

**EKOS<sup>®</sup> EndoWave<sup>™</sup>**  
**Ultrasound-Accelerated**  
**Thrombolysis System**

# How it works

- Ultrasound causes a reversible change to fibrin structure – elongates it and creates more space between clot components
- Allows lytic to access more of the clot.
  - Increased drug permeation
  - Constant infusion of fresh drug
  - Increased surface interaction



# Ultrasound-Enhanced Thrombolysis

- Low energy, high frequency (2 Mhz) ultrasound is radiated along the entire length of the infusion catheter (6-50cm.)
- Ultrasound does *not* fragment clot; it reversibly increases clot permeability to infused thrombolytic agents.
- Ultrasound power and local temperature are automatically controlled.



# EndoWave™ System

## 5F Peripheral System



6 - 50 cm Treatment Lengths



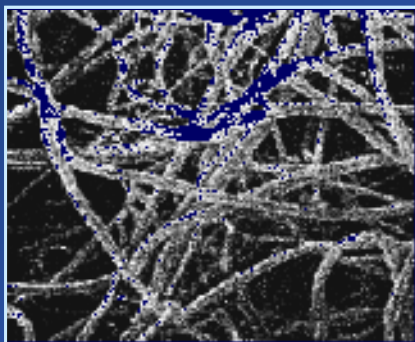
Portable Control Unit

# Ultrasound Accelerated Thrombolysis

## “Unlock the Clot” to Expose Receptor Sites

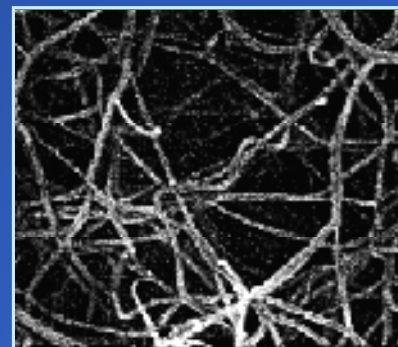
- **Primary Mechanism of Action**

- Ultrasound reversibly loosens fibrin strands, & reduces diameter ~ 44%.
- These physical alterations → 65% more individual strands are exposed.
- Dramatically increases thrombus permeability → exposes more plasminogen receptor sites for binding → faster fibrinolysis.
- No evidence of fibrin strand breakage/fragmentation → doesn't cause embolization.



Fibrin strands are tightly aggregated, impeding lytic penetration

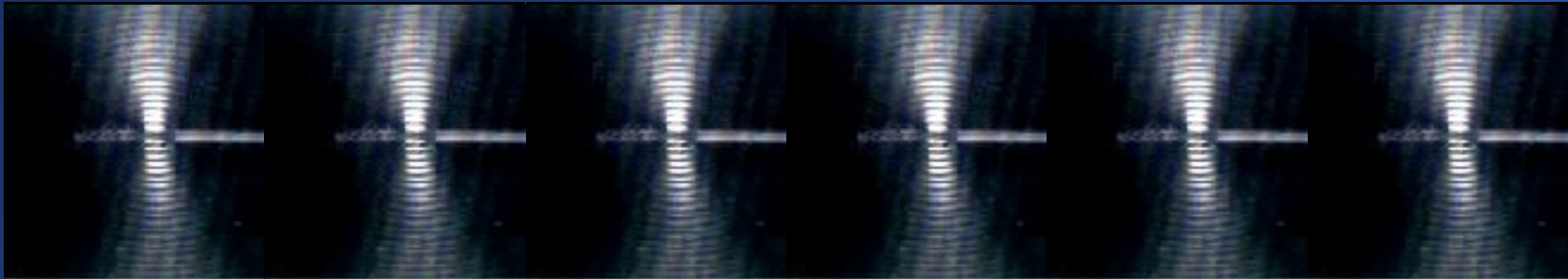
Without Ultrasound



Fibrin strands contract, promoting greater lytic penetration

With Ultrasound

# Acoustic Streaming



## EKOS 6 cm EndoWave® Catheter

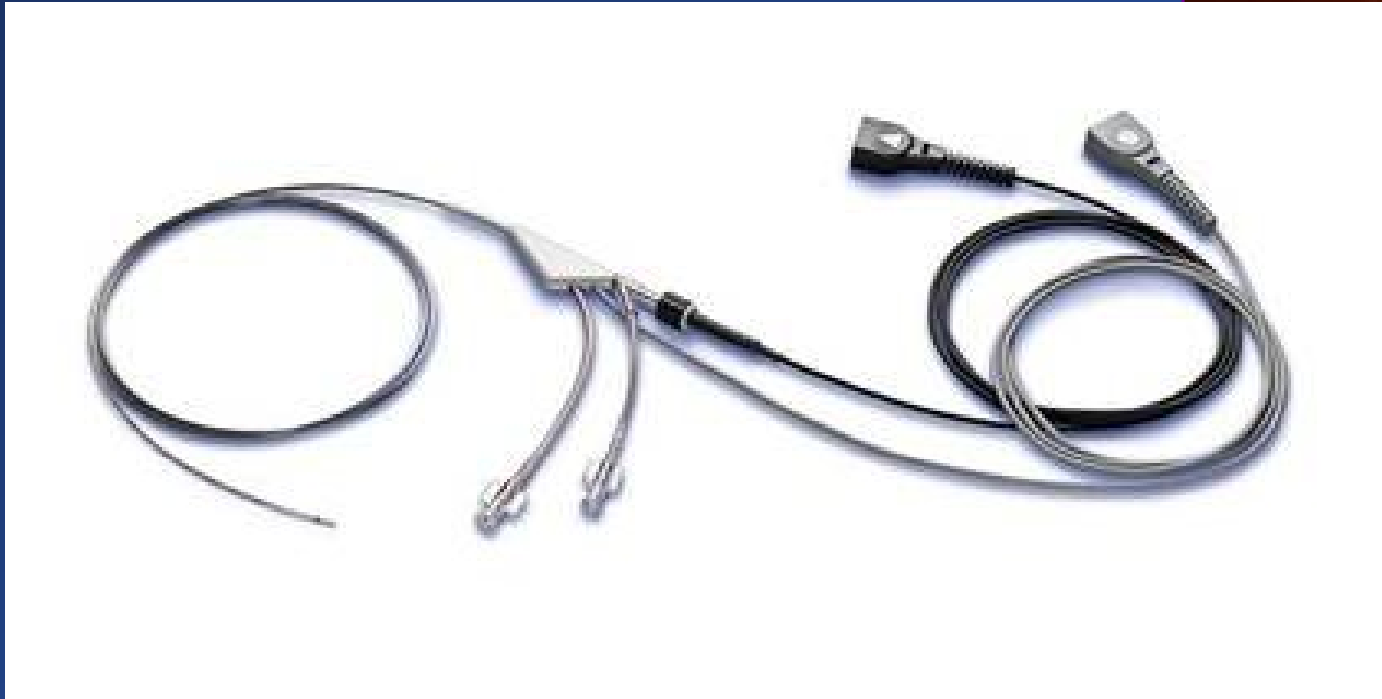
- Secondary Mechanism of Action
  - Ultrasonic waves pass through the thrombus all the way to the vessel walls; also through & behind venous valves.
  - Ultrasound physically drives/impells the drug through the & saturates clot; may also help to hold drug in occluded segment.
  - Thrombus exposed to ultrasound absorbed
    - 48% more t-PA in one hour,
    - 84% more t-PA in two hours, and
    - 89% more t-PA in 4 hoursthan thrombus not exposed to ultrasound. \*

\* Francis, Charles W. et al. Ultrasound Accelerates Transport of Recombinant Tissue Plasminogen Activator into Clots. Ultrasound in Medicine and Biology 21.3 (1995): 419-424.

# Safety

- Atar S, Luo H, Nagai T, et al. Arterial Thrombus Dissolution In Vivo Using a Transducer-Tipped, High-Frequency Ultrasound Catheter and Local Low-Dose Urokinase Delivery. *J Endovasc Ther* (2001) 8:282-290
- Soltani A. The Safety of Using Low-Intensity Ultrasound to Enhance Thrombolysis. *J Ultrasound Med* 25:S1-S118, (March 2006)
- Soltani A, Soliday C. Effect of Ultrasound on Enzymatic Activity of Selected Plasminogen Activators. *Thrombosis Research* (2006), in press.

# EndoWave Peripheral Catheter System

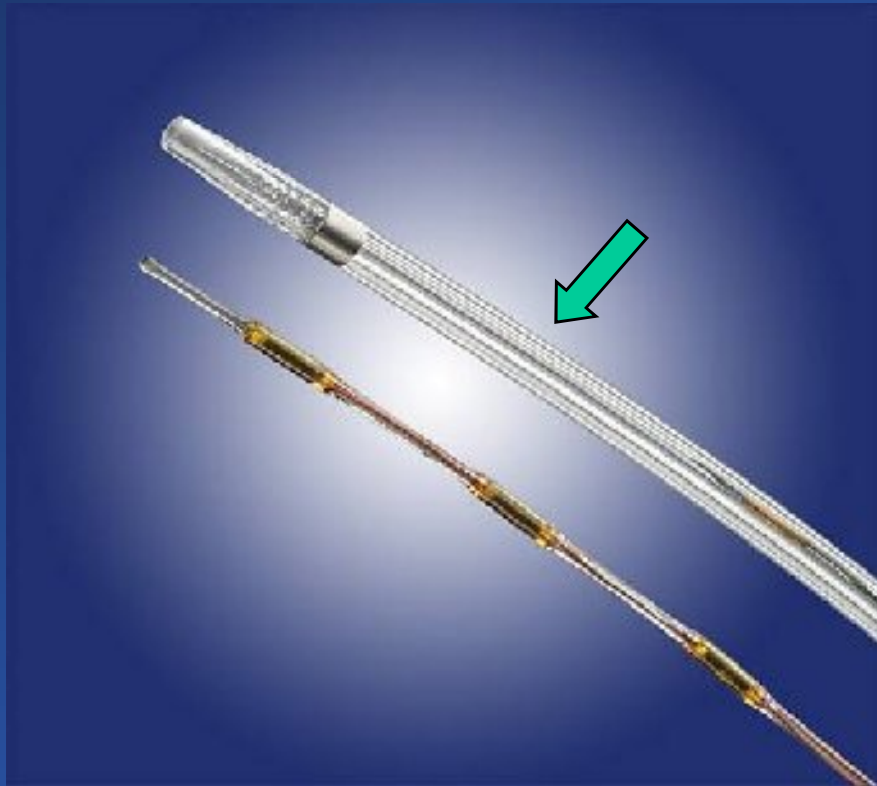


## Components

- Drug Delivery Catheter (DDC)
- Ultrasound Core (USC)



# Drug Delivery Catheter



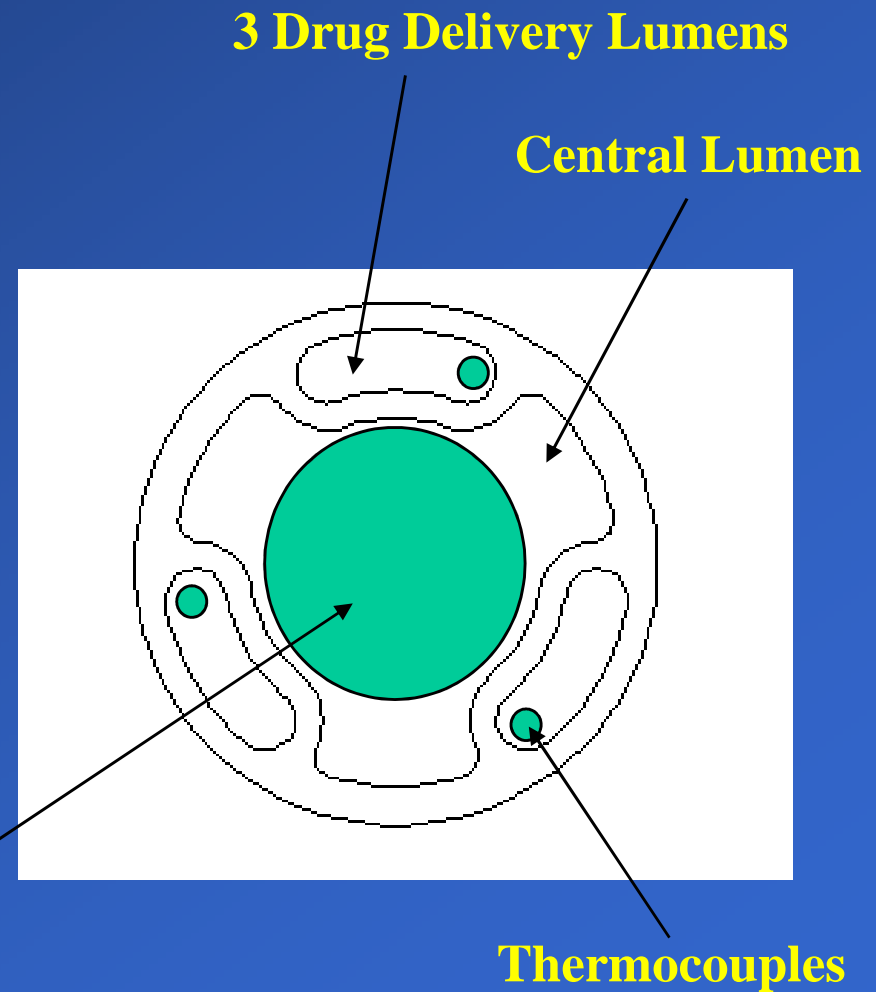
## Features

- 5.2 Fr catheter
- Flexible, kink resistant shaft
- 106 cm. working length
- Two radiopaque markers bracket the treatment zone
- 6, 12, 18, 24, 30, 40 and 50 cm treatment zones

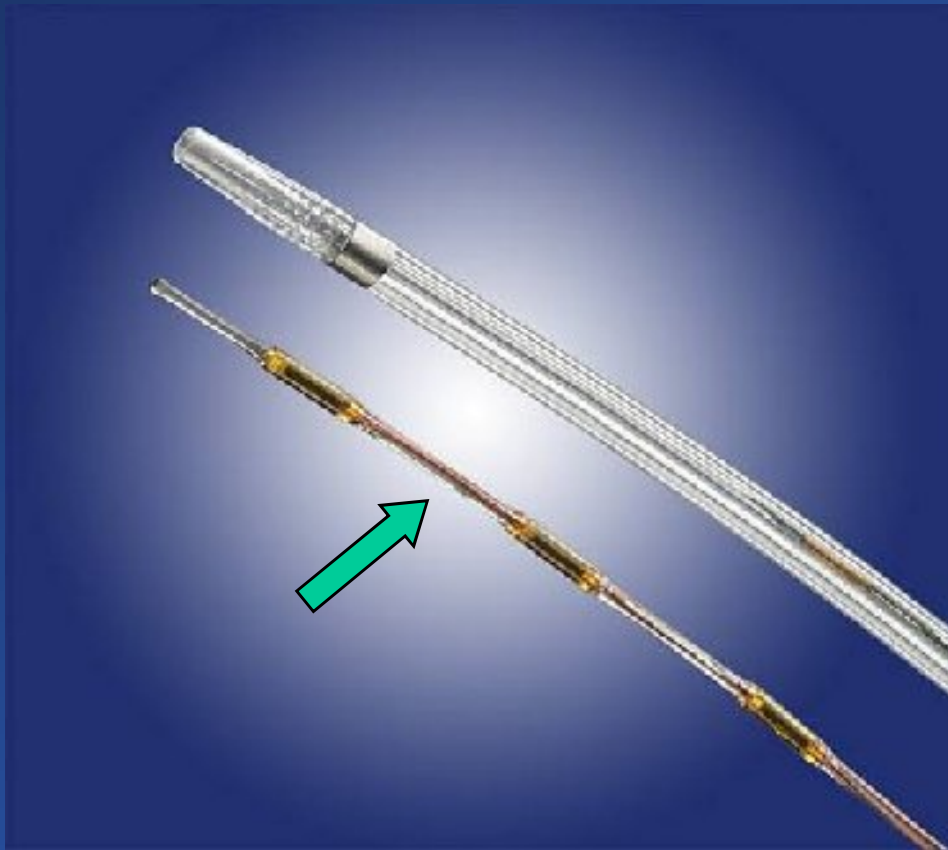
# Drug Delivery Catheter

- Central lumen accommodates a 0.035 in. guidewire and, later, the ultrasound core
- Coolant flows through central lumen and out the tip
- Thermocouples monitor temperature
- Drug flows through 3 drug lumens and out the side holes

**Ultrasound Core  
in central lumen**



# Ultrasound Core

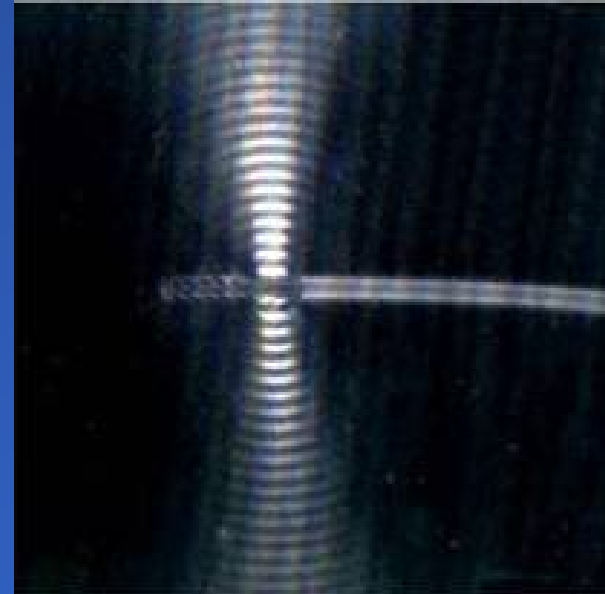
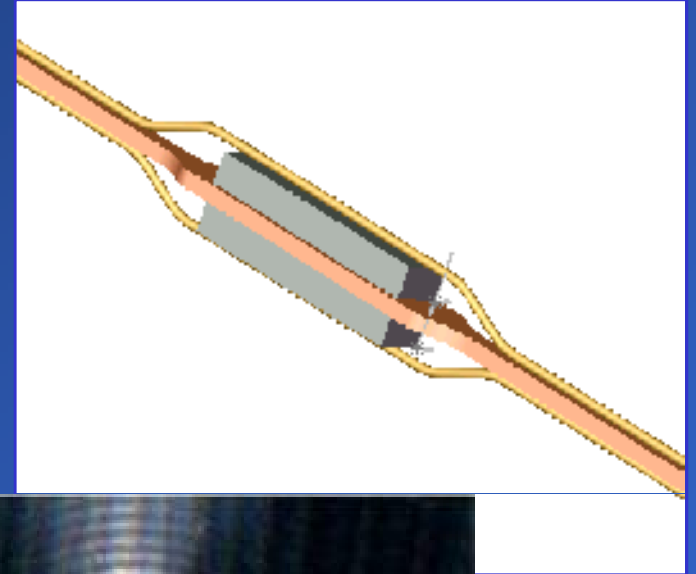


## Features

- Up to 30 ultrasound elements (5 groups of 6 elements)
- 6, 12, 18, 24, 30, 40 and 50 cm treatment zones
- Self-positioning in Drug Delivery Catheter

# Ultrasound Core

- Miniature 2.2 MHz acoustic transducers
- Ultrasound emitted radially



# EKOS PT-3 Control System

## Components

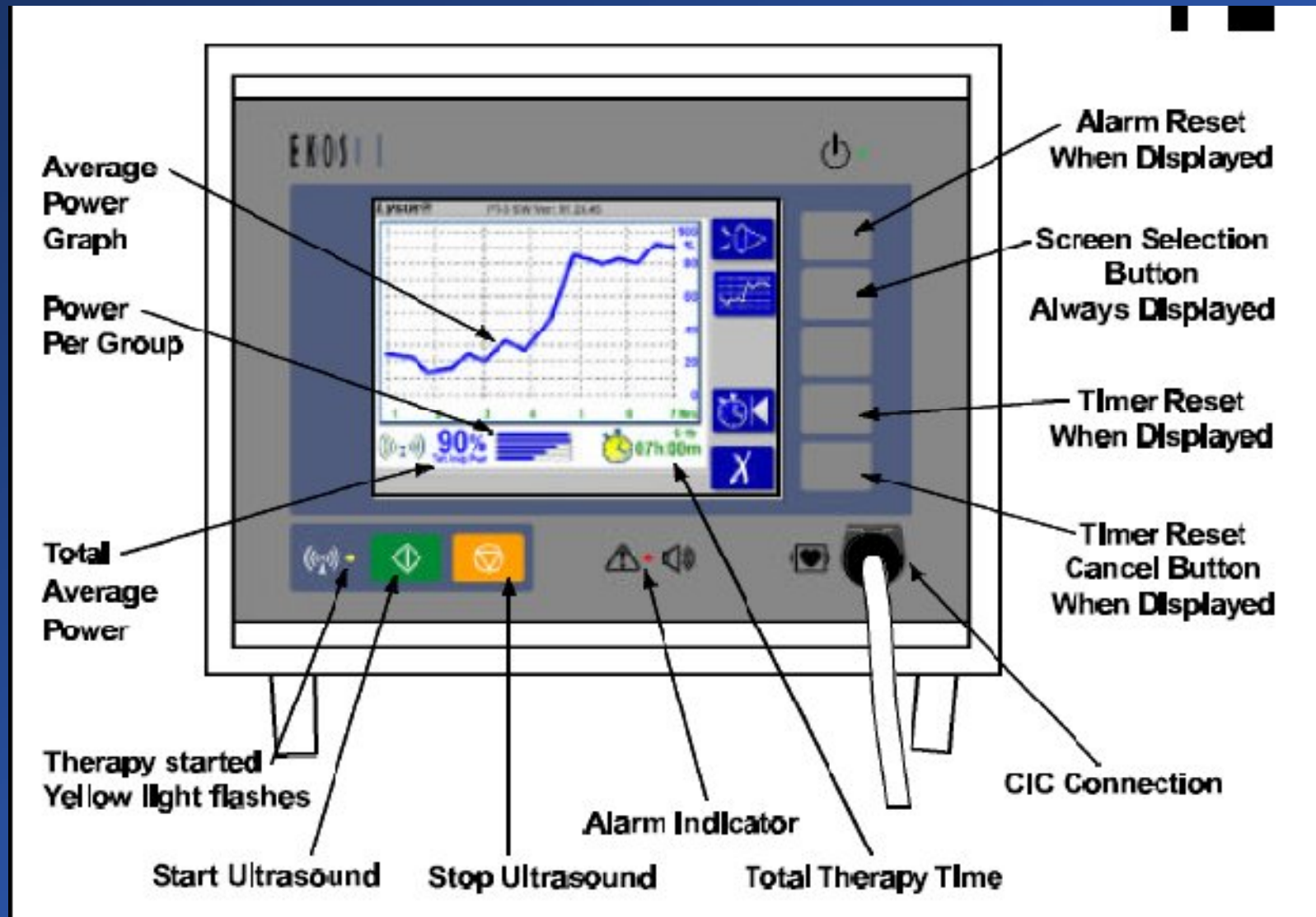
- PT-3 Control Unit
- Catheter Interface Cable



## Features

- Combines computer and power generator into single integrated unit
- Monitors connection integrity and operating parameters
- Auto-regulates power output to control ultrasound core temperature
- Records average power output, which, when displayed graphically, indicates a change in blood flow

# PT-3 Screen



# DVT Results

## EKOS EndoWave<sup>®</sup> System Summary (data as of 31 Oct 06)

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# DVT Demographics

Between January 2005 -March 2006  
treated 53 cases in 47 patients

- Average age = 50.8 years old  
(range 15 - 90 yo)
- 55% Male, 45% Female
- 60% lower extremity, 36% upper  
extremity, 4% other

# DVT Treated

- Average Clot length = 29 cm (4 -70 cm)
- 41% chronic, 41% acute, 17% acute on chronic
  - chronic defined as > 10 days
  - In 13% of the case, clot age not reported
- Lytic used
  - 42% Reteplase (rPA)
  - 26% Urokinase (UK)
  - 17% Alteplase (tPA)
  - 15% Tenecteplase (TNK)

# Comparative DVT Results at Final Angiogram

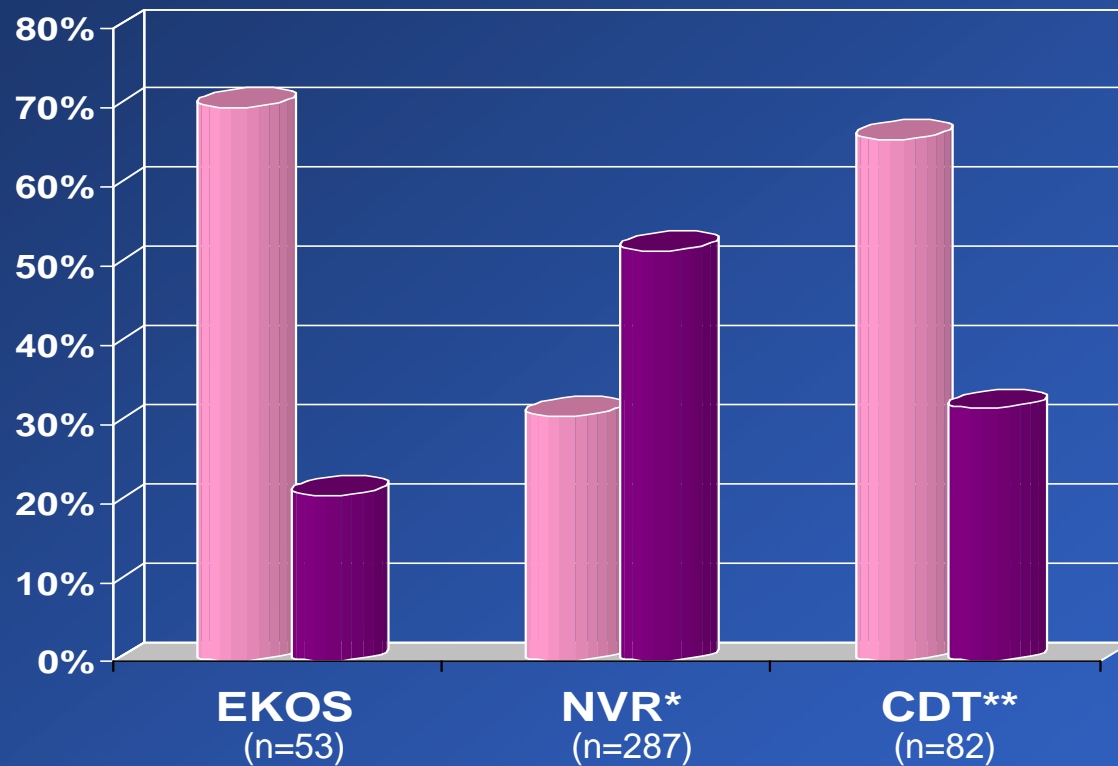
Case Result	EKOS (N=53)		NVR* (N=287)		CDT** (N=82)	
Complete Lysis	70%	37	31%	89	66%	54
Partial Lysis	21%	11	52%	149	32%	23
Refractory to Lysis	9%	5	17%	49	2%	2
Major Bleeding Rate	3.8%	2	11.4%	54/473	4.9%	4
Time to Final Angiogram	22.0 hrs (median)		53.4 hrs (average)		34.4 hrs (median)	

**Note: Results are Pre-Adjunctive Therapy for EKOS Data;  
Post-Adjunctive Therapy for NVR and CDT Data.**

\* Mewissen, et al. National Venous Registry. Radiology, 1999.

\*\* Grunwald and Hofmann. Catheter Directed Thrombolysis of DVT. JVIR, 2004.

# EKOS Achieves Greater Degree of DVT Clearance in Less Time



Complete Clearance  
Partial Clearance

Note:  
Results are Pre-Adjunctive  
Therapy for EKOS Data;  
Post-Adjunctive Therapy  
for NVR and CDT Data.

Therapy	Infusion Time (hrs)
EKOS (n=53)	22.0 (median)
NVR* (n=287)	53.4 (average)
CDT** (n=82)	34.4 (median)

\* Mewissen, et al, National Venous Registry. Radiology, 1999.  
\*\* Grunwald and Hofmann, Catheter-Directed Thrombolysis of DVT. JVIR, 2004.

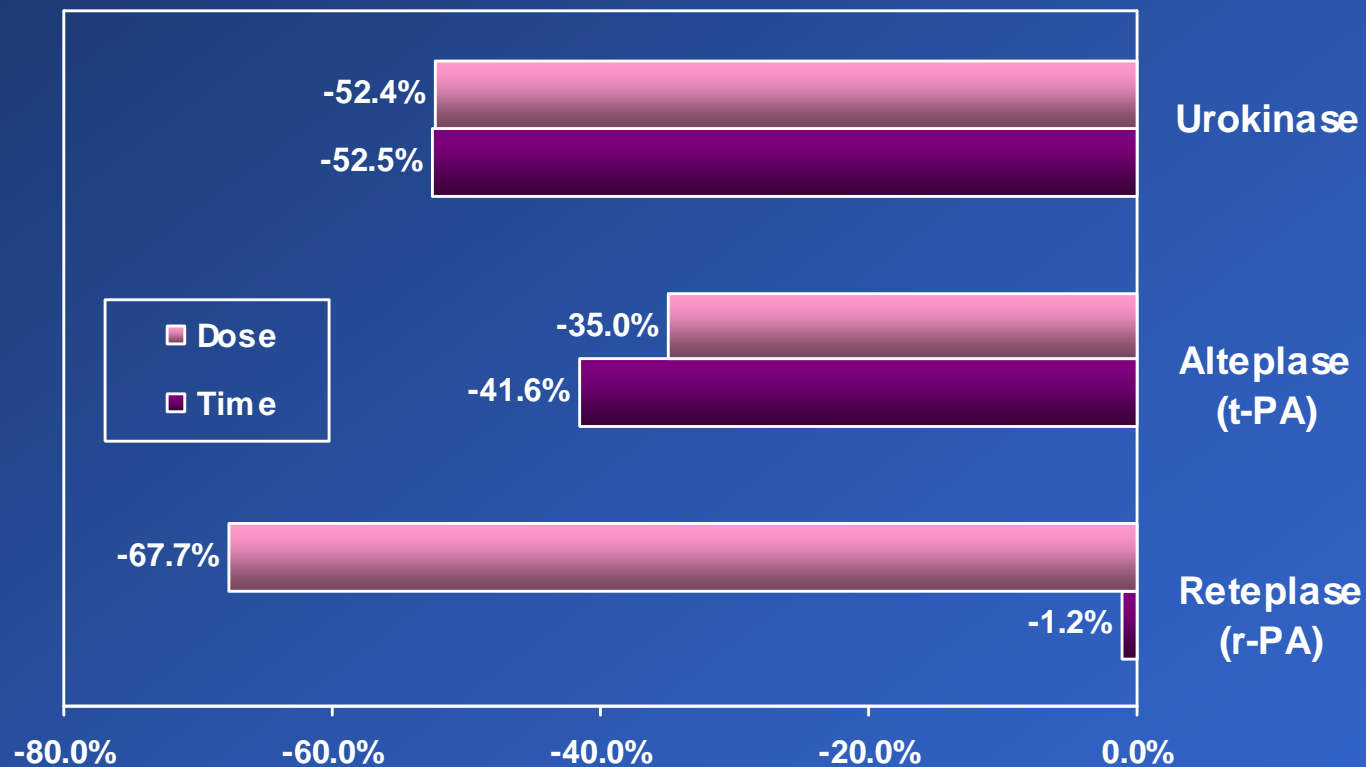
# EKOS Achieves DVT Clearance in Less Time with Lower Drug Dose

Case Result	Urokinase		Alteplase (t-PA)		Reteplase (r-PA)	
	EKOS (n=14)	CDT (n=38)	EKOS (n=9)	CDT (n=32)	EKOS (n=22)	CDT (n=12)
Median Drug Dose	2.02 MU	4.36 MU	14.0 mg	21.6 mg	6.9 U	21.4 U
Median Infusion Time	19.3 hr	40.6 hr	18.0 hr	30.8 hr	24.0 hr	24.3 hr

Comparison of EKOS Data to Catheter-Directed Thrombolysis (CDT)  
Data Reported by Grunwald and Hofmann, JVIR, 2004

# EKOS Achieves DVT Clearance in Less Time with Lower Drug Dose

Percent Reduction in Median Administered Dose & Infusion Time



Comparison of EKOS Data to Catheter-Directed Thrombolysis Data Reported by Grunwald and Hofmann, JVIR, 2004

# EKOS Demonstrates Advantages in Treating DVT

- Degree of Thrombus Clearance from EKOS Alone Exceeds Reported Results for Lysis Plus Mechanical Adjunctive Therapy.
  - Infusion Times and Drug Dose are Noticeably Reduced Compared with Catheter Directed Thrombolysis.
  - Complication Rates are Lower with No Reported Intracranial Hemorrhage.
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# Thank you, for your attention

- Be happy to answer any questions
  - Have a great time in N'Awlins!!!
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# PAO Results

## EKOS EndoWave<sup>®</sup> System Summary

(data as of 31 Oct 06)

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# PAO Demographics

Between September 2004 -March 2006  
treated 91 cases in 88 patients

- Average age = 70.3 years old  
(range 34 - 91 yo)
- 60% Male, 40% Female
- 64% grafts, 33% native, 3% stent-grafts

# PAO Treated

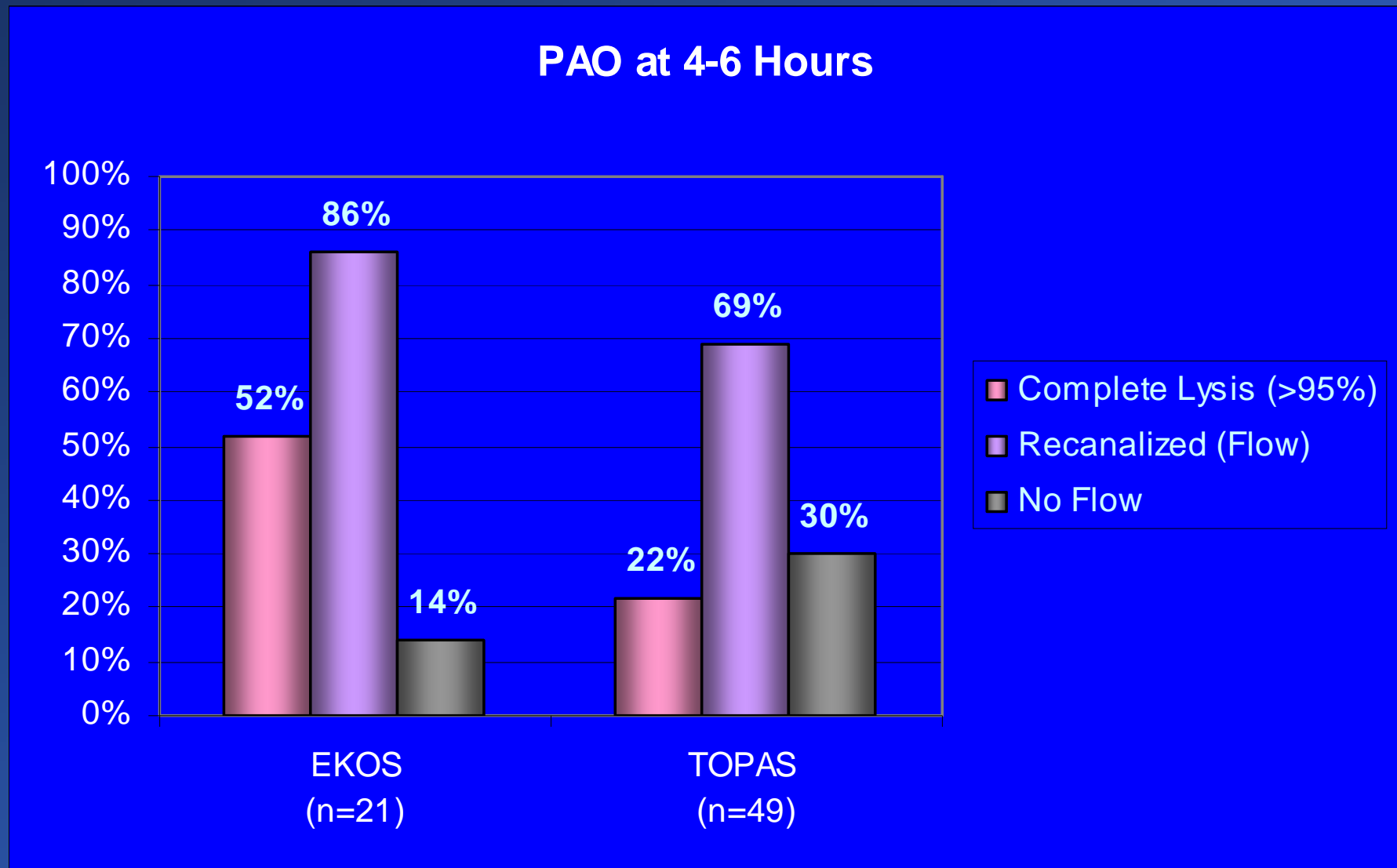
Average Clot length = 31 cm (3 -70 cm)

- 75% acute, 25% chronic
  - (chronic defined as > 14 days)
  - In 33% cases, clot age not reported
- Lytic used
  - 46% Retaplastase (rPA)
  - 24% Urokinase (UK)
  - 15% Alteplase (tPA)
  - 14% Tenecteplase (TNK)

# PAO Results at 4-6 hrs

	EKOS	TOPAS I
Complete Lysis	52% (11)	22% (11)
Recanalization (Partial + Complete Lysis)	86% (18)	69% (34)
No Flow	14% (3)	30% (15)
Total	21	49

# PAO Results at 4-6 hours



# PAO Results at Final Angiogram

	EKOS*	TOPAS II**
Complete Lysis	86% (78)	68% (167)
Partial Lysis	10% (9)	12% (29)
Refractory to Lysis	4% (4)	20% (50)
Total	91	246
Major Bleeding Rate	2.2% (2)	12.5% (32)
Mean Time to Final Angiogram	18.5 hrs ± 10.8 (3 - 70 hrs)	24.4 hrs ± 0.86

\*Clot up to one year in age, angiograms at convenience of operator

\*\*Ouriel, K., et. Al. NEJM, 338:16;1105-11; acute clot (< 2 weeks)

# PAO Results at Final Angiogram

