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 \(\rightarrow\) 99.5% effective
- Mohs is unique to dermatology, at present
- Can we *image* and *precisely remove* cancers in “real time”?
Uninvolved

Rim of BCC
Light Reflected (scattered) from Skin

- Polarized incident light
- Surface Fresnel reflectance (polarized)
- Single-scattered (polarized)
- Multiple-scattered (depolarized)
Polarization Imaging of Single Scattered Light

Polarizer filter at 90° to incident light polarization

Polarizer filter parallel to incident light polarization

\[ I_m - (I_m + I_s) \Rightarrow I_s \]

High-resolution, superficial image?

\[ \mu_s^{-1} \sim 100 \mu m \]
Imaging whole, intact surgery specimen with BCC

12 mm

710 nm, plain image  DI ~150 µm “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”

Selective Absorption → Wavelength
Thermal Confinement → Pulse duration

~ 1 million treatments / month

Blood vessels  Pigmented Cells
Tattoos  Hair
Fat?  Acne?
Selective light absorption $\rightarrow$ very local heating
Selective light absorption $\rightarrow$ very local heating

epidermis

Blood vessel

dermis
Selective light absorption
→ very local heating
→ selective repair
Laser Hair Removal

Pigmented hair shaft

Follicular Stem Cells (not pigmented)
Laser Hair Removal

Pigmented hair shaft

Follicular Stem Cells (not pigmented)

Subcutaneous Fat

Sebaceous gland

Stem cells

Epidermis

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

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

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

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

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

$\rightarrow$ Because of low $\rho c$, fat is a “sitting duck”
Fat and Water have nice “colors” in the NIR

Absorption coefficients

λ [nm]

α [cm⁻¹]

Human Fat

Water

915

1205

1715

2305
Ideally, ratio of photothermal heating for fat vs. water

Ratio of the temperature rises

Wavelength, nm

Subcutaneous fat / dermis
CH-selective Laser

Cold Window

Epidermis

Stem cells

Sebaceous gland

1-4 mm
Selective Fatty Tissue Targeting

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

3-5 μm thermal camera → ΔT

Energy meter → E

Sample
JLab FEL

Energy meter $\rightarrow$ E

Cold window

Sample

3-5 $\mu$m thermal camera $\rightarrow$ $\Delta T$
Subcutaneous Fat Necrosis induced \textit{in vitro} at 1208 nm (LDH activity stain)

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

melanin granules
Laser pulse targeting at the single cell level: Cytoplasmonic cavitation

A

melanin granules

B

0.5 µs after 5 ns pulse
Laser pulse targeting at the single cell level:

Cytoplasmic cavitation

melanin granules

0.5 µs after 5 ns pulse
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 J/cm². 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 ($\tau_t$)
- $\tau_t \approx \frac{d^2}{4\kappa}$ ($\kappa$ is thermal diffusivity)
- 1 $\mu$m object cools in $\sim$ 1 $\mu$s

Inertial Confinement
- Optical pulse < Acoustic relaxation time ($\tau_a$)
- $\tau_a \approx \frac{d}{v}$ ($v$ is sound velocity)
- 1 $\mu$m object relaxes in $\sim$ 1 nanosecond
Summary: tattoos

- Not a small problem
  $10^8$ people, $10^9$ treatments, $10^{11}$ $\$$
- Laser pulse-particle interactions have not been optimized
- Ps pulses @ tunable $\lambda$
- Fs pulse interactions?
- Designer tattoos are possible by nanoparticle engineering…
Thanks