Interventional Oncology

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Interventional Radiology
Ohio State University Medical Center

List of Interventional Oncology procedures

- Hepatic artery chemoembolization (TACE)
- Hepatic artery embolization (TAE)
- Hepatic artery radioembolization (SIRT)
- Portal vein embolization (PVE)
- Percutaneous thermal ablation:
  - RF and Microwave
- Cryoablation: Freezing tumors
- Chemical Ablation (PAE): absolute Ethanol
Trans-arterial Liver-directed Therapies for Metastatic NET

Octreotide

- Binds ssrt-2,3,5
- Relieves syndrome in 90%
- Decreases tumor markers
- Role in tumor stabilization
- Improved Progression Free Survival
  - 14.3 months vs 6 (p=0.00007)
  - PROMID study
## PROMID Study

- Phase III placebo controlled multicenter trial in Germany
- 85 patients over 7 years (2001 – 2008)
- WDNEC (Ki-67 <2%)
- 75% had tumor liver burden <10%
- 38% had carcinoid syndrome
- Median 4.3 months from dx to enrollment
- Improved PFS for Octreotide
  - 14.3 months vs 6 (p=0.00007)

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## Patient Selection

- Multidisciplinary Bi-weekly Conference
  - med onc, surg onc and IR
- Emphasis on curative therapies
  - Resection, Ablation
- TACE when not eligible for curative therapy
When to Intervene?

- Uncontrolled Symptoms
- Deterioration in Liver Function
- Increased Tumor Burden

How to Treat?

<table>
<thead>
<tr>
<th>Center</th>
<th>Type</th>
<th>Treatment</th>
<th>Response (RECIST)</th>
<th>TTP (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.D. Anderson</td>
<td>GI NET</td>
<td>TAE/TACE</td>
<td>24%</td>
<td>22.7</td>
</tr>
<tr>
<td>Univ. Pennsylvania</td>
<td>NET</td>
<td>TAE</td>
<td>n/a</td>
<td>10</td>
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<tr>
<td>Univ. Pennsylvania</td>
<td>NET</td>
<td>TACE</td>
<td>n/a</td>
<td>55</td>
</tr>
<tr>
<td>Washington University</td>
<td>GI NET</td>
<td>TAE/TACE</td>
<td>32%</td>
<td>20</td>
</tr>
<tr>
<td>Institut Gustave Roussy</td>
<td>GI NET</td>
<td>DEB-TACE</td>
<td>80%</td>
<td>15</td>
</tr>
<tr>
<td>Multi-center</td>
<td>GI NET</td>
<td>Y90</td>
<td>43%</td>
<td>22-28 MS</td>
</tr>
</tbody>
</table>

Gauer et al; Cardiovasc Intervent Radiol (2011) 34:566-572
**Why Bland Embolization?**

- M.D. Anderson 2005, (n=123)
- GI Carcinoid (n=69)
  - No difference in response rate / survival
- Islet Cell Carcinomas (n=54)
  - Response rate (TACE 50% vs TAE 25%) ns
  - Prolonged survival (TACE 31 vs TAE 18 months) ns

(Gupta et al; Cancer 2005)

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**LC Bead Product**

- 2 ml of LC Bead in saline
- 70 μm-150 μm, 100 μm-300 μm, 300 μm-500 μm and 700 μm-900 μm
## LC Bead Product

- 2 ml of LC Bead in saline
- 70 μm-150 μm, 100 μm-300 μm, 300 μm-500 μm and 700 μm-900 μm

![LC Bead Product Image](Image)

## Why Chemoembolization?

- U Penn: JVIR 2007, (n=67)
- No Difference in Severe Toxicities
  - TACE: 11/44 (25%)
  - Bland: 5/23 (22%)
  - 95% CI 0.4-4.0
- No difference in length of stay

(Ruutliainen: J Vasc Interv Radiol 2007)
Why Chemoembolization?

- 12 months Progression: TACE 0%, TAE 49%
- 3 Years: TACE: 35% were progression-free
- Symptom Control: Better with TACE
  - 15 months vs. 12 months (ns)
- Better Survival with TACE
  - 76% vs 68% at 2 years (ns)

(Ruutiainen: J Vasc Interv Radiol 2007)

Hepatic Artery Chemoembolization in 122 Patients with Metastatic Carcinoid Tumor: Lessons Learned

Mark Broomston · Osama Al-Saif · Dori Kremniki ·
Joseph J. Pinzone · Edward W. Martin · Bryan Palmer ·
Gregory Gay · Hooman Khabiri ·
E. Christopher Ellison · Manisha H. Shah

- Retrospective review of 122 patients
  - 1992 – 2004
- All patients considered “inoperable”
- Indications:
  - Liver tumor progression
  - Poorly controlled symptoms
  - Large tumor burden in liver

J Gastrointest Surg 2007;11:264-71
TACE: CAM

- Cisplatin 50 mg
  - No longer manufactured
- Adriamycin 30 mg
- Mitomycin 20 mg
- Ethiodol: 10 ml
- Volume: 20 ml

Liver Directed Therapy at OSU

- Lobar TACE
- Same Day Admit
- Octreotide Drip
TACE – OSU Experience

- Whole liver initially favored (75%)
  - Rarely done since 2004
- Complications 23%
- Mortality 5%
- Radiographic response = 82%
  - Median TTP = 19 months
- Biochemical response = 80%
  - Median TTP = 7 months
- Symptom response = 92%
  - Median TTP = 13 months

J Gastrointest Surg 2007;11:264-71

Complications: The European Experience

- Major: 5.9% of Procedures
  - Transient hepatic or renal failure
  - Liver abscess
- Death: 1.6% Procedures
  - Liver + renal failure
  - Septicemia

A Roche & T de Baere; Europ Radiol: 2003
## Predictors of Complications

- Tumor Burden > 70% (p=0.029)
- Bilioenteric anastomosis: Odds Ratio of liver abscess for TACE x67
- Whole Liver TACE vs. Partial (p=0.001)

(A Roche & T de Baere; Europ Radiol 2003)

## Contraindications

- Mostly Relative
- Hepatic Failure
  - Secondary to large tumor burden
- Portal Vein Thrombosis
  - Rare in NET patients
- Bilioenteric anastomosis
  - Abscess
Causes of Failure

- Poorly Vascularized Metastases
- Failure of TACE or failure to TACE?
- Failure in the dome:
  - Phrenic artery?
- Failure in the left lobe:
  - Left hepatic artery variant
- Intercostal Arteries

Post-embolization changes

<table>
<thead>
<tr>
<th>Fresh</th>
<th>Repeat</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
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</table>
Non-hepatic Arterial Supply

- Hepatic Artery
- Phrenic Artery
Progression After TACE

- Maximum response at up to 18 months
- Year 1-3: New lesions or progression of old lesions
- Threshold for re-treatment?
- Second line Therapy?

Repeat TACE

- Challenges of Re-embolization
- Success of re-TACE despite the appearance of the arteries, yet ultimately limited by the arteries
Second Line Therapy

- Repeat TACE- if good first response
- Switch to Y-90 if early failure?
- Increase Sandostatin
- Nuclear Therapy

Drug-Eluting Beads

- Biocompatible PVA hydrogel bead which can be loaded with chemotherapy
  - Doxorubicin: DEBDOX
  - Irinotecan: DEBIRI
- Combines chemotherapy and embolization
- Early experience
DC Bead Before and After Loading with Doxorubicin

Prior to Loading

Loaded with Doxorubicin

Loaded with Doxorubicin in Syringe

DC Bead Loading

- Negatively charged sulfonate interacts with positively charged doxorubicin hydrochloride or irinotecan hydrochloride
  - DC Bead Doxorubicin (DEBDOX)
  - DC Bead Irinotecan (DEBIRI)

Interaction of doxorubicin or irinotecan with $SO_4^{2-}$ groups displaces water from the hydration shells
## DEB TACE

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>N</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>2008</td>
<td>de Baere et al</td>
<td>20</td>
<td>PFS 15m</td>
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<tr>
<td>2011</td>
<td>Whitney et al</td>
<td>28</td>
<td>PFS 18m, OS 25m</td>
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<tr>
<td>2011</td>
<td>Gaur et al</td>
<td>18</td>
<td>PFS 14m</td>
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</tbody>
</table>

Potential advantages of traditional TACE:
- Consistent delivery
- Ease of use
- Ability to evaluate response
- ???Cost (Disadvantage?)

## DEB TACE

- Evidence not as mature as with conventional TACE
- Ongoing Trials
- Higher than expected Toxicity
  - Potential role: for selective treatment?
- No evidence or justification for Irinotecan
**Yttrium-90 Microspheres**

- Radiolabelled particles
  - TheraSpheres® - MDS Nordion (HCC)
  - SIRSpheres – SIRTex (CRC)
- Embolized into hepatic artery
- High dose radiation to tumor
- Low dose radiation to liver
- $\beta$ particle emission
  - 2-3mm of penetration

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**Yttrium-90 Microspheres**

![Microspheres Image](image-url)
Microspheres

“Video used with permission from Nordion (Canada) Inc.”
### Y-90 Results

- Kennedy: 148 patients, multiple centers
- 67% - No Toxicity (surprising)
- CR 3%, PR 60%, SD 23%, PD 5%
- High disease control - 95% control, mean survival 70 months
- Outpatient Process

(Am J Clin Oncol 2008;31: 000–000)

### Y-90 Process

- Outpatient treatment
- Angiographic Evaluation
  - presence of GI collaterals and lung shunting
- Y-90 Dose calculation and ordering:
  - 10 day delivery
- Actual treatment
- 4-6 weeks from referral to treatment
Ablation

Post Ablation
Ongoing Questions

- Is TACE superior to TAE?
- DEB-TACE for selective treatment?
- Y90: promising
- Role of Intra-arterial therapies early in the course of the disease
- RCT difficult due to small population size, heterogeneity

Ohio State University NET Program

<table>
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<tr>
<th>Endocrinologists</th>
<th>Clinic Team</th>
<th>Pathologists</th>
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<tbody>
<tr>
<td>Lawrence Kirschner</td>
<td>Linda Vaders</td>
<td>Wendy Frankel</td>
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<td>Manisha Shah</td>
<td>Paul Wakely</td>
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<td>Chad Galbraith</td>
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<td>Dori Klemanski</td>
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<td>Gail Davidson</td>
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<td>Medical Oncologists</td>
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<td>Manisha Shah</td>
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<td>Rich Goldberg</td>
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<td>Tanios Bekaii-Saab</td>
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<td>Interventional Oncologists</td>
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<td>Hooman Khabiri</td>
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<td>Gregory Guy</td>
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<td>Ali Rikabi</td>
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<td>Jamal Al Taani</td>
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<td>Surgical Oncologists</td>
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<td>Mark Bloomston</td>
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<td>Carl Schmidt</td>
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<td>Sherif Messiheldin</td>
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<td>Christopher Ellison</td>
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Patients & Families

Radiation Oncologists

Clinical Trials Office

Minden Collamore

Katie Warden

Geneticists

Albert de la chapelle
# Current Status of Vena Cava Filters in the Emerging Era of Retrievable Filters

Gregory E. Guy, M.D.  
Assistant Professor of Radiology  
Section of Interventional Radiology  
The Ohio State University College of Medicine

## OUTLINE

- Brief history of venous/IVC interruption  
- Evolution of vena cava filters  
- Expanding list of indications for filter placement  
- Growing number of vena cava filters placed annually  
- Introduction of retrievable vena cava filters
### VENOUS/IVC INTERRUPTION
#### MECHANICAL PREVENTION OF VTE

- Femoral vein ligation (late 1800s-1900s)
- IVC ligation (early-mid 1900s)
- Vena cava compartmentalization (mid-1900s)- sutures, clips, etc
- Vena cava filters (1960s-now)

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### MECHANICAL PREVENTION OF VTE
#### REASONS FOR FAILURE

- Contralateral disease
- Collateral vein formation
- Surface thrombus
### MECHANICAL PREVENTION OF VTE

#### REASONS FOR FAILURE

- Operative morbidity and mortality
- Venous stasis
- Abrupt decrease in systemic venous return

### MECHANICAL PREVENTION OF VTE

#### VENA CAVA FILTERS

- Mobin-Uddin umbrella (1967) percutaneous insertion 1974
  - Unacceptable rates of IVC thrombosis
  - Elevated “downstream” pressure
  - “Upstream” surface thrombus
<table>
<thead>
<tr>
<th>MECHANICAL PREVENTION OF VTE VENA CAVA FILTERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Greenfield vena cava filter (1973)</td>
</tr>
<tr>
<td>• percutaneous insertion 1984</td>
</tr>
<tr>
<td>• para-axial flow (intrinsic thrombolysis)</td>
</tr>
<tr>
<td>• over the wire delivery</td>
</tr>
<tr>
<td>• sheath 29.5 Fr OD</td>
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<table>
<thead>
<tr>
<th>VENA CAVA FILTERS CURRENT PERMANENT DEVICES</th>
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<tbody>
<tr>
<td>• Greenfield- steel 15 Fr.</td>
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<tr>
<td>• Greenfield- titanium 14.3 Fr.</td>
</tr>
<tr>
<td>• Bird’s nest 14 Fr.</td>
</tr>
<tr>
<td>• VenaTech 14.6 Fr.</td>
</tr>
<tr>
<td>• VenaTech LP 9 Fr.</td>
</tr>
<tr>
<td>• Simon nitinol 9 Fr.</td>
</tr>
<tr>
<td>• Trapease 8 Fr.</td>
</tr>
<tr>
<td>VENA CAVA FILTERS</td>
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<tr>
<td><strong>ABSOLUTE INDICATIONS</strong></td>
</tr>
<tr>
<td>• Contraindication to anticoagulation</td>
</tr>
<tr>
<td>• Complication of anticoagulation</td>
</tr>
<tr>
<td>• Failure of anticoagulation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VENA CAVA FILTERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RELATIVE INDICATIONS</strong></td>
</tr>
<tr>
<td>• <em>Massive PE</em></td>
</tr>
<tr>
<td>• <em>Iliofemoral thrombus</em></td>
</tr>
<tr>
<td>• Chronic or recurrent PE w/ PAHTN</td>
</tr>
<tr>
<td>• Patient non-compliance</td>
</tr>
<tr>
<td>• Unsteady gait or ataxia</td>
</tr>
<tr>
<td>• Venous thrombolysis</td>
</tr>
<tr>
<td>• Primary (spinal cord injury, multi-trauma)</td>
</tr>
<tr>
<td>• Peri-operative (primary or secondary)</td>
</tr>
</tbody>
</table>
### VENA CAVA FILTERS
#### SUMMARY OF TRENDS
#### LATE 1980s-EARLY 2000s

- Lower profile delivery systems
- Expanding indications

### VENA CAVA FILTERS TRENDS

- NHRS database 1979-1999
  - ~25x increase in annual VCF placements
- Single institution study 1995-2005
  - ~6x increase in annual VCF placements
- Increase in transient indications
- Increase in primary prevention
  - >50% multiple recent series
### VENA CAVA FILTERS
**RETRIEVABLE FILTERS**

- US approval ~2003
- All approved for permanent use
- Low rates of PE and IVC thrombosis
- High retrieval rates
- No maximum dwell time to retrieve

### VENA CAVA FILTERS
**RETRIEVABLE FILTERS**

- Celect (Gunther tulip)
- G2 (Recovery)
- OptEase
- Option
- ALN
# RETRIEVABLE VENA CAVA FILTERS

**ASSUMPTIONS**

- Low procedural complication rate
- Effective
- Low/no long term complications
- Retrievable filters have similar performance to permanent filters

# VENA CAVA FILTERS

**PERMANENT FILTERS: META-ANALYSIS**

- Procedural complications 4-11%
- Recurrent PE 2-5%
- IVC thrombosis 0-28%
- IVC perforation 0-40%
- Tilting, migration, other

- *good data lacking*
### VENA CAVA FILTERS  
**PREPIC STUDY GROUP**

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>• NEJM, 1998</td>
<td></td>
</tr>
<tr>
<td>• Circulation, 2005</td>
<td></td>
</tr>
<tr>
<td>• Nearly 400 patients</td>
<td></td>
</tr>
<tr>
<td>• Randomized anticoagulation and IVC filter anticoagulation alone</td>
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</tbody>
</table>

### VENA CAVA FILTERS  
**PREPIC STUDY GROUP**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>• Filter group reduction in PE (significant at 12 days) increase in DVT (significant)</td>
<td></td>
</tr>
<tr>
<td>• No difference in mortality</td>
<td></td>
</tr>
<tr>
<td>• No difference in post-thrombotic changes</td>
<td></td>
</tr>
<tr>
<td>• No difference in overall incidence of VTE</td>
<td></td>
</tr>
</tbody>
</table>
### RETRIEVABLE FILTERS

- Approval data short term
- Retrieval rates as low as 10%
- Observations
  - fracture
  - migration
  - perforation
- “one device for all”

- *good data lacking*

### RETRIEVABLE FILTERS

#### OUTCOMES- REVIEW

- Retrieval  34% (12-45%)
- PE  1.3% (0.7-4%)
- DVT  5.4% (0.8-14%)
- IVC stenosis/thrombosis  2.8% (0.6-8%)
RETRIEVABLE FILTERS
OUTCOMES- REVIEW

- Fracture
- Migration
- Perforation

- Most occurred >30 days after placement
## RETRIEVABLE FILTERS

### OUTCOMES

- Retrieval success inversely related to dwell times
- Reports of successful retrieval at long (years) dwell times

### REASONS FOR NON-RETRIEVAL

- No intent to retrieve
- Lost to follow-up
- Patient refusal
- Death
- Lack of familiarity
## RETRIEVABLE FILTERS
### REASONS FOR FAILURE TO RETRIEVE

- Trapped thrombus
- Incorporation into IVC wall (hook)
- Failure of strut collapse
- ?IVC perforation

## RETRIEVABLE FILTERS
### TRAPPED THROMBUS

- Controversy re: how much thrombus is “safe” to retrieve
- Options
  - retrieve vs initiate/continue anticoagulation
  - re-assess for retrieval
- Duration of anticoagulation unknown
### RETRIEVABLE FILTERS
#### PROPOSED ALGORITHM FOR RETRIEVAL

- Primary prevention (prophylactic)
- Secondary prevention (therapeutic)

### RETRIEVABLE FILTERS
#### ALGORITHM- PRIMARY

- Lower extremity venous duplex exam
- Bilateral iliac venograms
- IVC’gram
- Attempt retrieval
RETRIEVABLE FILTERS
ALGORITHM- SECONDARY

- Resume full anticoagulation
- IVC’gram
- Attempt retrieval
VENA CAVA FILTERS
SUMMARY OBSERVATIONS

- Vena cava filters are effective
- All filters may have complications
- The exact long term role of vena cava filters is unknown
- The long term performance of retrievable vena cava filters is evolving
RETRIEVABLE FILTERS
SUGGESTIONS

• More discriminate selection of filter type
• Better follow-up of filter patients
• Improve retrieval rates
dedicated follow-up “service”
?automated note on DC instructions
more widespread familiarity of devices