Microvascular Free Tissue Transfer

Physiology and Practice

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History of Tissue Transfer

1899 – Dorfler advocated use of all layers of vessels in repair

1907 – (Carrel) "The Surgery of Blood Vessels" (*JH Hospital Bull.*)

- 1st replantation of canine limbs
- 1st esophageal-intestinal interposition

1959 – (Seidenberg) human esophageal-intestinal interposition

1960 – (Jacobson/Suarez) operating microscope introduced (1 mm vessels)

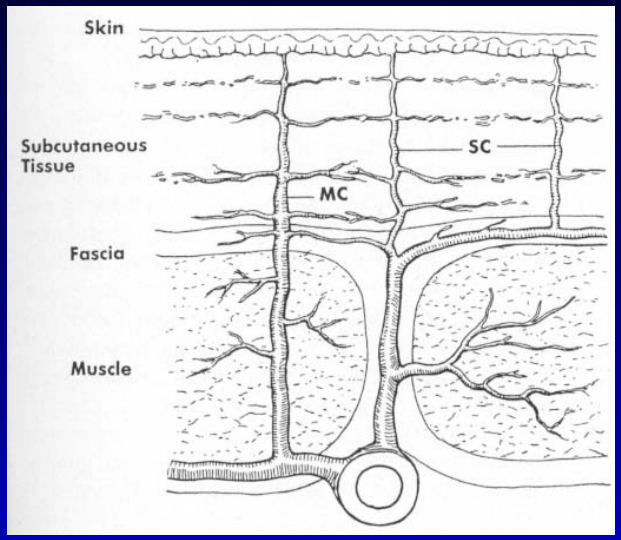
1966 – (Antia/Buch) fasciocutaneous transfer

1972 – (McLean/Buncke) omental flap to scalp

Flap Nutrient Flow

Zone I: Macrocirculation

- Cardiopulmonary circulation
- Musculocutaneous/septocutaneus arteries



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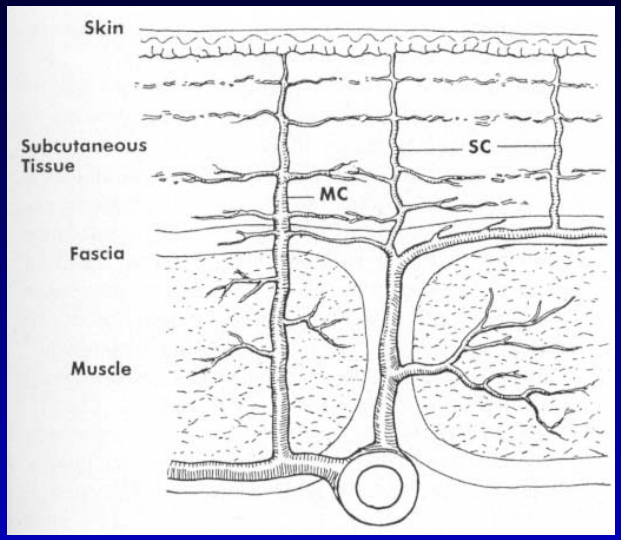
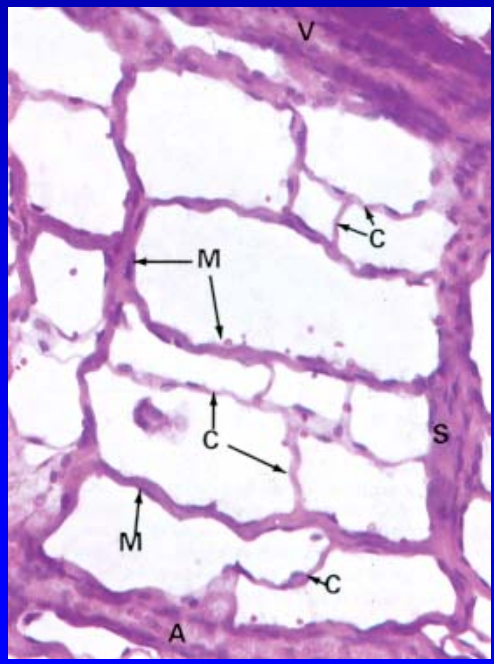
Zone II: Microcirculation

- Terminal arterioles (metarterioles)
  - discontinuous smooth muscle
  - shunt sphincters before capillaries
- Capillary system
  - devoid of smooth muscle
  - nutrient exchange & thermoregulation





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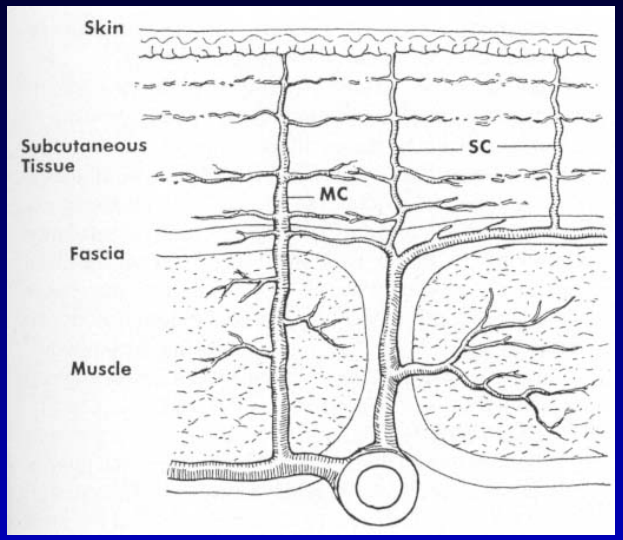
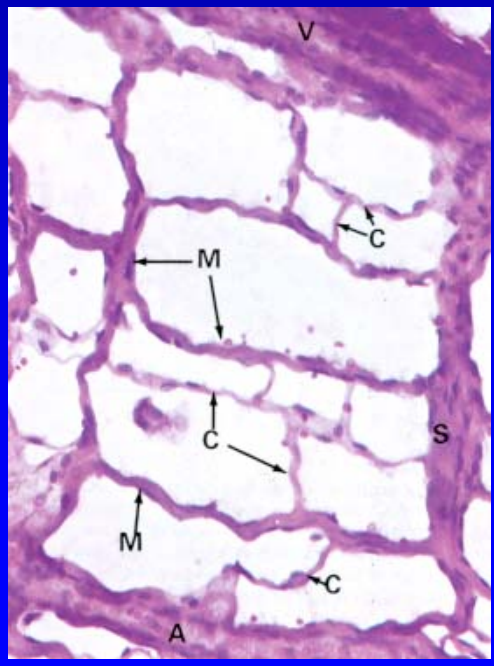
Zone III: Interstitium

- Proteoglycans/collagen
  - inhibit nutrient flow with dehydration
  - injury/inflammation → ↑ pressure & ↑ resistance to flow

Zone IV: Cellular systems





Blood Flow Regulation

Skin blood flow

- Varies constantly
- Maximal flow = 20x constricted flow

Extrinsic (α receptors)

- Sympathetics → NE
- Circulating catecholamines → NE & E
  - shunt sphincters *extremely sensitive* to catechols

Intrinsic

- Tissue metabolites
  - CO2, NO, lactate → dilation
  - potassium → constriction
- Kinins, histamine, serotonin
- **Prostaglandins**

Free Flap Physiology

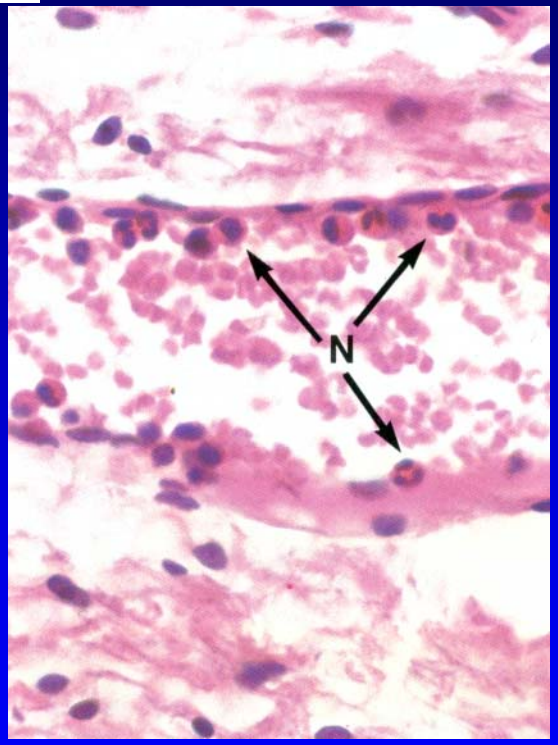
Responses to Ischemia

- Skin
  - *Anaerobic* metabolism preferred (glycolysis)
    - temperature regulation?
    - allows prolonged periods of anoxia
- Muscle
  - *Aerobic* metabolism essential (TCA cycle)
    - 2 hr anoxia – immediate recovery
    - 4 hr anoxia – prolonged recovery (edema)
    - 6 hr anoxia – no recovery (necrosis/infection)
      1. little histololgic change until ***reperfusion***
- Bone/Cartilage
  - Needs dependent on activity of constituent cells
  - Poor studies

Microcirculatory Response to Ischemia

Endothelial response

- *Aerobic* metabolism extremely important
  - *irreversible* injury in 2.5 min of anoxia
  - endothelial swelling narrows lumen
  - complete regeneration in 7 – 10 days (monocytes/pleuropotential myoepithelial cells)



Erythrocyte sludging

- stiff walls with low pH
- reduced with hematocrit below 30%

Leukocyte adherence

Interstitial swelling

- increases capillary pressure

Zone II/III failure in *No-Reflow Phenomenon*

Consequences of Vascular Injury

Endothelium

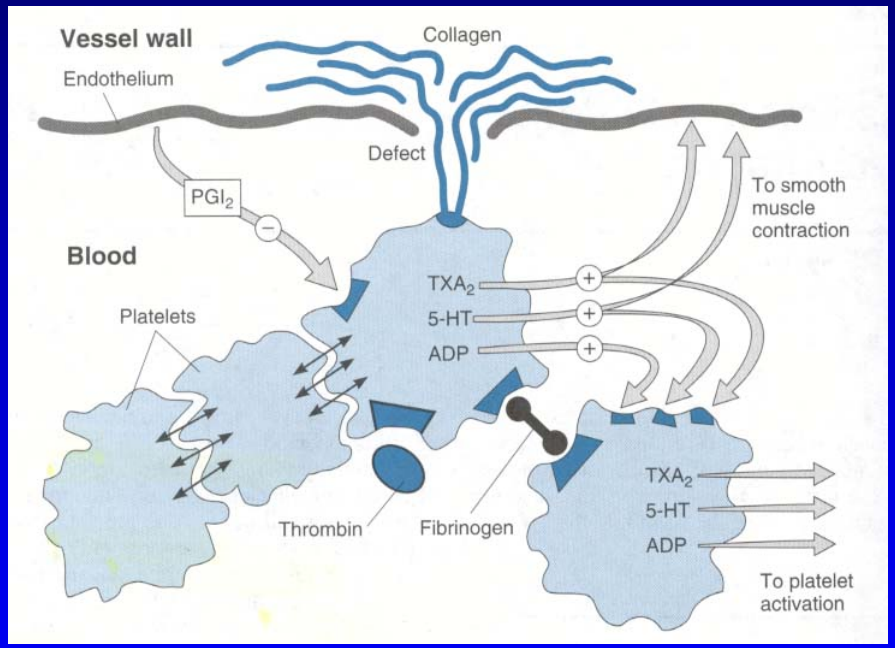
- Actively produces PGI_2
  - vasodilator
  - acts on distal arterioles

Basement membrane

- Exposed following endothelial loss
- Potent activator of platelets
- Rapid growth of clot (TxA_2)
  - vasoconstriction
  - vascular occlusion

Muscularis and adventitia

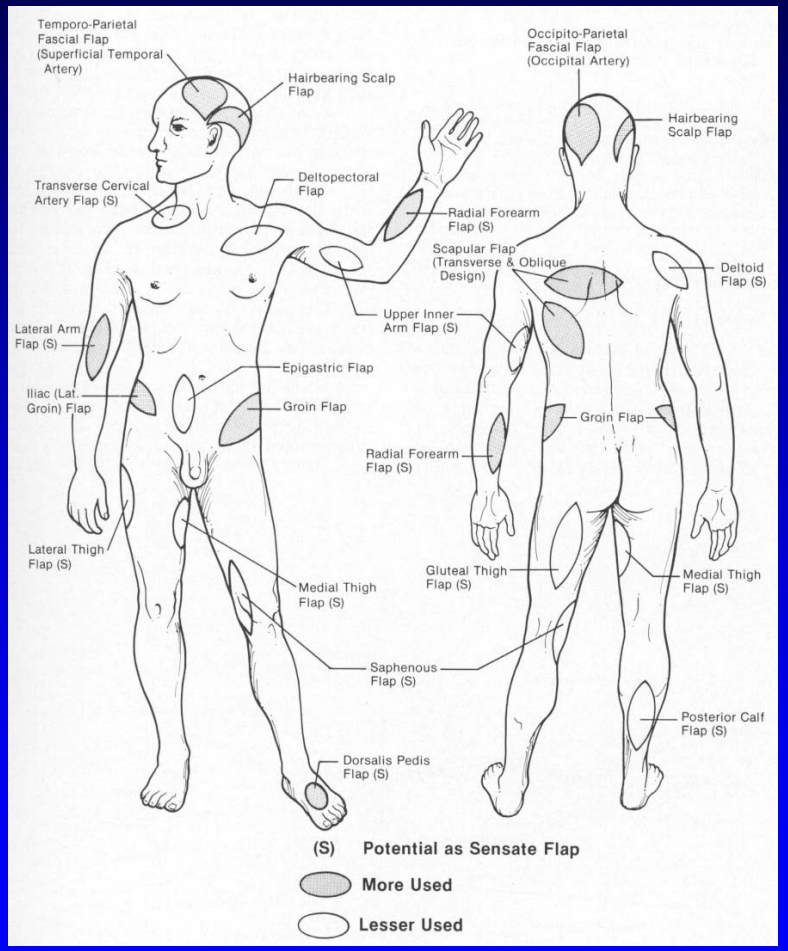
- Heals with scar deposition
- Extensive injury leads to ↓ patency and aneurysm



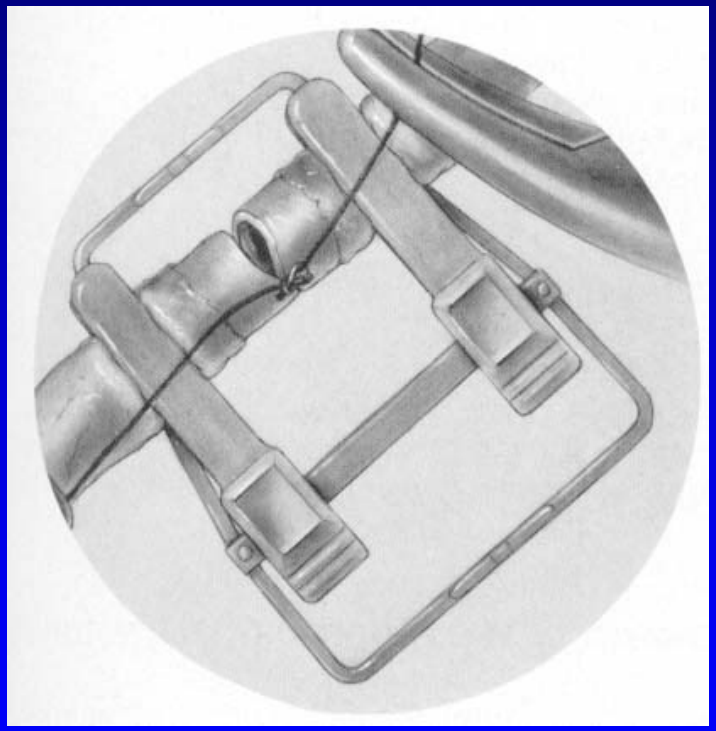
Principles of Microsurgery

Macrocirculation of Composite Tissue

- Segmental vasculature (axial flaps)
  - skin/fascia
  - skin/fascia & muscle
  - skin/fascia & bone +/- muscle
- Vessels 0.8 to 4 mm appropriate for transfer



Factors Affecting Anastomosis Patency



Technical

Flow factors

- Turbulence
- Smaller vessels more sensitive

Coagulation Factors

- PGI_2 → vasodilation
- TxA_2 → vasoconstriction

Spasm

- Vessel handling
- Blood, temperature, desiccation
- Circulating catecholamines
  - smoking
  - sympathetic activity stress/exogenous α-agonists

Free Flaps Outcomes

Prospective study of microvascular free-flap surgery and outcome (Khouri, *et al.*, PRS 1997)

- 493 free-flaps in 6 months at 60 centers
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- Post-op thrombosis 9.9% → 69% salvaged
  - recipient site chronic wound (OR = 2.9)
  - post-op SQ heparin (OR = 0.27)
- Intra-op thrombosis 8.3% → 95% salvaged
  - myocutaneous flaps (OR = 5.5)

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- Intra-op thrombosis 8.3% → 95% salvaged
  - myocutaneous flaps (OR = 5.5)
- Hematoma 9.4%
  - ↑ with obesity and vein graft use
  - ↓ with attending anastomosis, heparin irrigation intra-op, tobacco use

Evidence-based Free Tissue Transfer

Pre-operative

- Patient selection
- Vascular screening
- Smoking

Peri-operative

- Fluid status
- Anticoagulation

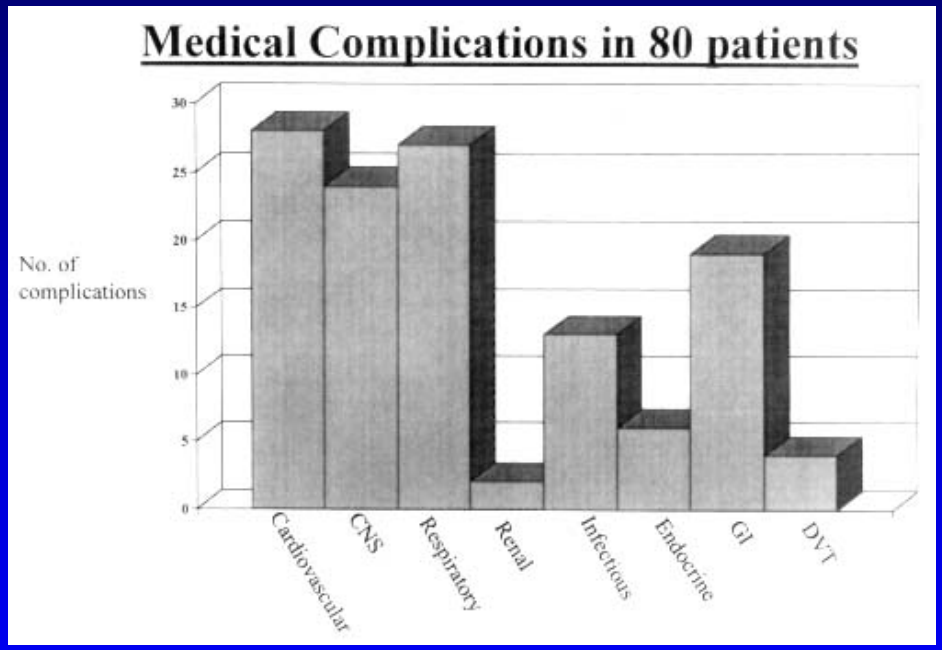
Post-operative

- Flap salvage

Patient Selection

Age

- Numerous studies
  - As independent variable → no increase in flap loss (Al Qattan, *Microsurg*, 1993; Chick, *PRS,* 1992; Khouri, *et al.,* PRS 1997)
  - 241 cases Head and Neck (Haughey, *Oto-HNS*, 2001)
    - 95% complete flap survival
    - Age 55 – 66
      1. Major complications OR = 14
    - Age > 66
      1. Major complications OR = 21



No age-associated flap complications with multivariate analysis

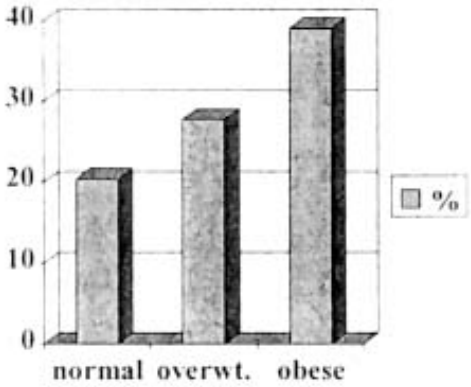
Patient Selection

Obesity

- 936 TRAM flaps (Chang, *PRS*, 2000)
- Flap complications by MLR = OR 2.5 (95% CI 1.3 – 4.7)
  - independent of comorbid conditions

Flap Complications

- 222 of 936 flaps (23.7%)
- Obese vs. Normal
  39.1% vs. 20.4 %
  $p = 0.001$
- Overwt. vs. Normal
  27.8% vs. 20.4%
  $p = 0.004$



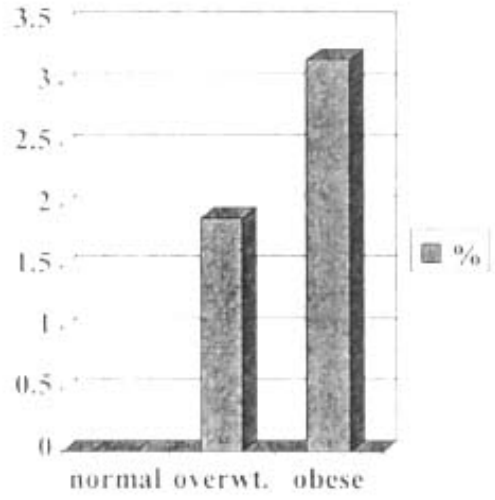
Patient Selection

Obesity

- 936 TRAM flaps
- Flap complications by MLR = OR 2.5 (95% CI 1.3 – 4.7)
  - independent of comorbid conditions

Total Flap Loss

- 8/936 flaps(0.9%)
- Obese vs. Normal
  3.2 % vs. 0 %
  $p = 0.001$
- Overwt. vs. Normal
  1.9 % vs. 0 %
  $p = 0.004$



Obesity correlates with ↑ flap loss and complications

Vascular Screening

Arteriosclerosis

- Most common risk factor for systemic vascular disease
- Independent risk factor for Zone I failure (Vlastou, Int Angiol, 1994)

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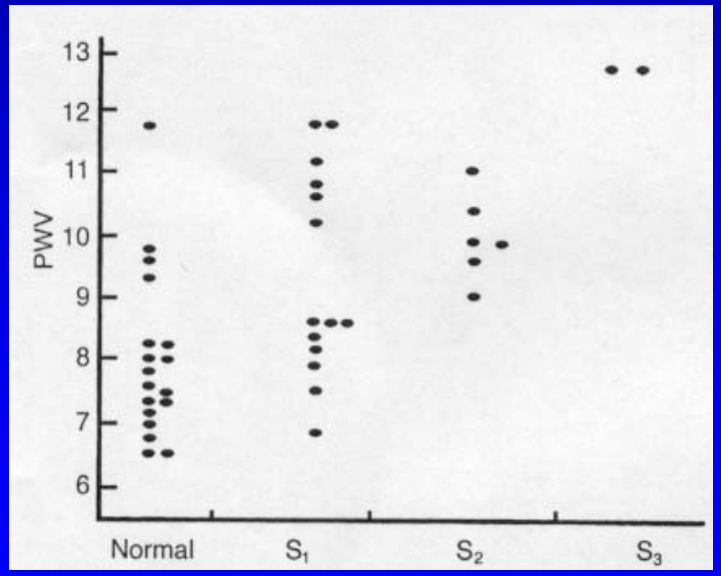
Pre-op screening

- None established
  - 40 patients with H & N malignancy evaluated (Kanoh, *Clin Otolaryngol*, 2000)
  - Identified severe arteriosclerosis in 2/40 by aortic pulse wave velocity (PWR)
  - Identified identical patients by fundoscopy



Smoking

Tobacco use

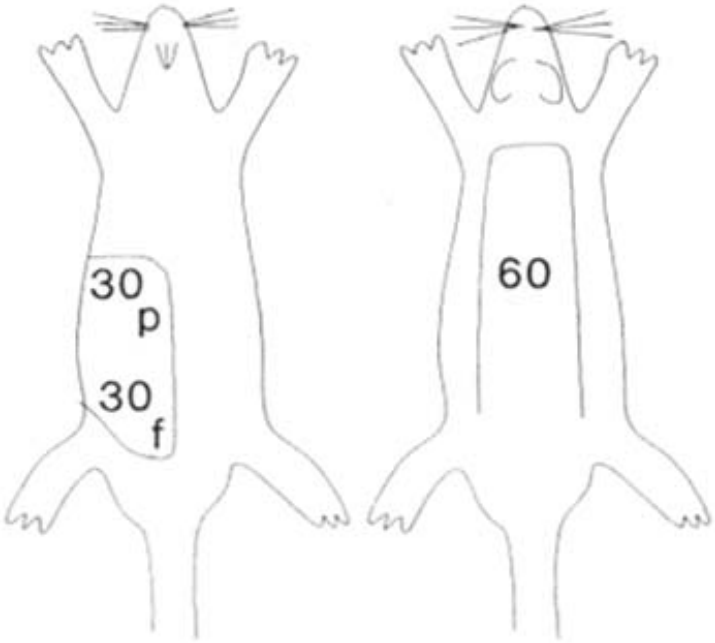
- Independent risk factor for arteriosclerosis
- Nicotine is vasoconstrictor
- Assoc. with poor wound healing
- Increased platelet aggregation
- Decreased oxygen transport (CO)

Tobacco and free tissue transfer:

- little known
- independent risk factor for flap complication OR = 5.3
  (95% *CI* 1.8 – 15.4; Haughey, *Oto-HNS*, 2001)
- animal model (van Adrichem, *PRS*, 1996)

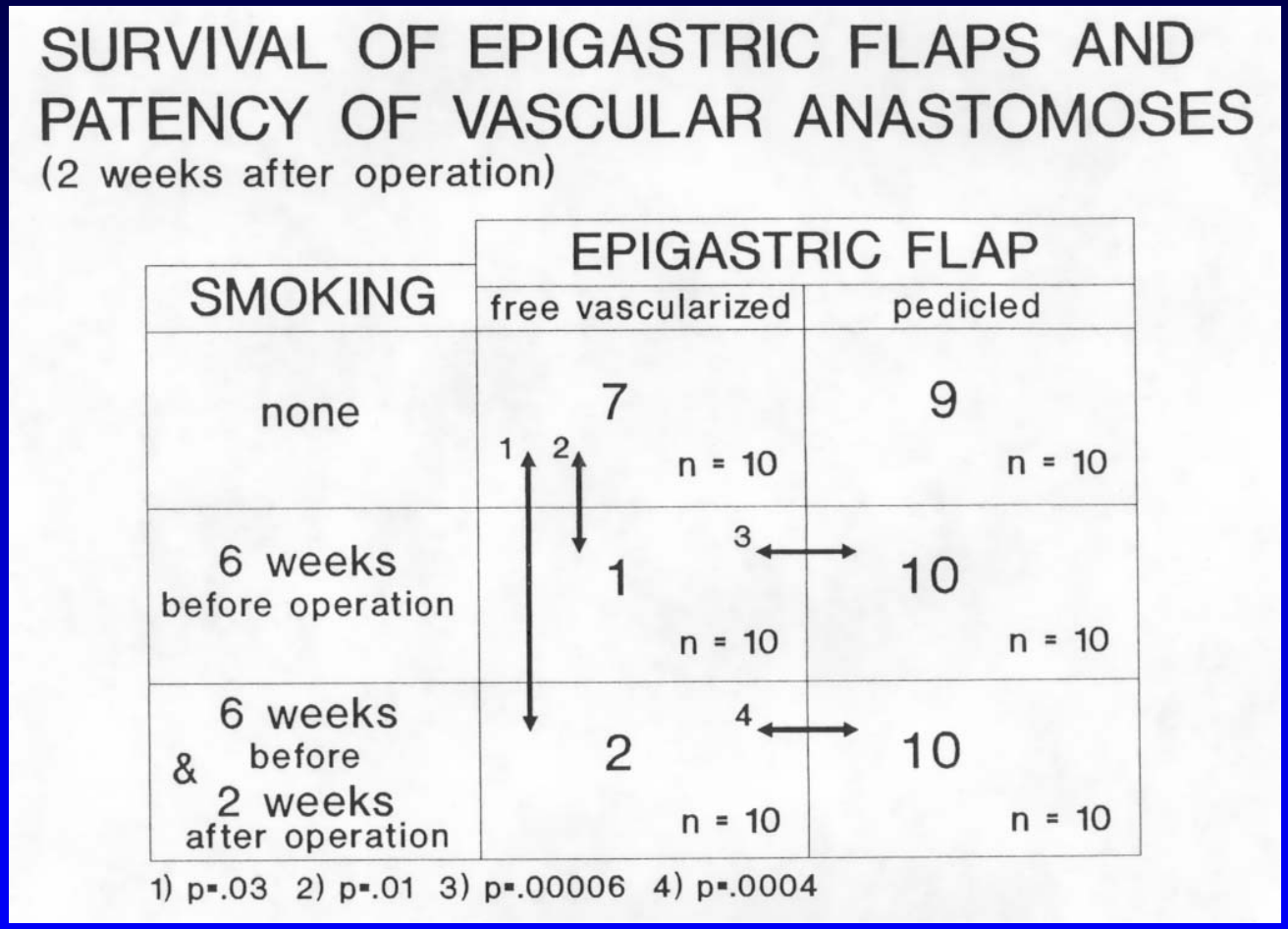
Smoking

EPIGASTRIC AND DORSAL FLAPS IN 60 RATS



SMOKING	EPIGASTRIC FLAP	
	free vascularized	pedicled
none	n = 10	n = 10
6 weeks before operation	n = 10	n = 10
6 weeks & before 2 weeks after operation	n = 10	n = 10

Smoking



SURVIVAL OF EPIGASTRIC FLAPS AND PATENCY OF VASCULAR ANASTOMOSES
(2 weeks after operation)

SMOKING	EPIGASTRIC FLAP	
	free vascularized	pedicled
none	7 n = 10	9 n = 10
6 weeks before operation	1 n = 10	10 n = 10
6 weeks & before 2 weeks after operation	2 n = 10	10 n = 10

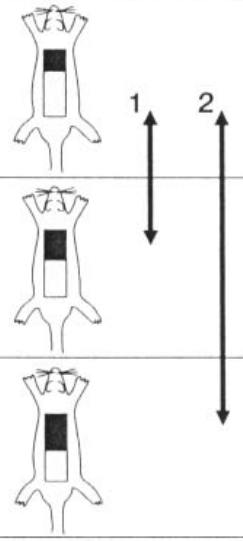
1) p=.03 2) p=.01 3) p=.00006 4) p=.0004

Smoking shows significant detrimental effect on free flap survival

Smoking

VITAL AREA OF AT RANDOM DORSAL FLAPS
judged on day 14 postoperatively,
as a percentage of the area on day of operation

SMOKING	ALL 60 RATS (n = 20 for every group)
none	65.4% (sd = 10.1)
6 weeks before operation	52.7% (sd = 11.2)
6 weeks & before 2 weeks after operation	47.5% (sd = 6.3)

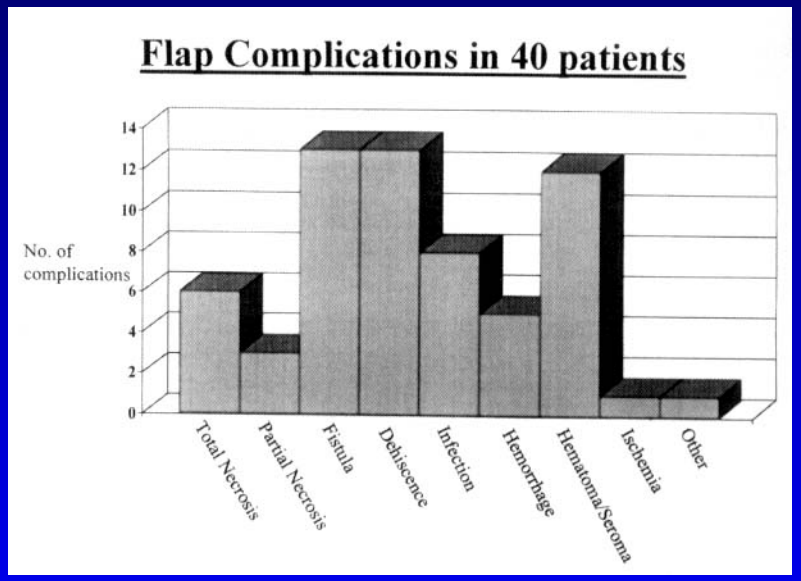


* 1: p=.002 / 2: p=.002 / all:p=.00001
* After subdivision of groups into free and pedicled epigastric flaps the results differed < 1%

Smoking significant detrimental effects on Zone II/III survival

Perioperative Considerations

Fluid management



- Presumed to be related to flap edema
- 141 H & N free flaps (Haughey, *Oto-HNS*, 2001)
  - > 7 L crystalloid assoc. with:
    - **flap complication** (OR = 2.75; 95% *CI* 1.1 – 6.7)
    - **major medical complication** (OR 5.1; 95% *CI* 1.6 – 16.2)
  - flap failures avg. 9.5 L fluid (range 3.7 – 11)
- Marker for anesthetic practice?

Large volume of crystalloid associated with flap complications

Anticoagulation

Peri/postoperative anticoagulation

- Very difficult to find consensus
- Many studies
  - retrospective
  - poorly controlled
  - practice patterns vary
    - by physician
    - by patient
- Survey of 106 microvascular surgeons (Glicksman, *PRS*, 1997)

	Elective		
	Preop	Intraop	Postop
No treatment	84%	49.1%	29.3%
Aspirin	16%	1.9%	34.9%
Heparin	0%	29.2%	5.7%
Dextran	0%	19.8%	30.1%

Anticoagulation Types

Aspirin

- Inhibits cyclooxygenase *irreversibly*
  - low dose → blocks TxA_2
  - low dose does not change endothelial prostaglandins

Heparin

- Binds antithrombin III
  - accelerates clotting factor protease activity
- May decrease basement membrane electronegativity
- Decrease platelet binding?

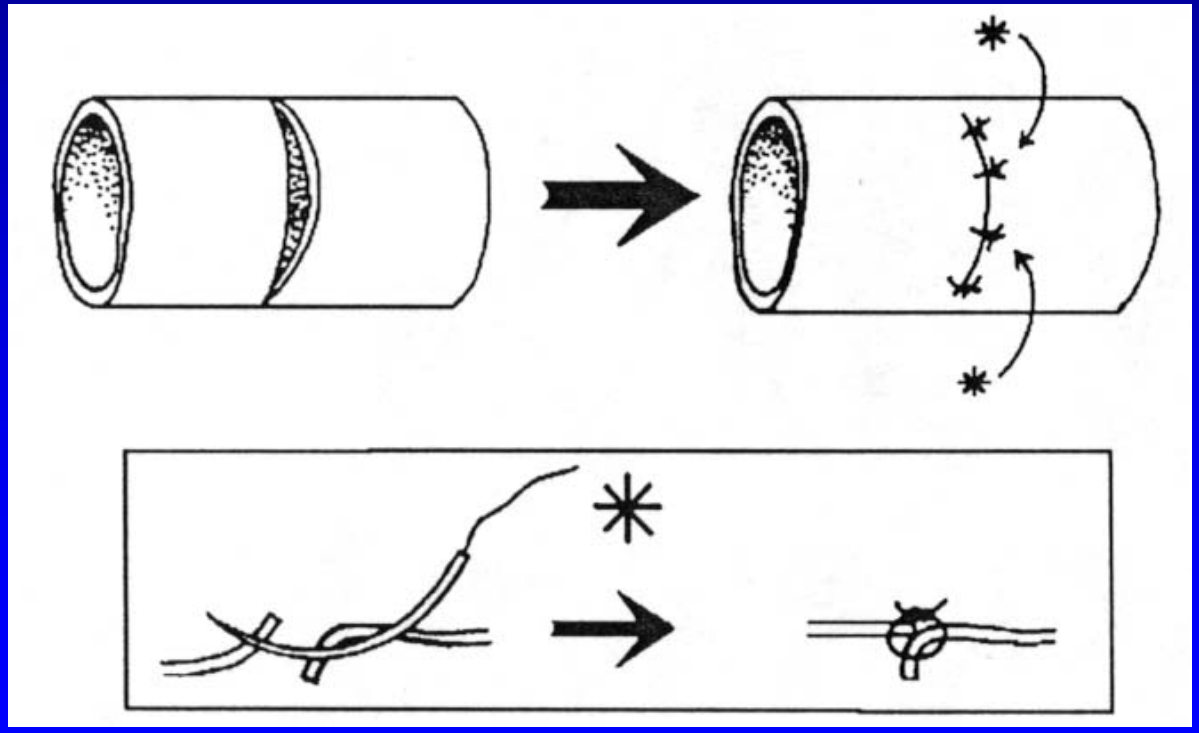
Dextran

- Plasma expander → lowers viscosity
- Lowers platelet adherence
- Alters fibrin structure

Animal Model of Thrombosis

Effect of aspirin on Zone I and Zone II (Peter, *PRS*, 1997)

- Wistar rats
- Femoral artery/vein division & ligation



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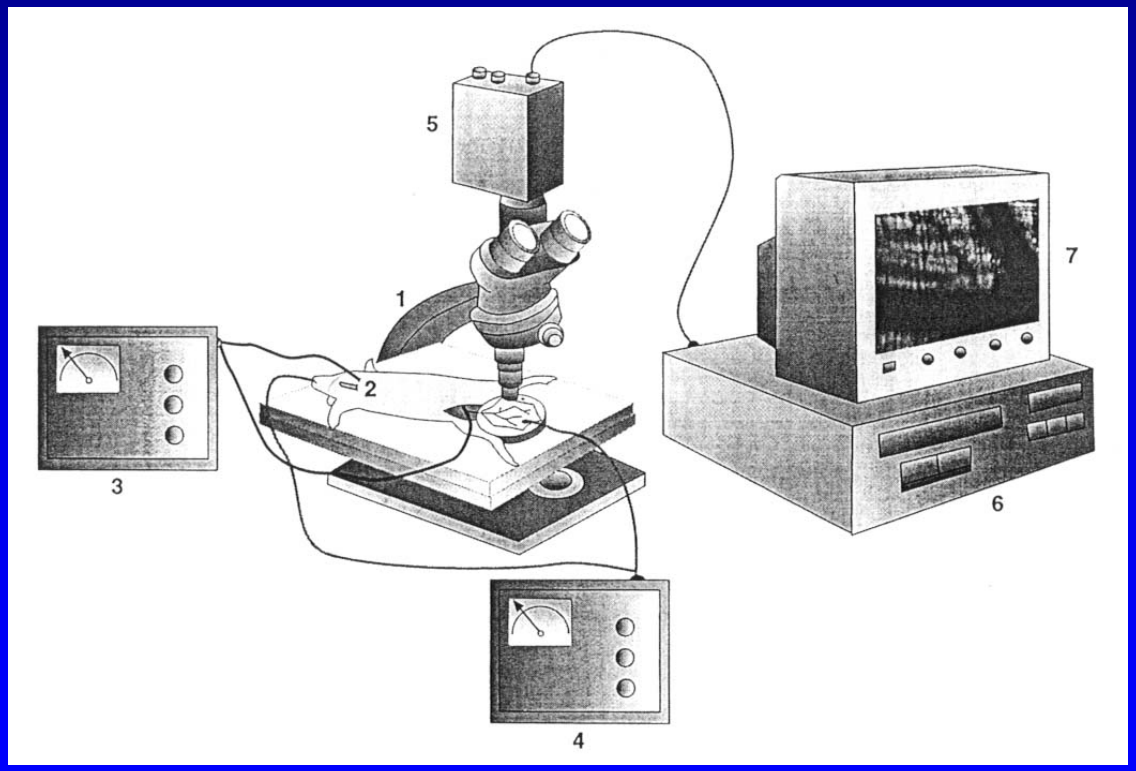

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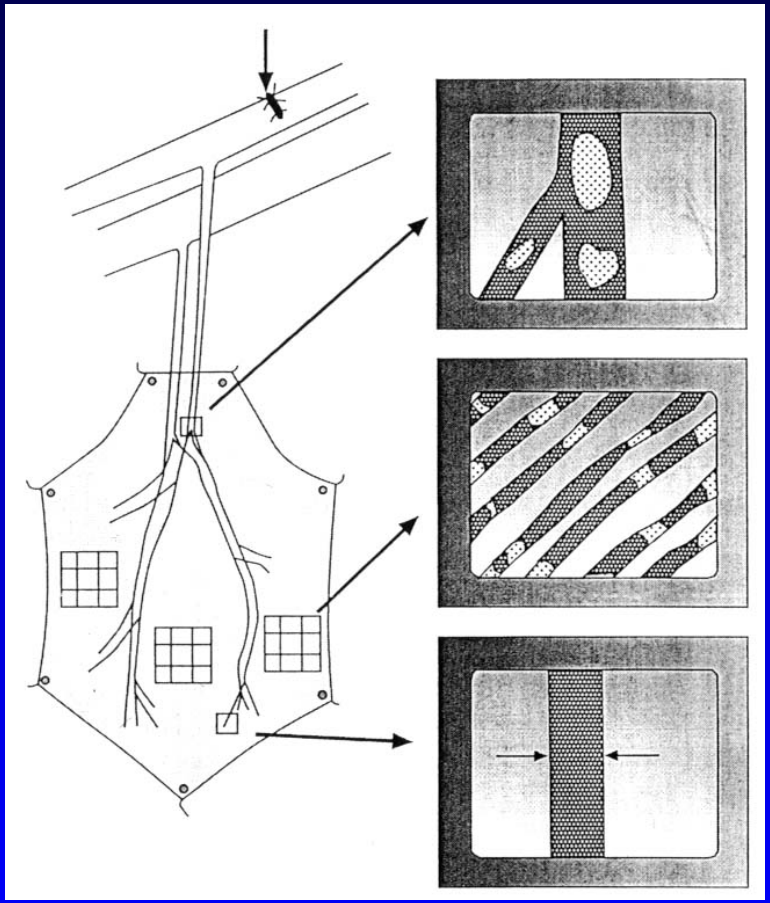
- Femoral artery/vein division & ligation
- Cremaster dissection
- Microscopic evaluation
  - transillumination
  - temperature
  - followed over 6 hr



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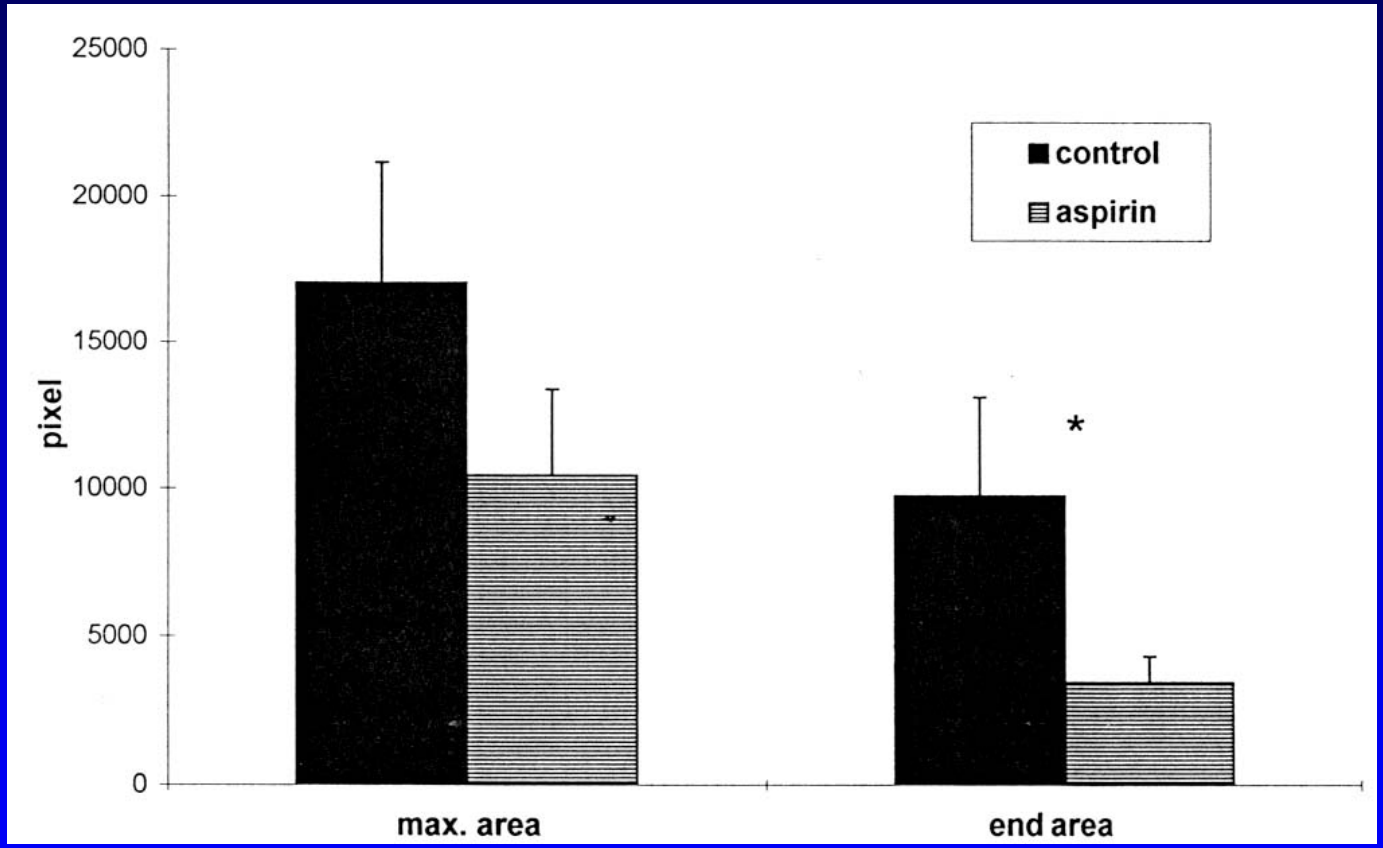

Arterial Thrombus size

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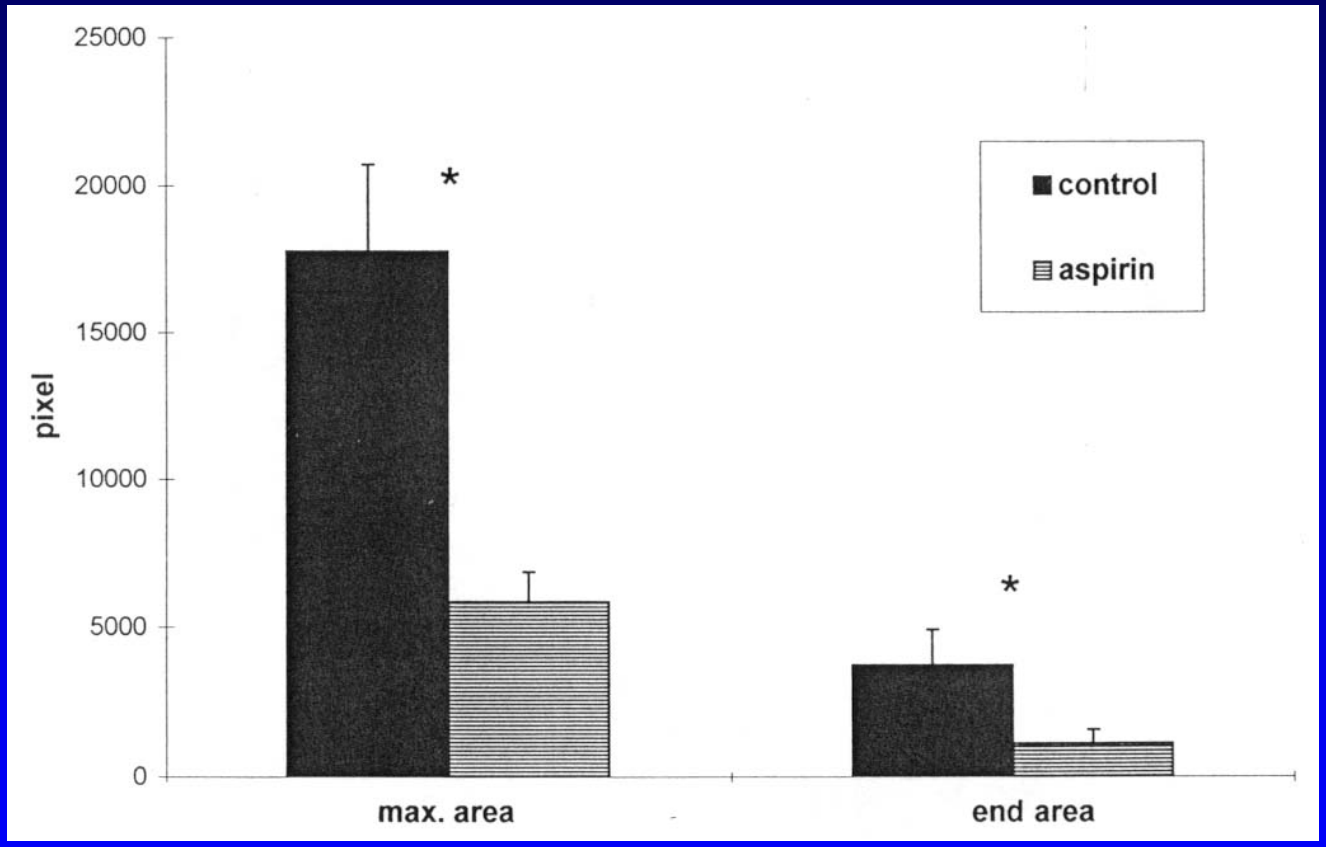
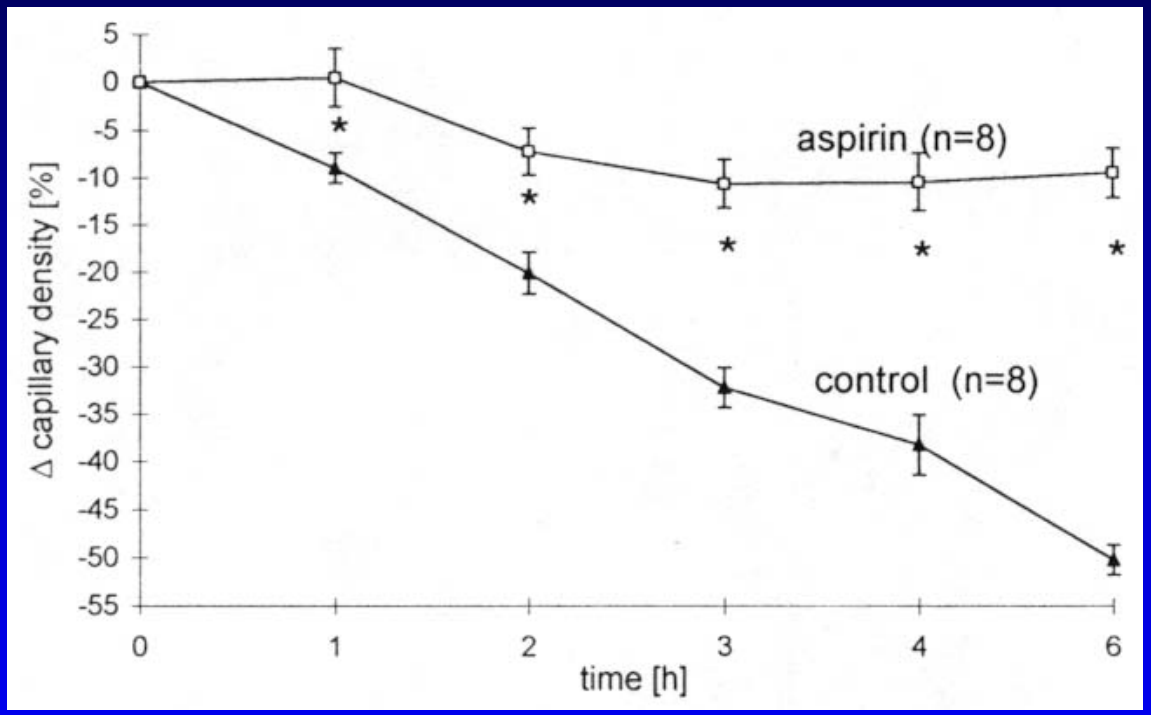


Venous Thrombus size

Animal Model of Thrombosis

Effect of aspirin on Zone II (Peter, *PRS*, 1997)



Capillary Perfusion

<u>Microemboli A1 – A2</u>

control = 15.9 +/- 14.3

aspirin = 55.0 +/- 39.8

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    - propose greater influence of shear activation of platelets at artery than biochemical activation (TxA_2/PGI_2)
  - ASA increases capillary perfusion (Zone II) *despite* greater emboli
    - previous study showed ↓ emboli but *no* improved flow with heparin
    - hypothesize reduced thrombus stability with ASA
    - hypothesize vasoconstriction (TxA_2) more important than microemboli

Anticoagulation in Practice

Aspirin

- Commonly used
- No statistically significant studies

Dextran

- Widely used → no supporting data

Heparin

- Benefit *trend* shown for low-dose heparin and bolus heparin (Kroll, *PRS*, 1995)

Thrombosis, Flap Loss, and Hematoma

Group	*n*	Flap Loss	Thrombosis	Hematoma
All flaps	517	21 (4.1%)	30 (5.8%)	36 (7.0%)
No heparin	227	10 (4.4%)	14 (6.1%)	12 (5.3%)
Low-dose heparin	192	2 (1.0%)	4 (2.1%)	13 (6.8%)
Bolus heparin	46	0 (0.0%)	1 (2.2%)	3 (6.5%)
High-dose heparin	30	3 (10%)	4 (13.3%)	6 (20%)
Dextran 40	22	6 (27.2%)	7 (31.8%)	2 (9.1%)

Free Flap Failure

How to repair following failure? (Wei, *PRS*, 2001)

- 42/1235 HNS flaps failed (3.4%)
  - 23 total & 19 partial failures

Outcome	Management (no. of cases)		
	Second Free Flap	Regional Flap	Conservative
Successful	16	8	6
Complicated			
Major	1	2	1
Minor	0	5	3
Total	17	15	10
Days of hospitalization	44	75	42

Consider second free flap despite failure

Summary

- **Few good studies to base decisions**
  - large, prospective studies by flap type and indication necessary
- **Pre-operative health influences result**
  - smoking, obesity, peripheral vascular disease
- **Intra-operative fluid load important**
  - hematocrit, anesthetic agent, pressors also factors
  - technical factors critical
- **Post-operative management poorly understood**
  - consider patient risk factors
  - ASA warrants further study
  - second free flap is an option following flap failure