

# Catheter Directed Thrombolysis

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Stanford Vascular Conference

9/12/05

# Catheter Directed Thrombolysis

- Background
- Patient selection
- Clinical Trials
- Techniques
- Adjuncts
- Future Directions

# Background

- History
  - First intravascular instillation 1955 – Tillet
  - First series 1965 - Clifton
  - Routinely utilized since '80's
  - Efficacy established by Berridge et al in 1991
    - Superiority of rt-PA, safety of catheter directed vs. systemic

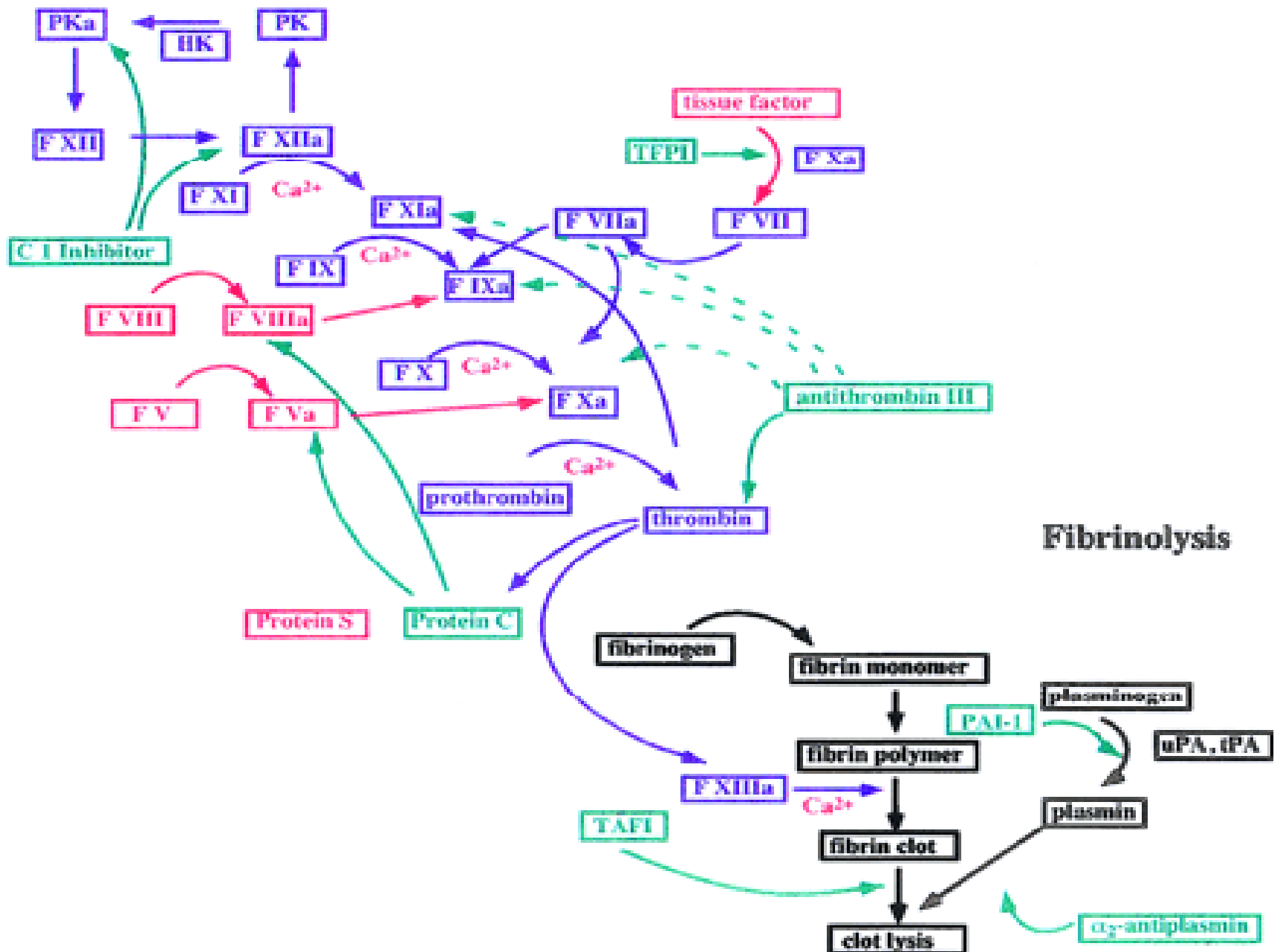


# Background

- Thrombolytic agents
  - Plasminogen activators
    - Cleave peptide bond to convert plasminogen to plasmin
    - Plasminogen delivered into thrombus
      - Lyses clot – breakdown of fibrinogen
      - Protected from inhibitors

## Contact Phase Activation (Intrinsic Pathway)

## Tissue Factor Pathway (Extrinsic Pathway)



# Background

- Thrombolytic Agents
  - Streptokinase
    - First described
    - Derived from Streptococcus
    - Antigenic potential – allergic reactions
    - Must bind with plasmin or plasminogen to activate and be able to convert second plasminogen to plasmin

# Background

- Thrombolytic Agents
  - Urokinase
    - Derived from human urine, kidney cells
    - Directly activates plasminogen
    - Non-antigenic
    - Recombinant form available
  - Prourokinase
    - Activated by plasmin to form urokinase
    - Amplification
    - Fibrin specific
      - Preferentially binds fibrin bound plasminogen in thrombus

# Background

- Thrombolytic Agents
  - Tissue plasminogen activator (t-PA)
    - Naturally produced by endothelial cells
    - Fibrin specific
    - Has been bioengineered to lengthen half-life
      - alteplase, reteplase

# Background

- Objectives of Catheter directed thrombolysis (CDT)
  - Dissolve thrombus and restore perfusion
  - Identify underlying lesion
  - Allow for definitive correction



# Background

## Secondary benefits

- Urgent to elective
- Re-establish inflow/outflow for bypass
- Convert major operation to less extensive
- Avoid intimal injury from balloon thrombectomy
- Establish patency for inaccessible small vessels
- Reduce level of amputation

# Patient selection

- Good candidates
  - Acute occlusion of relatively inaccessible vessels
  - Wound complications
  - Popliteal aneurysm acute thrombosis
  - Acute thrombosis in proximal arteries
  - Thrombosed SVG grafts (>1 yr old)

# Patient selection

- Poor Candidates
  - Acute embolus of large artery, easily accessible
  - Acute post-op bypass thrombosis
  - “modest ischemia”
  - Severe ischemia with limb viability imminently threatened

# Results

- Rochester Trial
  - Ouriel et al. 1994, single center, randomized
  - 114 pts with acute ischemia (<7days) randomized
    - Catheter directed thrombolysis (UK) vs operative revasc
  - Equal limb salvage at 1 year (80%)
  - Improved survival at 1 year of CDT (84% vs 58%)
    - Related to periprocedural cardiopulmonary complications
  - Equal 30 day mortality
  - 70% success of thrombolysis

# Results

- Surgery vs Thrombolysis for Ischemic Lower Extremity trial (STILE)
  - 393 pts randomized to surgery, rt-PA, or UK
  - No consideration of duration of ischemia
  - Halted at first data review
    - Equivalent 30 day death (5%) and amputation (6)
    - Significantly more morbidity with CDT (21% vs 16%)
    - CDT conveyed advantage for acute ischemia
    - Operative intervention better for chronic ischemia
  - No difference in safety/efficacy of urokinase vs rt-PA but shorter time to lysis with rt-PA (8 vs 16 hrs)

# Results

- Surgery vs Thrombolysis for Ischemic Lower Extremity trial (STILE)
  - More bleeding complications with CDT
    - Worse with lower fibrinogen or longer PTT
  - Surgery better for native iliofem or fempop dz
  - CDT better for acute graft ischemia
  - Highest risk patients (diabetic, infrapop, critical ischemia) randomized to CDT had survival advantage at 1 yr (7% vs 32% mortality)

# Results

- Thrombolysis Or Peripheral Arterial Surgery for acute ischemia (TOPAS)
  - 544 pts randomized to primary surgery vs. UK
    - Amputation free survival comparable at 1yr (68%)
    - Fewer major surgeries for CDT patients
    - Worse bleeding complications for CDT patients

# Results

- Consistent findings from STILE and TOPAS
  - 1-year mortality for acute limb ischemia 10-20%
  - Treatment of occluded grafts better outcome than treatment of native arteries
  - Risk of bleeding higher with CDT
    - Worse in proportion to induced coagulopathy
  - Risk of intracranial bleed 1-2% with CDT
  - CDT patients require fewer open surgical procedures

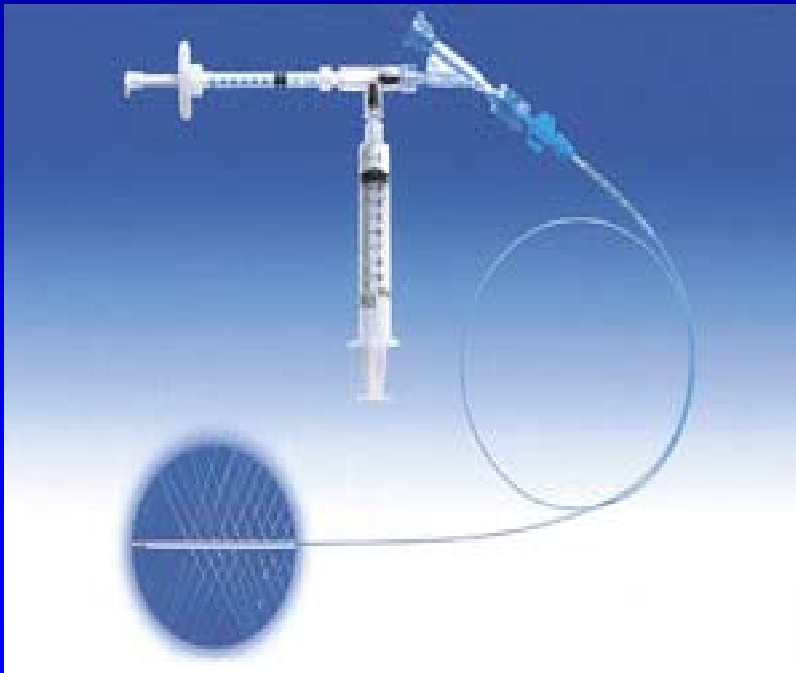
# Results (comparing CDT agents)

- PURPOSE Trial (Recombinant prourokinase vs. urokinase)
  - Bleeding dose dependent
  - Rate of in-hospital amputation or death worsened for distal embolization during CDT
- Rt-PA vs Urokinase for fem-pop dz–Mahler et al.
  - Integrated mechanical techniques
  - Rt-PA better for pure lysis
  - Results better with mechanical techniques as adjunct
    - C/w STILE trial
    - Dosing iniquity
- Better lysis with higher dose, bolus dosing

# Techniques

- Consensus Document for CDT in lower limb arterial occlusion - 1998
- Guide wire traversal test
  - Higher success if can traverse entire occluded vessel
- “thrombus lacing”
  - Higher success with intrathrombus bolus

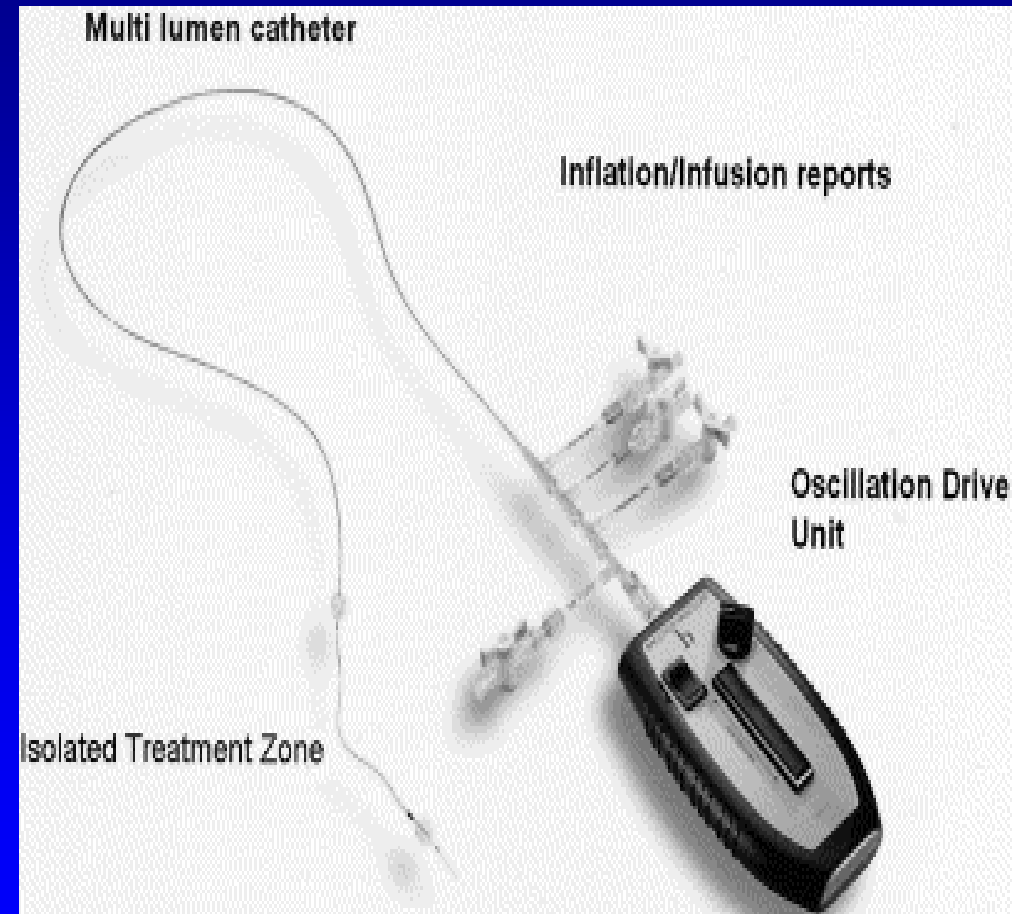
# Techniques



- “pulsed spray” – forceful injection
  - Increased working surface area
  - Once antegrade flow established, no benefit to additional pulsed spray vs infusion
  - Greenberg et al – in vitro model with PTFE comparing pulsed spray vs continuous infusion
    - Time to reperfusion less, more complete with infusion, more emboli than infusion

# Techniques

- Percutaneous mechanical thrombectomy
  - Device dependent
  - High risk patients not candidates for thrombolysis
  - Adjunct to CDT



Trellis thrombectomy device

# Adjuncts

- Platelet inhibitors
  - ASA
  - Plavix
  - GIIbIIIa inhibitors
    - Abciximab – fewer embolic episodes
- Heparin
  - Worsens bleeding if given systemically
  - No benefit if subtherapeutic
  - Intra-arterial use might lessen bleeding risk and deliver more beneficial dose

# Intra-operative CDT

- High degree of residual thrombus after balloon thrombectomy
  - Bolus and or infusion of thrombolytics is effective
    - 20-30 min
  - Isolated limb perfusion technique
  - Extra-corporeal pump

# Summary

- CDT is good first line therapy for appropriate patients
- CDT increases bleeding risk
  - 2% intracranial hemorrhage
- Acute limb ischemia is associated with significant morbidity/mortality
- Further device and agent investigation needed
- Intraoperative therapy can be valuable adjunct to surgery

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