

***Controversies Surrounding the
Optimal Therapy for Extensive Leg
DVT: The Newly NHLBI-Funded
ATTRACT Trial***

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Disclosures

❖ **Research support for the ATTRACT Trial:**

- ❖ Bacchus Vascular - Financial Support
- ❖ BSN Medical (Jobst) - Donate Stockings
- ❖ Genentech - Donate Study Drug (rt-PA)
- ❖ Possis/MEDRAD - Financial Support

The ATTRACT Trial

- ❖ **Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis**
 - NHLBI-funded, Phase III, open-label, multicenter RCT
 - Pharmacomechanical Catheter-Directed Thrombolysis
 - 692 patients with symptomatic, acute proximal DVT
 - 28 U.S. Centers, enrollment to begin 4th quarter 2008
 - PI = Dr. Suresh Vedantham (Washington University)
 - Study Chair = Dr. Samuel Z. Goldhaber (Harvard)

Controversy

- ❖ ACCP (2004): Only when DVT => acute limb threat
 - Buller HR et al. Chest 2004; 126(3):401S-428S.
- ❖ SIR (2006): Use for ambulatory patients with acute iliofemoral DVT at low bleeding risk
 - Vedantham S et al. J Vasc Interv Radiol 2006.
- ❖ ACCP (2008): Extensive acute proximal DVT at low bleeding risk, good functional status (Grade 2B)
 - Kearon C et al. Chest 2008; 133:454S-545S.

***The Post-Thrombotic Syndrome
(PTS)***

Acute DVT is a Chronic Disease!

<u>Author/Yr</u>	<u>N</u>	<u>Journal</u>	<u>2-yr PTS</u>
Prandoni 1996	355	Ann Intern Med	23%
Brandjes 1997	96	Lancet	23%
Prandoni 2004	90	Ann Intern Med	25%
Partsch 2004	37	Int Angiol	46%
Van Dongen 2005	244	J Thromb Haemost	30%

IT'S THE CLOT, STUPID!

- ❖ Post-Tx change in clot burden predicts recurrent VTE
 - Prandoni P et al. Ann Intern Med 2002; 137:955-960. (n = 313)
 - Hull RD et al. Am J Med 2005; 1118:456-464. (analyzed 11 RCTs)
- ❖ Time to therapeutic PTT with UFH predicts recurrent VTE
 - Hull RD et al. Arch Intern Med 1997; 157(22):2562-2568.
- ❖ Early ambulation/compression reduces 2-year rate of PTS
 - Partsch H et al. Int Angiol 2004; 23:206-212. (small RCT)

Clot Removal Prevents PTS

<u>Author/Year</u>	<u>Intervention</u>	<u>PTS Rates</u>	<u>RRR</u>
Elliott 1979	Systemic SK	92% vs 35%	62%
Arnesen 1982	Systemic SK	67% vs 24%	64%
Plate 1984	Modern Surg Thrombectomy	93% vs 58%	38%
Turpie 1990	Systemic TPA	56% vs 25%	55%
AbuRahma 2001	CDT - UK/TPA	70% vs 22%	69%

Clot Removal Prevents PTS

❖ Successful clot lysis in > 85%; better 1-yr patency, long-term symptom resolution, & QOL; less reflux.

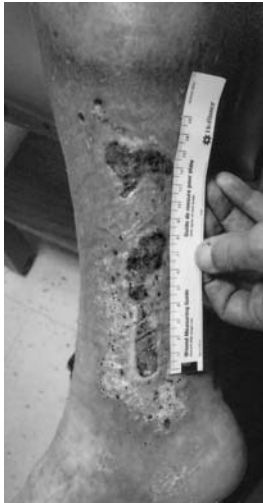
- Mewissen MW et al. Radiology 1999; 211:39-49.
- Comerota AJ et al. J Vasc Surg 2000; 32:130-137.
- AbuRahma AF et al. Ann Surg 2001; 233:752-760.
- Elsharawy M et al. Eur J Vasc Surg 2002; 24:209-214.

❖ BUT: Small studies, none were multicenter RCTs

1. Does PCDT Prevent PTS?

- ❖ **Primary Endpoint: Occurrence of PTS at 24 months follow-up (by the Villalta PTS Scale)**
- ❖ 80% power for 33% PTS reduction (5%, 2-sided)
- ❖ **Secondary Endpoint: PTS Severity**
 - Evaluate at 6, 12, 18, and 24 months.
 - Villalta, CEAP, Venous Clinical Severity Score

2. Does PCDT Improve LATE QOL



- ❖ Presence and severity of PTS correlate with impaired QOL in graded fashion
 - Kahn SR et al. Arch Intern Med 2002.
- ❖ PTS is lifelong, irreversible, costly via medical care & work disability
- ❖ **ATTRACT will assess general (SF-36) and disease-specific (VEINES) QOL at 6,12,18, and 24 months**

3. Does PCDT Improve EARLY QOL?

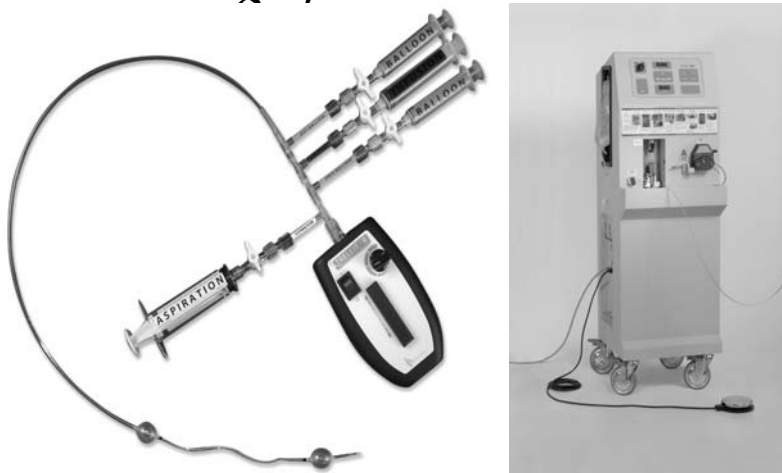


- ❖ Inflammation, congestion, and patient hardship are directly caused by the presence of clot!
- ❖ ATTRACT will evaluate leg pain (Likert scale), swelling (calf circumference), and early QOL (SF-36, VEINES-QOL measures) at 10 and 30 days

4. Is PCDT Safe Enough?

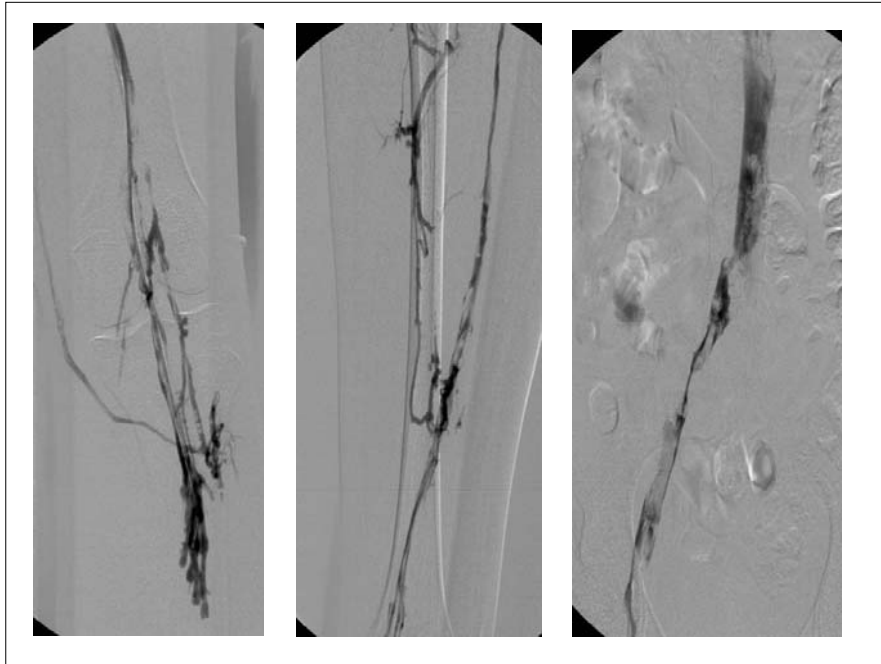
- ❖ Systemic thrombolysis trials => 14% major bleeds
 - Goldhaber SZ et al. Am J Med 1984; 76:393-397.
- ❖ CDT Registry => 11% major bleeds, 0.4% ICH
 - Mewissen MW et al. Radiology 1999; 211:39-49.
- ❖ ATTRACT will assess major bleeding, ICH, PE, recurrent VTE, and death at 10 days and 2 years

*Single-Session
Pharmacomechanical CDT: Safe
Enough for Prime-Time?*

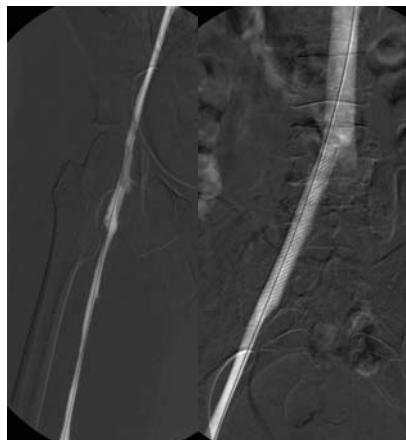


5. Is PCDT Cost-Effective?

- ❖ Economic outcomes will be compared, aided by a cost diary that all subjects will keep.
- ❖ If PCDT prevents PTS but is more costly, a formal cost-effectiveness analysis will be conducted to determine the incremental cost per quality-adjusted life-year (QALY) gained.



6. *Is Clot Removal the Key?*



- ❖ Can initial clot burden stratify long-term risk of PTS and tell us who should get PCDT?
- ❖ Does residual clot burden post-PCDT predict PTS risk?
- ❖ ATTRACT will quantitatively assess thrombus burden pre- and post-PCDT and enable these correlations to be made

7. Does PCDT "Save" Valves?

- ❖ Valvular reflux frequently seen in PTS patients
 - Markel A, et al. J Vasc Surg 1992; 15:377-384.
 - Prandoni P et al. J Thromb Haemost 2005; 3:401-402.

- ❖ CDT studies => valve function preserved
 - Elsharawy M et al. Eur J Vasc Surg 2002; 24:209-214.

- ❖ ATTRACT US Substudy (n = 142) will compare reflux rates and determine if reflux predicts PTS.

ATTRACT – Consider these Patients!

Include: Symptomatic Proximal DVT

- ❖ **EXCLUDE patients with:**
 - ❖ Higher bleeding risk, CNS lesions
 - ❖ Phlegmasia or massive PE
 - ❖ Symptom duration > 2 weeks
 - ❖ Same-leg DVT in the last 2 years
 - ❖ Non-ambulatory or short life-expectancy
 - ❖ Active cancer

ATTRACT - A Community Project

- ❖ NHLBI leadership in tackling PTS
- ❖ SIR Foundation – active collaboration
 - ❖ American Venous Forum
 - ❖ American College of Phlebology
- ❖ Industry: Bacchus, BSN, Genentech, Possis

❖ **INVESTIGATORS:**

- ❖ Radiology (52), Surgery (33), Internal Medicine (30), Emergency Medicine (28), Economics (1), Statistics (1)

Thanks to the ATTRACT Steering Committee!

- ❖ David Cohen, MD
- ❖ Anthony Comerota, MD
- ❖ Samuel Goldhaber, MD
- ❖ Heather Gornik, MD
- ❖ Jim Julian, PhD
- ❖ Michael Jaff, DO
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- ❖ Stephen Kee, MD
- ❖ Andrei Kindzelski, MD, PhD
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