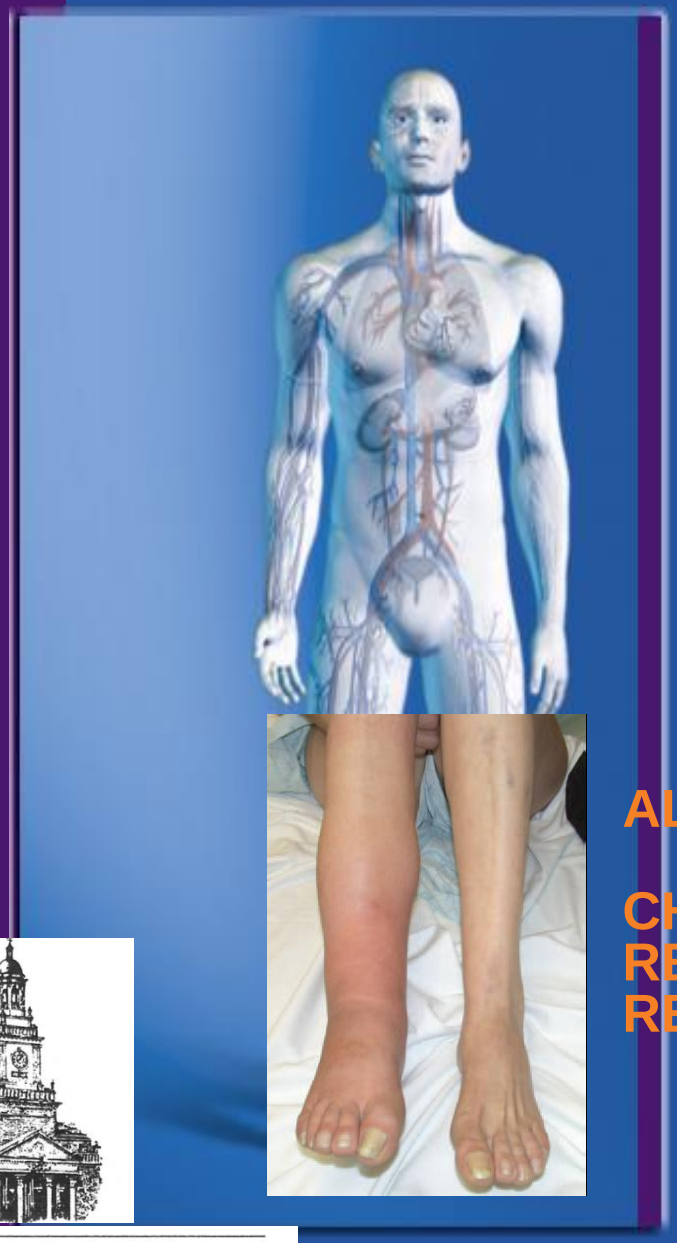
CACVS 2018



Endovascular Management of DVT: Has Anything Changed with ATTRACT Trial?

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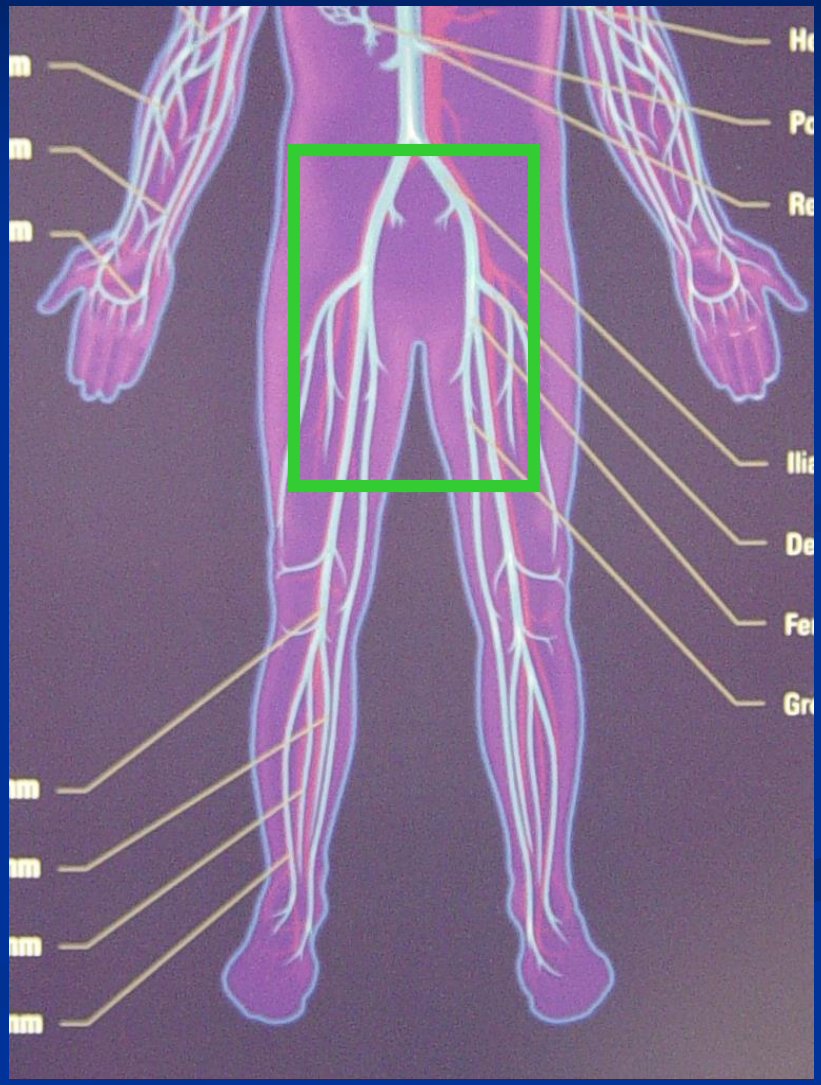
Venous Thromboembolism (DVT & PE)

- >2 million Deep vein thrombosis
- >200,000 deaths from pulmonary embolism
- Even after 6 months of anticoagulation following first VTE event, risk of subsequent VTE is increased by 5-12% annually.

Ilio-Femoral DVT

Endovascular Specialists:

- View ilio-femoral DVT as fundamentally different from physiologic considerations as well as more severe disease manifestation
- BUT it is rarely distinguished from other forms of DVT by other physicians.



Post thrombotic syndrome

- Most physicians treat all cases of proximal DVT the same.
- MUST differentiate between iliofemoral DVT and infrainguinal DVT.
- Iliofemoral DVT ⟶ Virulent post-thrombotic morbidity.

20 -60% of Pts with DVT
800,000/Yr cases of Post-Thrombotic Syndrome

Incidence and cost burden of post-thrombotic syndrome.
AU
Ashrani AA, Heit JA
J Thromb Thrombolysis. 2009 Nov;28(4):465-76.

Post Thrombotic Syndrome

- Chronic leg heaviness
- Leg aching
- Venous claudication
- Edema
- Venous varicosities
- Chronic skin changes
- Ulceration

Ilio-Femoral DVT
Long Term Clinical Status and QOL

- ***Conclusions***
- Venous claudication developed in almost 50%
- Limited ambulation in 15%
- Marked hemodynamic impairment
- Markedly reduced QOL

Delis KT et al
Ann Surg 2004;239(1):118

Ilio-Femoral DVT
Treatment Objectives

- Minimize or eliminate the Embolic potential of the existing Thrombus
- Prevent further Thrombosis

- Restore Venous Patency (remove obstruction)
- Preserve Venous Valvular function

Anticoagulation

DOES

- Minimize or eliminate the Embolic potential of the existing Thrombus
- Prevent further Thrombosis

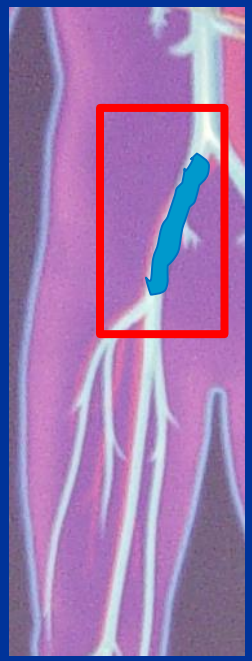
DOES NOT

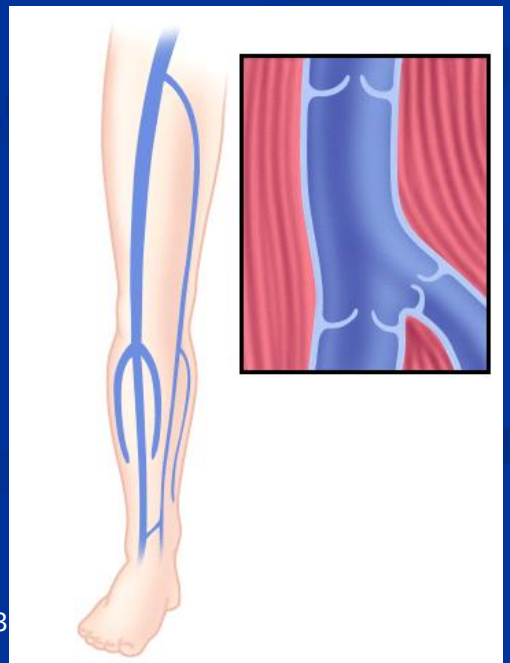
- Restore Venous Patency (remove obstruction)
- Preserve Venous Valvular function

Ilio-Femoral DVT
Ambulatory Venous Hypertension

Combination of Obstruction + Valvular Incompetence

Highest Venous Pressure and most severe morbidity





Indications for Endovascular Therapy

- Functional patient with ilio-femoral DVT
- No Major risk factors for the use of thrombolytic
- “But” can use Mechanical Thrombectomy
- Need to be anticoagulated with Heparin and Coumadin
- Phlegmasia Cerulea Dolens

Ilio-Femoral DVT
Improved Outcome with Early Resolution

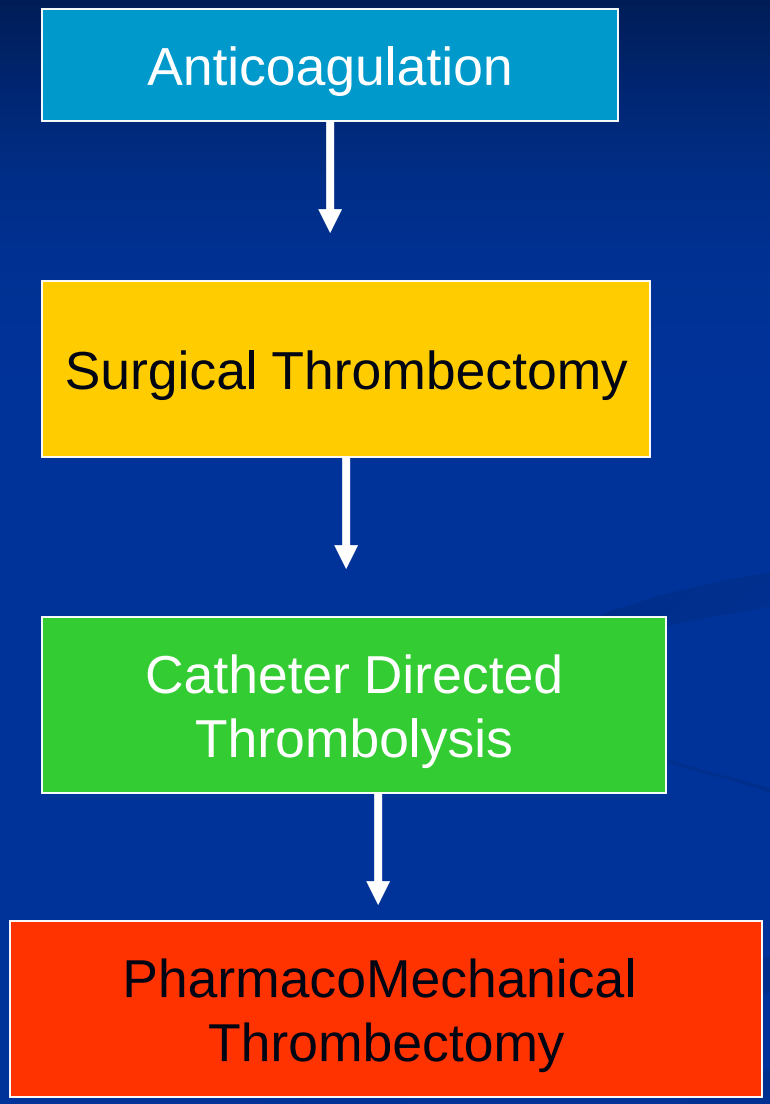
Randomized Trial: Iliofemoral DVT
Venous Thrombectomy vs. Anticoagulation
(Follow-up @ 6 mos, 5 yrs, 10 yrs)

- **Patients randomized to thrombectomy showed:**
  1. Improved patency — $P < 0.05$
  2. Lower venous pressures — $P < 0.05$
  3. Less leg swelling — $P < 0.05$
  4. Fewer post-thrombotic symptoms — $P < 0.05$

Compared to anticoagulation

Plate G, et al. *JVS*; 1984
Plate G, et al. *Eur J Vasc Surg*; 1990
Plate G, et al. *Eur J Vas Endovasc Surg*; 1997

Mangagment of Ilio-Femoral DVT



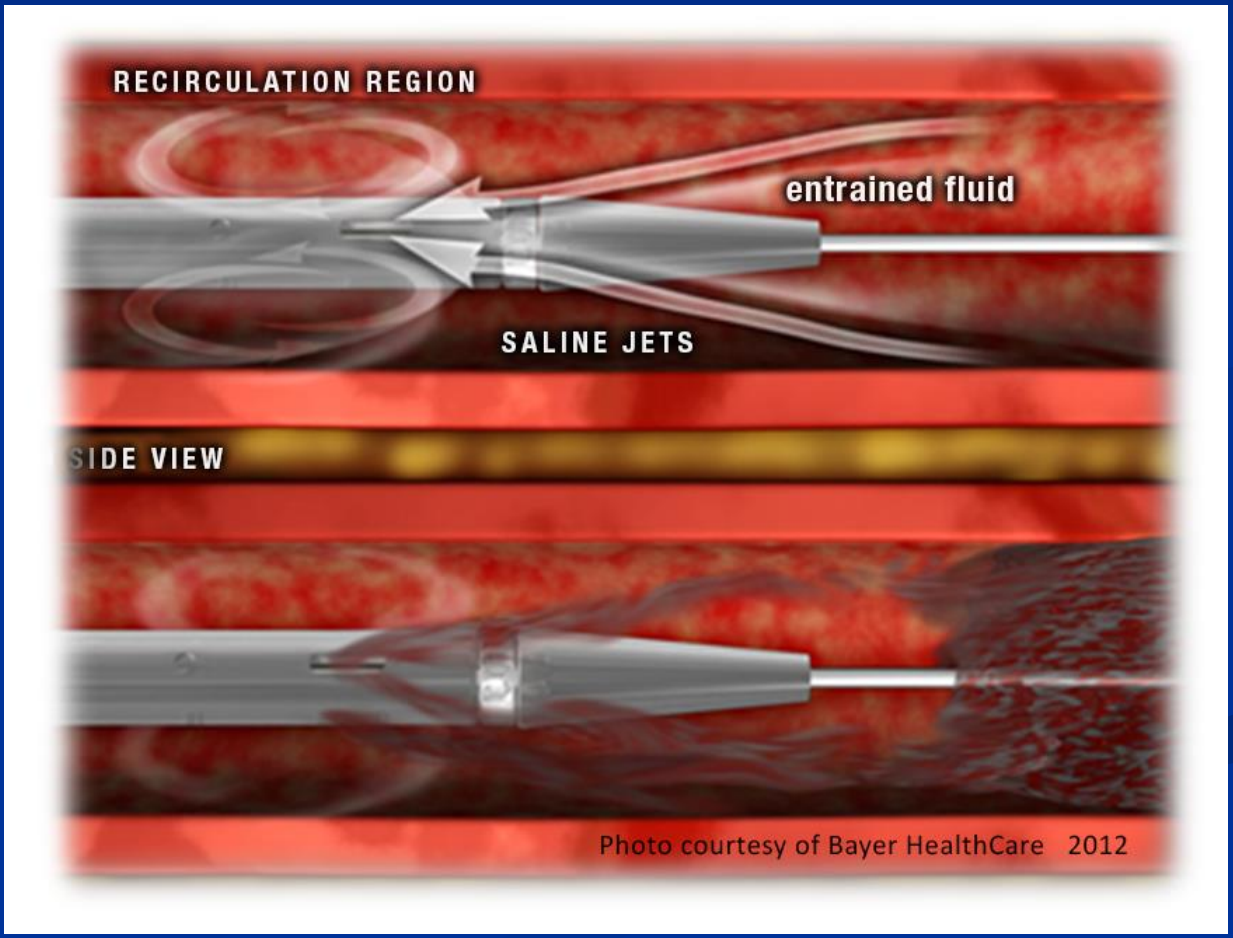
Combination of Mechanical Thrombectomy and Thrombolysis

- Combination therapy is even more Powerful
- Initially reduces more thrombus burden
- Exposes a greater area of the thrombus surface to lytic agent
- Decrease Dose and Infusion time for thrombolytic drugs
- One Retrospective study, PMT greatly reduced both time of lysis (40% reduction) and Lytic drug dose (60% reduction).

Device/ Techniques

Popliteal Vein

Treating DVT with AngioJet



Treating DVT: Meet the Players

EKOS Lysis System

PEARL Comparison

Treatment of LE DVT

		PEARL	Venous Registry*	CaVenT**	
				CDT	STD
Onset of DVT Symptoms	Acute	67% (≤14 days)	66% (≤10 Days)	100% ≤21 days	
	Chronic	33% (>14 days)	16% (>10 Days)	NA	
	Acute & Chronic	NA	19%	NA	
Primary Lytic		TPA	Urokinase	TPA	NA
CDT Drip Times *(mean)*		17 hrs	48 hrs	57.6 hrs (2.4 days)	NA
Procedure Times	CDT (N=29)	40.9 hrs	NA	NA	NA
	CDT+PPS/RL (N=172)	22.0 hrs	NA	NA	NA
	PPS/RL (N=115)	2.0 hrs	NA	NA	NA
Bleeding Complications		5% (major & minor combined)	11% (major); 16% (minor)	22% (major & minor combined)	0%

*Mewissen MW, Seabrook GR. Radiology 1999:211:39-49

**Enden , Haig Y. . Lancet 2012:379:31-38

PEARL Comparison

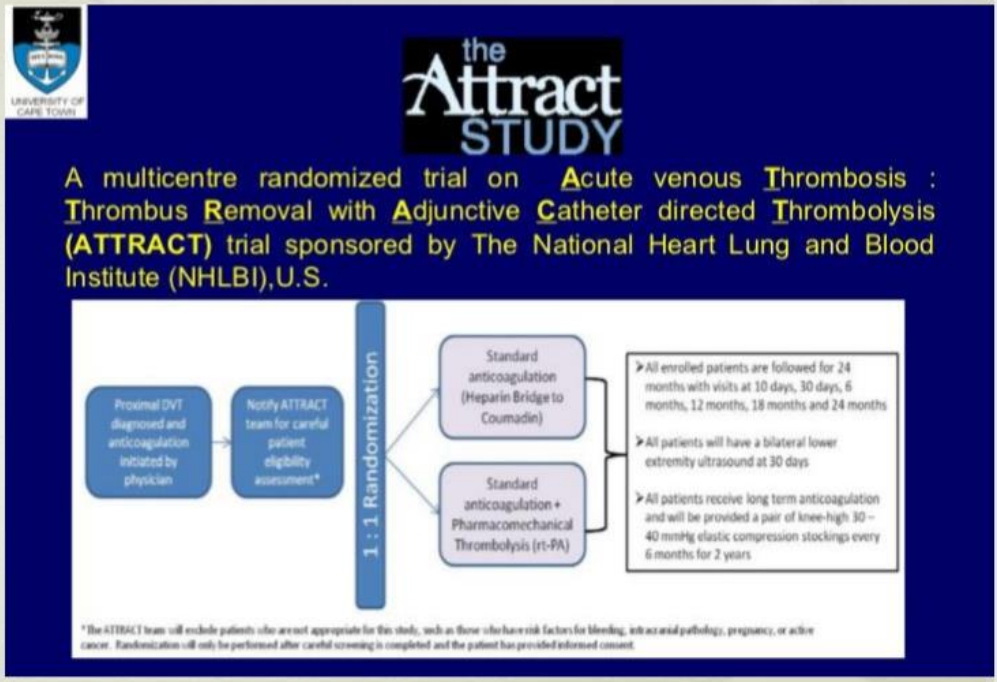
Treatment of LE DVT

		PEARL	Venous Registry*	CaVenT**	
				CDT	STD
Overall % Thrombus Removal		96%	83%	89%	NA
By Lytic Groups: % thrombus Removal	CDT (N=28)	93%	NA	NA	
	CDT+PPS/RL (N=167)	97%	NA	NA	
	PPS/RL (N=113)	95%	NA	NA	
Acute: % Thrombus Removal		97%	86%	89%	
Chronic: % Thrombus Removal		95%	68%	NA	
Acute & Chronic: % Thrombus Removal		NA	76%	NA	
Primary Patency		NA	6 Mon=65%; 12 Mon=60%	6 Mon = 65.9%	6 Mon = 47.4%
Freedom from Rethrombosis		6 Mon= 87%; 12 Mon=83%	NA	NA	NA

*Mewissen MW, Seabrook GR. Radiology 1999:211:39-49
**Enden , Haig Y. . Lancet 2012:379:31-38

The “Open Vein Hypothesis”

- Development of PTS is associated with persistent venous thrombosis
- Does active elimination of DVT prevent PTS?
- Support comes from studies linking:
  - Poor thrombus clearance to venous valve dysfunction and recurrent VTE[8,9]
  - Residual venous thrombus or valve incompetence and PTS[10]
  - Systemic thrombolysis, surgical thrombectomy or CDT to reduced incidence of PTS[11-14]



ATTRACT Trial Design

- Multicenter, randomized, open-label, assessor-blinded, parallel two-arm, controlled clinical trial sponsored by National Heart, Lung, and Blood Institute of the U.S. National Institutes of Health

- SIR Foundation, Boston Scientific, BSN Medical, Covidien/Medtronic, and Genentech provided additional support

- 692 subjects enrolled in 56 US Centers followed for 24 mo
  - 337 randomized to PCDT
  - 355 randomized to no PCDT

ATTRACT Trial Objectives

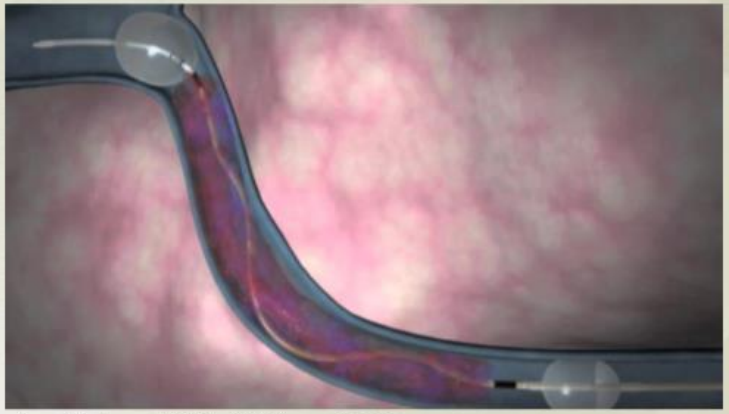
- Primary objective:
  - Determine if PCDT with standard DVT therapy reduces development of PTS after 24 month follow-up compared to standard DVT therapy alone
- Secondary objectives:
  - Evaluate for major bleeding, symptomatic VTE and death
  - Venous disease-specific QOL
  - Relief of acute DVT symptoms
  - Pretreatment predictors of response to PCDT in preventing PTS
  - Compare medical costs and cost-effectiveness
  - Determining technical, anatomical and physiologic endpoints of therapy

ATTRACT Trial – Standard DVT Therapy

- Weight-based low molecular weight heparin or IV unfractionated heparin then Warfarin
- International guidelines for INR 2-3, duration of therapy (3 months or longer)
- 30-40 mmHg knee-high elastic compression stockings at 10 day follow-up

ATTRACT Trial – PCDT Intervention

- One of three methods for rt-PA delivery (max 25 mg initially; max 35 mg total)
  1. "Isolated Thrombolysis" with Trellis Peripheral Infusion System (Covidien, Inc.)
  2. "PowerPulse Thrombolysis" with AngioJet Rheolytic Thrombectomy System (Boston Scientific)



https://i.ytimg.com/vi/50LzxuleYUc/maxresdefault.jpg

ATTRACT Trial – PCDT Intervention

- One of three methods for rt-PA delivery (max 25 mg initially; max 35 mg total)
  3. "Infusion-First Thrombolysis" with multisidehole catheter through thrombus, up to 1 mg/h rt-PA for max 30 hours
     - Subsequent therapy with balloon maceration, aspiration thrombectomy and/or mechanical thrombectomy allowed for residual thrombus

http://www.angiodynamics.com/images/userfiles/Unifuseillustration.jpg

ATTRACT Trial – Endpoints and Efficacy

- ≥90% thrombus clearance with restored flow
- 35 mg maximum rt-PA dose or 30 h maximum infusion time reached
- Overt clinical bleeding or other complications necessitating cessation

- Evaluation for PTS in index limb at 6-24 months after randomization
- Villalta PTS scoring used
  - Combines patient and clinician evaluation
  - PTS defined as Villalta score > 5 or presence of ulcer

ATTRACT Trial
Initial Result SIR 2017

- PCDT not found to reduce incidence of PTS compared to AC alone
  - PTS 46.7% for PCDT vs 48.2% for no-PCDT (p= 0.56)
  - Recurrent VTE higher in PCDT vs no-PCDT (12.5% vs 8.5%; p=0.09)
  - Major and any bleeding rates statistically higher in PCDT arm (1.7% vs 0.3%; p=0.49 and 4.5% vs 1.7%; p=0.034) – in line with prior studies
    - NO intracranial or fatal hemorrhages

ATTRACT Trial – Initial Results SIR 2017

- IFDVT vs femoropopliteal DVT (FPDVT)
  - Trends to more benefit in IFDVT
  - Study not powered to sufficient power to statistically significant differences between subgroups

Good News

- Leg pain and swelling significantly improved in PCDT vs. no-PCDT out to 30 days (p=0.019 and p=0.05)
  - PCDT helpful for acute symptoms
- 25% fewer patients in PCDT arm developed moderate or severe PTS vs no-PCDT (17.9 % vs 23.7%; p=0.035)
  - “Open Vein hypothesis”

Good News

- In IFDVT mod-severe PTS was 18.4% vs 28.2% in PCDT vs no-PCDT
- In FPDVT little difference (17.1% vs 18.1% moderate to severe PTS)
- PCDT was less effective in patients ≥ 65 y/o

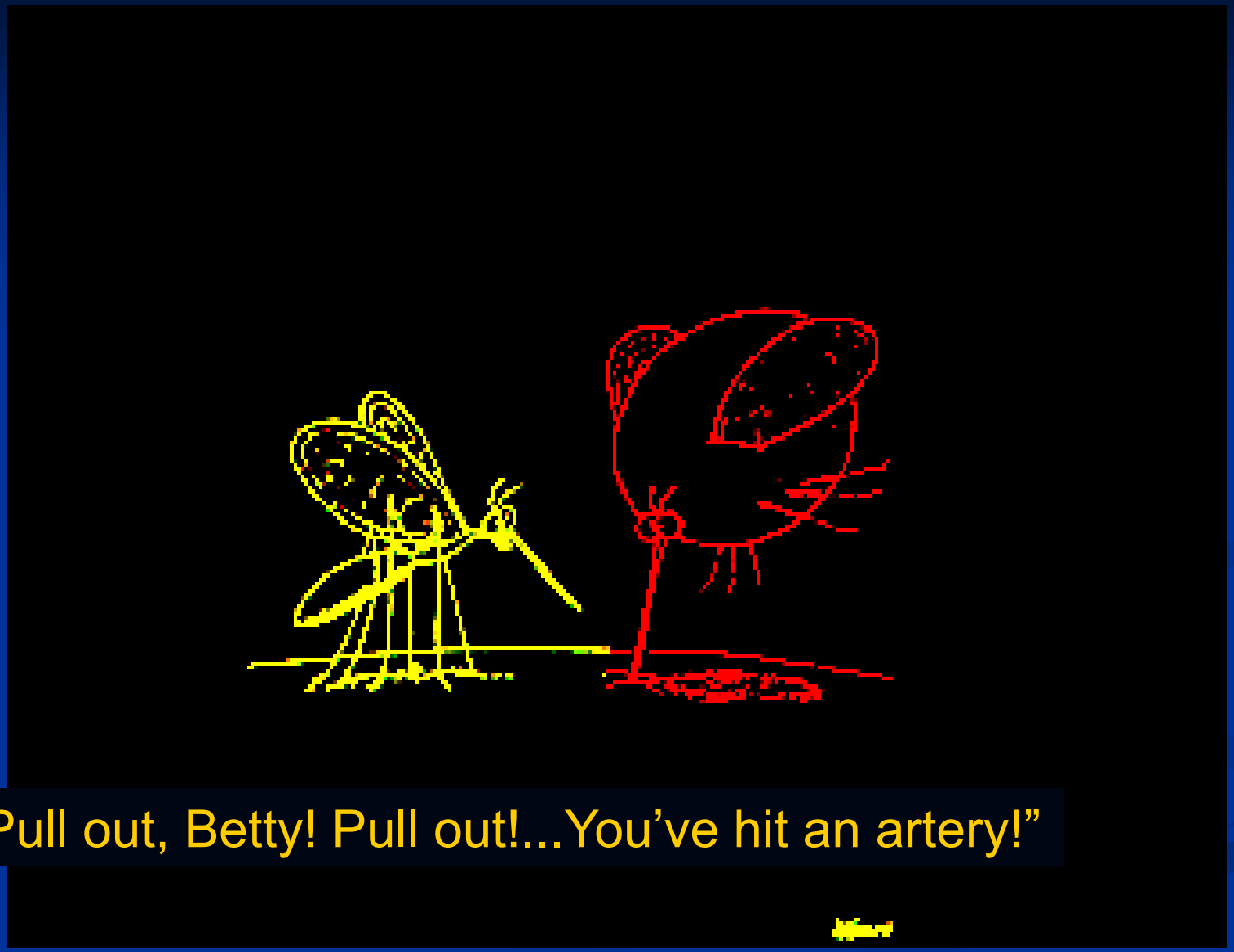
ATTRACT Summary and Learning Points

ATTRACT Trial Summary and Learning points

- Ambitious well-designed RCT, failed primary endpoint, but not the end
- Helps us strategize for appropriate care
- Who to and not to treat
  - Same as CaVenT: iliofemoral DVT, younger and functional patients
  - Femoropopliteal DVT alone patients do not derive same benefit
  - Older patients do not derive same benefit
  - Prevent bleeding and cost in inappropriate patients

Summary: Acute Ilio-Femoral DVT

- Medical management is associated with higher PTS compare to endovascular management
- There is increasing evidence that early thrombus resolution with endovascular intervention is associated with improved outcome in Ilio-Femoral DVT
- Pharmacomechanical decreases procedure time, decrease amount of thrombolytic used


“Pull out, Betty! Pull out!...You’ve hit an artery!”