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

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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)

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

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

Charles T. Dotter M.D.
THE ROOTS OF INTERVENTIONAL RADIOLOGY

- Treated the first patient with catheter assisted vascular dilation

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THE “DO NOT FIX” CONSULT
THE DO NOT FIX PATIENT SCALES MOUNT HOOD WITH DR. DOTTER 1965

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Timeline of discovery

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

1990's-Present
- Drug eluting stents
- Drug eluting beads
- Radiopaque bead
- Navigation platforms
- Continued efforts to modify and perfect catheters, stents, baskets, and procedures

Golden Age
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
- 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

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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, C B C T, 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

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CT

Tracking

Work-Station

US

EM Field Generator + Software
+/- Tracked Needle +/- Tracked
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Targeting a Hidden Tumor: arterial phase enhancing HCC

Pre → Targeting → Tracking & Insertion → Post

J Vasc Interv Radiol 2010:S257-63
PET GUIDED BIOPSY: METABOLIC INTERVENTIONS

31 of 36 PET-guided biopsies diagnostic

Radiology 2011;260:848-56
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)

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RISK FACTORS FOR HCC

Rare inherited disorders:
- Tyrosine deficiency
- Alpha1-antitrypsin deficiency
- Porphyria cutanea tarda
- Glycogen storage diseases
- Wilson disease

Toxins: Flavotoxins, Arsenic, Tobacco, Alcohol

Hepatitis B,

Ethnicity: Asian, Pacific Islander, Sub-Saharan

Cirrhosis/Fatty liver

Hereditary hemochromatosis

Male

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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
CHILD PUGH SCORING

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

<table>
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<th>Clinical/biochem.</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td>Encephalopathy (grade)</td>
<td>None</td>
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<td>3-4</td>
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<tr>
<td>Ascites</td>
<td>None</td>
<td>Slight</td>
<td>moderate</td>
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<tr>
<td>Albumin</td>
<td>&gt;3.5</td>
<td>2.8-3.5</td>
<td>&gt;2.8</td>
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<tr>
<td>Prothrombin time (sec)</td>
<td>1-4</td>
<td>4-6</td>
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<tr>
<td>Bilirubin -- Primary biliary cirrhosis</td>
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<td>2-3</td>
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<td></td>
<td>1-4</td>
<td>4-10</td>
<td>&gt;10</td>
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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 °C or in excess of 60 °C for most cell type”

ABLATION AND TRANSARTERIAL EMBOLIZATION
CRYOABLATION

- Percutaneous
- Cryoablation probe(s) introduced into tumor and cooled to -40°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

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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

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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, dessicated tissue; is capable of generating very high temperatures, often in excess of 100°C
- Does not require grounding pads
The tip of the RFA probe is placed in the liver tumour under ultrasound or CT guidance.

The RFA probe is 'deployed' (opening up the prongs at its tip). The probe is connected to the generator and the tumour destroyed.

Once destruction is completed, the probe is withdrawn.
INDICATION FOR ABLATION -- HCC

- Very early to early stage disease
- Localized tumor < 3 cm 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%
  - Intraperitoneal 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

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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 anesthetia eval)**
- **EDUCATION**
  - ANTICIPATORY GUIDANCE
  - RISKS
  - POST EMBOLIZATION SYNDROME
- **INFECTION RISK ANALYSIS**
- **ANTIBIOTICS**
- **BOWEL PREPS- CHOLANGIOCARCINOMA/ AMPULARY/ WHIPPLE OTHER SURGICAL CONCERNS**

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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-platinum
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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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 >2 mg/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

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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%

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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
- 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

Radiation
10 Gy

Fri

Radiation
10 Gy

Mon

Radiation
10 Gy

Wed

Radiation
10 Gy

Thu

Radiation
10 Gy

2 weeks

Fri

TACE

Ablation

Mon

Wed
FEEDING VESSEL DETECTION: UN-TANGLE TORTUOSITY & OVERLAP REFERENCING A “3D ROADMAP”
AUTO FEEDER DETECTION W DUAL PHASE ENABLES SELECTIVITY
ANGIOGRAM PRE-TACE
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

PLEASE JOIN US TO CELEBRATE THE 50TH ANNIVERSARY OF
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
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

Electromagnetic Field Generator

EM Sensor

TRUS Probe

Ultrasound

Fusion Workstation

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Fusion Biopsy Set up
PROSTATE FUSION BIOPSY
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
Targets are mapped and saved

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WHAT THE STANDARD TRUS BIOPSY MAY MISS

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WHAT THE STANDARD TRUS BIOPSY MAY MISS
WHAT THE STANDARD TRUS BIOSY MAY MISS
FUSION FOCAL LASER ABLATION

1 cm active tip of 980 nm Laser catheter

Medtronic/Visualase Workstation

Perineal template

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TRANSPERINEAL APPROACH W/ MR THERMAL DOSE GUIDANCE

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PHASE-SENSITIVE IMAGES REFLECT REAL-TIME THERMAL MAPS

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POST-TREATMENT T1+G D M R DEMONSTRATED GOOD AGREEMENT WITH DAMAGE ESTIMATE

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BRINGING IT ALL TOGETHER

• The Science
• The Art
• The Happy Ending
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.
Fractures (red arrows) of varying ages and healing phases.

Osteomalacia 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 osteodystrophy.
• Sclerotic density ?tumor?
• <2x1 cm, 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
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

http://www.nature.com/ki/journal/v76/n7/fig_tab/ki2009246f1.html
• 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 cryo-ablation 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 IC EBALL SURROUNDING TUMOR

• Joint is spared damage that would have been caused by surgical resection (hemipelvectomy)
PROBLEM FIXED:
TUMOR INDUCED OSTEOMALACIA GONE
& FGF, CA, PHOS, VIT D NORMAL
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,

Dr. Levy  Dr. Chang  Dr. Krishnasamy  Dr. Wood  Dr. Pinto
AND....THANK YOU!

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