Interventional Oncology

Hooman Khabiri, MD
Assistant Professor of Clinical Radiology
Interventional Radiology
Ohio State University Medical Center

Trans-arterial Liver-directed Therapies for Metastatic NET

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

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)

Rinke et al, JCO 2009

When to Intervene?

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

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

How to Treat?

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

Gauer et al; Cardiovasc Intervent Radiol (2011) 34:566-572

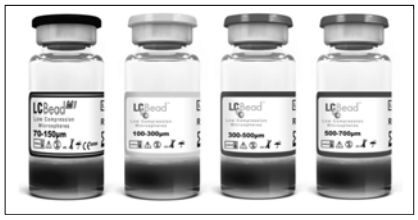
Why Bland Embolization?

- 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)

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

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

(Ruutiainen: 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)

TACE: CAM

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

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

Mark Bloomston · Osama Al-Saif · Dori Klemanski · Joseph J. Pinzone · Edward W. Martin · Bryan Palmer · Gregory Guy · 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

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

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)

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

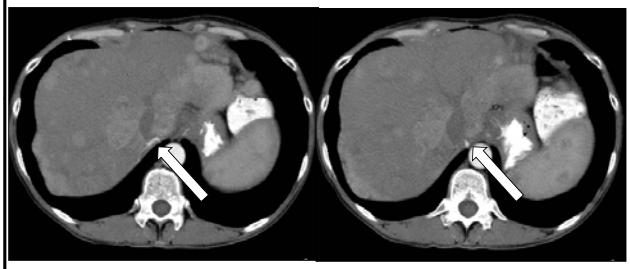
Contraindications

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

Causes of Failure

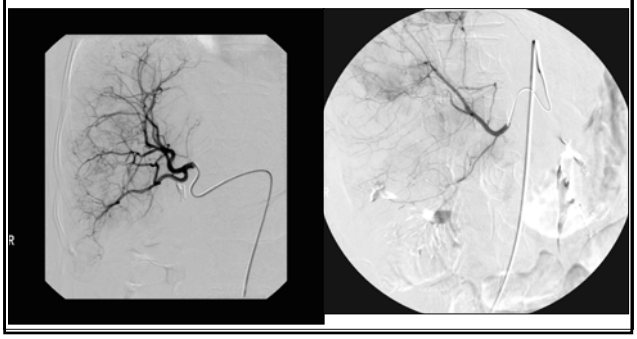
- ?Poorly Vascularized Metastases
- Failure of TACE or failure to TACE?
- Failure in the dome:
  - Phrenic artery?
- Failure in the left lobe:
  - Left hepatic artery variant
- Intercostal Arteries

Unresponsive Lesions



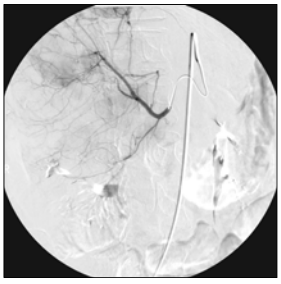
Post-embolization changes

Fresh Repeat

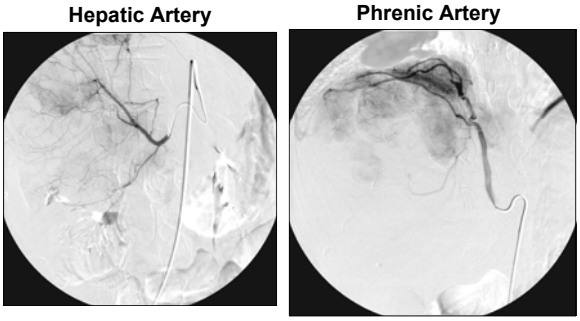


Non-hepatic Arterial Supply

Hepatic Artery Phrenic Artery

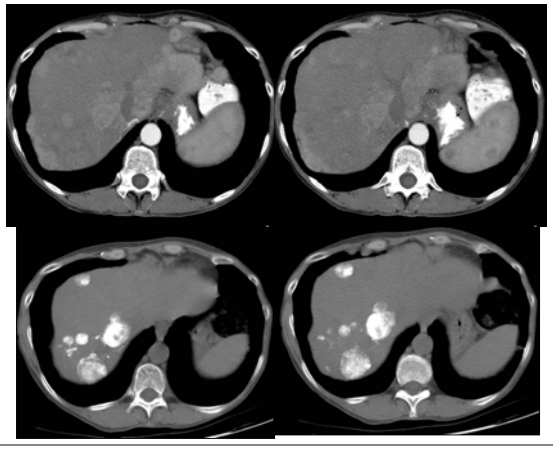


Non-hepatic Arterial Supply



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

DC Bead Before and After Loading with Doxorubicin

Prior to Loading

Loaded with Doxorubicin

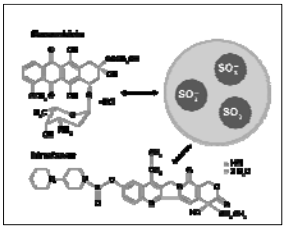
Loaded with Doxorubicin in Syringe

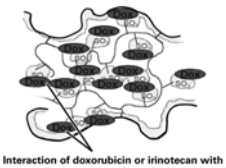
Drug-Eluting Beads

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

DC Bead 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_3^- groups displaces water from the hydration shells

DEB TACE

Year	Author	N	Outcome
2008	de Baere et al	20	PFS 15m
2011	Whitney et al	28	PFS 18m, OS 25m
2011	Gaur et al	18	PFS 14m

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

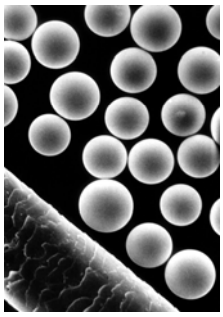
Yttrium-90 Microspheres

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

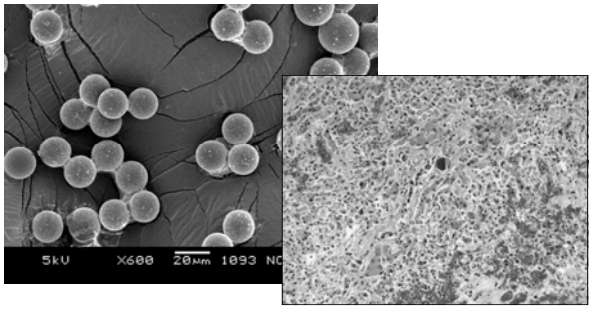
DEB TACE

- **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



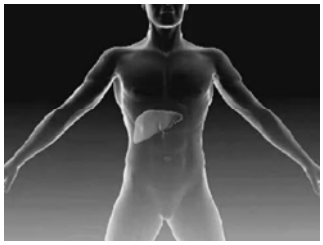
Microspheres



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)*

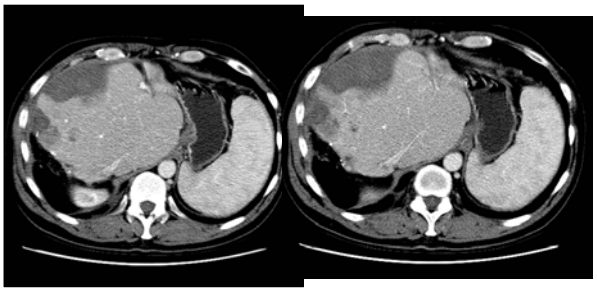


"Video used with permission from Nordion (Canada) Inc."

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

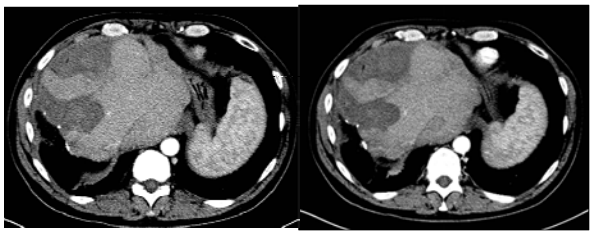
Ablation



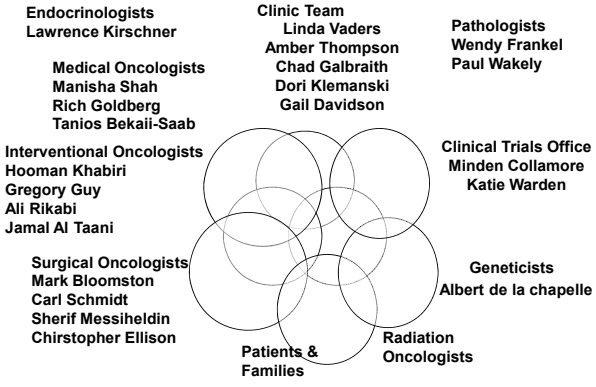
Ongoing Questions

- 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

Post Ablation



Ohio State University NET Program



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

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)

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

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

- Greenfield vena cava filter (1973)
  percutaneous insertion 1984
  para-axial flow (intrinsic thrombolysis)
  over the wire delivery
  sheath 29.5 Fr OD

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

VENA CAVA FILTERS CURRENT PERMANENT DEVICES

- Greenfield- steel 15 Fr.
- Greenfield- titanium 14.3 Fr.
- Bird's nest 14 Fr.
- VenaTech 14.6 Fr.
- VenaTech LP 9 Fr.
- Simon nitinol 9 Fr.
- Trapease 8 Fr.

VENA CAVA FILTERS
ABSOLUTE INDICATIONS

- Contraindication to anticoagulation
- Complication of anticoagulation
- Failure of anticoagulation

VENA CAVA FILTERS
SUMMARY OF TRENDS
LATE 1980s-EARLY 2000s

- Lower profile delivery systems
- Expanding indications

VENA CAVA FILTERS
RELATIVE INDICATIONS

- *Massive PE*
- *Iliofemoral thrombus*
- Chronic or recurrent PE w/ PAHTN
- Patient non-compliance
- Unsteady gait or ataxia
- Venous thrombolysis
- Primary (spinal cord injury, multi-trauma)
- Peri-operative (primary or secondary)

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

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
RETRIEVABLE FILTERS

- Celect (Gunther tulip)
- G2 (Recovery)
- OptEase
- Option
- ALN

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

- NEJM, 1998
- Circulation, 2005
- Nearly 400 patients
- Randomized
  - anticoagulation and IVC filter
  - anticoagulation alone

RETRIEVABLE FILTERS

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

- *good data lacking*

VENA CAVA FILTERS
PREPIC STUDY GROUP

- Filter group
  - reduction in PE (significant at 12 days)
  - increase in DVT (significant)
- No difference in mortality
- No difference in post-thrombotic changes
- No difference in overall incidence of VTE

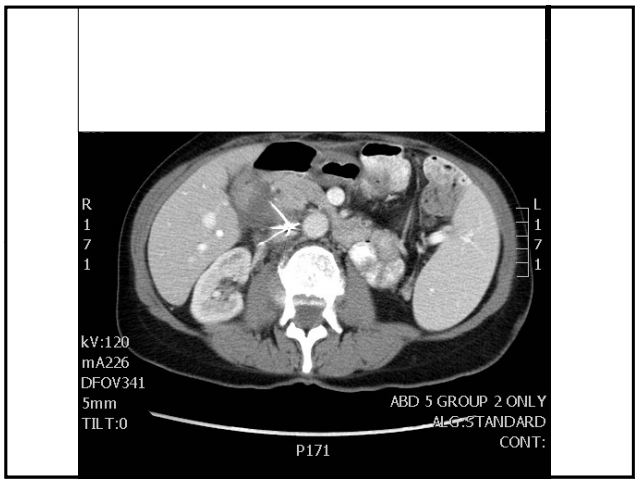
RETRIEVABLE FILTERS
OUTCOMES- REVIEW

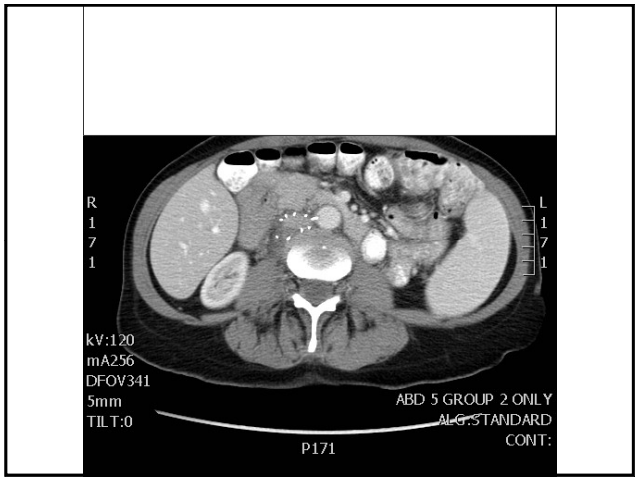
- Retrieval 34% (12-45%)
- PE 1.3% (0.7-4%)
- DVT 5.4% (0.8-14%)
- IVC stenosis/thrombosis 2.8% (0.6-8%)

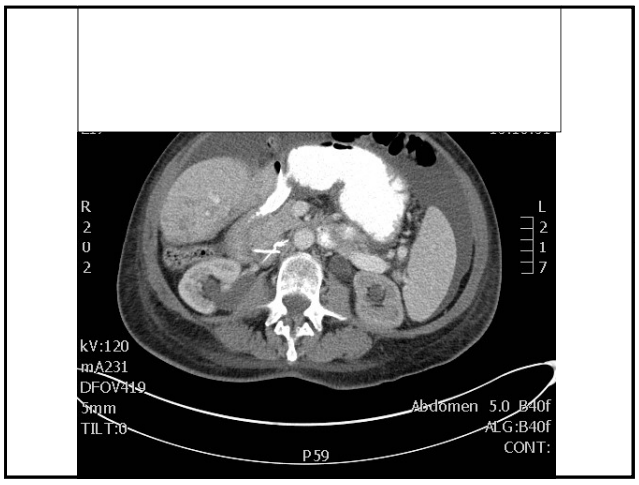
RETRIEVABLE FILTERS OUTCOMES- REVIEW

- **Fracture**
- **Migration**
- **Perforation**

- **Most occurred >30 days after placement**

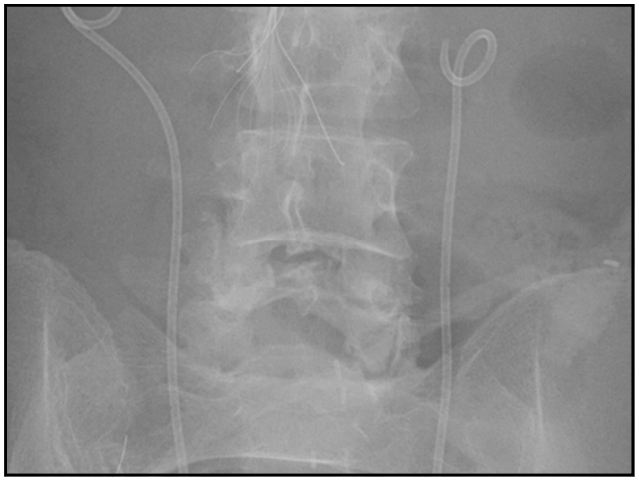

R
1
7
1
L
1
7
1
kV:120
mA226
DFOV341
5mm
TILT:0
ABD 5 GROUP 2 ONLY
ALG:STANDARD
CONT:
P171


R
1
7
1
L
1
7
1
kV:120
mA256
DFOV341
5mm
TILT:0
ABD 5 GROUP 2 ONLY
ALG:STANDARD
CONT:
P171



RETRIEVABLE FILTERS OUTCOMES

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



RETRIEVABLE FILTERS 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
- Incorportation into IVC wall (hook)
- Failure of strut collapse
- ?IVC perforation

RETRIEVABLE FILTERS
PROPOSED ALGORITHM FOR RETRIEVAL

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

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
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

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

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