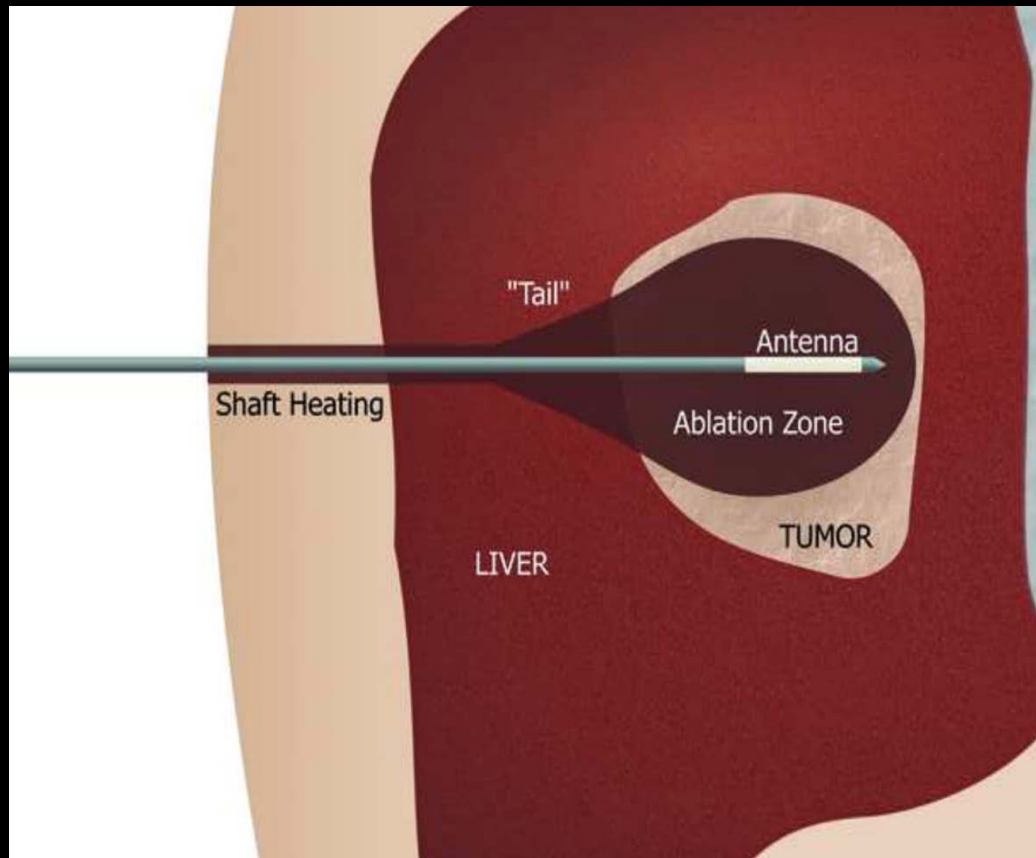
- ❖ Electrode probes deliver an alternating high-frequency electrical current (460 to 500 kHz)
- ❖ Ion agitation is converted by friction into heat
- ❖ Tissue temperature is increased
- ❖ Cellular death occurs via thermal coagulation necrosis

# RFA CONSIDERATIONS

- "Heat sink" effects
- Compromised sphincter of Oddi
  - Levaquin and Flagyl prep
- Adjacent structures
  - Diaphragm
  - Abdominal wall
  - Capsule
  - Bowel
- Size



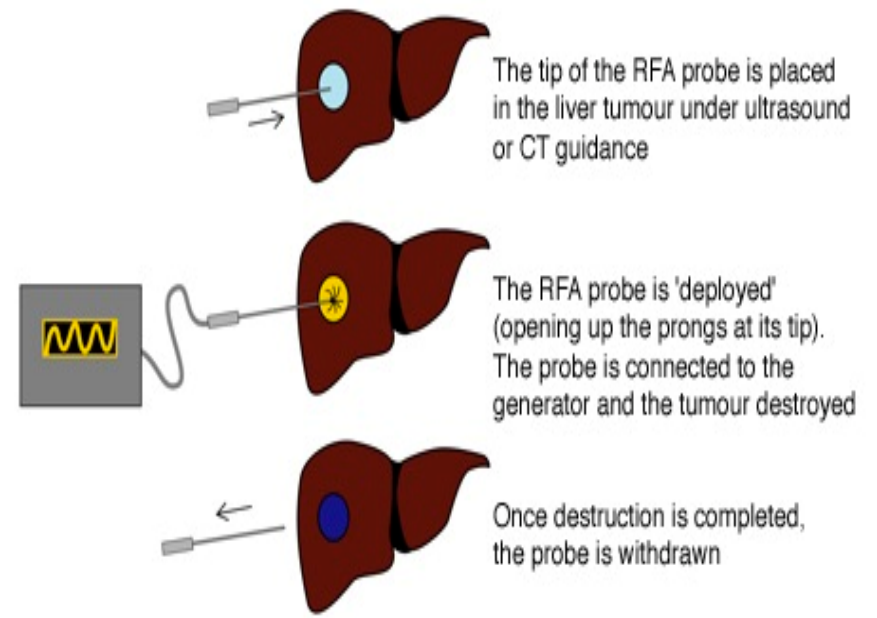
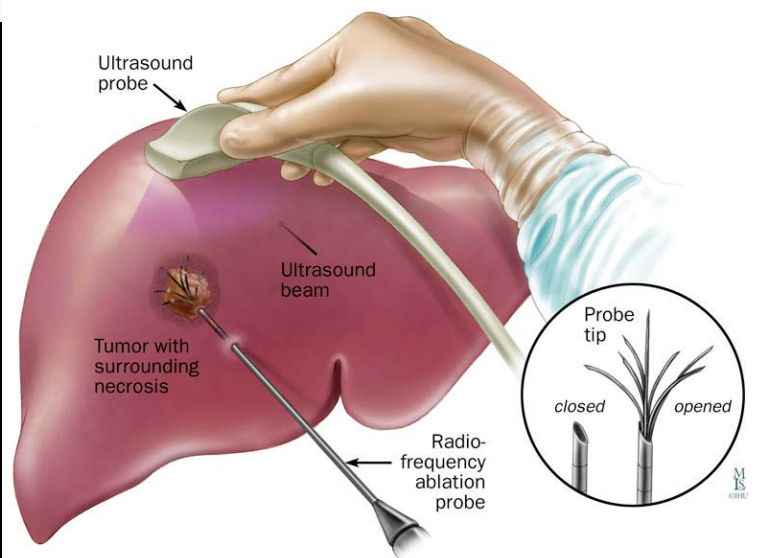
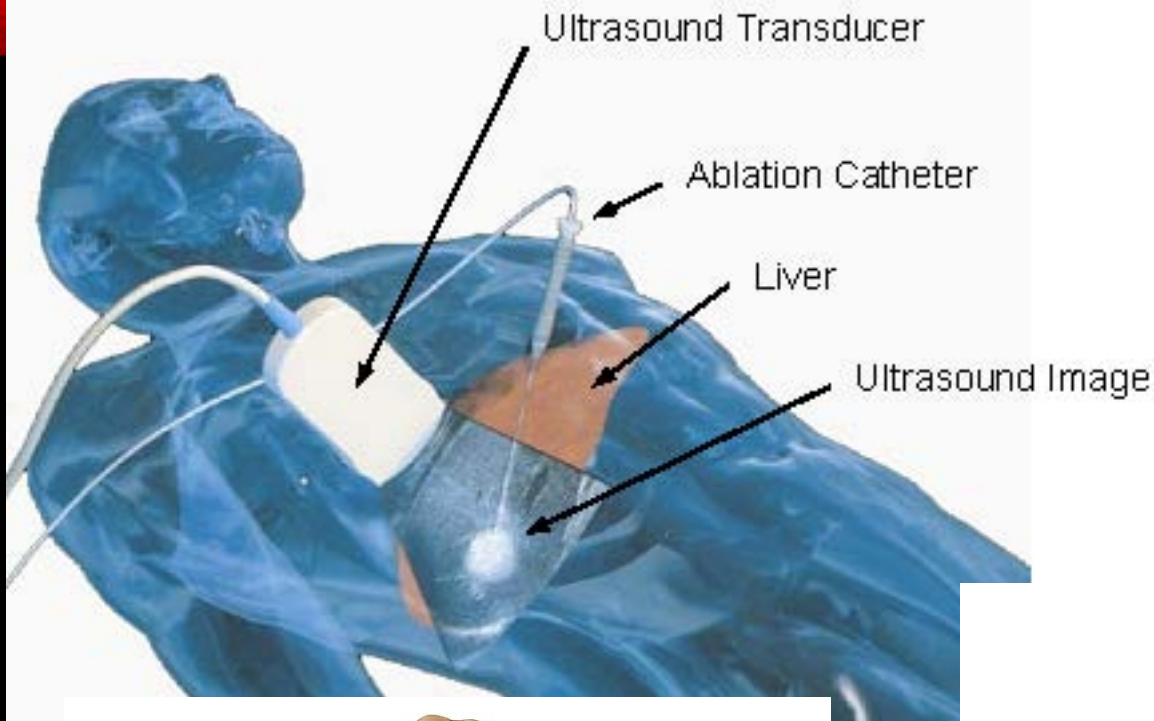
# MICROWAVE



faster heating over a larger volume of tissue with less susceptibility to "heat sink effects"

effective in tissues with high impedance such as lung or charred, desiccated tissue; is capable of generating very high temperatures, often in excess of 100° C

does not require grounding pads



# INDICATION FOR ABLATION --HCC

- Very early to early stage disease
- Localized tumor <3cm at its longest axis
- Less than or equal to 5 tumors
- Cirrhosis: Child Pugh Class A-B
- Nonsurgical patients

# CONTRAINDICATIONS

- A tumor located <1 cm from the main biliary duct—may lead to stenosis
- Intrahepatic bile duct dilation
- Anterior exophytic location of the tumor—risk of tumor seeding
- Bilioenteric anastomosis –increased risk of infection

# POTENTIAL COMPLICATIONS

- More Common 2.2-3.1%
  - Intraoperative bleeding
  - Liver abscess
  - Intestinal perforation
  - Pneumo- or hemothorax
  - Bile duct stenosis
  - Post RFA Syndrome
    - Fever, fatigue, nausea
- Tumor seeding (0.5%)
- Procedure mortality (0.1-0.5%)
  - sepsis
  - hepatic failure
  - colon perforation
  - portal vein thrombosis

# ADVERSE COMPLICATIONS

- Procedure mortality (0.1-0.5%)
  - SEPSIS
  - HEPATIC FAILURE
  - COLON PERFORATION
  - PORTAL VEIN THROMBOSIS

# PATIENT PREP FOR IR

- **STOPPING BLOOD THINNERS**
  - ASA
  - HEPARIN
  - NEWER DRUGS-PLAVIX, ETC.,
- **PLATELETS >50K**
- **GENERAL ANESTHESIA ISSUES (NIH anesthesia eval)**
- **EDUCATION**
  - **ANTICIPATORY GUIDANCE**
  - **RISKS**
  - **POST EMBOLIZATION SYNDROME**
- **INFECTION RISK ANALYSIS**
- **ANTIBIOTICS**
- **BOWEL PREPS-CHOLANGIOCARCINOMA/AMPULARY/WHIPPLE**  
**OTHER SURGICAL CONCERNS**

# NIH SOP FOR ABLATION AND TAE

- Admit
- General anesthesia
- NPO after midnight
- Peri-operative antibiotics and Foley type urinary catheter placement
- Bedrest post-procedure
- Frequent VS
- Comfort meds: PCA, Ketorolac IV 15-30mg every 6 hrs. x 5 days
- Antibiotics for 2 days for TAE/TACE
- Lab tests: CBC, and electrolytes for 2-3 days



# CHEMOEMBOLIZATION

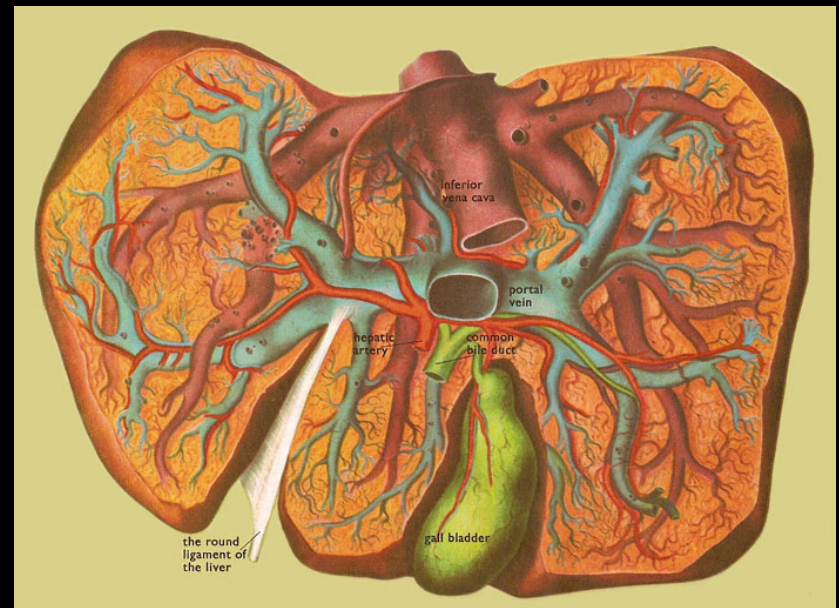
- Treatment with a mixture of chemotherapy and embolic agents, typically as oily chemoembolization or drug-eluting bead chemoembolization.
- ***Oily chemoembolization***, mixture of chemo- therapeutic agents
  - ethiodized oil (Lipiodol) followed by embolization with particles such as calibrated micro- spheres, polyvinyl alcohol, or Gelfoam (absorbable gelatin sponge).
- ***Drug-eluting bead chemoembolization***

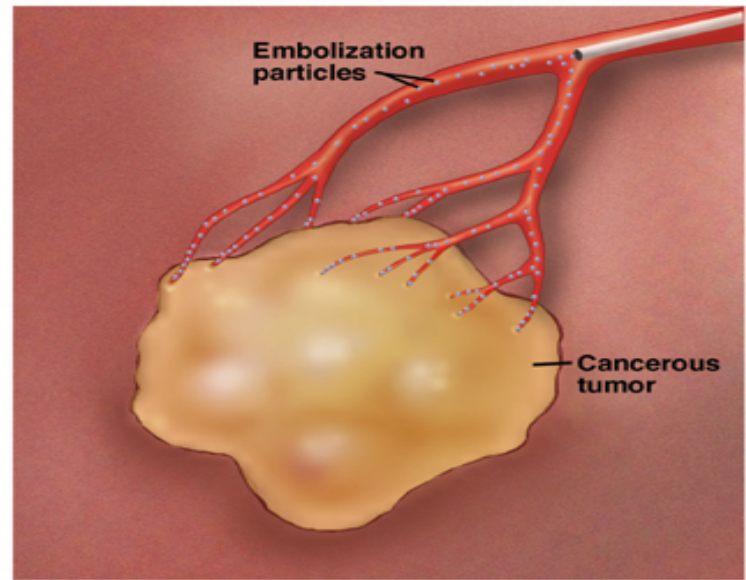
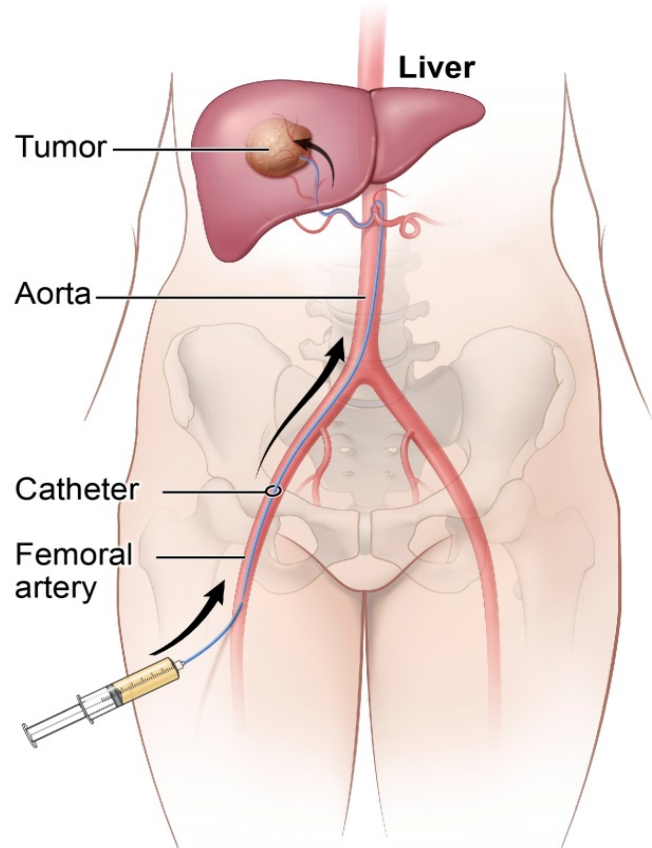
the infusion of calibrated microspheres that are designed to bond with chemotherapeutic agents and release the drugs over time following treatment.

  - Doxorubicin
  - Irinotecan
  - Mitomycin C
  - Adriamycin
  - Cis-platin

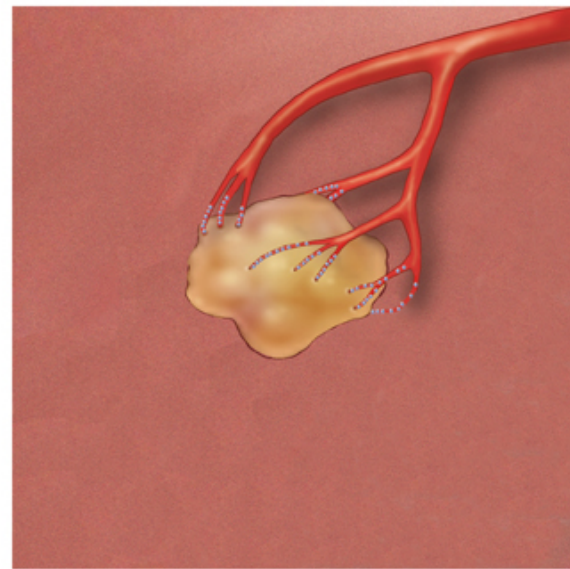
# INTRA-ARTERIAL ADMINISTRATION

- Tumors receive 80-100% of their blood supply from hepatic artery
- Normal liver receives > 75% of its blood supply from portal vein





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© Society of Interventional Radiology, www.SIRweb.org

# INDICATIONS

- ❖ UNRESECTABLE INTERMEDIATE-STAGE HCC (CHILD PUGH CLASS A/B)
- ❖ NO VASCULAR INVASION
- ❖ LIVER-DOMINANT HEPATIC MALIGNANCIES WHO ARE NOT CANDIDATES FOR CURATIVE RESECTION
- ❖ ONE < 5 CM OR THREE TUMORS < 3 CM
- ❖ BRIDGE TO TRANSPLANT (ONLY CURE FOR HCC)
- ❖ PALLIATION FOR METASTATIC DISEASE COLORECTAL CANCER AND NEUROENDOCRINE CANCERS

# CONTRAINDICATIONS

- ❖ DISEASE IN >50% OF LIVER
- ❖ COMPLETE PORTAL VEIN THROMBOSIS
- ❖ BILIRUBIN >2MG/DL
- ❖ LDH >425
- ❖ AST >5X UNL

# EXPECTED COMPLICATIONS

- **POST EMBOLIZATION SYNDROME OCCURS IN ALMOST ALL PATIENTS IN SOME DEGREE**
  - **FEVER**
  - **PAIN**
  - **INCREASED WBC**
  - **FATIGUE**
  - **NAUSEA/VOMITING**

# ADVERSE COMPLICATIONS

- **UNCOMMON And SERIOUS**

- **LIVER FAILURE—2.3%**
- **HEPATIC ABSCESS--<1%**
- **SURGICAL CHOLECYSTITIS--<1%**
- **GI BLEEDING/ULCERATION--<1%**
- **PULMONARY EMBOLUS--<1%**
- **DEATH WITHIN 30 DAYS 1%**

# CASE STUDY

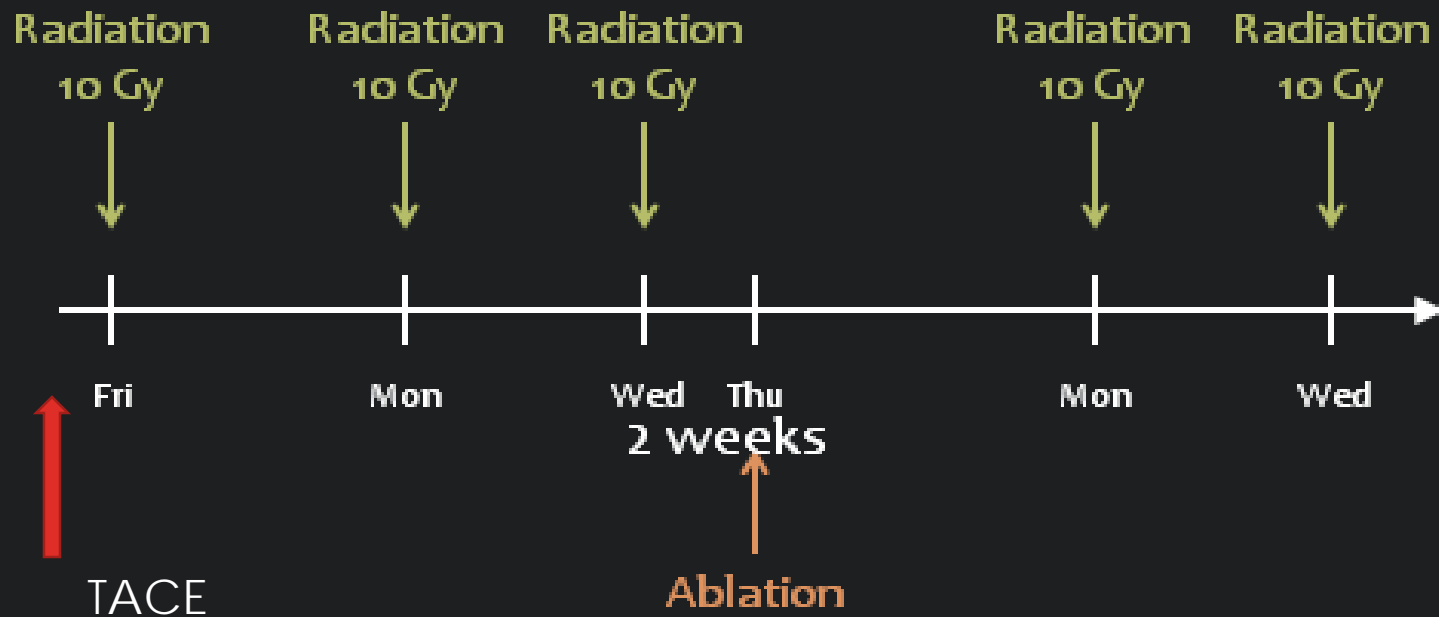
- 76 y.o. Filipino with history hemochromatosis
- Diagnosed with a large hepatoma
- Complicated cardiac medical history: EF<25%, AICD/Pacemaker
- Not a surgical candidate
- Neg. Hep. B, C, D
- Plan to treat with combined standard of care chemoembolization and then enroll in protocol that combined thermal ablation with external beam radiation



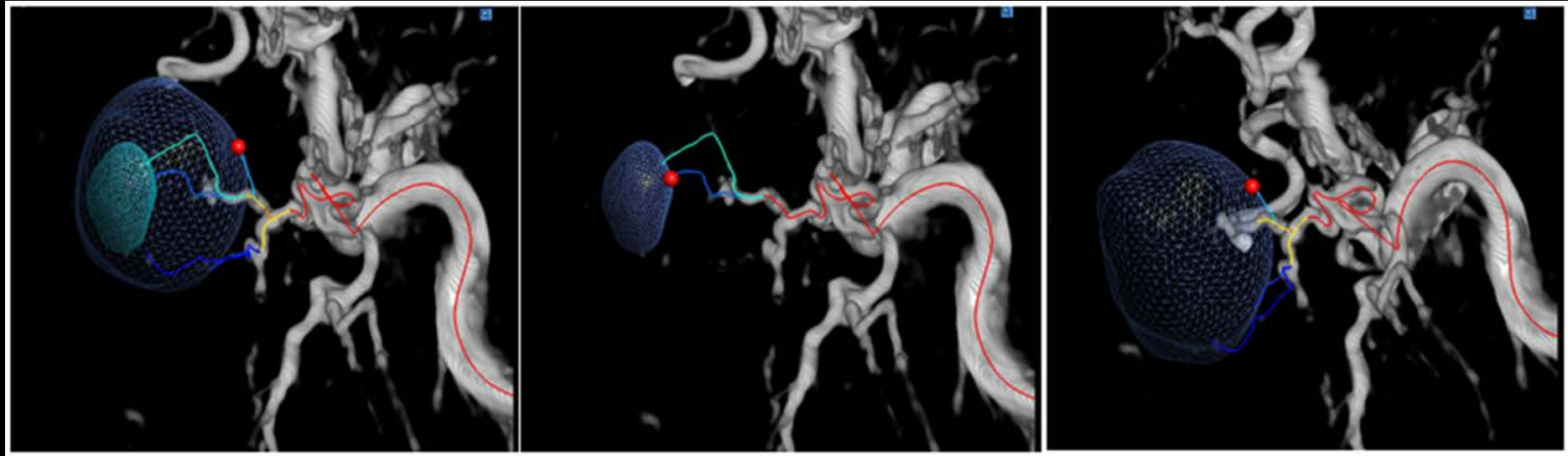
# PRE-OP

- Consultation with cardiology, hematology, ICU, internal medicine
- AICD response to therapies?
- AICD rep. on stand-by to reprogram
- Risk of MI high as known triple vessel disease-inoperable
- Chest pain during a CT
- ICU admit post-procedure

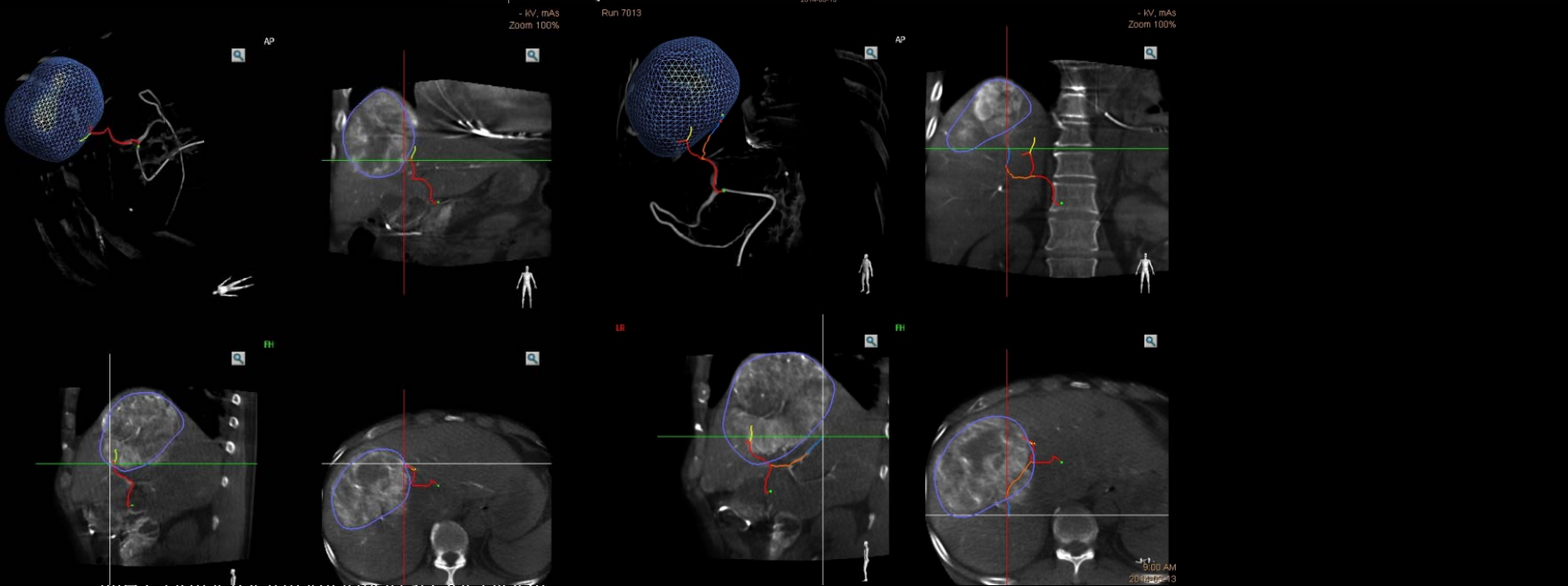
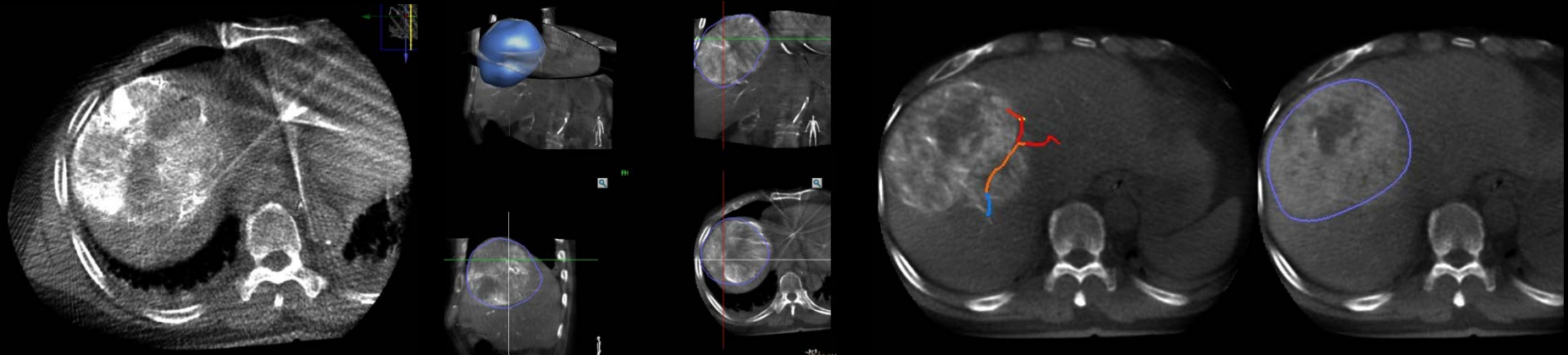
# Treatment plan



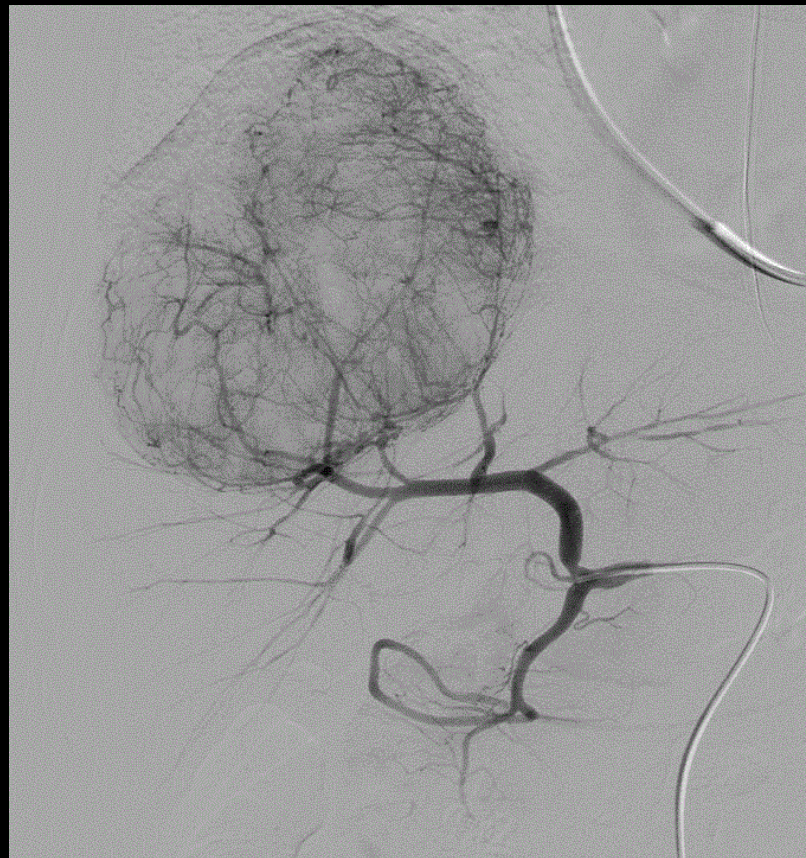
# FEEDING VESSEL DETECTION: UN-TANGLE TORTUOSITY & OVERLAP REFERENCING A "3D ROADMAP"



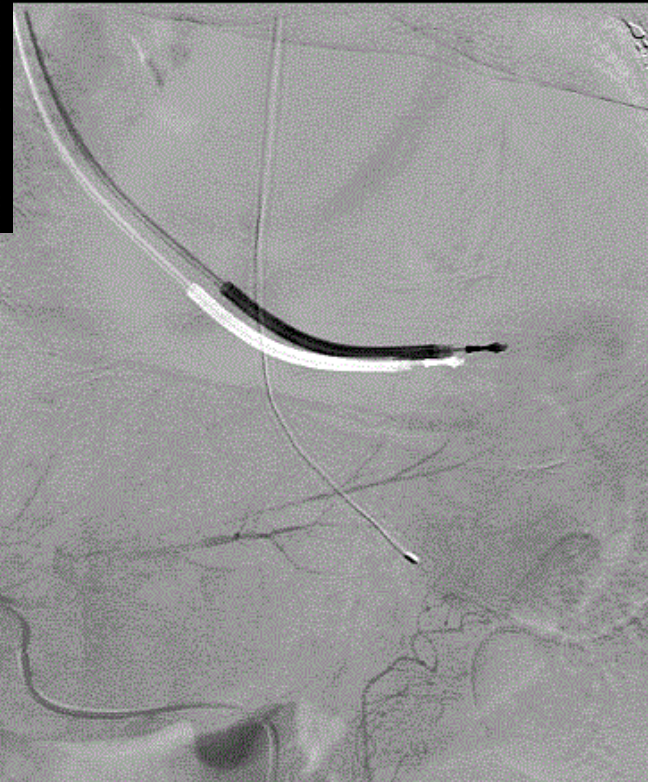
# AUTO FEEDER DETECTION W DUAL PHASE ENABLES SELECTIVITY



# ANGIOGRAM PRE-TACE



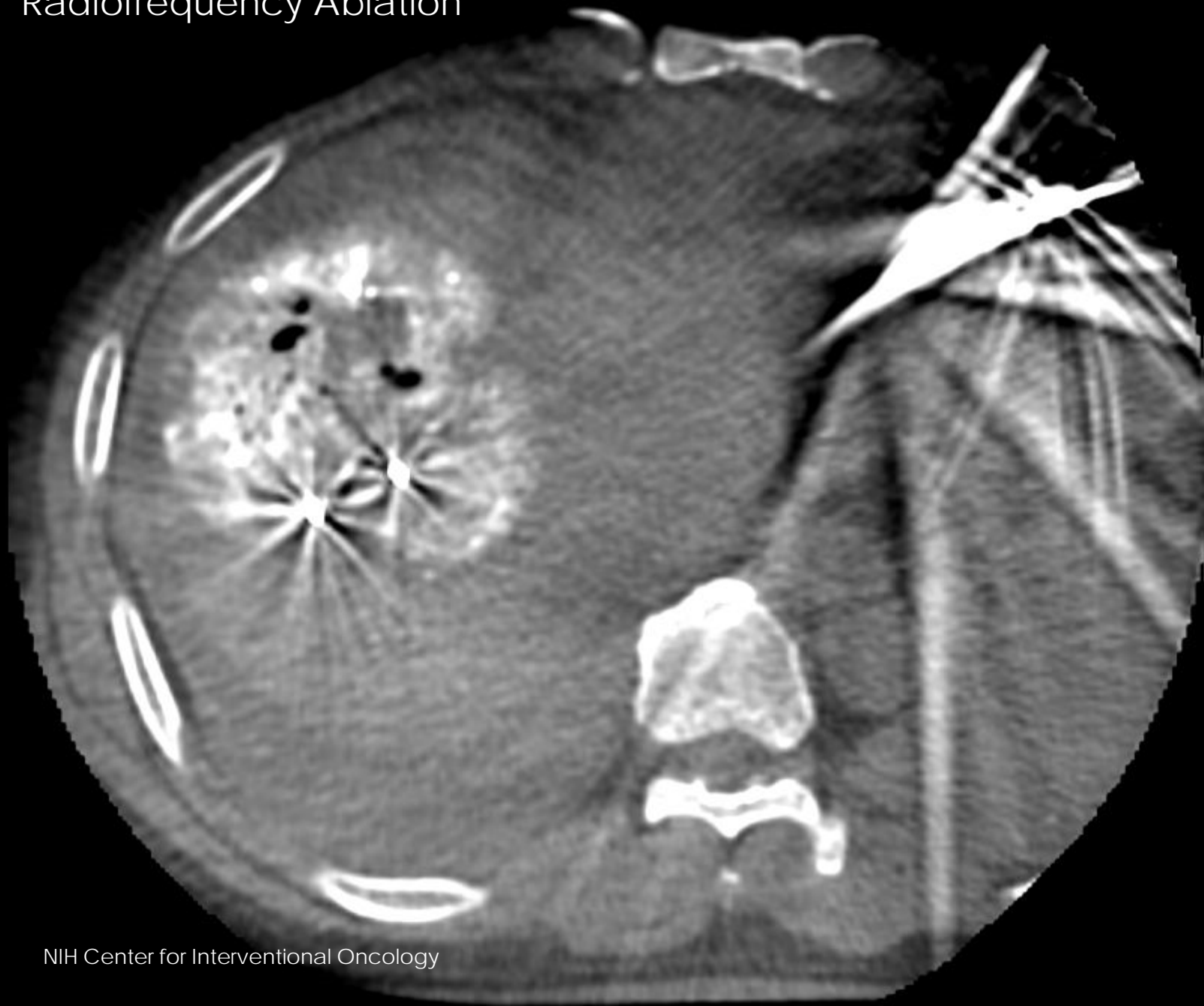
# POST TACE



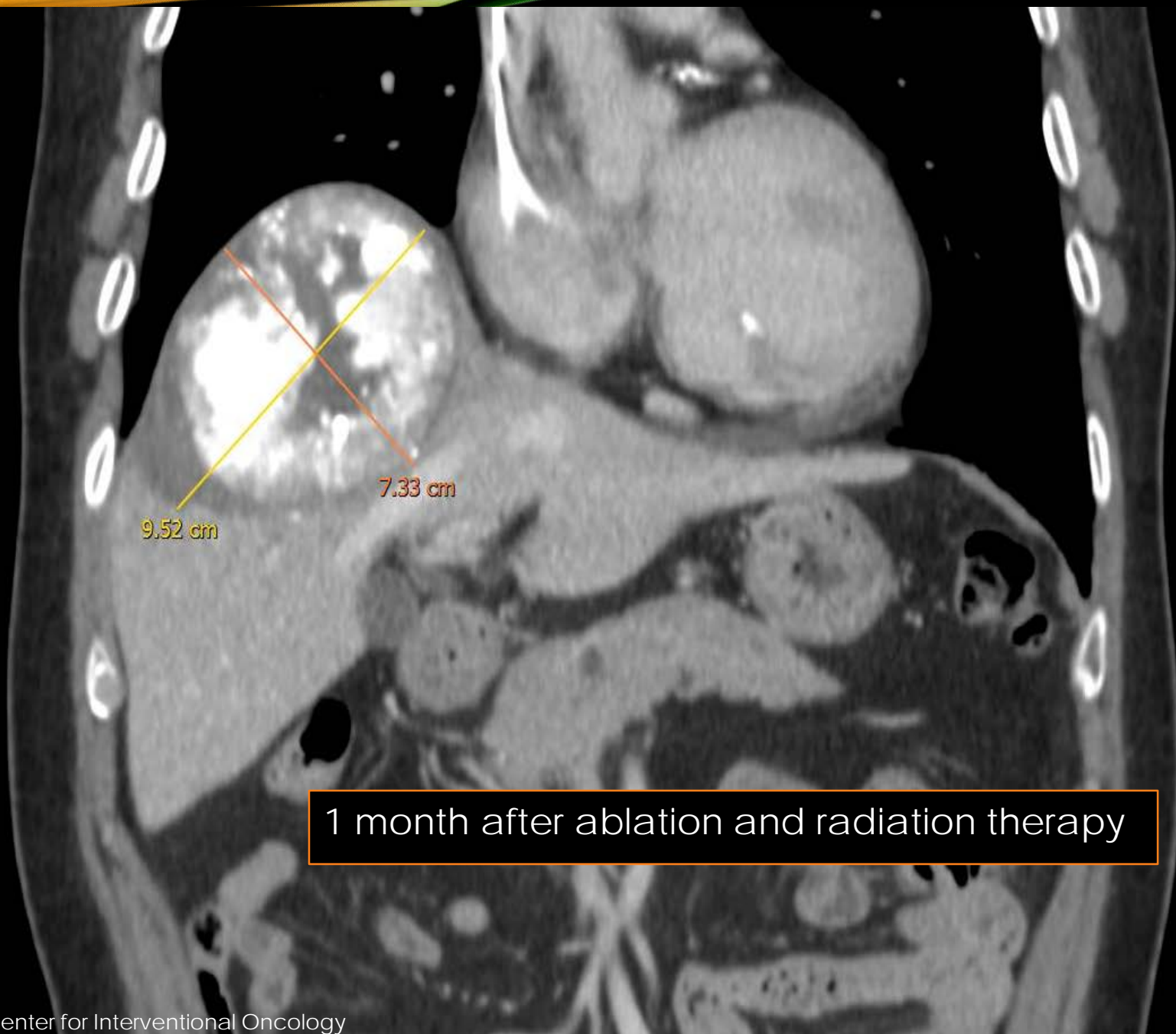
1 month after TACE  
Before ablation and radiation



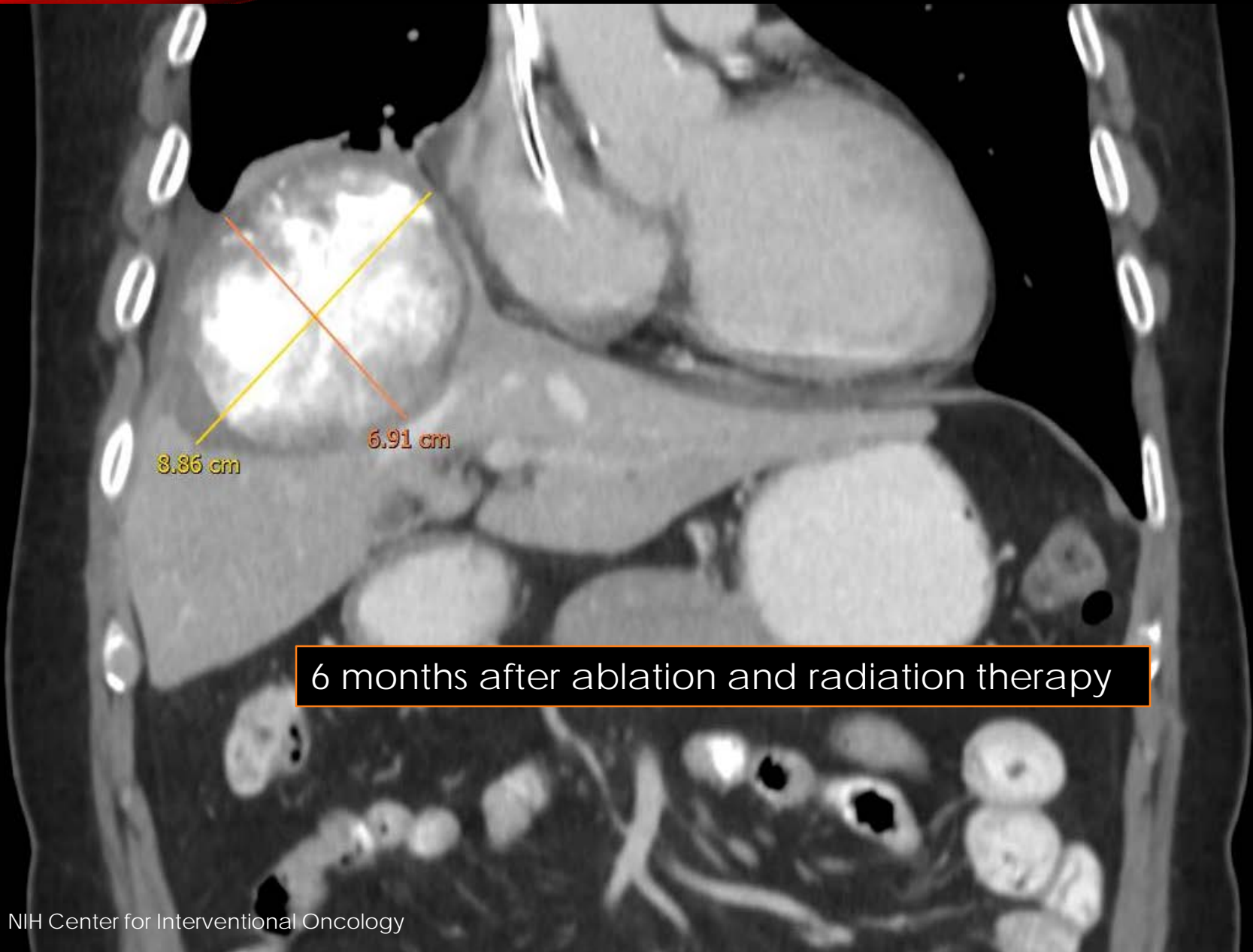
# Radiofrequency Ablation





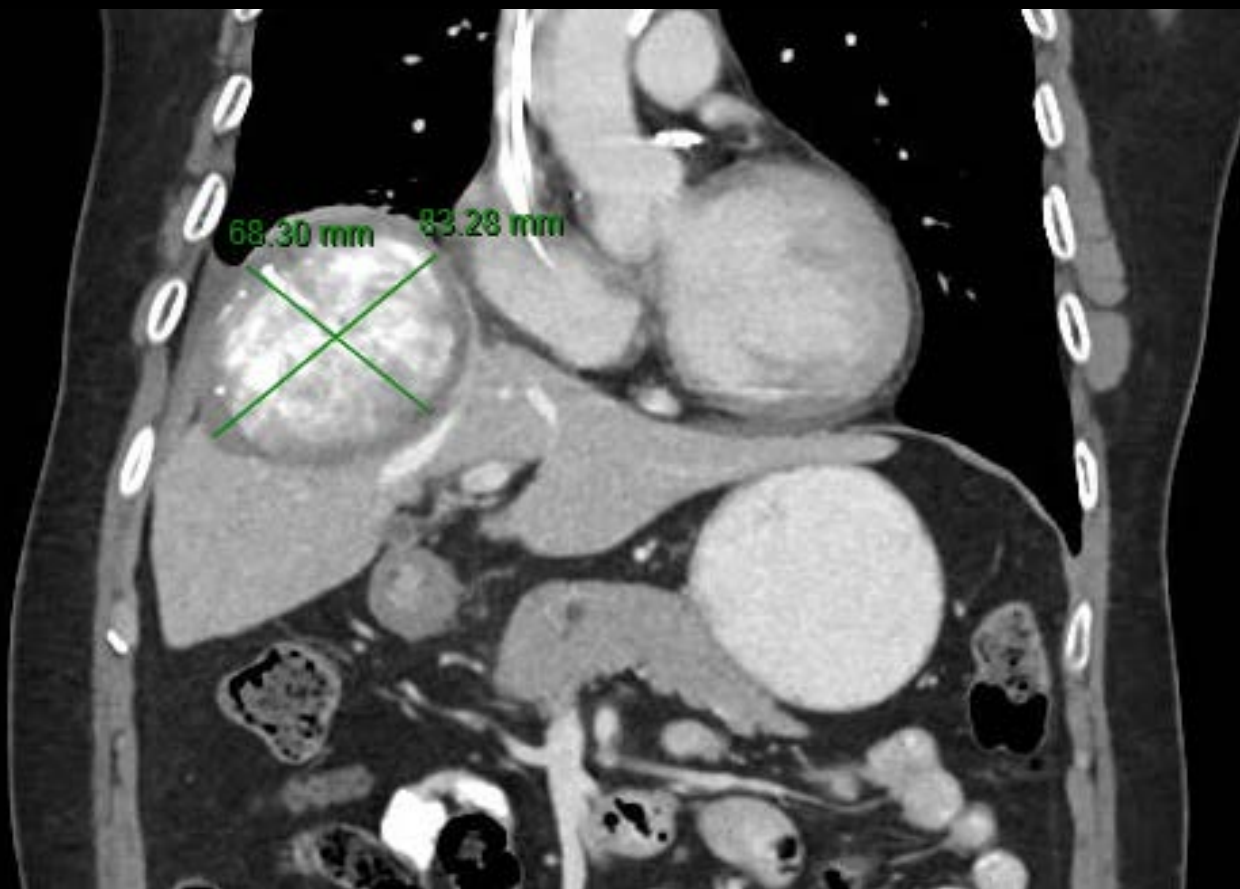


1 month after ablation and radiation therapy



6 months after ablation and radiation therapy

Post RFA and Radiation 17 months



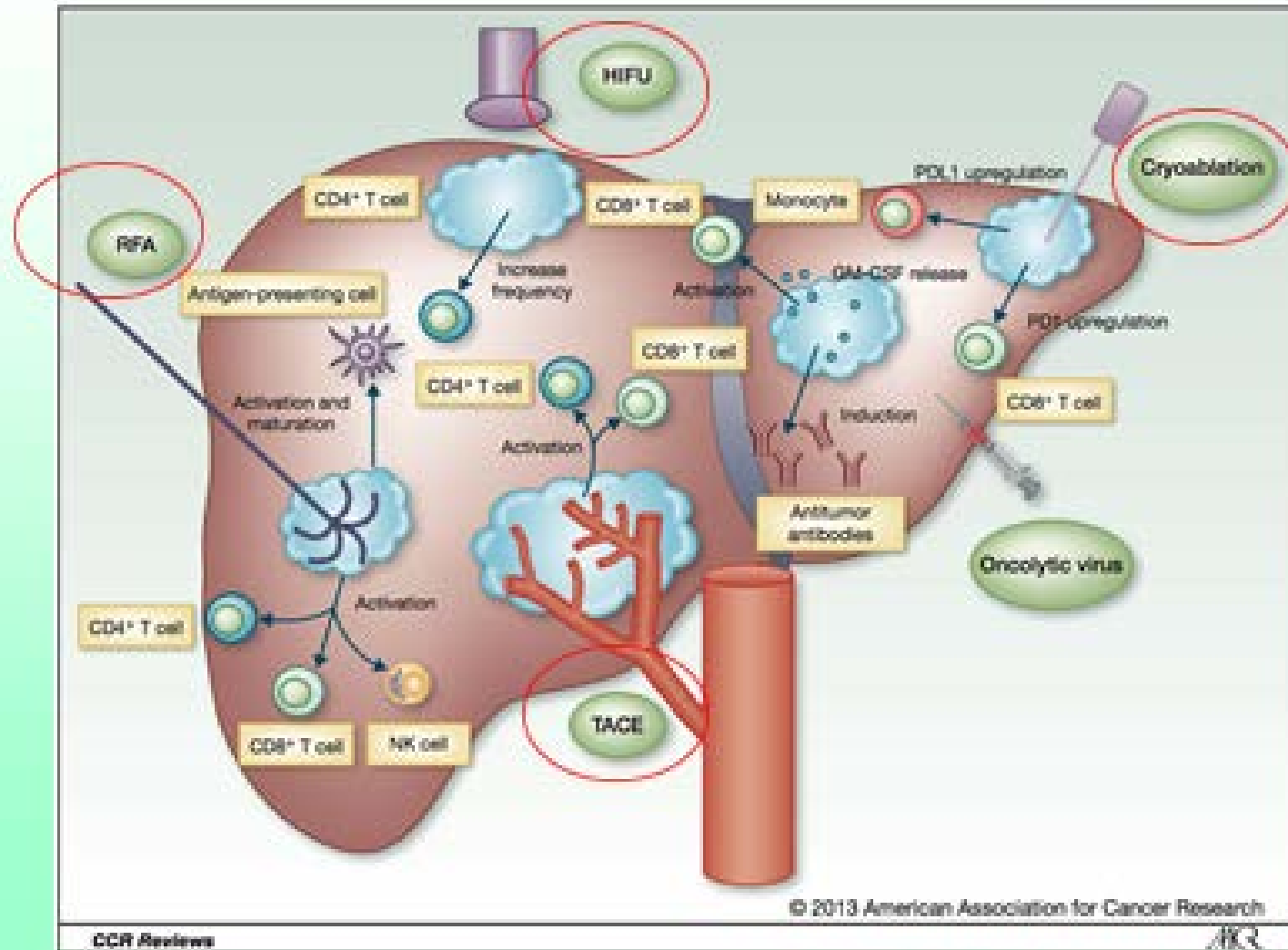
# WHY WE GO TO WORK



# TREATMENT OF LIVER MALIGNANCIES SYSTEMIC + TACE OR ABLATION

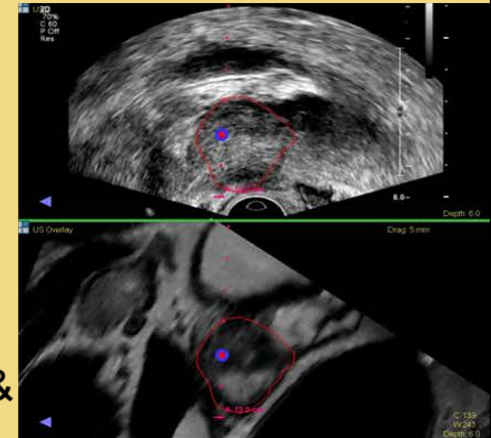
- a “check point” Inhibitor anti-CTLA-4, Tremelimumab, (Treme)
- Treme enhances anti-tumor immunity by blocking tumor induced immune suppression of cytotoxic T cells.
- Add a local inflammatory response: thermal or cryoablation or transarterial chemoembolization, TACE, (drug loaded beads with Doxorubicin) to enhance the activity of Treme.
- Protocol enrolls Hepatocellular cancer, and biliary tract (Cholangiocarcinoma) into cohorts using either a thermal ablation, cold ablation, cryoablation or TACE

# Ablation Immunotherapy



# Fusion Biopsy

1. PSA up, MRI abnormality or active surveillance of known prostate cancer
2. Diagnostic Multi-parametric MRI:
  - Read & export 3D MRI info: Prostate contour & suspicious lesions
3. Registration MRI with real-time TRUS for display of targets & needle guide trajectory
4. TRUS + MRI fusion to guide the biopsy needle to the visible suspicious lesions seen on MRI
  - Needle depth insertion monitored on TRUS / fusion
5. Track, map, & record the locations of targeted and standard TRUS biopsies for later referencing
  - (esp. important for active surveillance patients who will return for repeat biopsies, after an interval)



# FINDING THE PROSTATE CANCER

67 yr old, PSA = 21.4

6 prior random bx, over 10 yrs, all negative

3 MRI-based targets

All random cores negative

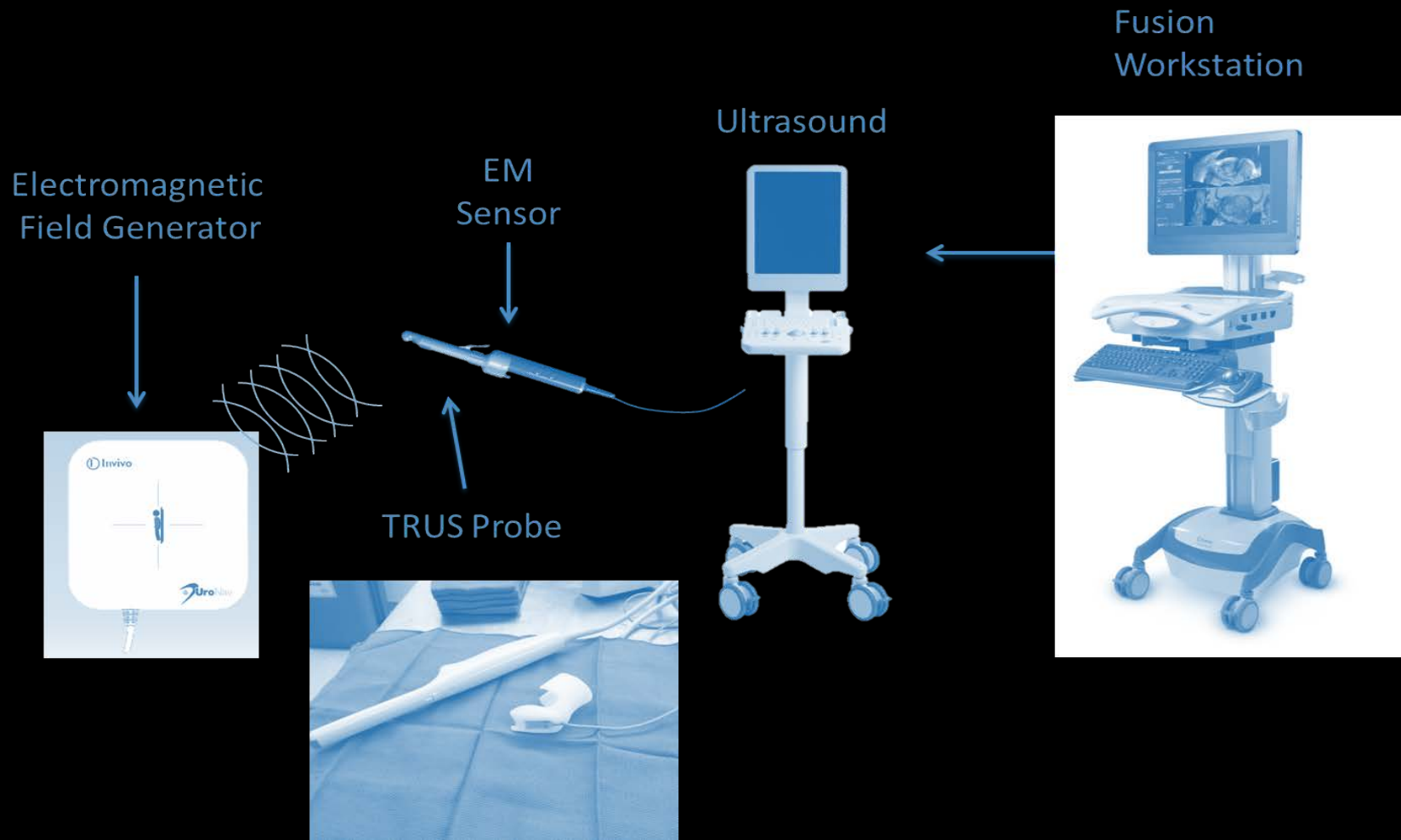
All targeted biopsy cores positive, Gleason 7



# PATIENT PREP

- Exam
- Labs
- Urinalysis and culture
- Education
- Prophylactic antibiotic- usually Levofloxacin
- Fleets enema

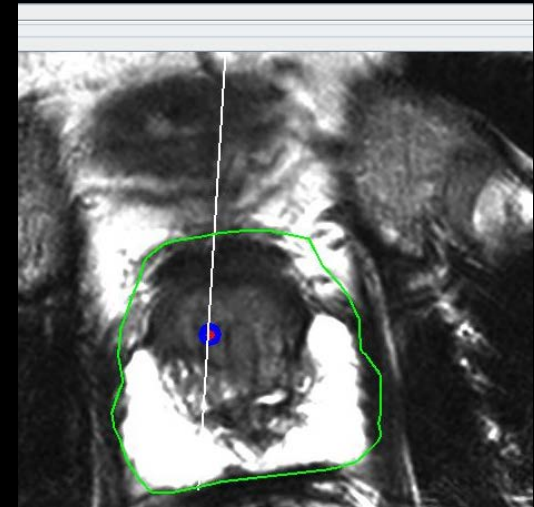
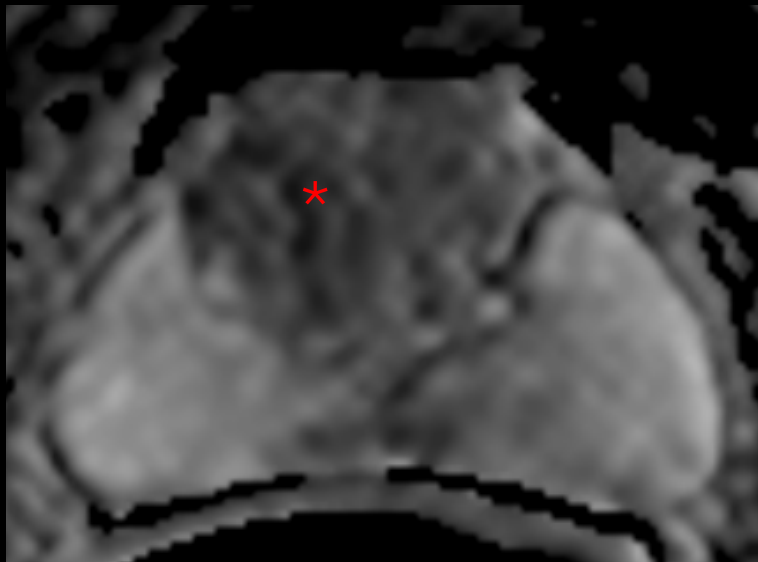
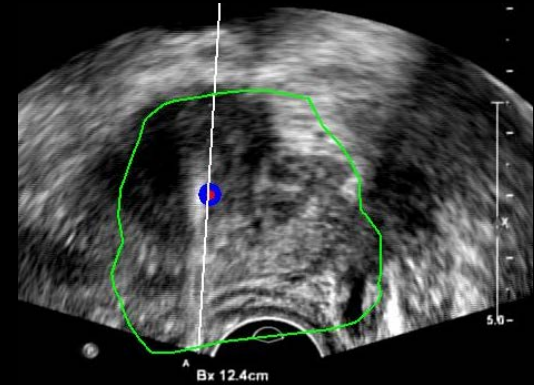
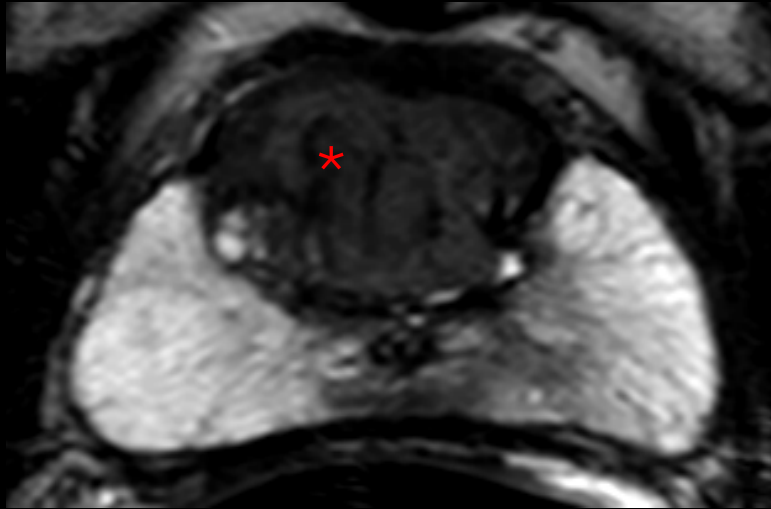
# EM Fusion-guided Technique



# Fusion Biopsy Set up



# PROSTATE FUSION BIOPSY



Live Freeze



U/S Probe In Range

Layout

Target

Add Associate Delete

mr target1- right posterio

Rename Show Current

Blend



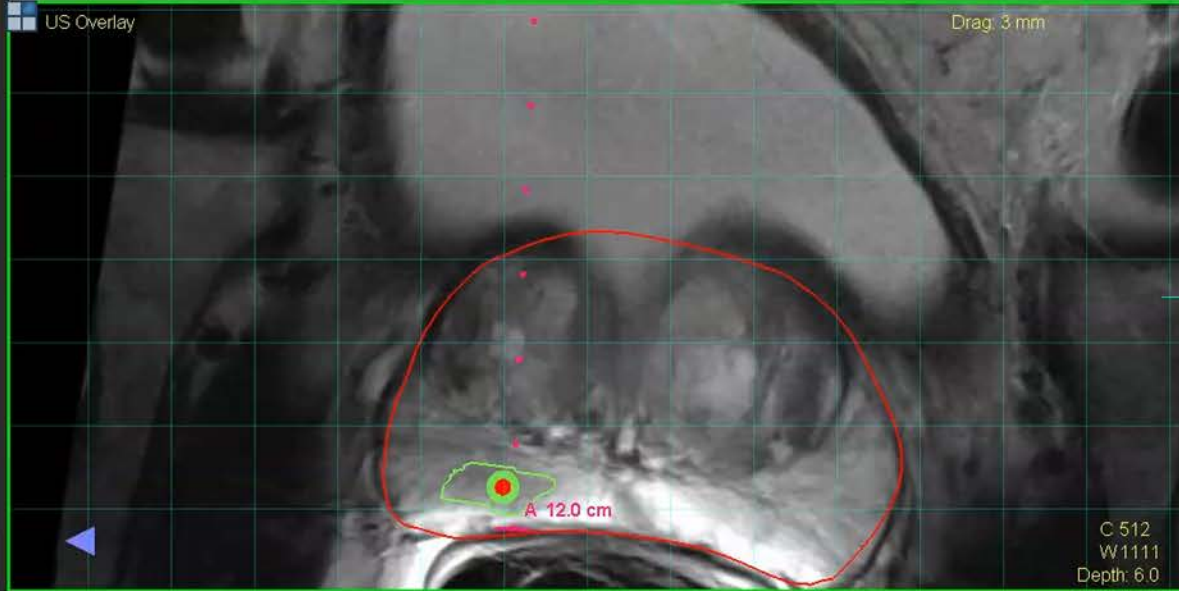
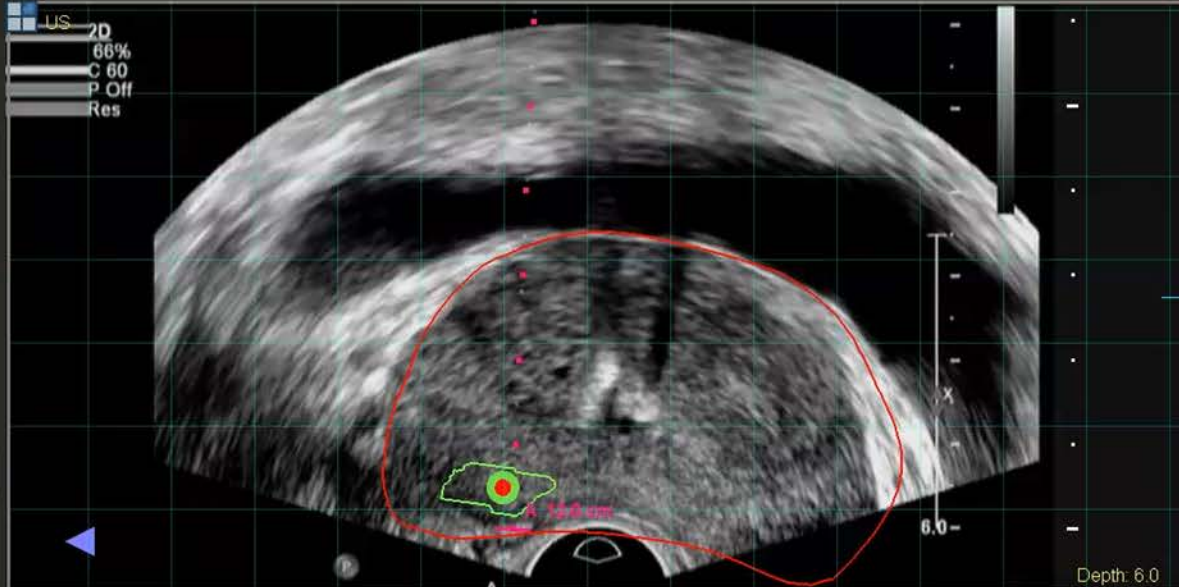
08-07-2013  
12:10:07

Motion Comp

Clear Comp

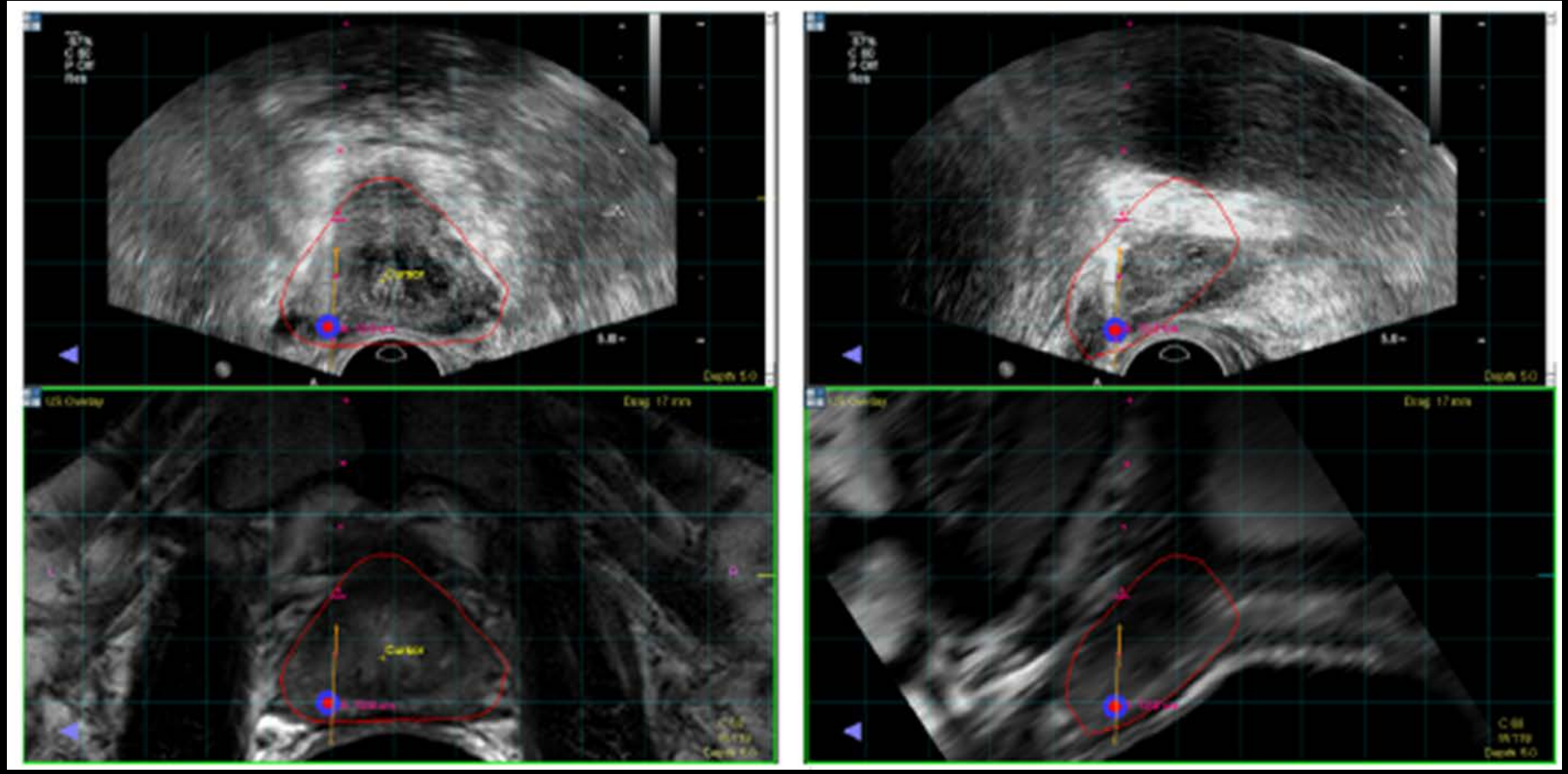
Distance to Target:  
n/a

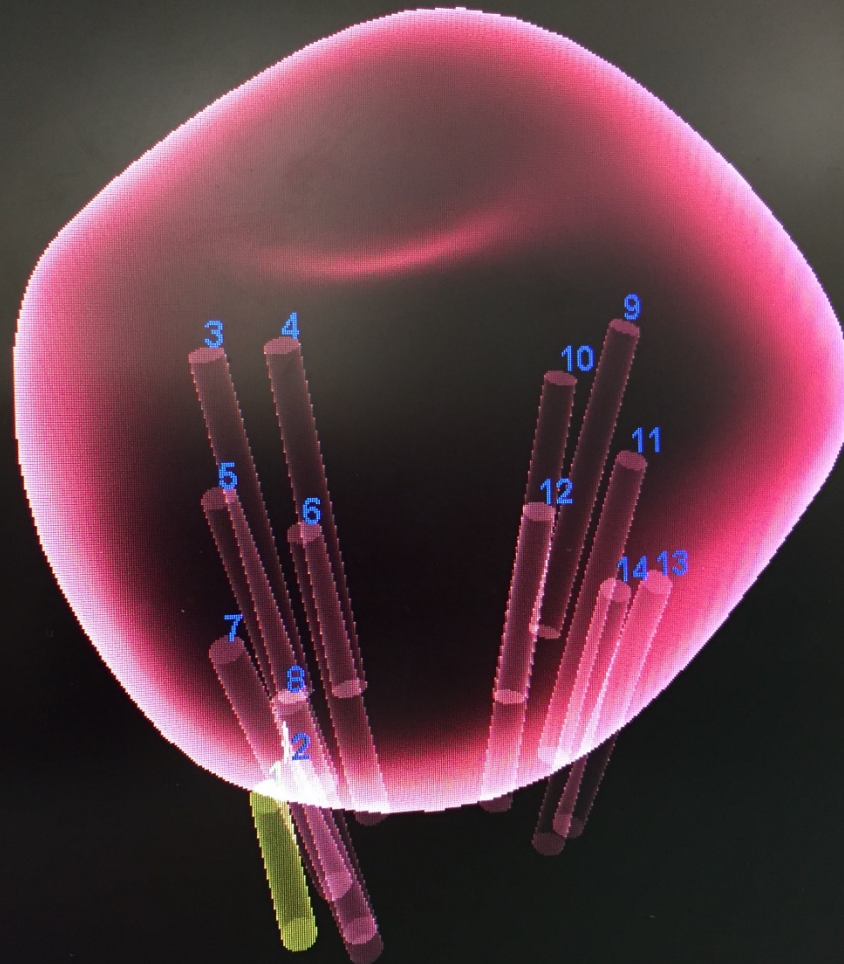
Back Done



Big red dot is center of target  
Small red dots are needle path  
Needle depth is from visual TRUS  
feedback  
Orange line records specimen location

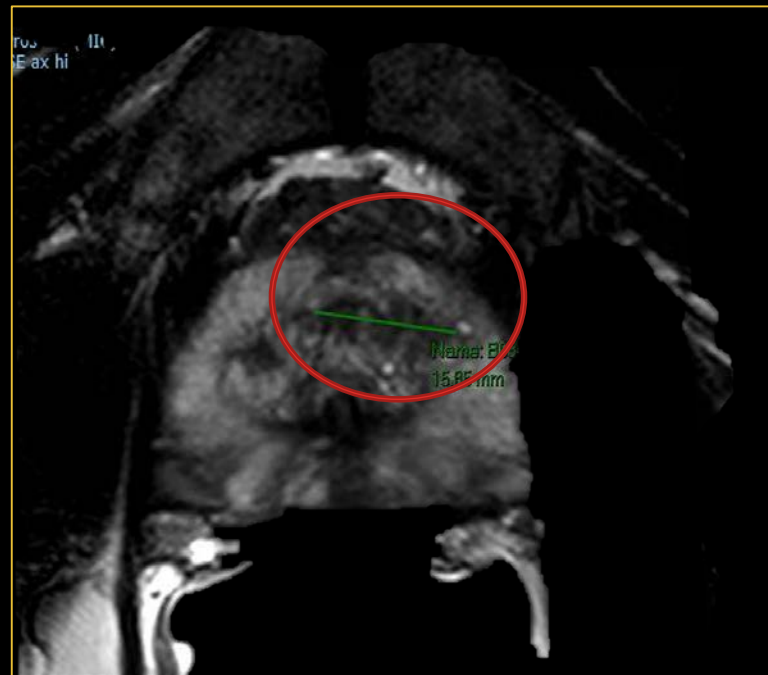
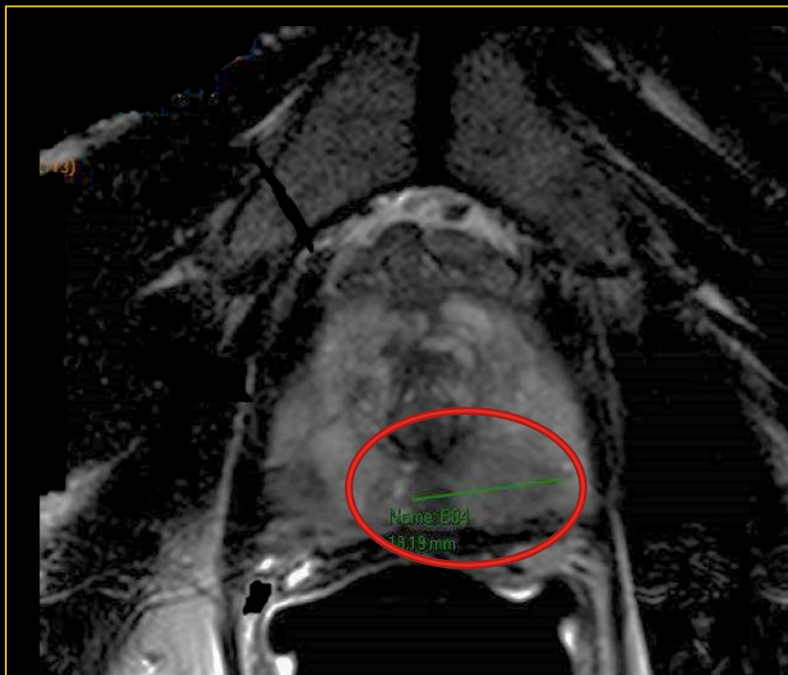
# NEEDLE IN ACTION





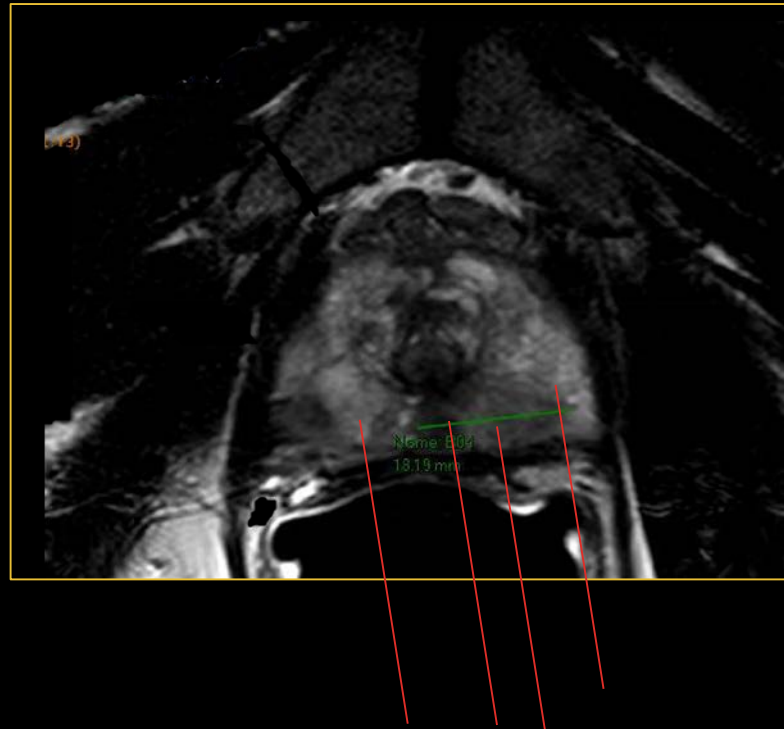
Targets are mapped and saved

# WHAT THE STANDARD TRUS BIOPSY MAY MISS

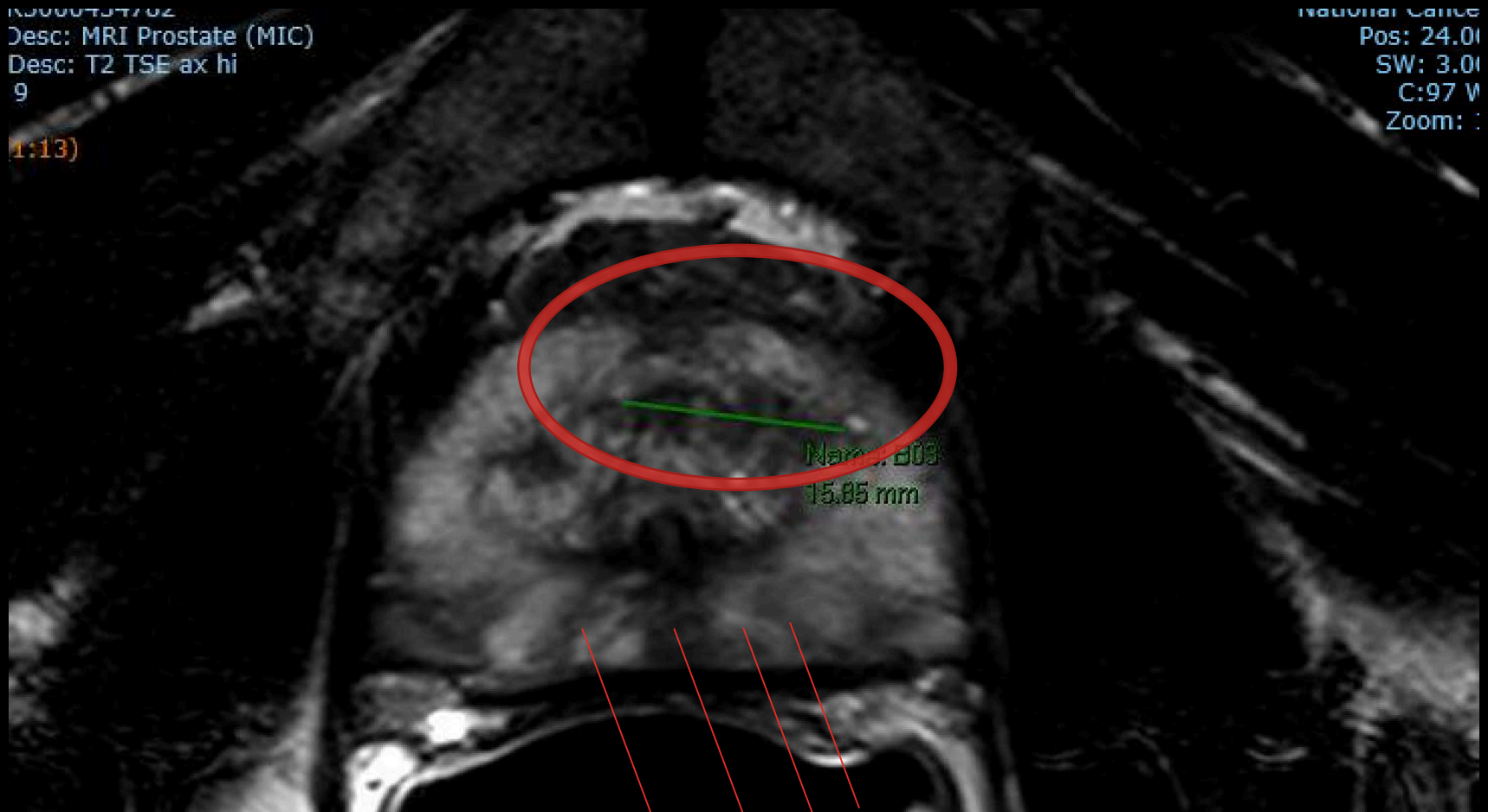




# WHAT THE STANDARD TRUS BIOPSY MAY MISS



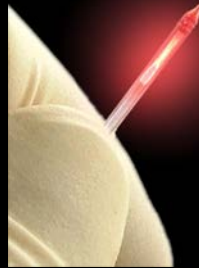
# WHAT THE STANDARD TRUS BIOPSY MAY MISS



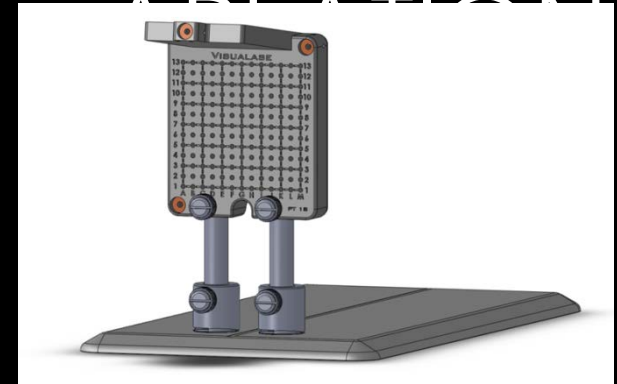
# FUSION FOCAL LASER ABLATION



Medtronic/Visualase  
Workstation

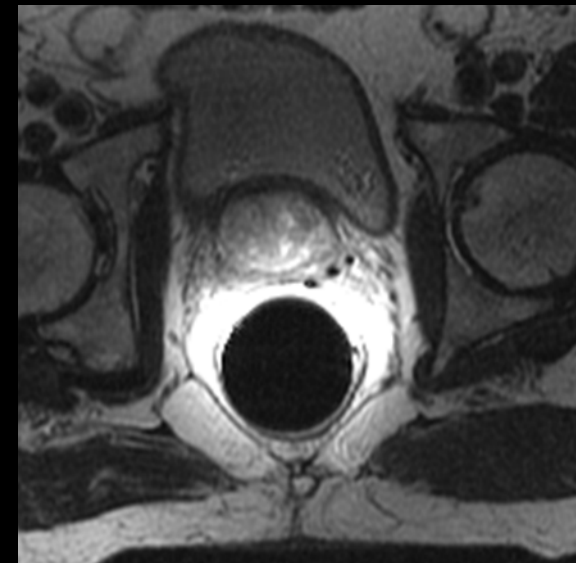
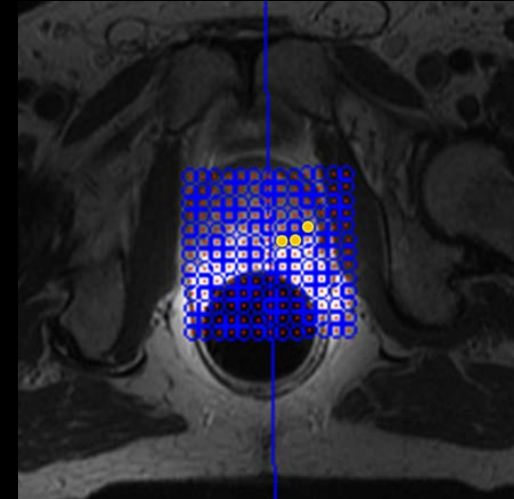
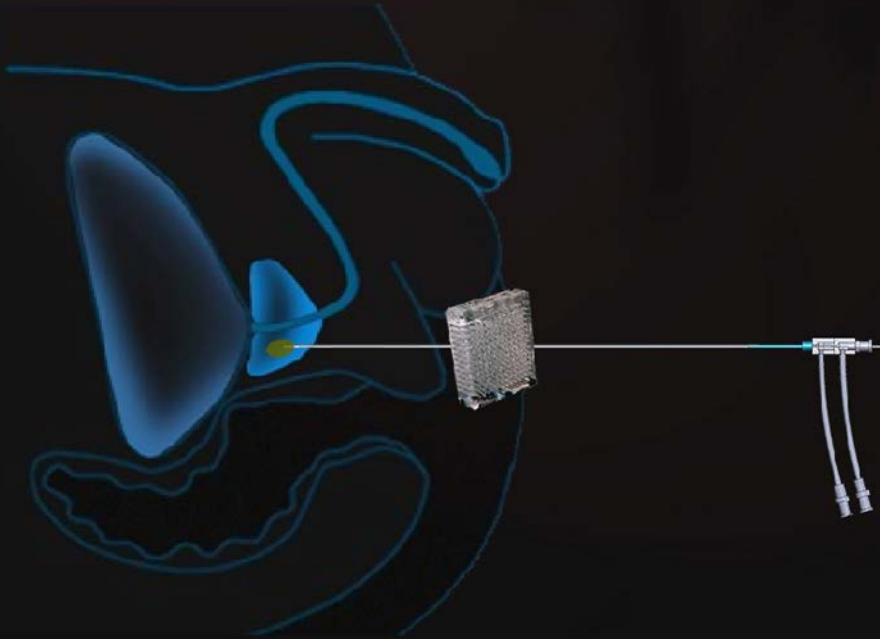


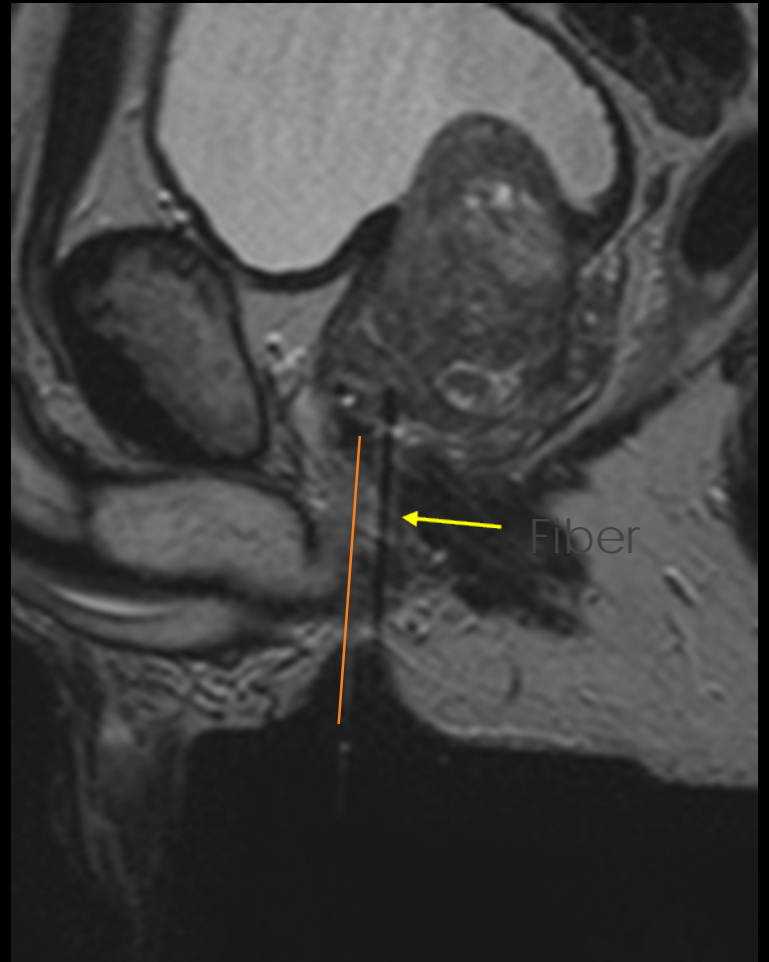
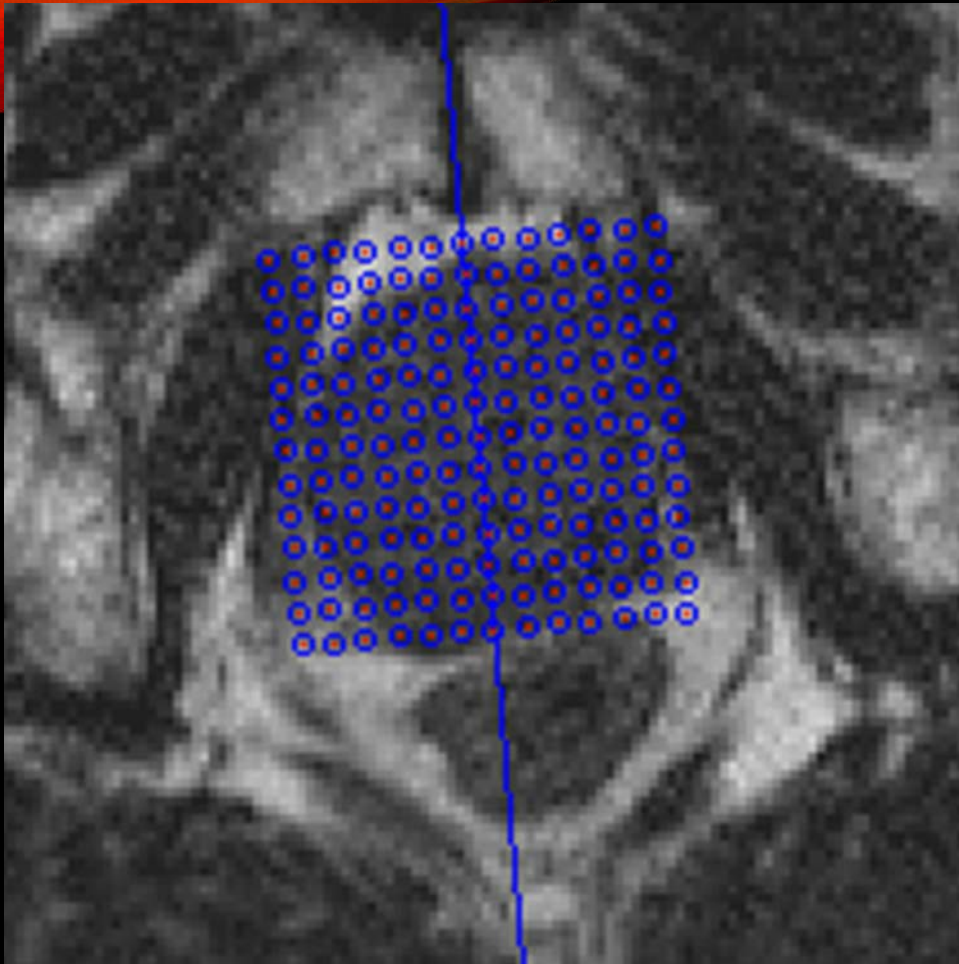
1 cm active tip of  
980 nm Laser  
catheter



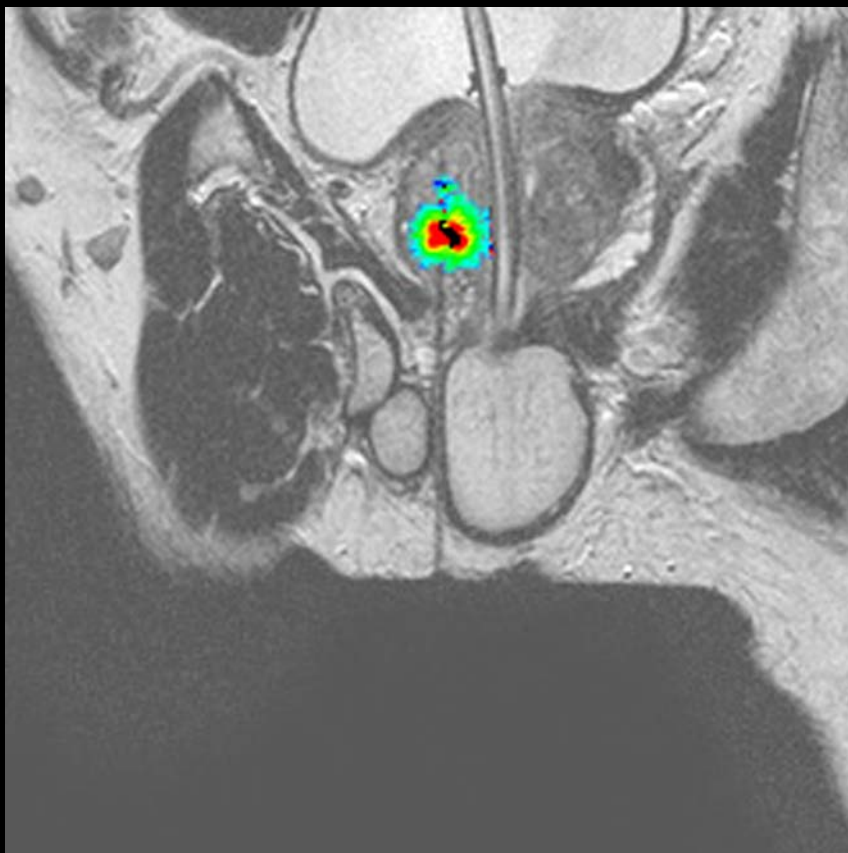
Perineal  
template

# TRANSPERINEAL APPROACH W/ MR THERMAL DOSE GUIDANCE

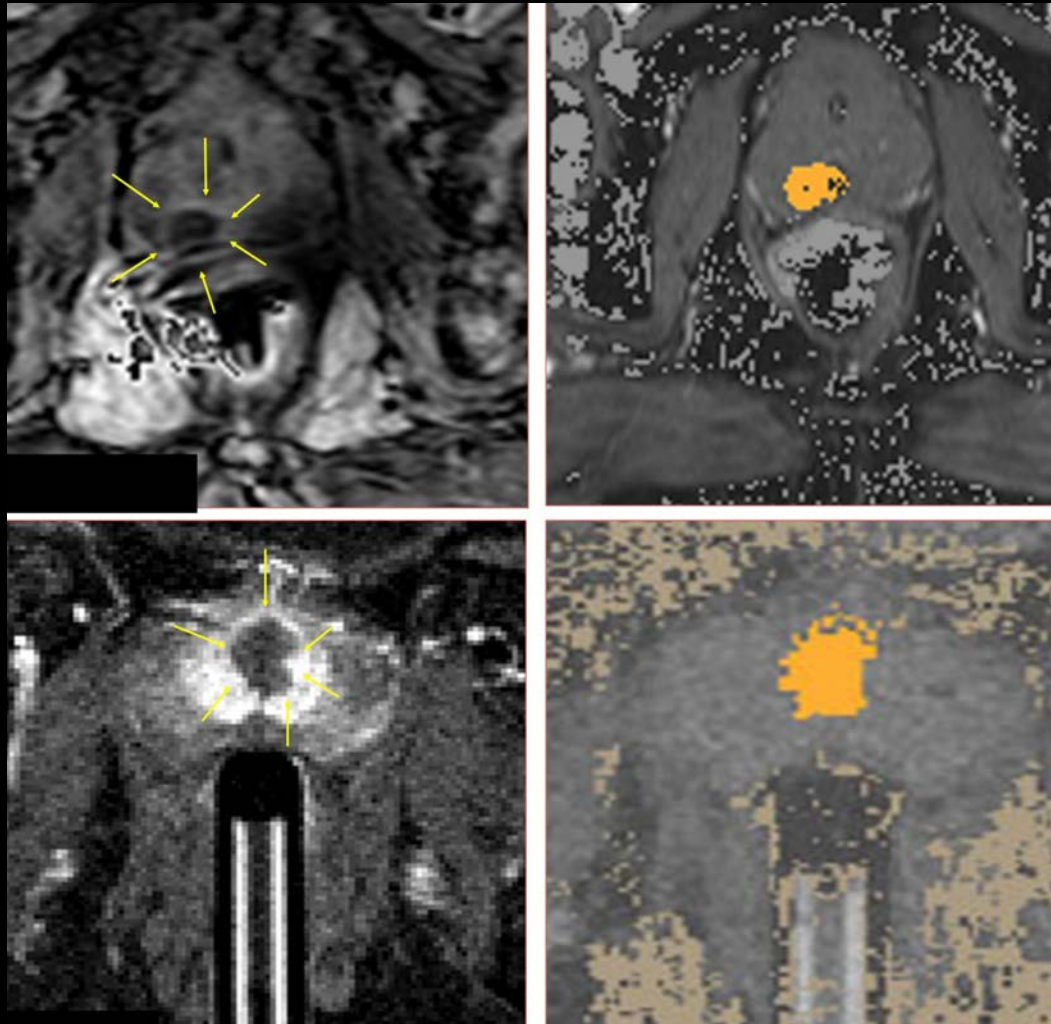




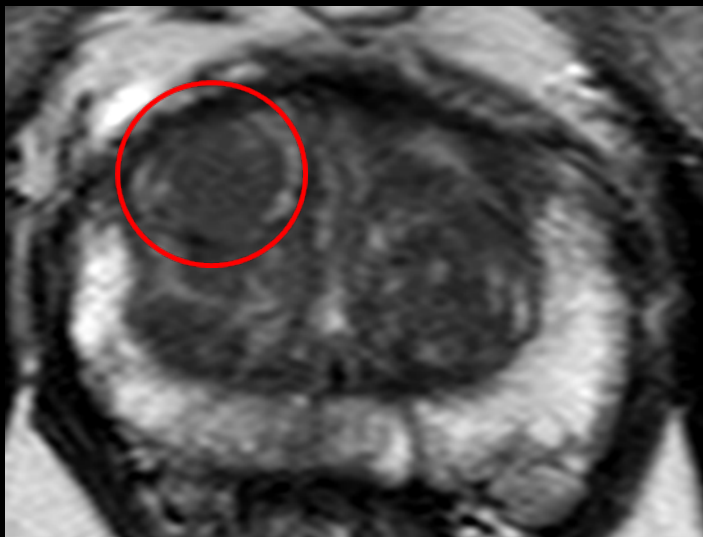
# PHASE-SENSITIVE IMAGES REFLECT REAL-TIME THERMAL MAPS



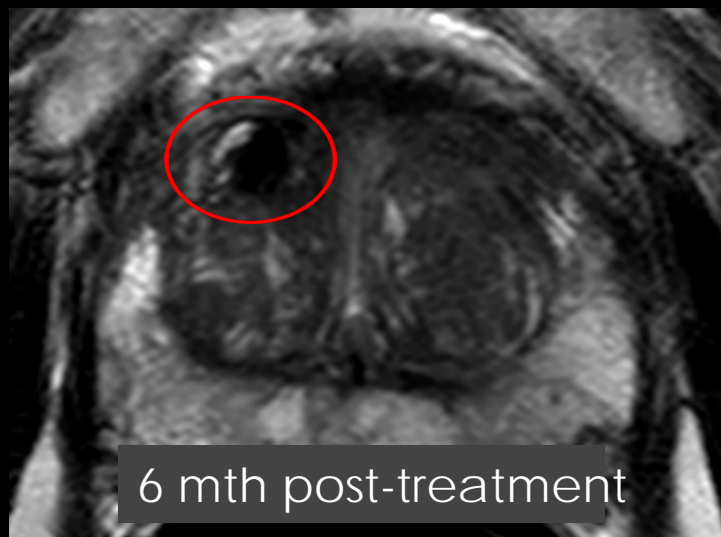
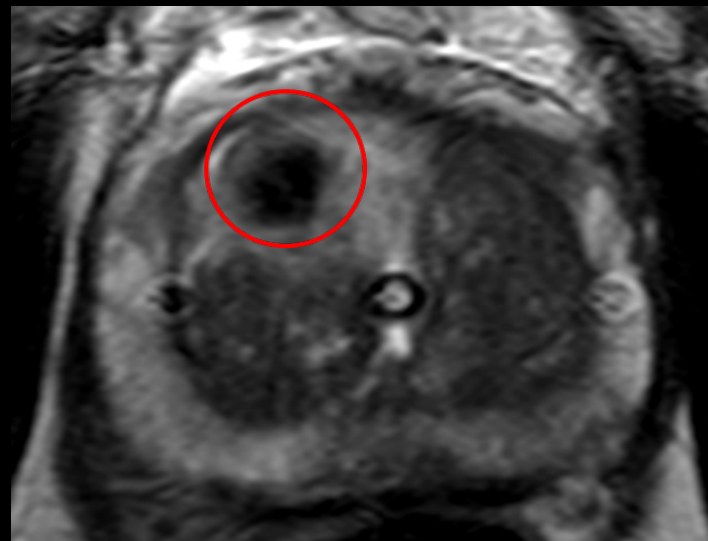
# POST-TREATMENT T1+GD MR DEMONSTRATED GOOD AGREEMENT WITH DAMAGE ESTIMATE



Pre-treatment



Immediate  
Post-treatment



6 mth post-treatment



1 year post-treatment



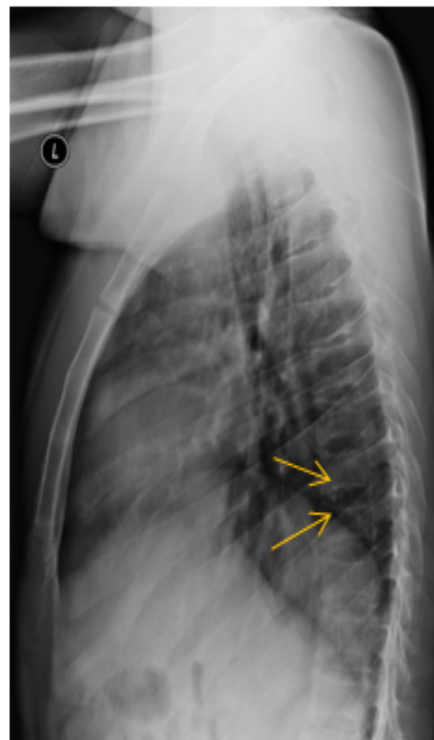
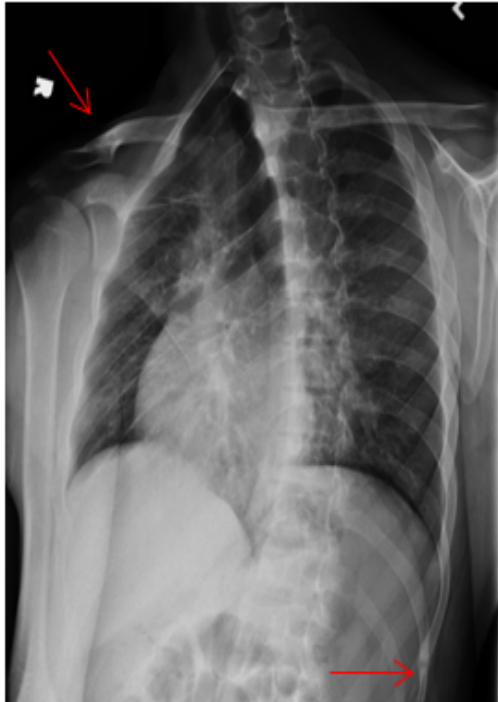
# BRINGING IT ALL TOGETHER

- 
- The Science
    - The Art
  - The Happy Ending

# CASE STUDY

- A 22 year old wheelchair-bound X 1 year with multiple repeated bone fractures all over body, over a 3 year period, after progressive immobility
- Prior to age 19 when his symptoms began, he was previously a very active athlete and weightlifter.

# RADIOLOGY CLUES



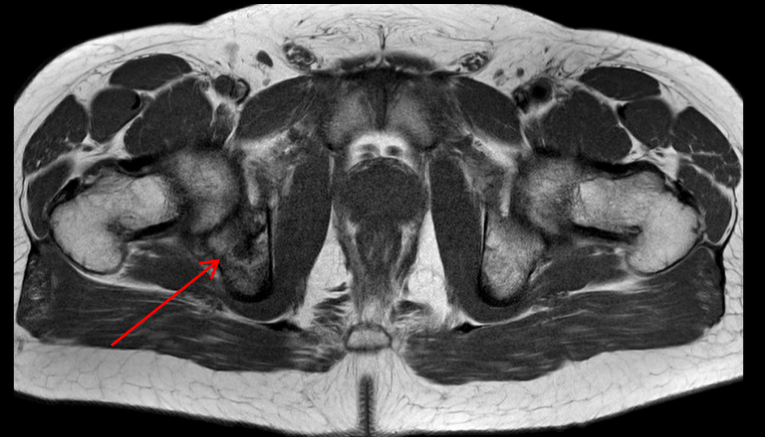
Fractures (red arrows) of varying ages and healing phases.

Osteomalacea shows as decreased density  
and chalky indistinct trabeculae (white arrows).

In the spine, fishmouth shape between vertebrae (orange arrows) can also be seen  
in sickle cell, osteoporosis, and renal osteodystrophe.

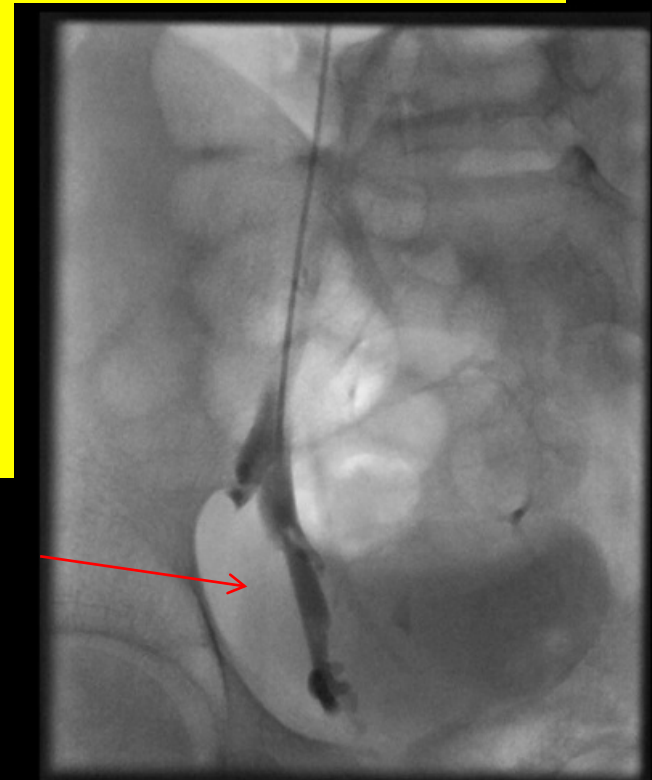
# IMAGING

- Sclerotic density ?tumor?
- <2x1cm, in acetabulum touching hip joint
- Low signal with enhancement same region on MRI
- Gallium 68 Dotatate PET CT showed a "hot spot" over acetabular mass



# VENOUS SAMPLING

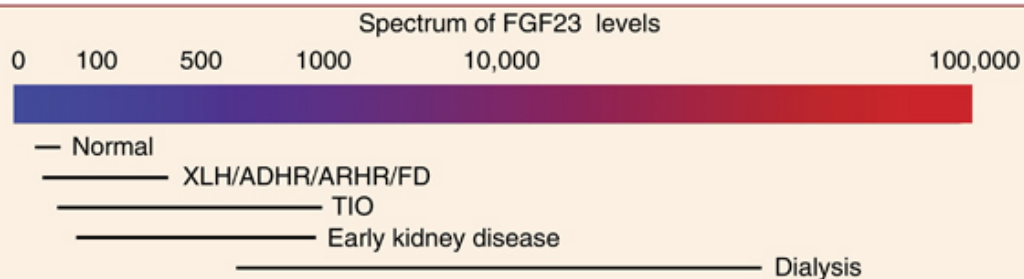
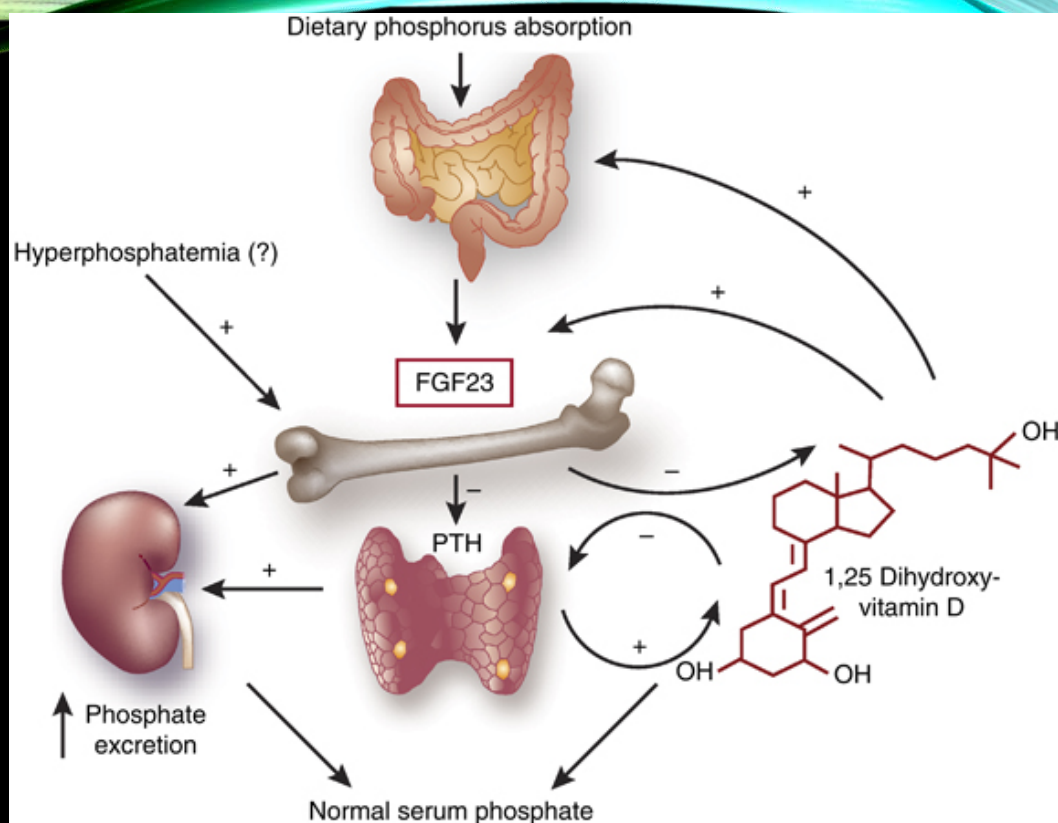
- Catheter sampling of internal iliac veins that drain the region of the acetabulum find markedly elevated FGF-23 (Fibroblast Growth Factor-23) in venous drainage (1800 pg/ml, normal < 50)
- Confirms diagnosis
- Localizes tumor definitively



# FGF-23 & PHOSPHATE REGULATION

Fibroblast growth factor 23 (FGF23) regulates serum phosphate levels within a narrow range, despite wide fluctuation in dietary intake, by a series of classic negative endocrine feedback loops involving:

- 1,25-dihydroxyvitamin D (1,25D),
- parathyroid hormone (PTH),
- urinary phosphate excretion, &
- dietary phosphorus absorption

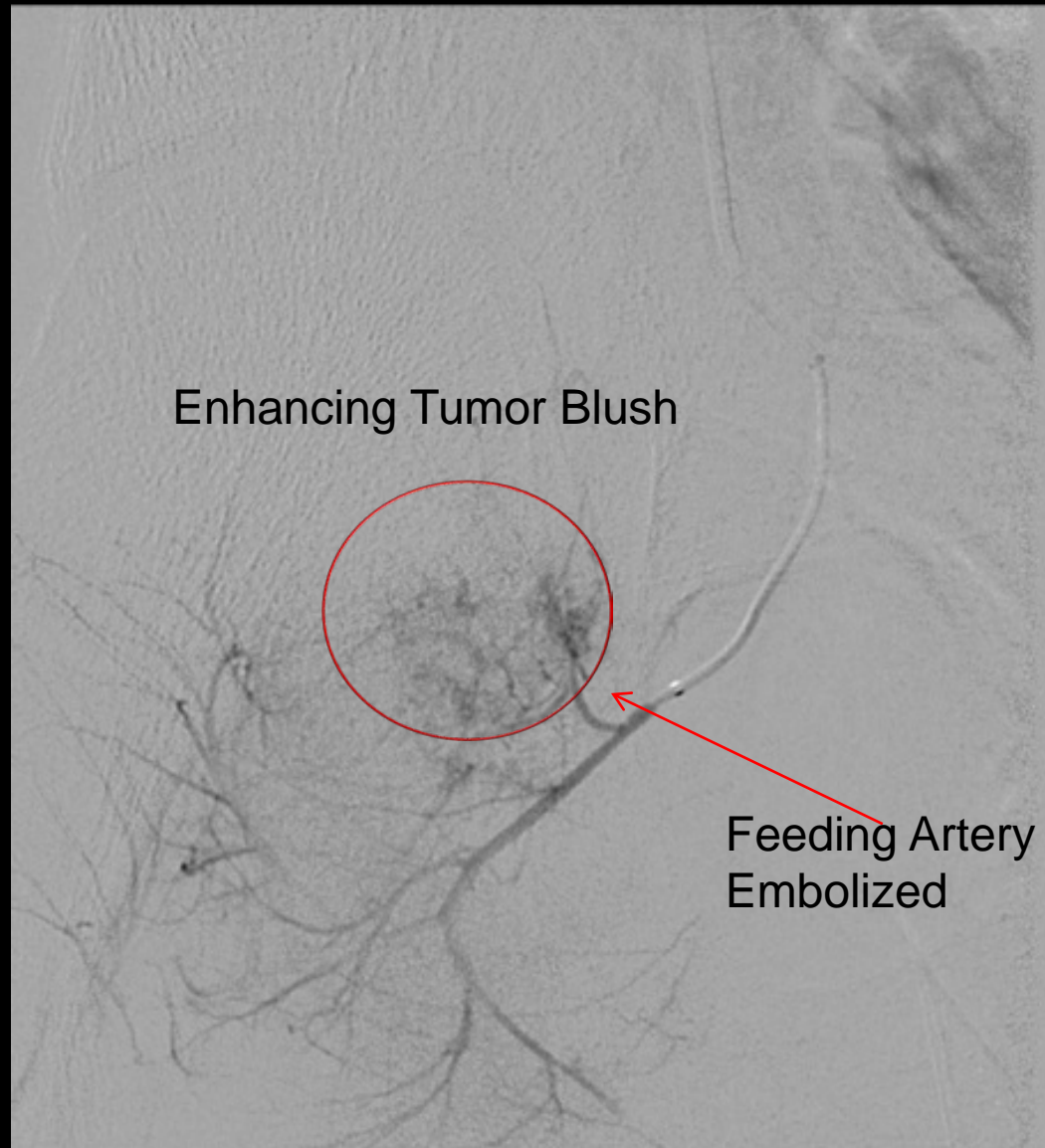


Metabolic characteristics of primary versus secondary syndromes of FGF23 excess

	FGF23	Serum Pi	Urinary Pi	1,25D	PTH
1° FGF23 Excess	↑	↓ ↓	↑	↔ / ↓	Variable
2° FGF23 Excess	↑ ↑ ↑	↔ / ↑	↑	↓ ↓	Variable / ↑ ↑

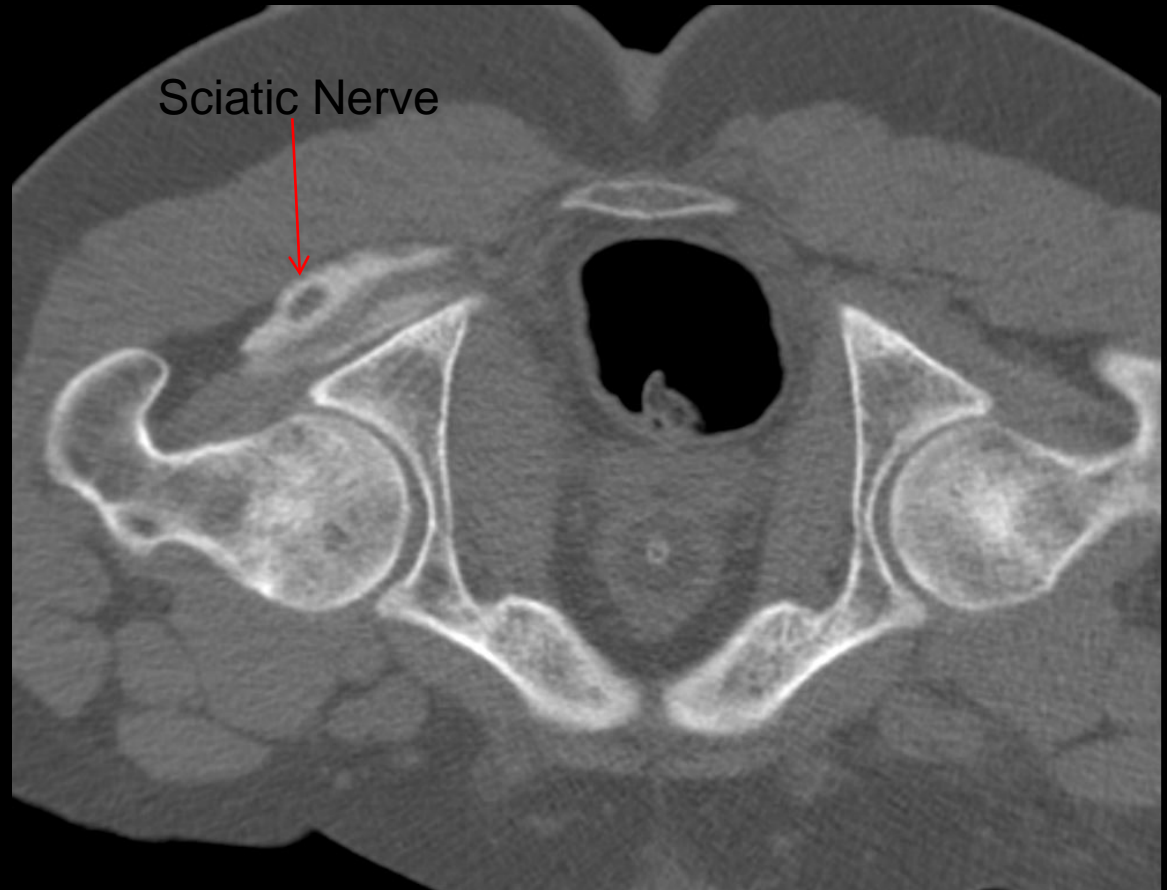
# EMBOLIZATION TO DECREASE BLOOD SUPPLY

- Small collagen plugs & powder are injected locally into artery supplying tumor to devascularize tumor prior to ablation



# HYDRODISSECTION TO PROTECT SCIATIC NERVE

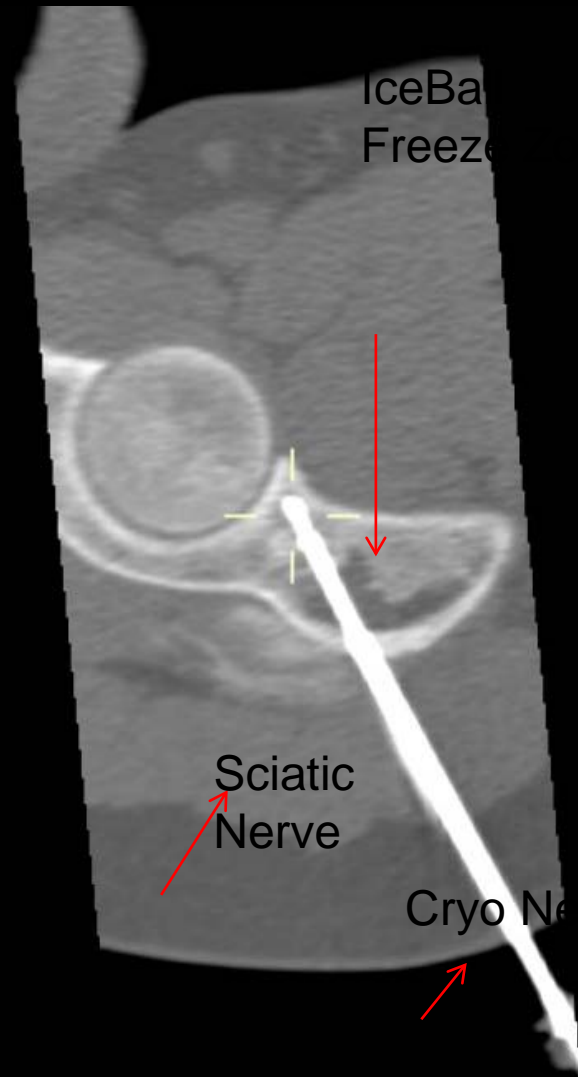
- Contrast is injected percutaneously prior to cryoablation to blanket & protect nerve from thermal damage





# CRYO-ABLATION NEEDLE IN SUSPECT TUMOR

- Cryo-ablation needle is placed into tumor after drilling cortical bone pathway so ice ball covers tumor & misses nerve



# POST-ABLATION MRI WITH EDEMA FROM ICEBALL SURROUNDING TUMOR

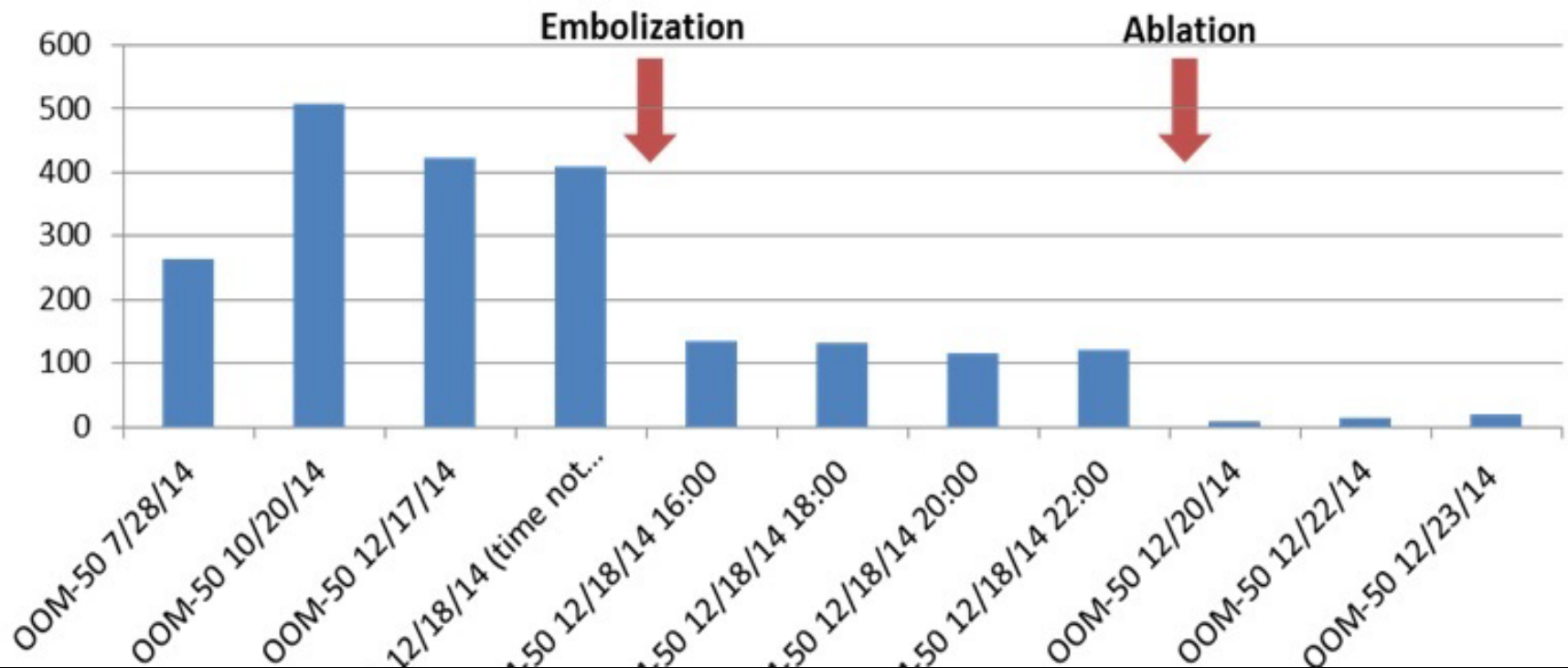
- Joint is spared damage that would have been caused by surgical resection (hemipelvectomy)



# PROBLEM FIXED:

TUMOR INDUCED OSTEOMALACEA GONE  
& FGF, CA, PHOS, VIT D NORMAL

## iFGF23 Before/After Embolization and Ablation OOM-50



# HAPPY ENDING—HE WALKED DOWN THE AISLE



# SUMMARY

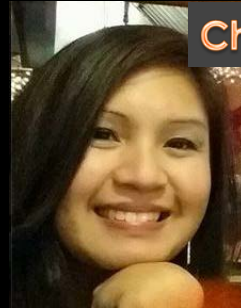
- Interventional Radiology is a safe and effective option to surgical (open) procedure to obtain a diagnosis of cancer
- Multiple modalities are available in the IR clinic to cure and palliate solid tumor primaries and metastases

# THANK YOU

John, Linsey, MJ, Andrew, Erica,  
Debbie Steve, Alisa and Debbie,



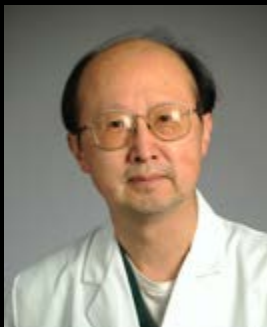
Julie



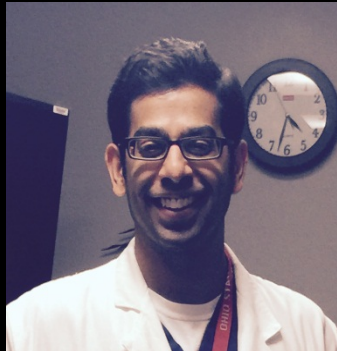
Charisse



Dr. Levy



Dr. Chang



Dr. Krishnasamy



Dr. Wood



Dr. Pinto

AND...THANK YOU!

