

# Pesky Problems Poised for Laser Surgery

- Why use photons in medicine/surgery?

*Selectivity* (but, how?)

# Pesky Problems Poised for Laser Surgery

- Why use photons in medicine/surgery?

*Selectivity* (but, how?)

- Cancer
- Acne
- Fat
- Tattoos

# Skin Cancer

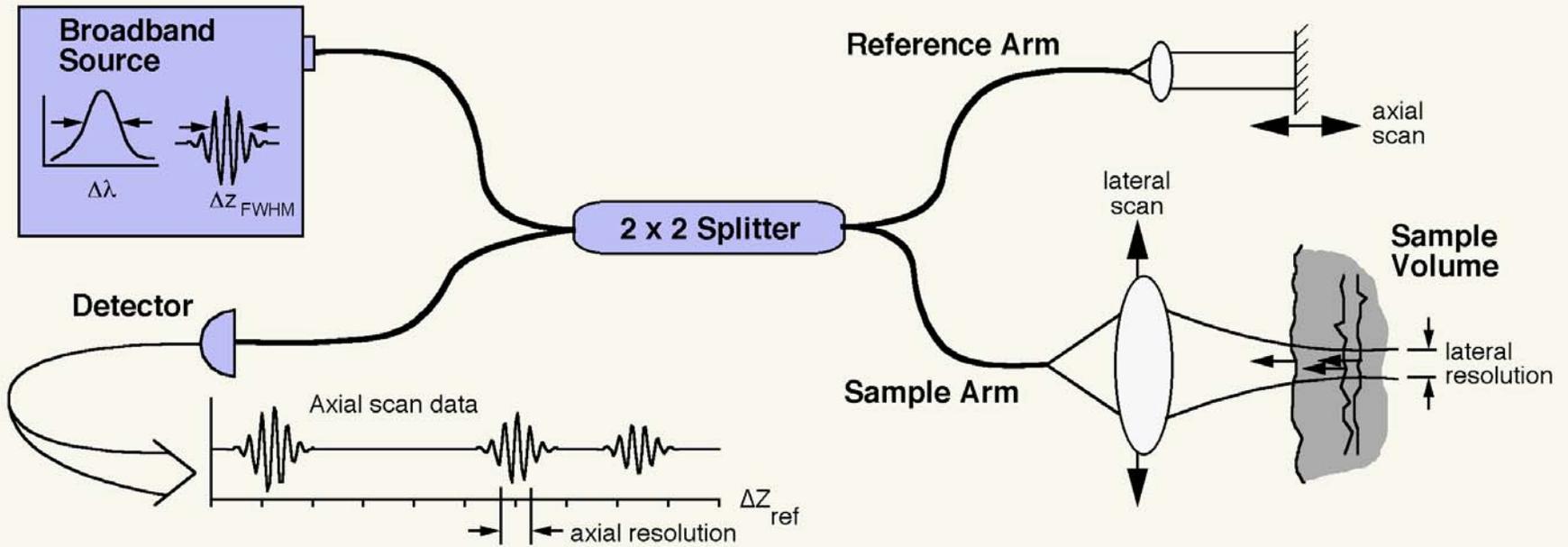
## How poetic to treat it with light...

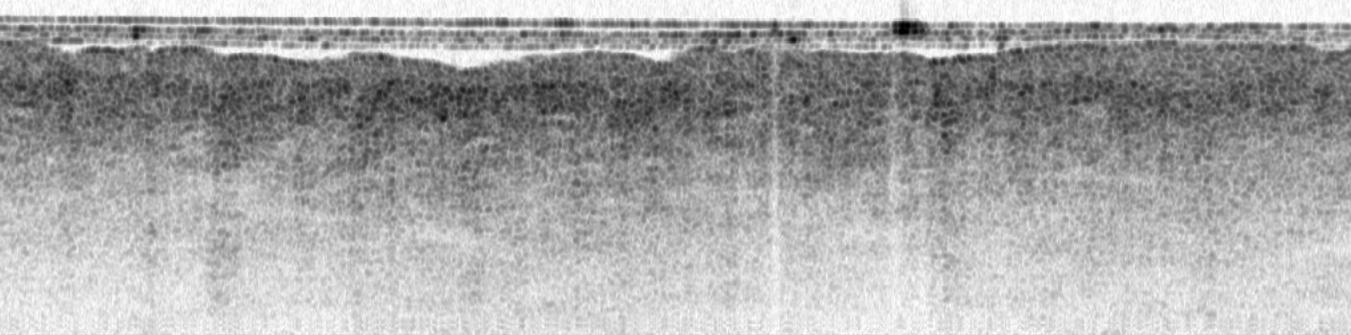
- Caused by sun exposure
- US statistics:
  - Basal cell carcinoma: > 1 million/year
  - Squamous cell carcinoma: ~ 100 k/year
  - Melanoma: ~ 30 k/year, ~ 8 k deaths
- Unguided surgery is 90% effective for BCC
- Mohs technique = surgeon runs back and forth to a microscope → 99.5% effective
- Mohs is unique to dermatology, at present
- Can we *image* and *precisely remove* cancers in “real time”?





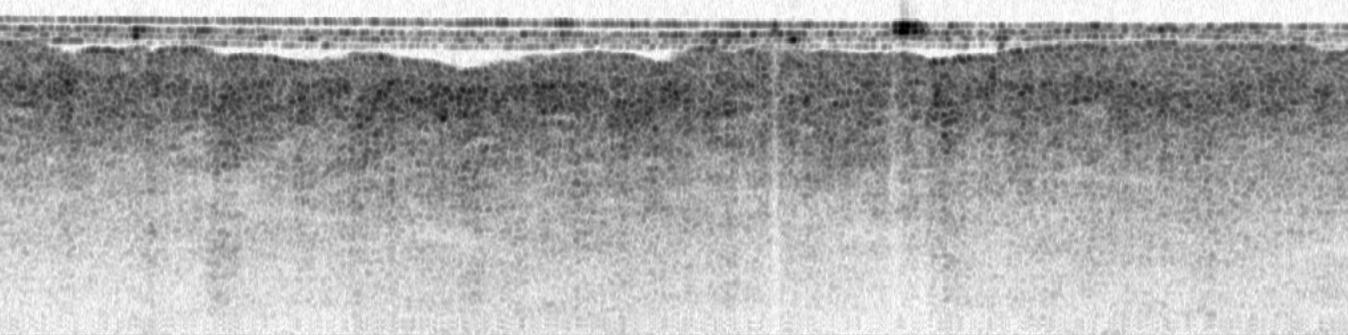
# OCT schema



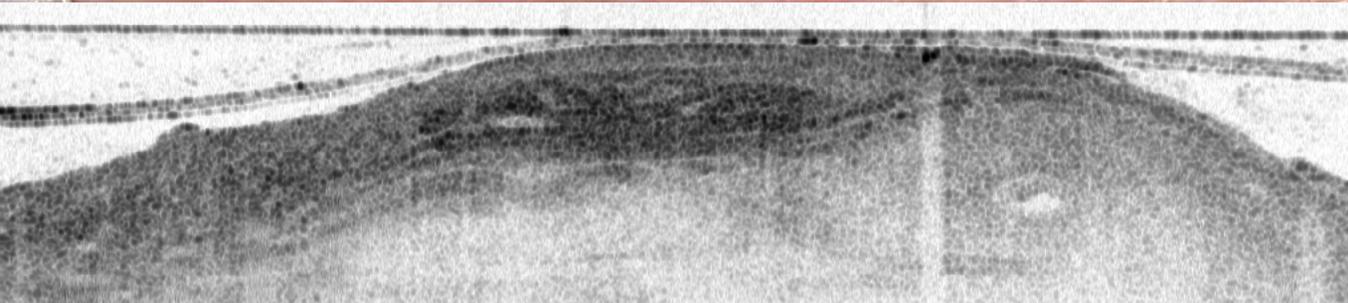


**Uninvolved**



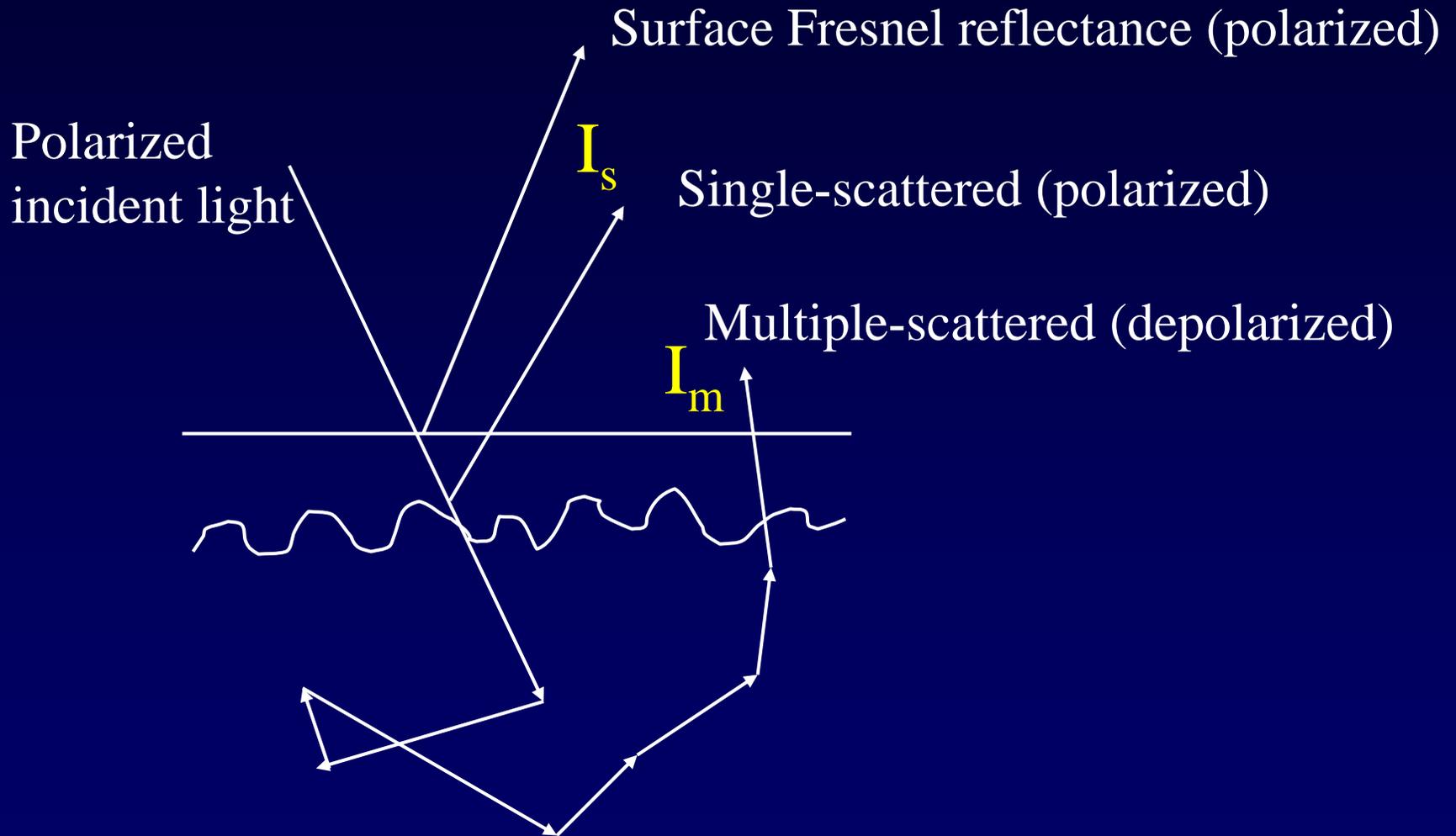


**Uninvolved**



**Rim of BCC**

# Light Reflected (scattered) from Skin

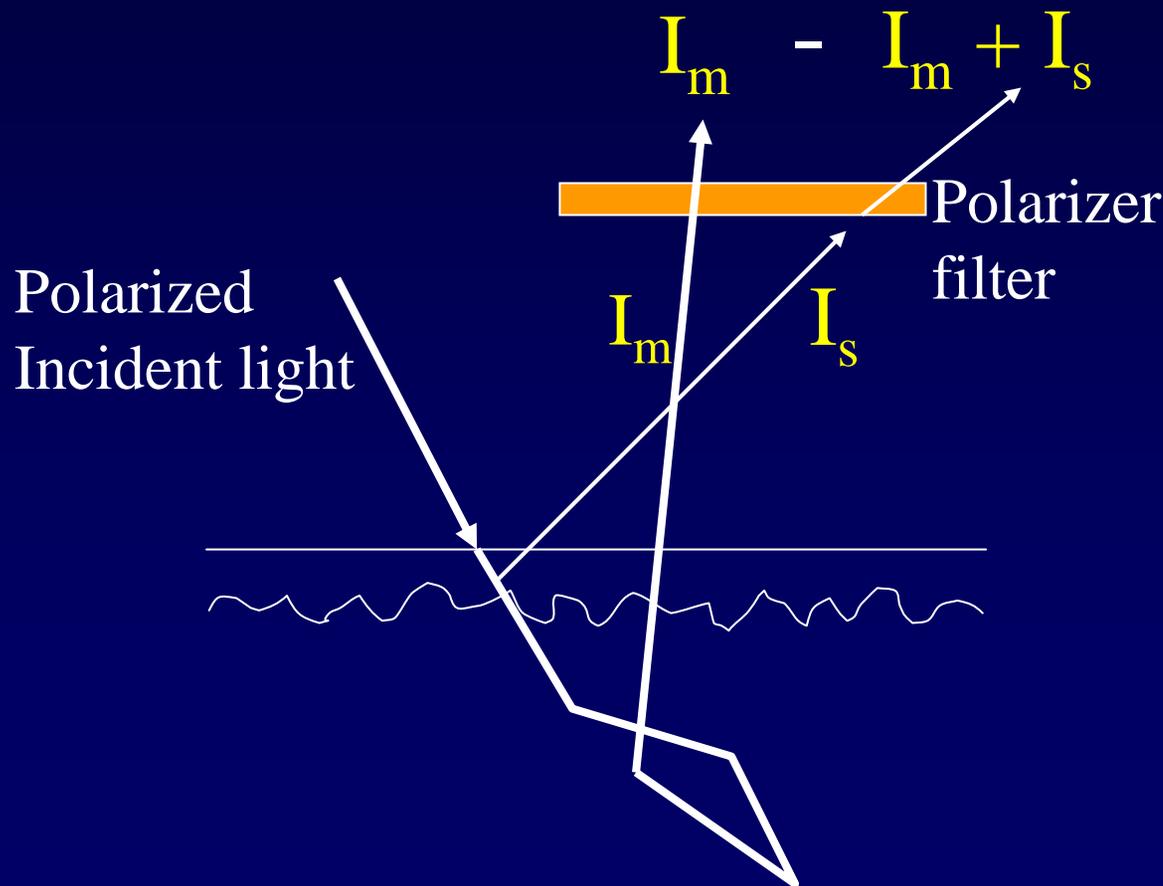


# Polarization Imaging of Single Scattered Light

Polarizer filter at  $90^\circ$   
to incident light  
polarization

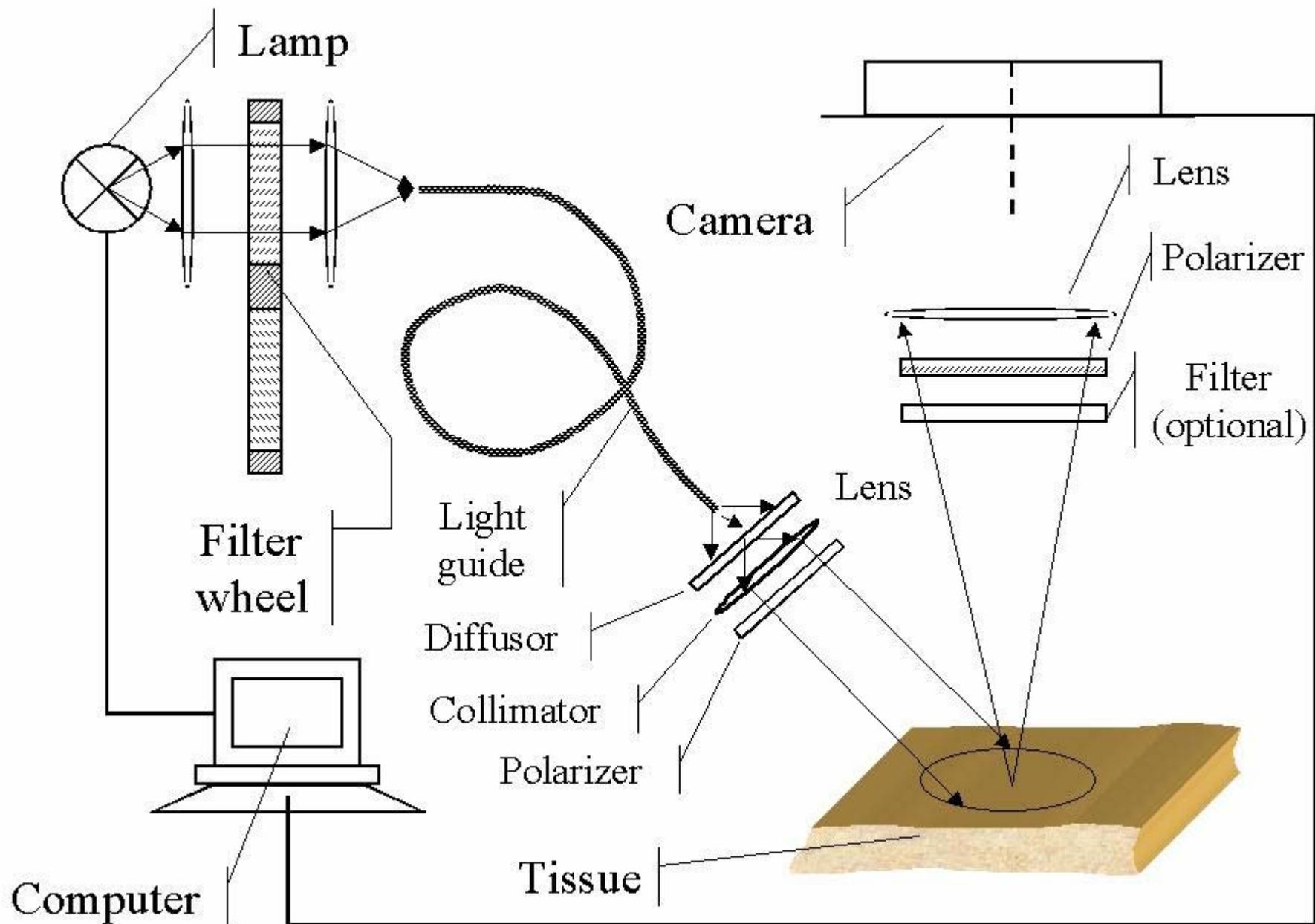
Polarizer filter  
parallel to incident  
light polarization

Single-scattered  
light image



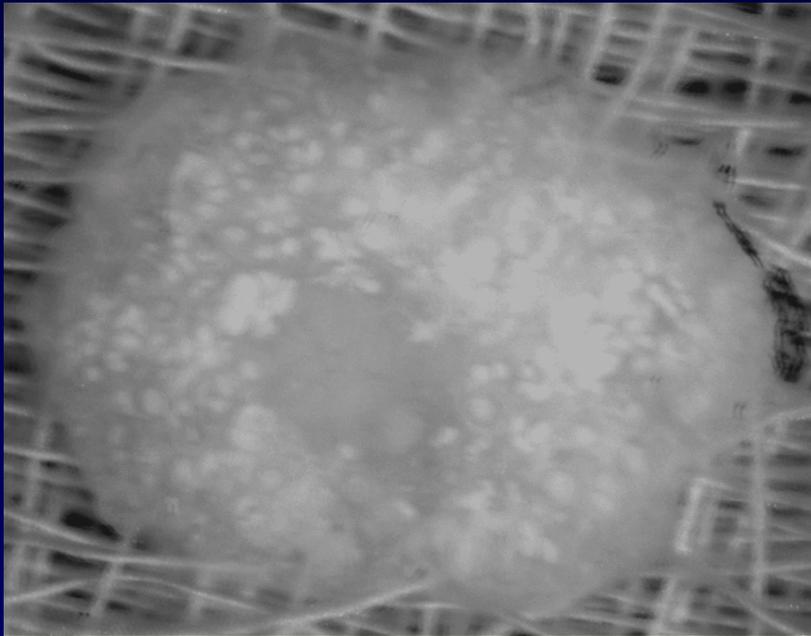
$$\Rightarrow I_s$$

High-resolution,  
superficial  
image?  
 $\mu_s^{-1} \sim 100 \mu\text{m}$

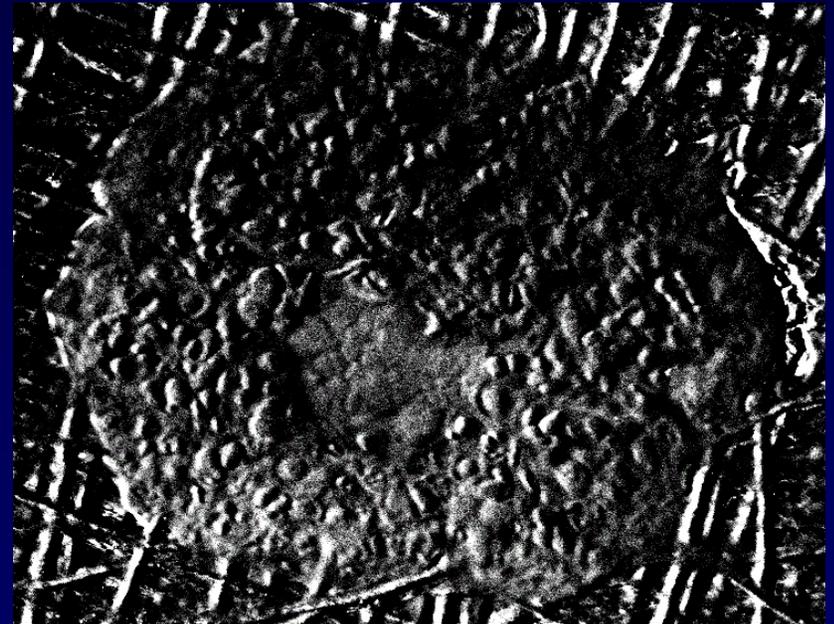


# Imaging whole, intact surgery specimen with BCC

← 12 mm →

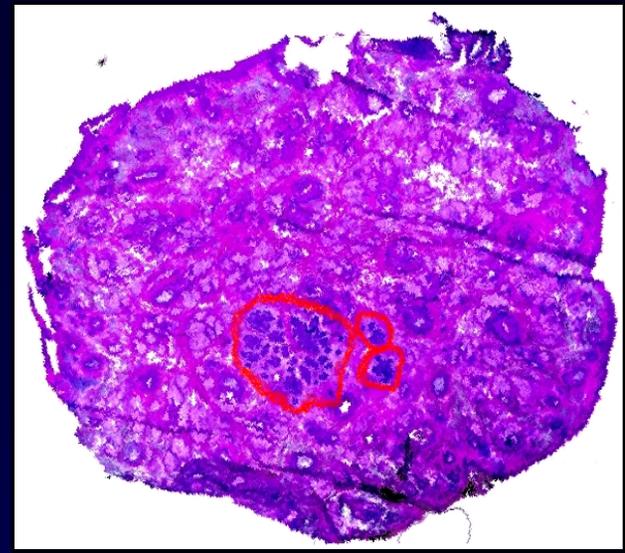
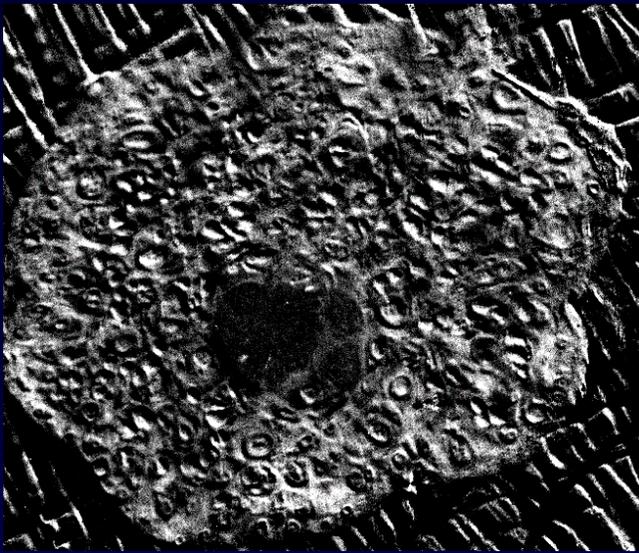


710 nm, plain image

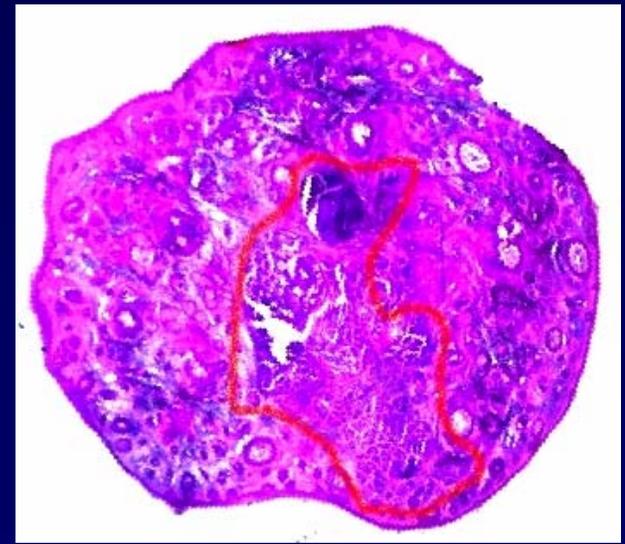
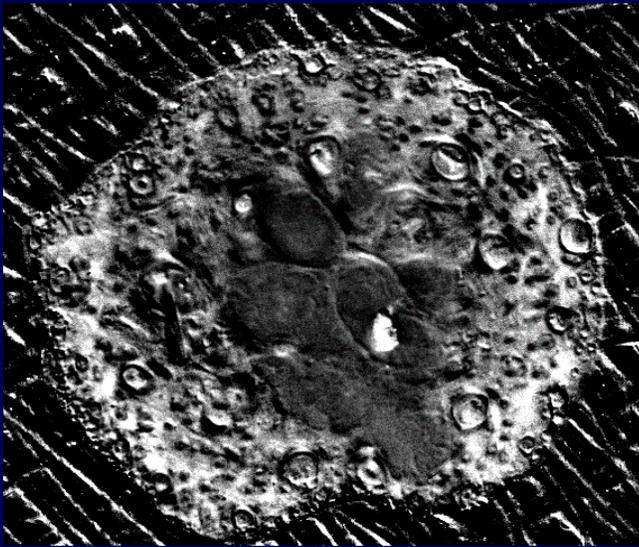


DI  $\sim 150 \mu\text{m}$  “section”

Images courtesy of Anna Yaroslavsky, PhD (Harvard)

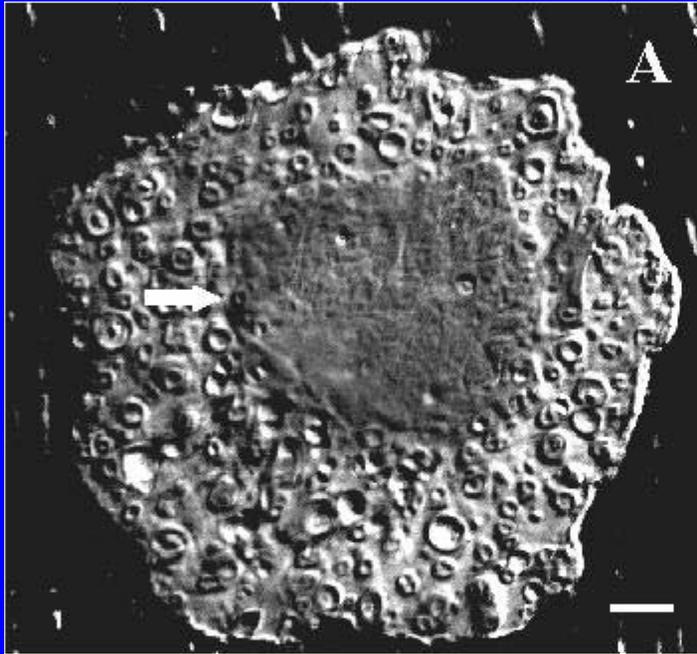


620 nm, nodular BCC stained with TB

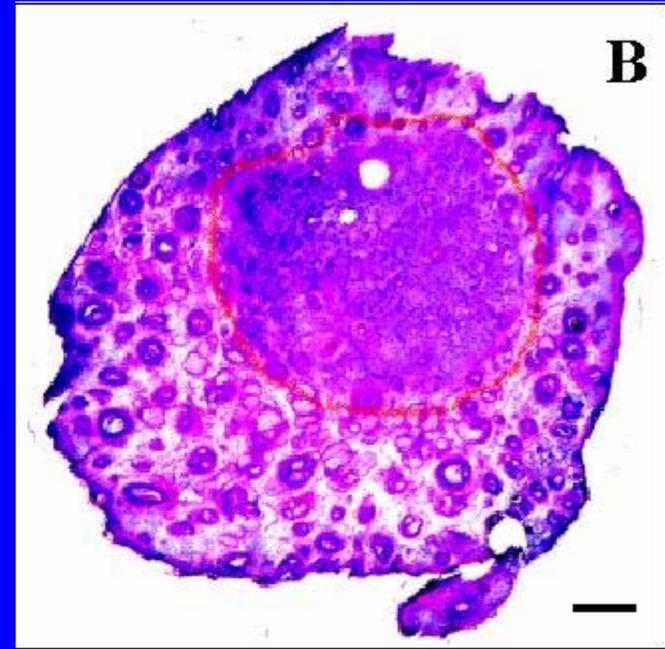


620 nm, nodular BCC stained with MB

# Morpheaform (infiltrating) BCC



Intact, 600 nm, TB-stained



H&E stain of Mohs section

Images courtesy of Anna Yaroslavsky, PhD (Harvard)

# Next step?

## Cancer surgery should be a video game

Real-time imaging

+ laser ablation

= new surgical platform

# “Selective Photothermolysis”

RR Anderson, JA Parrish Science 220:524-527 (1983)

Selective Absorption → Wavelength

Thermal Confinement → Pulse duration

~ 1 million treatments / month

Blood vessels

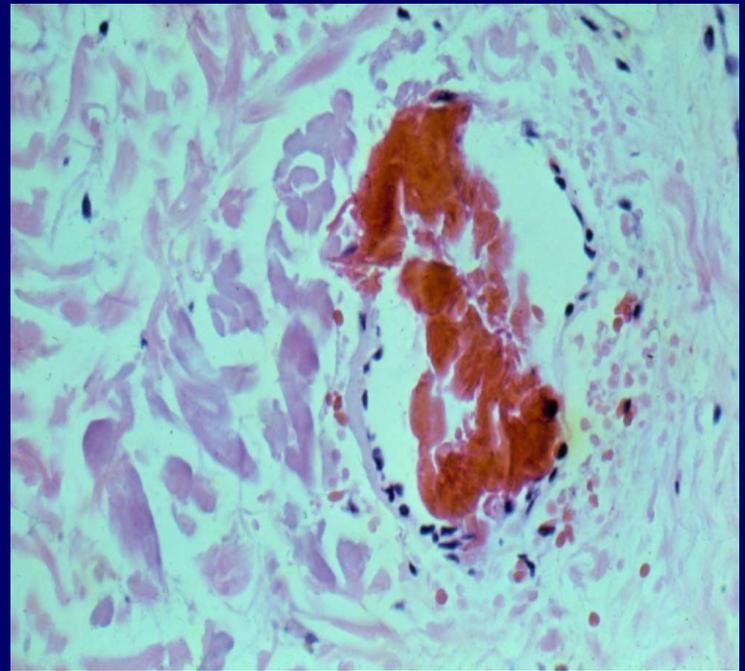
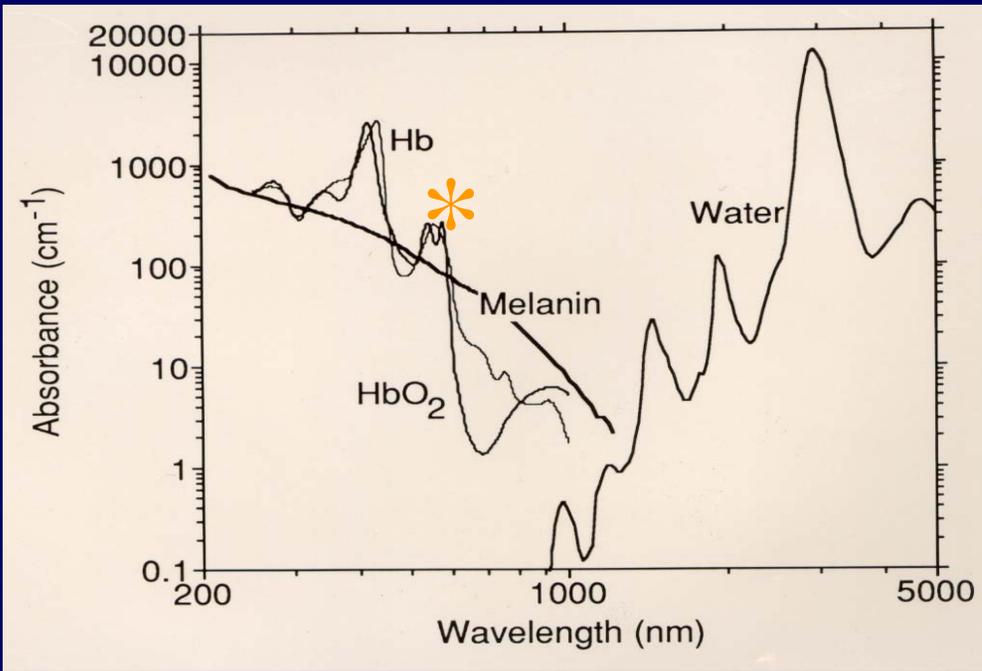
Pigmented Cells

Tattoos

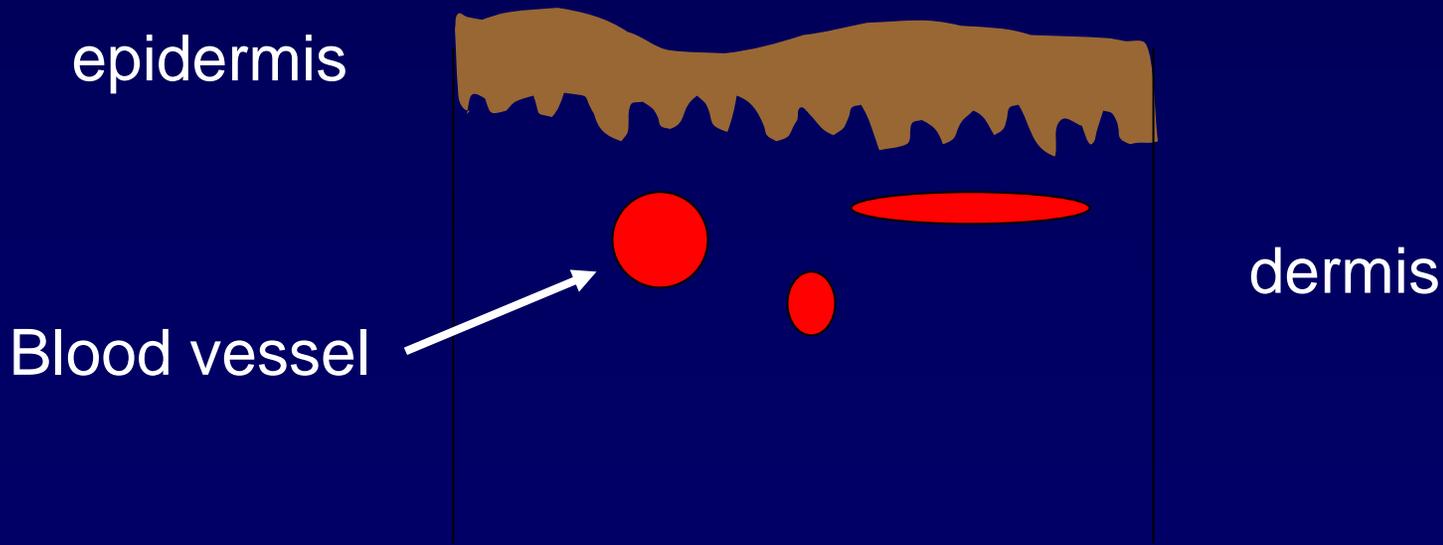
Hair

Fat?

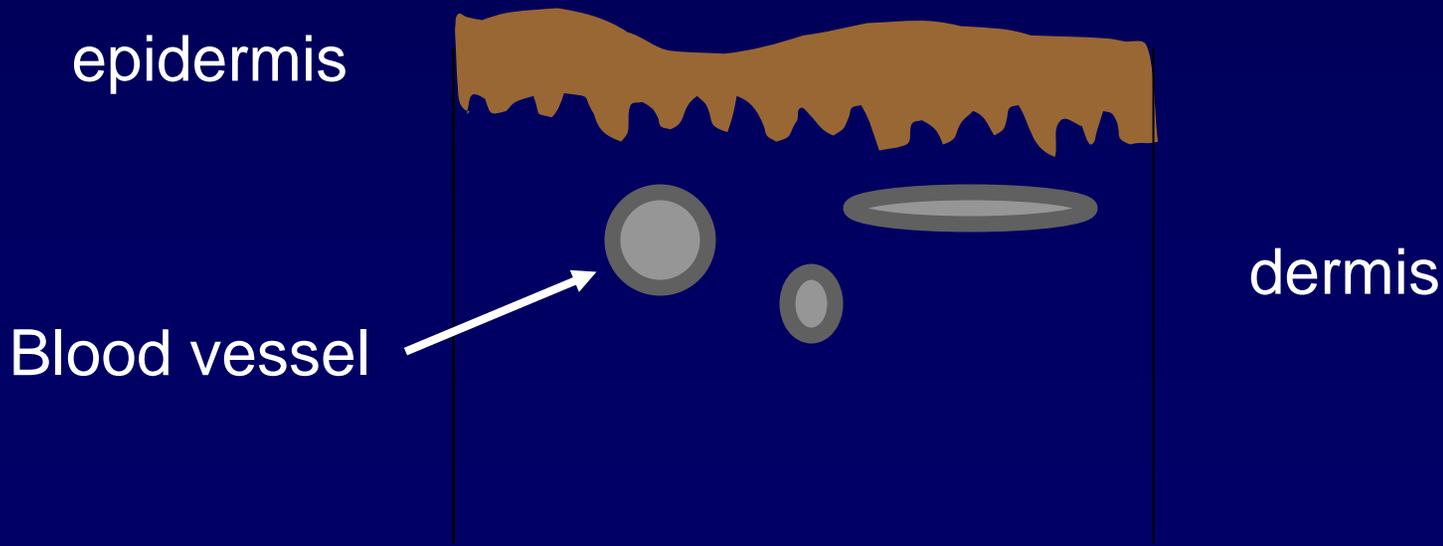
Acne?



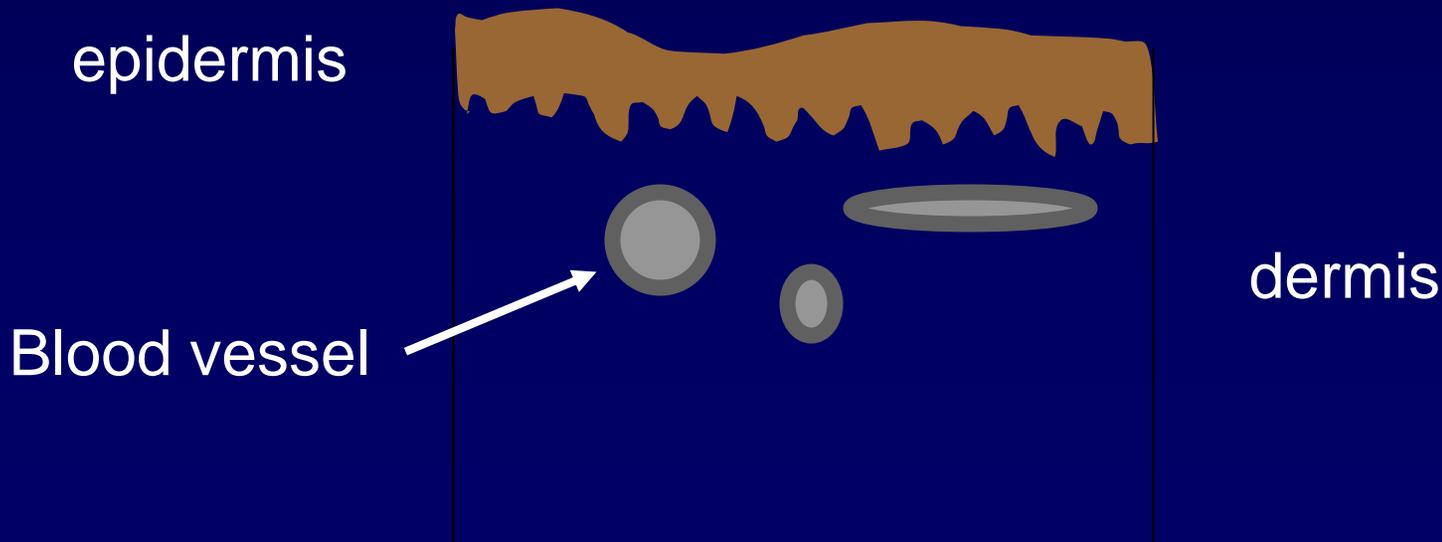
*Selective* light absorption  
→ very local heating



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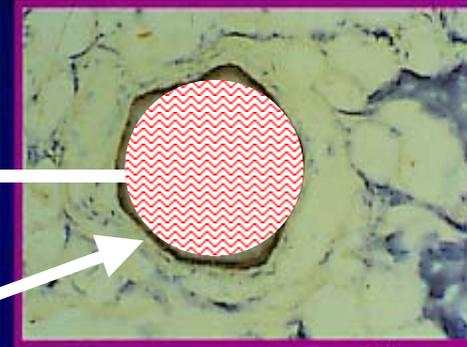
*Selective* light absorption  
→ very local heating  
→ selective repair



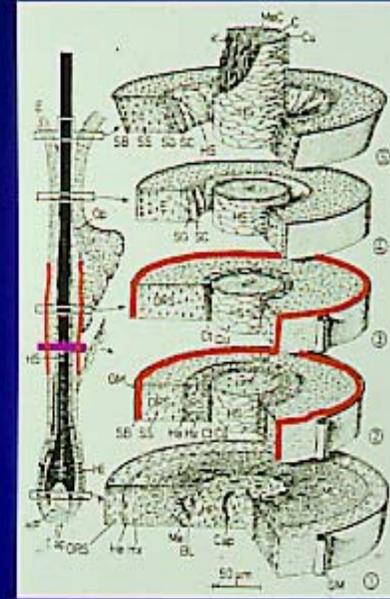
# Laser Hair Removal

Pigmented hair shaft

Follicular Stem Cells  
(not pigmented)



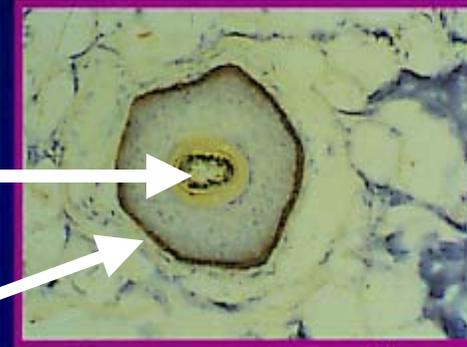
NBTC  
C8 / 144B



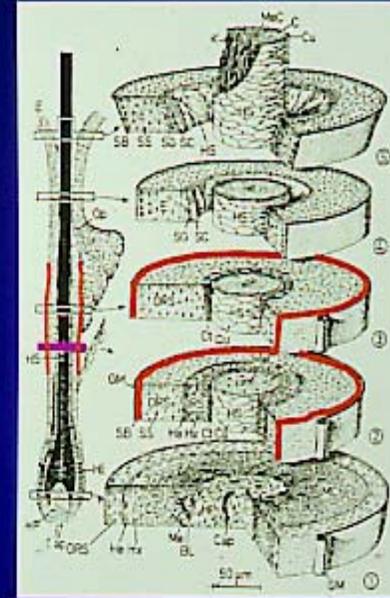
# Laser Hair Removal

Pigmented hair shaft

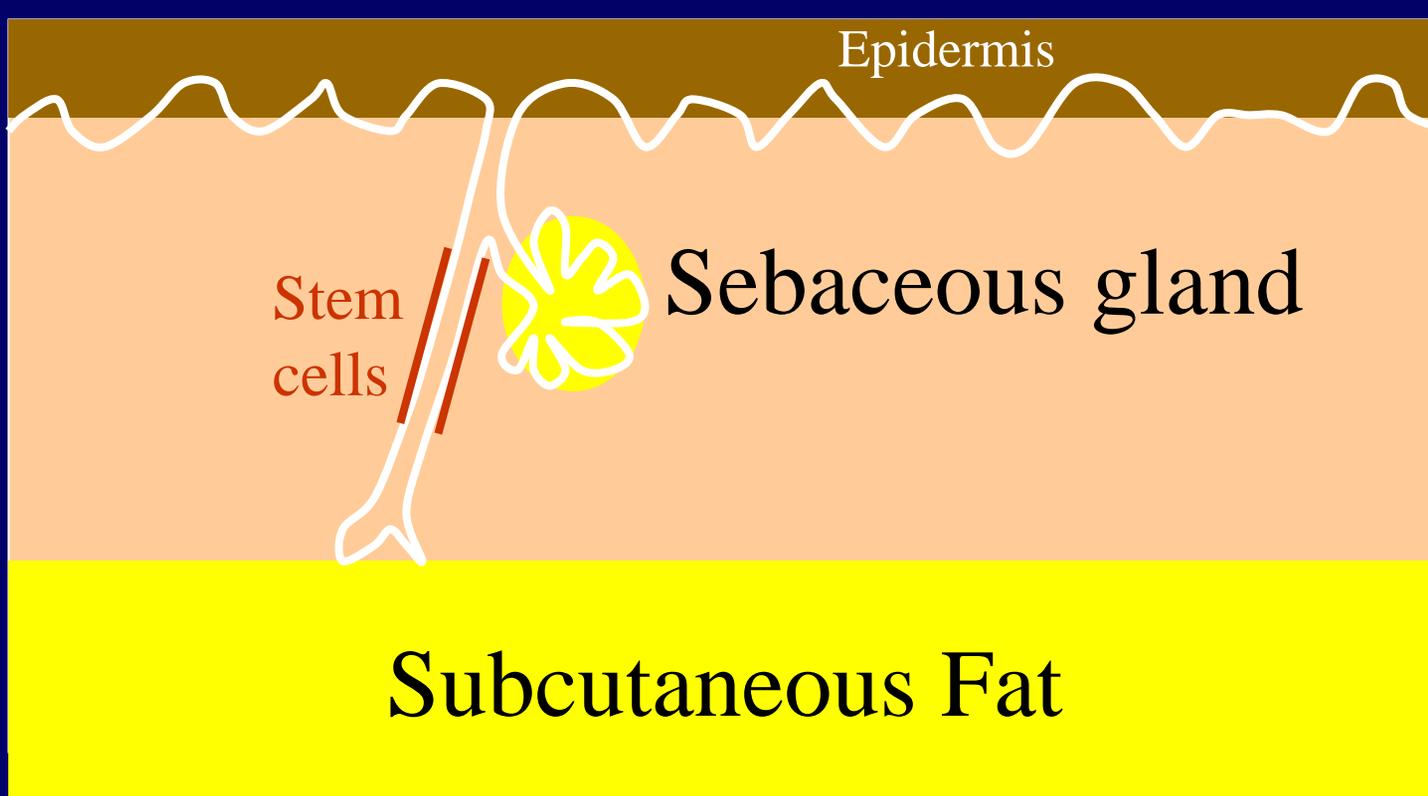
Follicular Stem Cells  
(not pigmented)



NBTC  
C8 / 144B



*Altshuler GB et al Extended theory of selective photothermolysis.  
Lasers Surg Med 2001;27:1-17*



1-4 mm

# Photo-thermal Excitation

$$\Delta T = (E\mu_a / \rho c)$$

$\Delta T$ : Temperature rise

E: Energy density

$\mu_a$ : Absorption

$\rho$ : Density

c: Heat capacity

$$\rho_{\text{fat}} = 0.85 \text{ g cm}^{-3}$$

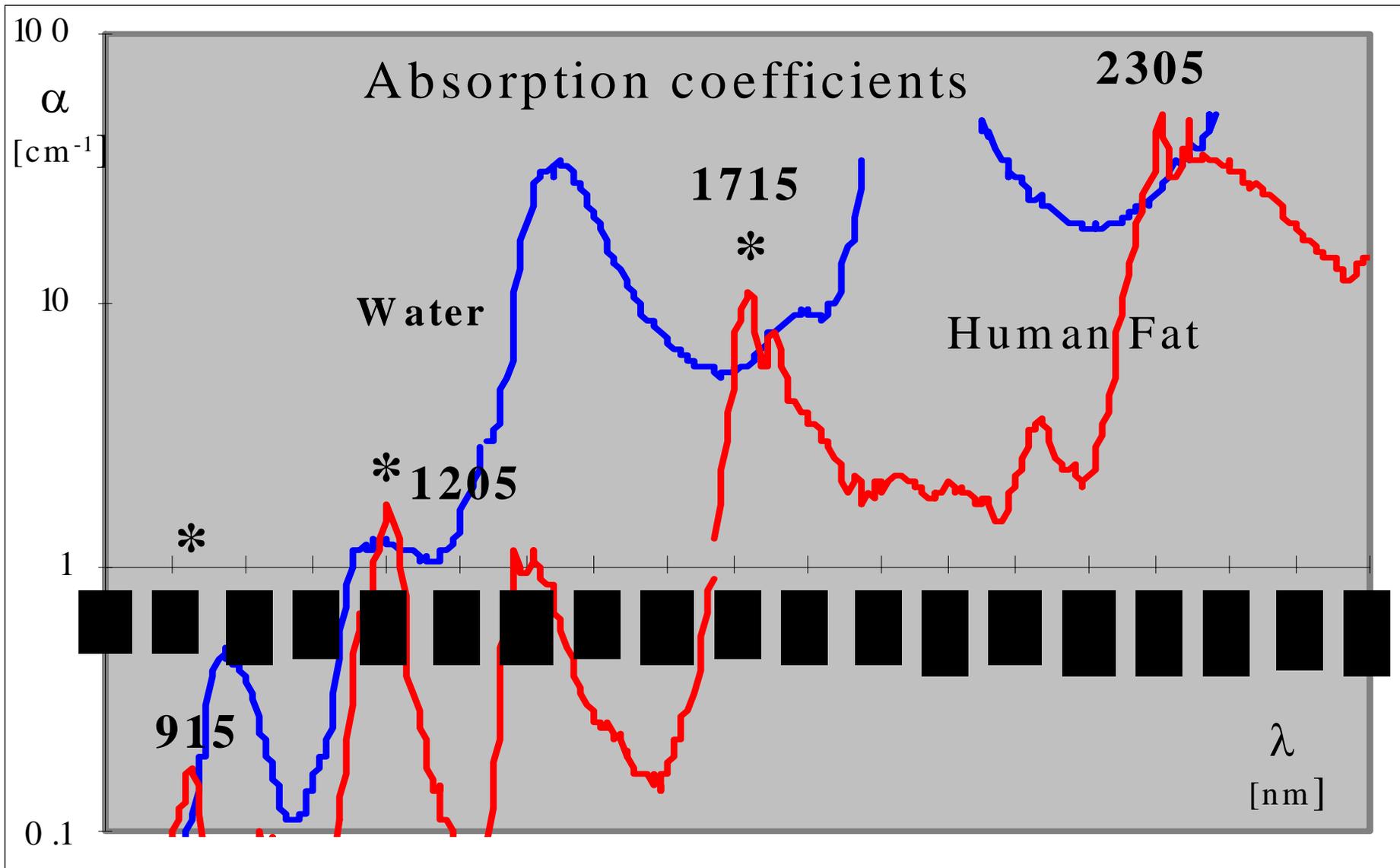
$$\rho_{\text{dermis}} = 1.08 \text{ g cm}^{-3}$$

$$c_{\text{fat}} = 2.3 \text{ J g}^{-1} \text{ K}^{-1}$$

$$c_{\text{dermis}} = 3.5 \text{ J g}^{-1} \text{ K}^{-1}$$

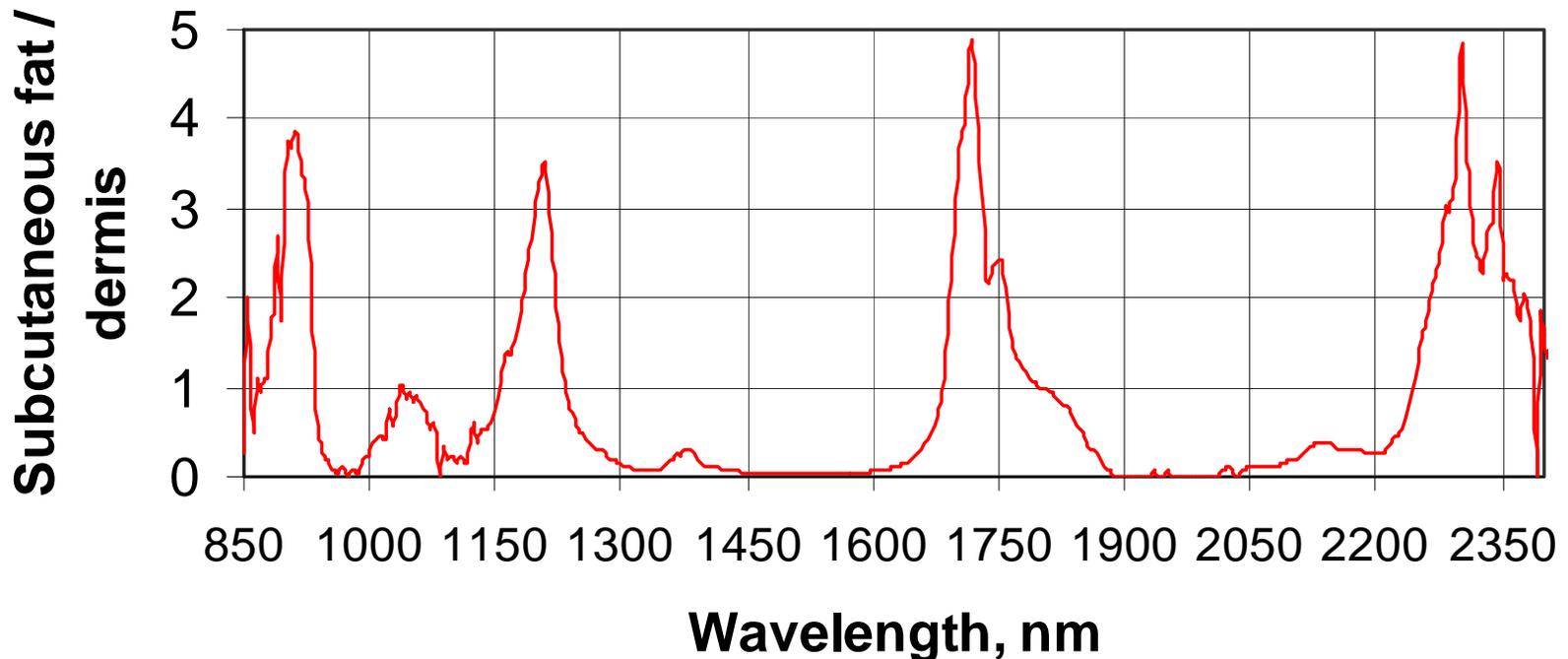
→ Because of low  $\rho c$ , fat is a “sitting duck”

# Fat and Water have nice “colors” in the NIR

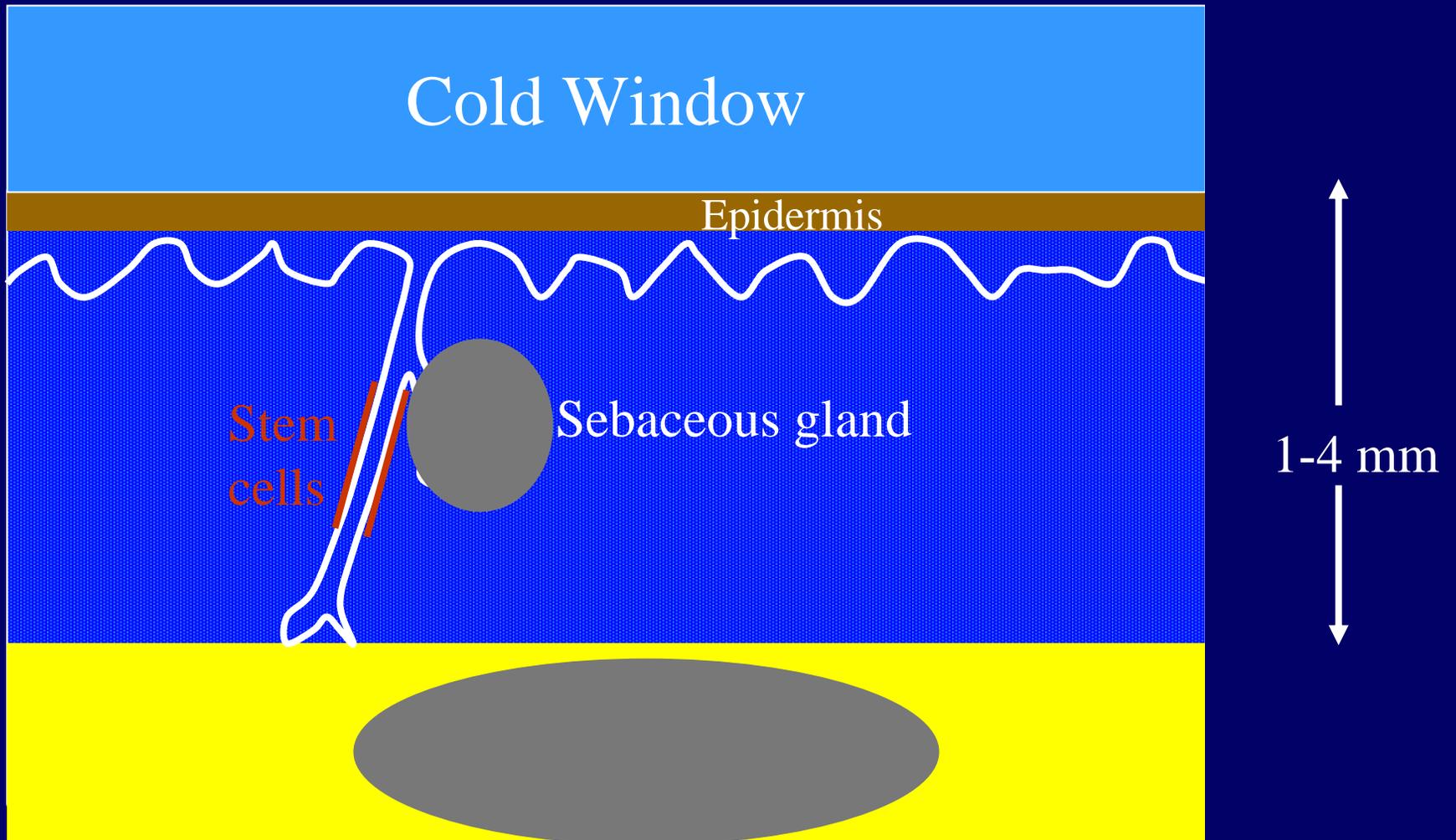


# Ideally, ratio of photothermal heating for fat vs. water

## Ratio of the temperature rises



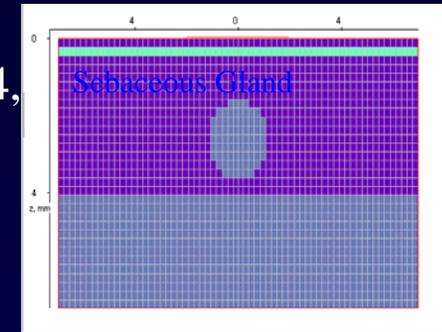
# CH-selective Laser



# Selective Fatty Tissue Targeting

## Monte Carlo Simulations :

Sebaceous gland (depth = 2.5 mm, radius = 1.0 mm  
 $n=1.45$ ,  $\mu_a=0.17$  /mm,  $\mu_s'=0.58$  /mm) below epidermis ( $n=1.4$ ,  
 $\mu_a=0.039$  /mm,  $\mu_s'=0.79$  /mm) and capillary layers ( $n=1.37$ ,  
 $\mu_a=0.04$  /mm,  $\mu_s'=0.3$  /mm) within 3.8 mm thick dermis  
( $n=1.4$ ,  $\mu_a=0.035$  /mm,  $\mu_s'=0.2$  /mm) irradiated by focused  
beam ( $\lambda = 1200$  nm  $r= 2$  mm, focusing depth = 3.5 mm )



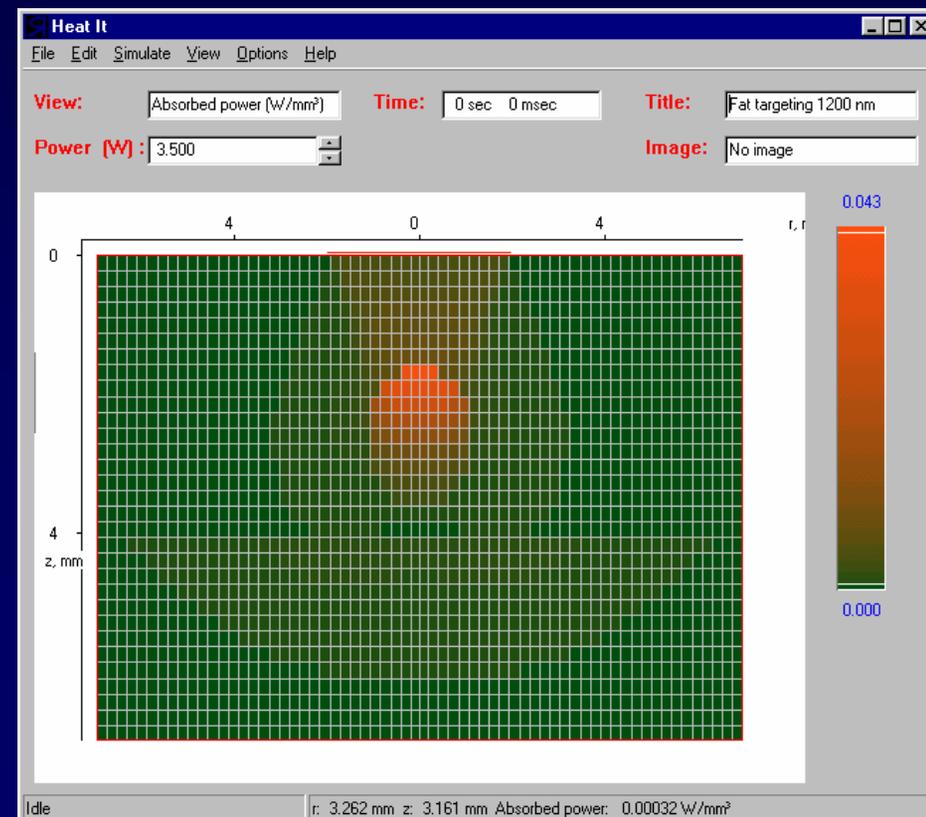
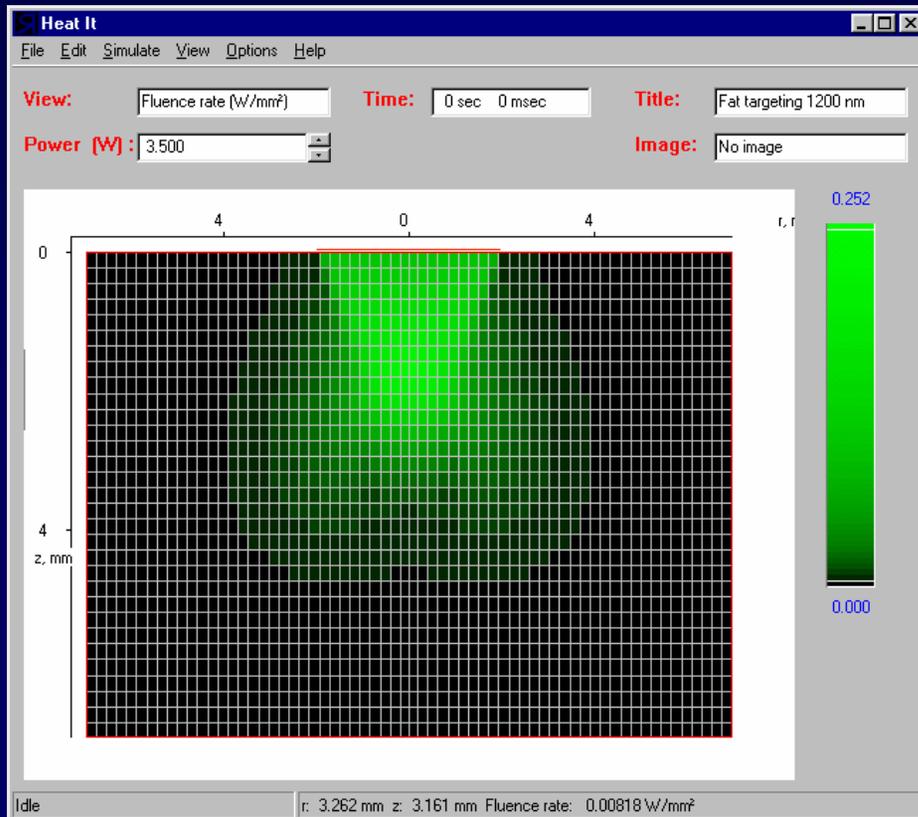
Epidermis

Blood

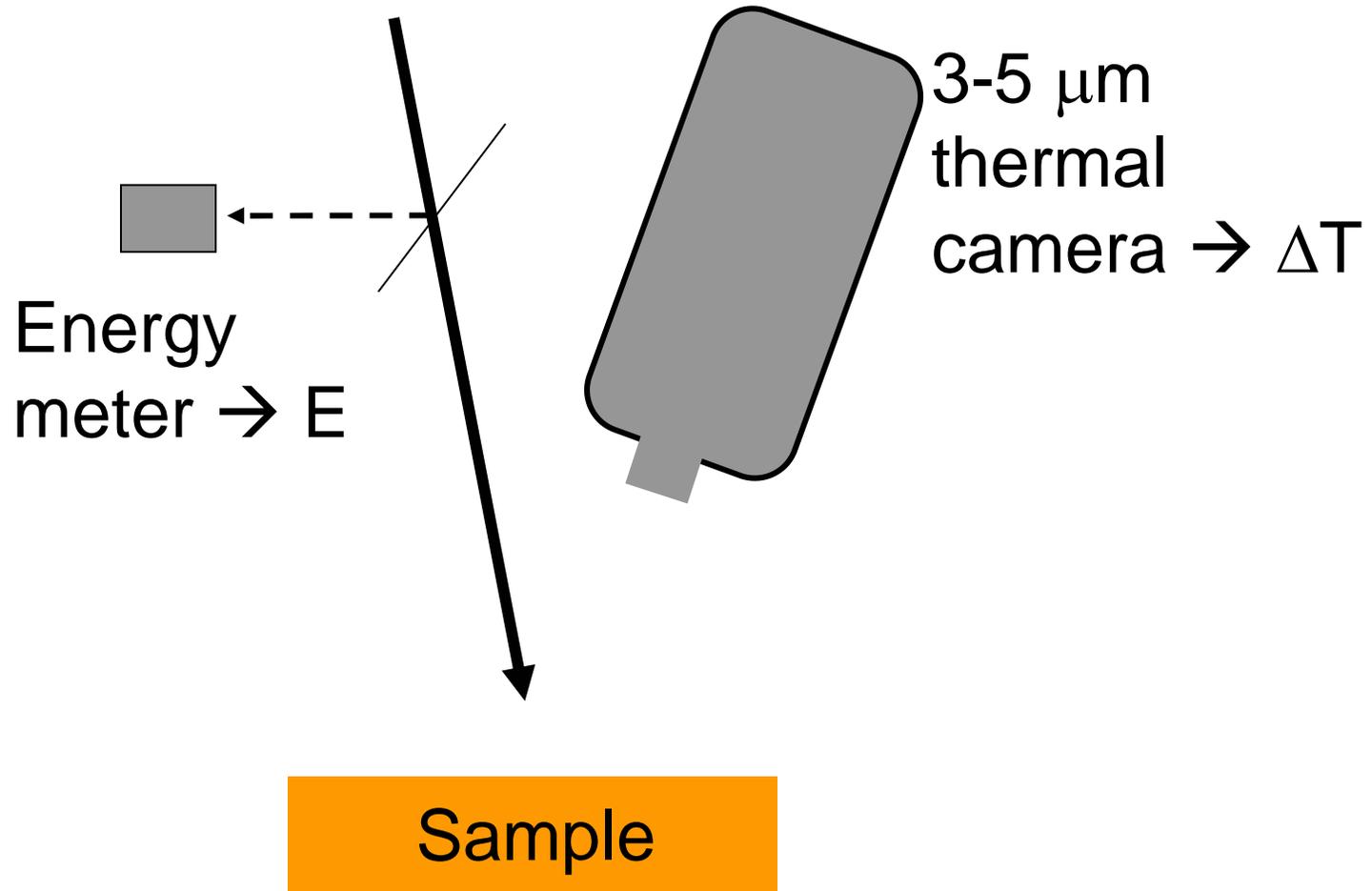
Dermis

Subcutaneous

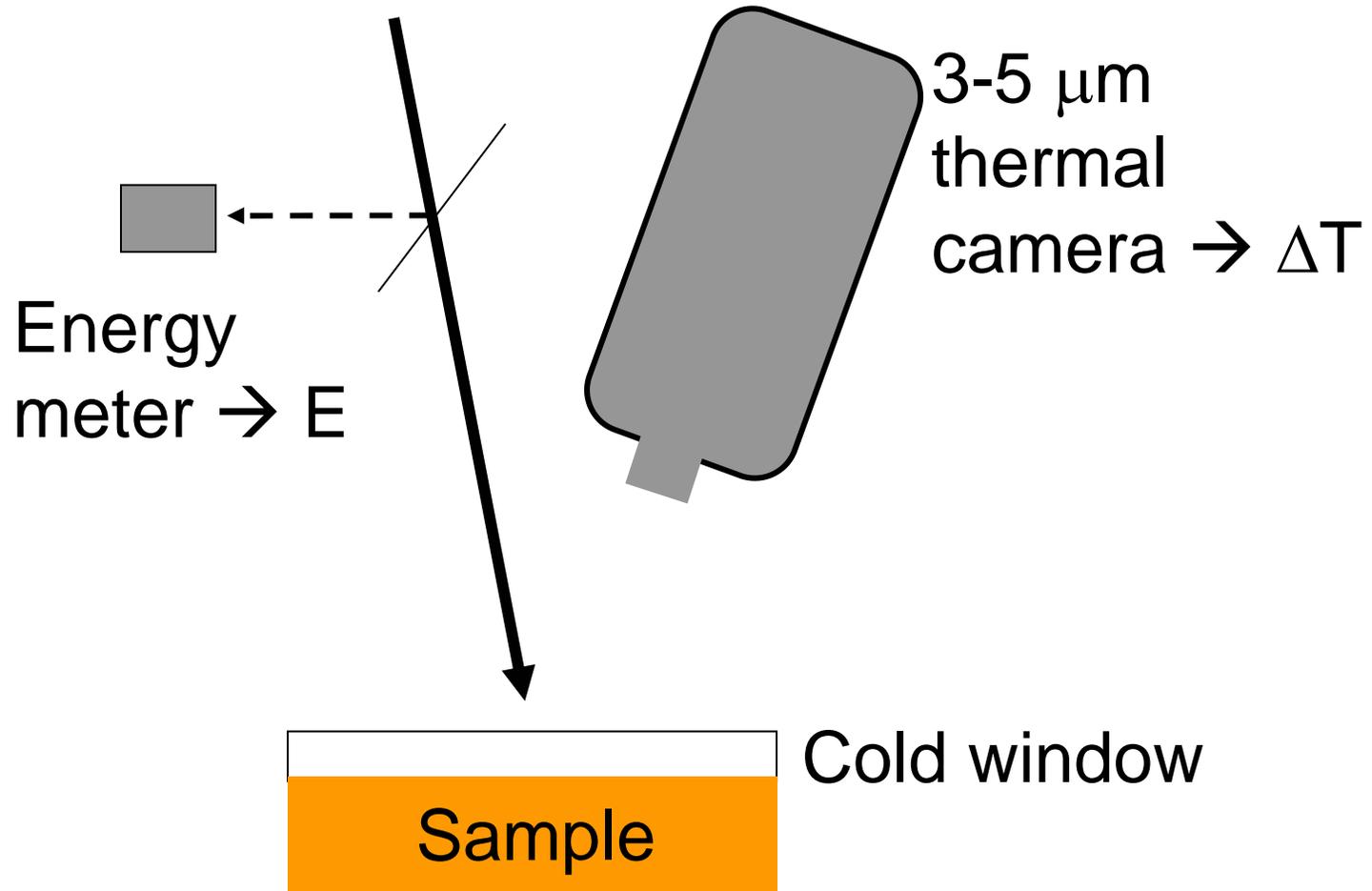
Fat



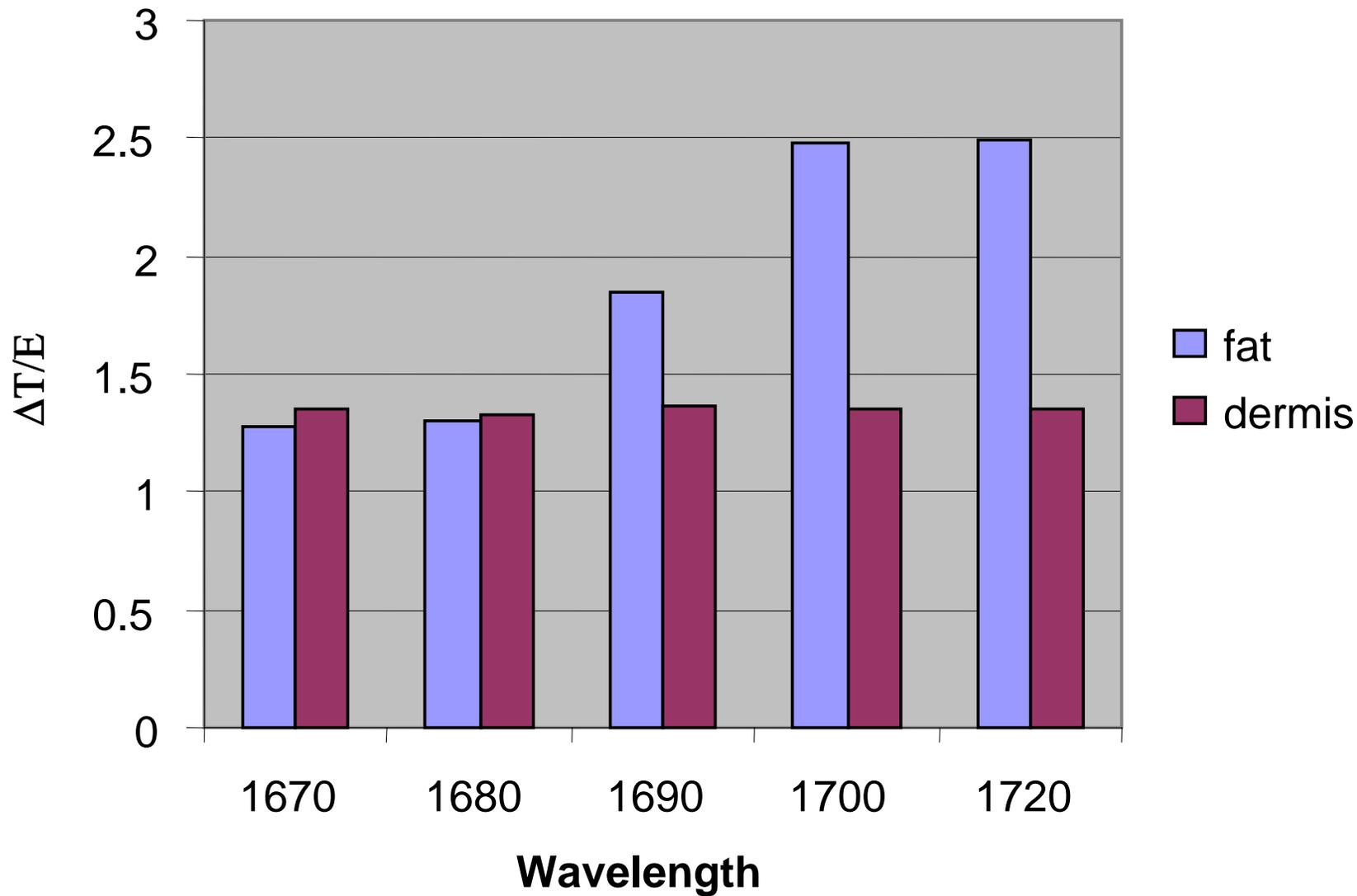
# JLab FEL



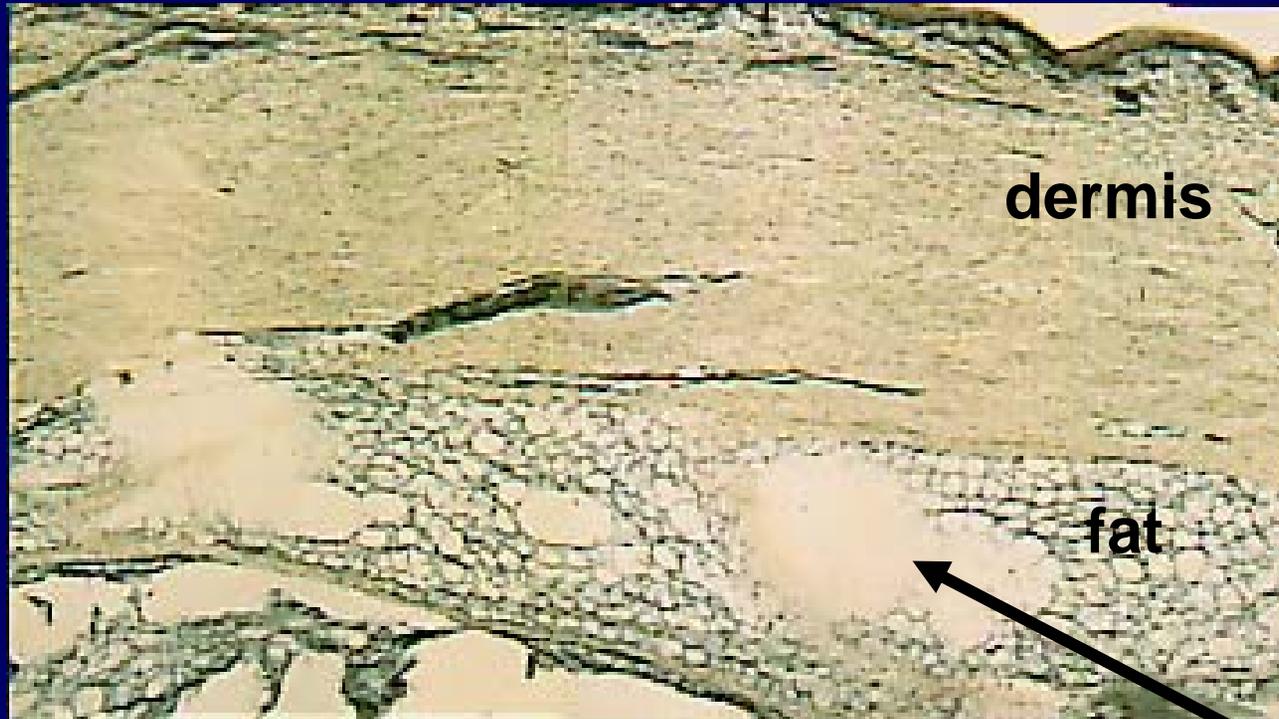
# JLab FEL



# $\Delta T/E$ vs. Wavelength (J-Lab FEL)



# Subcutaneous Fat Necrosis induced *in vitro* at 1208 nm (LDH activity stain)



dermis

~ 1 mm

fat

Laser-induced fat  
necrosis, achieved  
“through” the dermis

# What next?

- More power ( $> 100$  W) at 1210 nm band
- Photothermal excitation spectroscopy
- Thermal damage mapping by NTBC animal and human skin, fat, atherosclerotic arteries
- Animal studies (mice, 2006)
- FEL body sculpting? 😊

# Tattoos are part of being Human

- Ancient
  - 6000 year-old “iceman” had ~10 carbon tattoos
- Modern
  - ~ 20% of US college students
  - ~ 100 different “inks”, not regulated
  - Injected by artists with no medical training
  - RRR for hepatitis = 4 to 7
  - \$50 investment, lasts a lifetime
  - 30% will regret the tattoo
  - Women choose better...



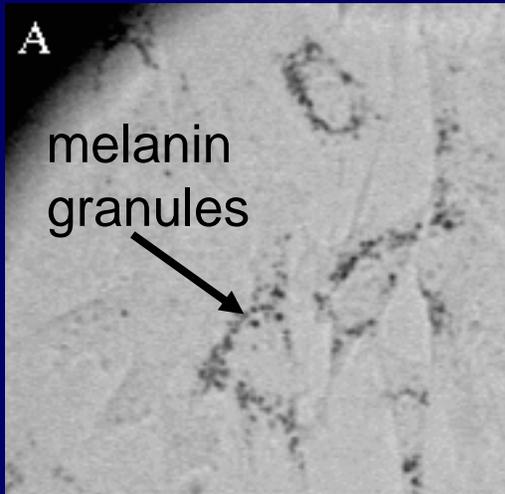


Tattoos are also nanoscale, intracellular particles of pigment. Laser pulses (ns) are used for tattoo “removal”.

- ~ 1 million/year seek removal
- ink is trapped in cells
- laser releases ink particles
- ink → lymph nodes
- 6-12 painful \$\$ treatments
- think B4 you ink....

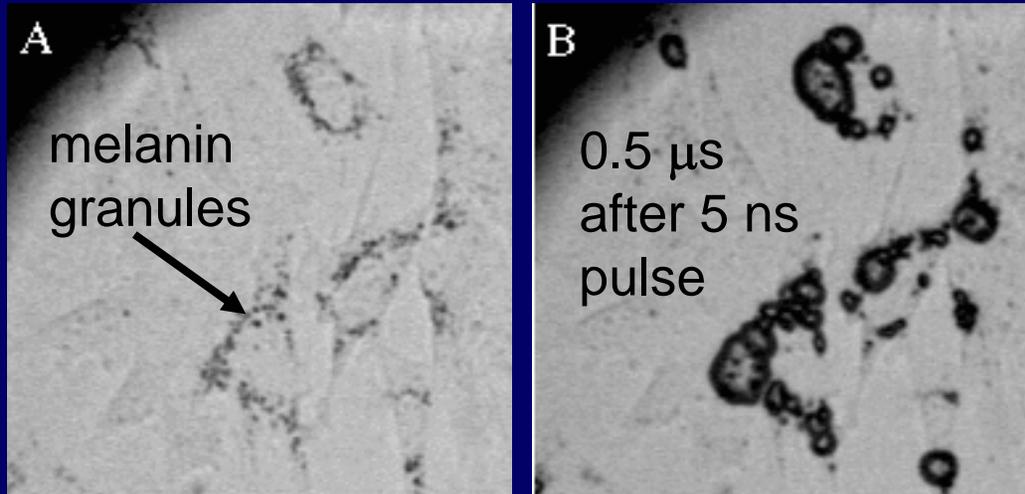
# Laser pulse targeting at the single cell level:

## Cytoplasmic cavitation



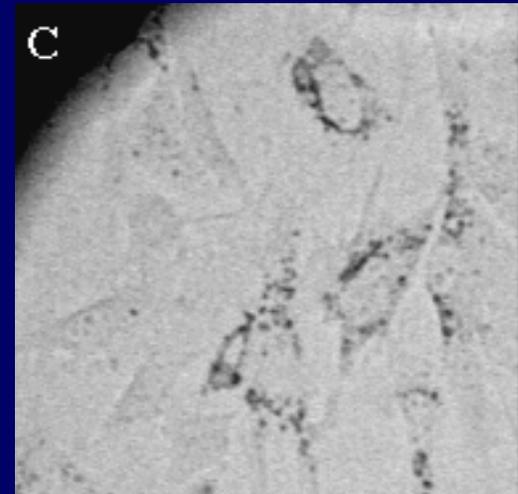
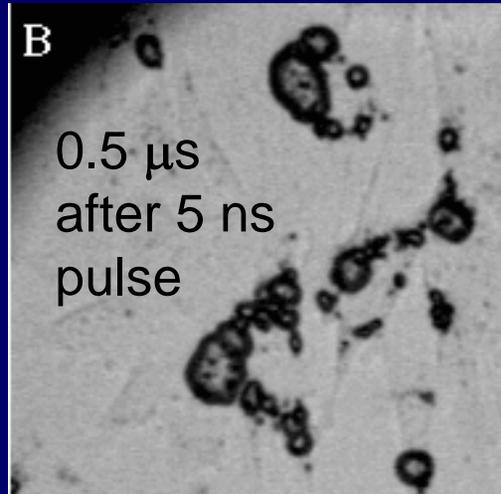
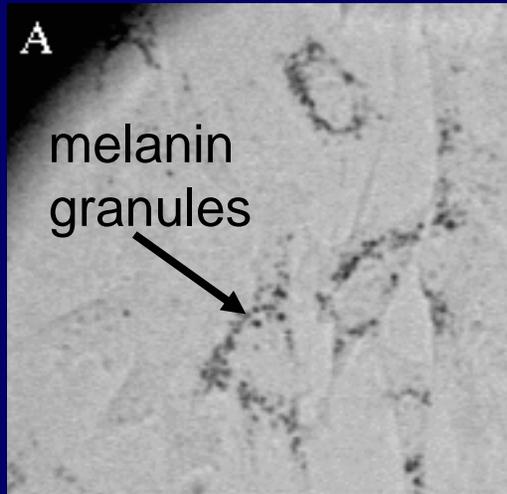
# Laser pulse targeting at the single cell level:

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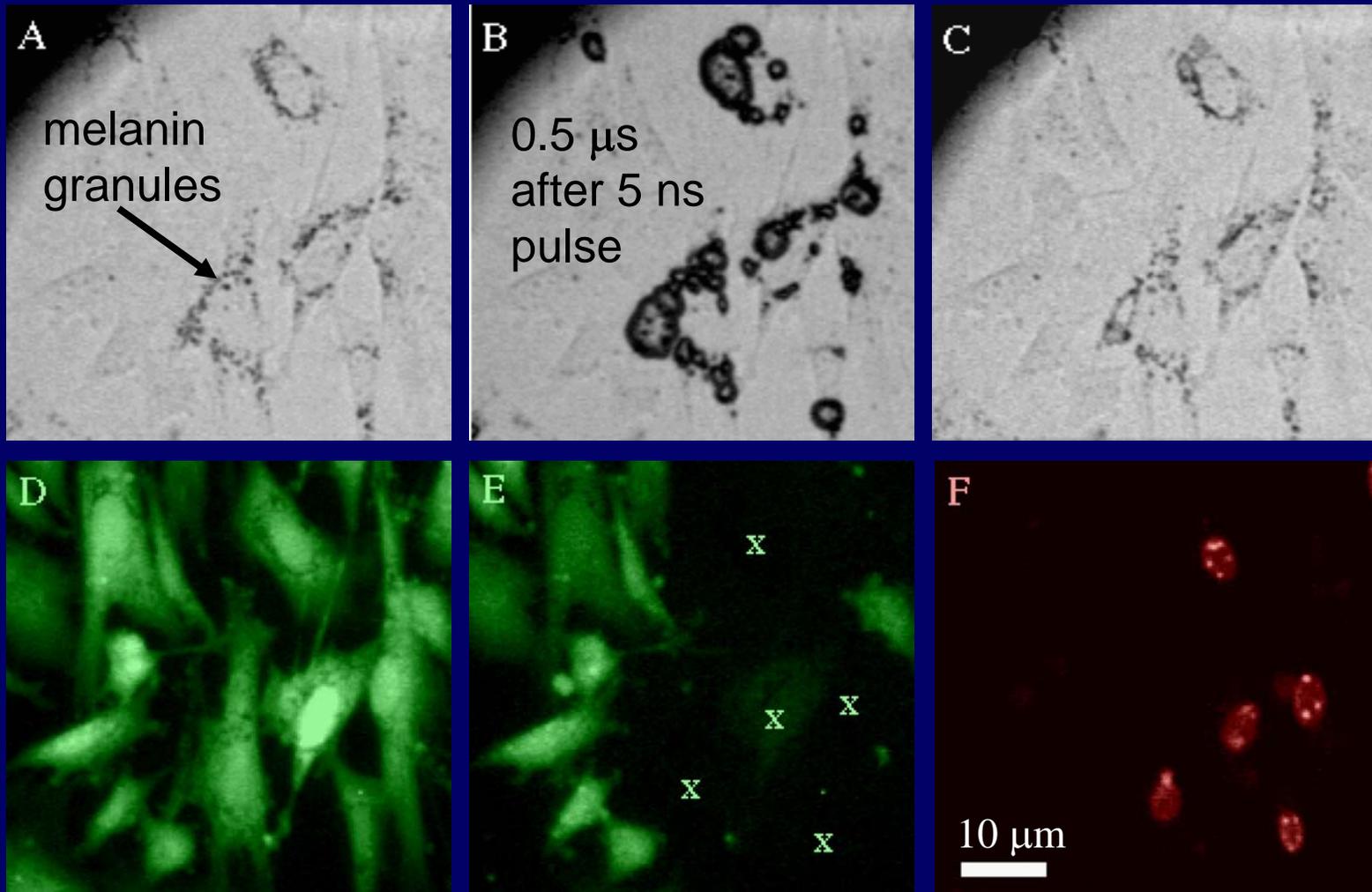
# Laser pulse targeting at the single cell level:

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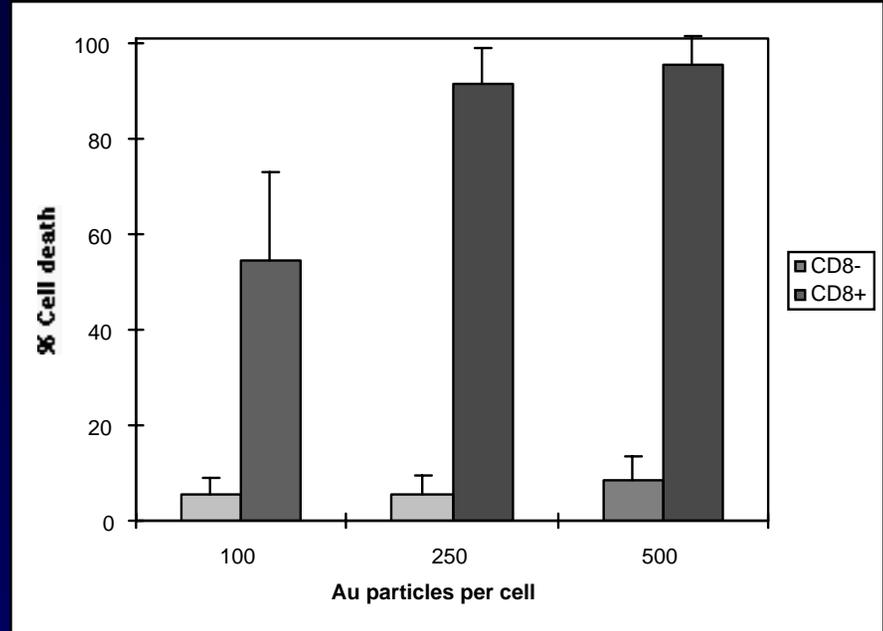
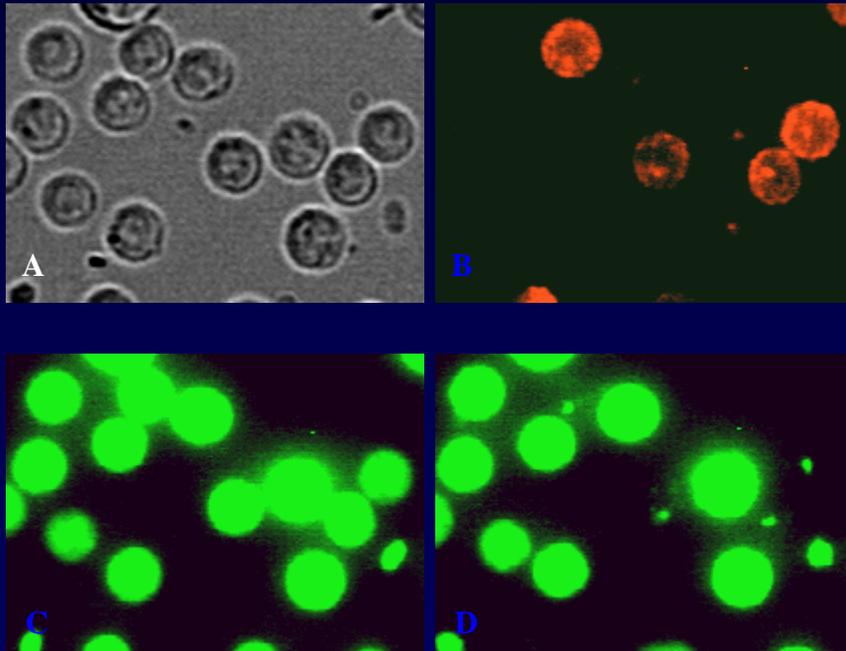


# Laser pulse targeting at the single cell level:

→ New treatment of glaucoma



# Selective Targeting of CD8+ T Cells (30 nm gold Nanoparticles)



- (A) T lymphocytes labeled with 30 nm gold particles
- (B) Cells double-labeled with anti-CD8 phycoerythrin (PE) fluorescent probe
- (C) and (D) Cells are irradiated with 20 nsec, 565 nm laser pulses at a fluence of  $0.5 \text{ J/cm}^2$ . Calcein-AM fluorescence before and after irradiation indicates loss of viability in CD8+ cells.
- (E) Results of selective killing of human lymphocytes using 30 nm gold particles directed against the CD8 membrane receptor.

# Nanoscale Particle Targeting

## Thermal Confinement

- Optical pulse < Thermal relaxation time ( $\tau_t$ )
- $\tau_t \cong d^2/4\kappa$  ( $\kappa$  is thermal diffusivity)
- 1  $\mu\text{m}$  object cools in  $\sim 1 \mu\text{s}$

## Inertial Confinement

- Optical pulse < Acoustic relaxation time ( $\tau_a$ )
- $\tau_a \cong d/v$  ( $v$  is sound velocity)
- 1  $\mu\text{m}$  object relaxes in  $\sim 1$  nanosecond

# Summary: tattoos

- Not a small problem  
10<sup>8</sup> people, 10<sup>9</sup> treatments, 10<sup>11</sup> \$
- Laser pulse-particle interactions have not been optimized
- Ps pulses @ tunable  $\lambda$
- Fs pulse interactions?
- Designer tattoos are possible by nanoparticle engineering...

Thanks