Laser Tissue Interaction – Technology meets medicine
Aesthetic Laser Industry

Why the excitement?
71% of patients who have cosmetic surgery earn less than $60,000 per Year*

All ages and incomes consider cosmetic procedures**

34.8 million light-based equipment procedures performed in 2006***

More than $17.24 billion spent in 2006 on aesthetic procedures worldwide***

The media is fueling the anti-aging buzz

Lunchtime Facelifts Are The Newest Skin Treatment

THE OPRAH WINFREY SHOW
The Latest Breakthroughs in Reducing the Signs of Aging
Procedure volume for light-based skin procedures continues to grow.

Worldwide Procedure Volume for Light-Based Skin Rejuvenation

Year 2005 2006 2007 2008 2009 2010
Procedures (million) 10 20 30 40 50 60

Worldwide Procedure Volume for Light-Based Epilation, 2005-2010

Year 2005 2006 2007 2008 2009 2010
Procedures (million) 10 20 30 40 50 60

2006 Medical Insight, Inc/www.miinews.com
Industry Information

- Cutera Website
  - www.cutera.com

- American Society of Aesthetic Plastic Surgery (ASAPS)
  - www.surgery.org

- American Academy of Dermatology (AAD)
  - www.aad.org

- American Academy of Ophthalmology (AAO)
  - www.aao.org

- American Society for Laser Medicine and Surgery (ASLMS)
  - www.aslms.org
Industry Competition

- Highly competitive Market

- Many competitors in this industry – the following are several major competitors
  - Cutera
  - Lumenis
  - Sciton
  - Syneron
  - Alma
  - Palomar
  - Cynosure
  - Candela
Laser Tissue Interaction
Goal of Lasers in Aesthetics / Medicine

- Target specific structures without damaging surrounding tissue
- Enable less invasive procedures with lower risk of complication
  - Lentigines
  - Glaucoma
- Dermatology and Ophthalmology
  - Accessibility
Anatomy of the Skin

The anatomy of your skin:

- Epidermis
- Dermis
- Subcutaneous tissue (fat)
- Connective tissue
- Muscles
- Artery
- Vein
- Nerve

- Sweat pores
- Squamous epithelial cells
- Basal cells
- Sweat glands
- Melanocytes
- Oil (sebaceous) gland
- Erector muscle of hair

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Normal Skin Histology

- **Epidermis (5 Primary Layers)**
  - Stratum Corneum at top
  - Varies in thickness by body part

- **Dermis (2 Primary Layers)**
  - Papillary Dermis
  - Reticular Dermis
  - ~2mm thick (varies)

- **Hypodermis below Dermis**
  - Adipose tissue / connective tissue
  - 10-30mm thick
Skin Histology Cont.

http://upload.wikimedia.org/wikipedia/commons/2/20/Skinlayers.png


Skin, thick H&E

- epidermis
- dermal papillae
- dense irregular connective tissue
- dermis
- hypodermis
- adipose tissue

Mechanisms of Laser Interaction

Photo Chemical
- Acne
- PDT (Photo Dynamic Therapy)

Photo Thermal
- Vascular (Face and Leg Veins)
- Rejuvenation (Wrinkles, texture, age spots)
- Resurfacing
- Hair Removal, etc.

Photo Acoustic
- Tattoo
Photochemical Action

- Light induced chemical reaction
- Uses Endogenous or Exogenous Chromophores
- PDT (Photo Dynamic Therapy)
  - Spectral absorption curve determines optimal light sources
  - Typical action is a chemical reaction that releases a free radical oxygen
  - Free radical oxygen is highly volatile
- Used for Acne (one example)
  - P.Acne Bacteria also has an absorption spectrum with a photochemical reaction
  - Part of the reason acne tends to clear up after time at the beach
Photo Acoustic

- Uses shockwaves to destroy tissue or target structures

- Dermatology examples:
  - Q-switched lasers (~50ns pulse duration)
    - Little to no thermal damage
    - Target ink particles in the upper dermis
  - Tattoo Removal
    - Targeting requires wavelengths that absorb in ink colors
    - Typically requires 3 distinct wavelengths (multiple color tattoos)
      - YAG, Ruby, KTP

- Ophthalmology examples
  - Secondary Cataracts (Q-YAG)
  - Vision correction (Excimer laser)
Most common application of lasers in Dermatology and Ophthalmology (retinal)

Very dependant upon the use of the Theory of Selective Photothermolysis

Lasers and Light used typically range from ~400nm to 10,600 nm
Theory of Selective Photothermolysis

- Photothermolysis (Greek)
  - Photo meaning light
  - Thermo meaning heat
  - Lysis meaning destruction.

- Translation: Selective Photothermolysis
  - Using light to selectively heat an object, resulting in its destruction, while preserving surrounding tissue
Regardless of IPL (Intense Pulsed Light) or Laser, the goal is to:
- Heat the desired targets ...
  - In the case of hair and vessels, to the point of destruction
  - ...without excessive heating, and damage, to surrounding tissue

Selective Photothermolysis requires the right combination of ALL of the following parameters safety and consistently achieve the desired target response.
- Wavelength
- Pulse Duration
- Power
- Spot Size
- Cooling (consistent safety)
- ... all selected to treat a specific patient and condition
Primary Chromophores for Thermal Tx

Reduced & Oxy-hemoglobin
- vascular lesions

Melanin
- pigmented lesions, hair
- Primarily in hair and epidermis
  - some dermal pigment

Water
- General tissue incision, excision, ablation, volumetric heating
- Water exists in every cell
Light Sources: Lasers and Lamps

- **Laser**
  - Single Wavelength or “Color”
  - Controllable beam: Can be delivered via fiber
  - Adjustable Spot Sizes
  - Typically smaller treatment area

- **Lamp**
  - Range of Wavelengths
  - Highly divergent light: Lamp placed near target tissue
  - Fixed treatment area (based on size of window)
  - Typically, large treatment area
Desired Response:

1. Sufficient light reaches target
2. Light absorbed by target (chromophore)
3. Absorbed light converts to heat
4. Temperature rise in target sufficient to provide desired effect
5. Minimal heating of surrounding tissue
Key Parameters of Light Sources

- **Wavelength**
  - What is the absorbing target?

- **Spot Size**
  - How large and how deep is the target?

- **Pulse Duration**
  - What is the size of the target?

- **Fluence**
  - How much energy is necessary to thermally treat the target?

- **Cooling**
  - Can enough energy be delivered to the target while protecting the epidermis

Selective Photothermolysis requires the right combination of parameters for safe and effective treatments.
Absorption (Melanin and Hemoglobin)

- Different Targets are absorbed differently according to wavelength

Absorption Spectrum
(Logarithmic)

Absorption (1/cm)

Wavelength (nm)

532 KTP 585 Pulsed Dye
694 Ruby 755 Alexandrite 808 Diode
940 Diode 1064 YAG
Absorption (Melanin, Hemoglobin, and Water)

Absorption Spectra

Absorption (1/cm) vs. Wavelength

- Hemoglobin
- Deoxy Hemoglobin
- Water
- Melanin
Absorption (Water)

Water Absorption by Wavelength

![Graph showing water absorption by wavelength](image)
Wavelength: Effect on Depth of Penetration

- Wavelength and depth of penetration (given comparable fluence)
  - In visible to near IR, depth of penetration increases with wavelength over the range absorbed by melanin and hemoglobin.
    - Shorter wavelengths experience more scattering.
    - More of the longer wavelengths reach deeper targets.
  - Water absorption limits depth of longer wavelengths
Selection of Spot Size

- Smaller spot sizes reduce penetration at a given wavelength, due to increased impact of scatter.

- Large Spot Sizes for:
  - Deep Targets
    - Hair removal, deep reticular veins
  - Large Area Coverage
    - Epidermal melanin
    - Bulk dermal heating

- Small Spot Sizes for:
  - Small, shallow targets
  - Where high fluences are required (such as telangiectasia)
Thermal Relaxation Time (TRT)

- The time it takes for an object to cool to 50% of the temperature achieved immediately after laser exposure.

- Thermal relaxation time also affects the time that it takes for an object to heat.
  - Short thermal relaxation times cool and heat rapidly.
  - Long thermal relaxation times cool and heat slowly.
Utilize a pulse width short enough to confine heating to the desired target without excessive heating of adjacent tissue (pulse width shorter than the target’s TRT)

\[ \text{YET} \]

long enough to minimize epidermal heating (pulse width longer than epidermal TRT)

Nominal pulse duration = $\frac{1}{2}$ TRT to TRT
Prior to the light exposure, the target is approximately the same temperature as the surrounding tissue.

The target object is heated during the pulse of light.
- As light is absorbed, the temperature of the target increases.

As the target becomes hotter than the surrounding tissue, heat will begin to flow from the target to the surrounding skin. (Conduction)
Selection of Pulse Duration

- Small objects in the skin cool off faster than large objects.
  - Greater surface area relative to absorption area
  - Tea cup vs. large pot of hot water.
    - Tea cup cools off much faster, but also heats up much faster
    - Tea cup has a short thermal relaxation time relative to a large pot of water

- For maximum heating efficiency, heating should occur rapidly enough so that most of the heat is confined to the target.

- In order to provide efficient heating of the target, the optimal pulse duration for a small object is usually shorter than for a large object.
Commonly Used Laser Pulse Durations by Application

- The pulse durations listed below are short enough to efficiently heat the target but long enough to provide minimal heating of the epidermis
  - Estimates (each hair, vein, etc. must be evaluated independently)

  - Microvasculature (capillary loops, blush)
    Laser Genesis procedure: 0.3 ms

  - Fine telangiectasia / fine hair: 10-20 ms

  - Spider veins / medium hair: 20-30 ms

  - Reticular leg veins / coarse hair: 40-60 ms

  - Epidermis: ~5-10ms
    - Longer than this allows heat to exit the epidermis, reducing risk of burns
    - Much shorter prevents the epidermis from heating. Pulses must be less than ~0.4 ms to provide safety.

  - For bulk heating of dermis with Titan, common pulse durations are 3-5 seconds.
Fluence

- Fluence = J / cm²
- Describes the average energy density of the entire pulse
- Fluence is typically the final parameter adjusted, based on clinical response
- Fluence is ONLY significant once pulse duration, wavelength and spot size are all set correctly
- Multiple systems with equal fluence, but different pulse durations / spot sizes will result in significantly different clinical outcomes
  - Can range from safe and efficacious treatments to high rate of complications even though fluence is the same
  - Joules is time and power dependent, but the body and selectivity require specific pulse durations for targeting and efficacy
Fluence, Pulse Duration & Spot Size Combinations

- The graph below shows some commonly used Cutera settings and peak power.
- The combination of parameters is what is critical to determine clinical efficacy.
- To provide 60 J/cm² in 10ms (a setting used for hair removal), a system must have a minimum power shown by the blue line.
- With less power, a system can still achieve the required fluence, but only at a pulse duration that is ineffective for some treatments.
- Cutera’s lasers provide high peak power capability over a wide range of pulse durations for maximum versatility in parameter selection.
Cooling

- The epidermis has melanin
  - Melanin absorbs most wavelengths creating a competing chromophore
  - Without cooling, the epidermis will heat while the target heats

- Primary types of cooling
  - Contact Copper, Contact Sapphire, Cryogen Spray, Bulk air cooling

- Pre-Cooling
  - Reduces initial temperature allowing safe temperature rise during Tx
    - Copper, Sapphire, Cryogen, Bulk Air
  - Ideally pre-cooling controls the skin temp to achieve the same temperature prior to every pulse (challenging with bulk air)

- Post-Cooling
  - Extracts heat from tissue to prevent bloom and reduce time at elevated temperature
    - Copper, Sapphire, Bulk Air

- Parallel Cooling
  - Cools during pulse delivery
    - Sapphire
  - Most significant if pulse duration is long relative to thermal conduction time in tissue (> ~100ms)
    - Thermal conduction time in tissue (essentially water with heat extraction from vessels) increases with the square of distance
      - 4ms cools ~30um
      - 400ms cools ~300um
Lasers in Use
Hair Removal

- **Target:**
  - Melanin in the hair

- **Wavelength:**
  - Melanin absorption, low hemoglobin absorption and low water absorption
  - Low enough melanin absorption to penetrate through the epidermis (>750nm)

- **Depth of Treatment**
  - Must penetrate deeply to reach the hair bulb

- **Problems:**
  - Melanin is the target for Selective Photothermolysis
  - The epidermis has melanin
  - Heat must be retained in the hair follicle to treat

- **Solution to Problem:**
  - Must provide epidermal cooling
  - Pulse durations >5 ms to protect the epidermis
  - Pulse durations <100 ms to confine heat to the hair follicle
  - Smaller hairs require shorter pulse durations
Melanin is in the epidermis & hair

The more melanin, the more heat

Epidermal safety is determined by the amount of melanin & laser parameters
- Skin type & tan
- Wavelength
- Fluence
- Cooling

Growth Stage of the Hair
- Anagen
- Catagen
- Telogen
Vascular Lesions
Vascular (Leg and Facial Veins)

Spider Veins (0.5 – 1.5 mm)
- blue, purple or red

Fine Spider Veins (< 0.5 mm) - red

Deep Reticular Veins (1 – 4 mm)
- blue
Vascular Treatments

- **Target:** Hemoglobin

- **Wavelength**
  - Anything from 500-600
  - Not between 600-900
  - Anything from 900-1064

- **Pulse Duration**
  - Maintain thermal confinement to target vessels (5-60 ms)
  - Shorter pulse durations for small diameter, longer for large diameter

- **Problem**
  - Melanin is more highly absorbed than hemoglobin
  - Larger vessels tend to be deeper
  - Multiple sized vessels

- **Solution**
  - Wavelength Selection for high hemoglobin to melanin contrast
  - Cooling to protect the epidermis
  - Multiple spot sizes to match vessel size and depth
Optimal vascular results require sufficient hemoglobin but minimal melanin absorption. For vascular treatments, important wavelengths include 532 nm, 585 nm, 694 nm, 755 nm, 810 nm, and 1064 nm for FD Nd:YAG, Pulsed Dye, Ruby, Alex, and Diode Nd:YAG, respectively.
Vascular treatment:
- Hemoglobin absorption (blood vessels) is good
- Melanin absorption (epidermis) is bad
- 500 – 600 nm and 940-1064 nm lasers are best for vascular treatments
Pigmented Lesions
Pigmented Lesion Treatments

- Target: Melanin
- Wavelength
  - 500-700 nm (High melanin absorption)
- Pulse Duration
  - Shorter pulses are more aggressive
  - Longer pulses allow for more gradual heating – safer for darker skin types and low contrast pigmented lesions
- Problem
  - Cooling reduces the efficacy when treating pigment because the treatment intentionally heats the epidermis
- Solution
  - On-Demand Skin Cooling
  - Pulse Duration Selection
Laser Genesis

- Target: Hemoglobin in microvasculature (papillary dermis) and bulk heating
- Wavelength
  - 1064 nm Nd:YAG
- Pulse Duration
  - Very short microsecond pulses
- Problem
  - Melanin is more highly absorbed than hemoglobin
- Solution
  - Microsecond pulses thermally confine heat to targets smaller in size than the epidermis
  - The epidermis is subsequently a large target and is not heated to damage levels making the laser modality safe for all skin types and tanned skin
  - High frequency pulsing cumulatively heats the papillary dermis and upper reticular dermis
Hemoglobin absorption used to heat (not damage) fine upper vascular plexus

Water absorption used to conduct heat into upper dermis

Results in reduction of diffuse redness and stimulation of new collagen production
Skin Laxity

- Target: Water
- Wavelength
  - 1100-1800 nm
  - Wavelengths below 1100 nm absorb in melanin and hemoglobin increasing risk to the epidermis
    - Increases variability across patients (limiting efficacy)
    - Limits skin types safely treated by the device
- Pulse Duration
  - Long pulse durations to provide safe heating for collagen contraction
- Problem
  - Bulk heating does not have thermal confinement yet the treatment needs to spare the epidermis
  - There is no “specific” chromophore for the laser to target
  - Short pulse durations do not localize heating to the depths desired for efficacy and can create burns
- Solution
  - Contact cooling over the entire epidermis being treated
  - Target water absorption and control the amount of absorption to control depth
  - Provide long pulses to heat and maintain volumetric heating
Sustained heating of the dermis

Treatment Objectives
- Collagen contraction
- Long-term: stimulation of collagen remodeling
- Epidermal protection
Designed to absorb in water yet penetrate deeply for optimal results

Absorption Spectra

Titan Spectrum

Water Absorption
Collagen Contraction

- Heat disrupts the bonds linking the collagen
- Collagen coil “relaxes” resulting in a shorter, thicker strand
New Collagen Growth – Long-term
- Thermally induced wound response
- Happens gradually (3 – 6 months)
- Improves skin texture
Pearl

Resurfacing Laser
What are we trying to treat?
How do we treat this best (from a physician and patient perspective)?

<table>
<thead>
<tr>
<th>Location</th>
<th>Depth</th>
<th># of Tx Full Cover</th>
<th>Down Time Full</th>
<th># of Tx Frac.</th>
<th>Down Time Frac.</th>
<th>Full Coverage or Fractional?</th>
<th>Cutera Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lentigines</td>
<td>Epidermis &lt;100 micron s</td>
<td>1-2</td>
<td>3-4 days</td>
<td>4-6</td>
<td>2-3 days</td>
<td>Full – best results in the fewest treatments with less days of total downtime.</td>
<td>Pearl</td>
</tr>
<tr>
<td>Texture / Fine lines and wrinkles</td>
<td>Epidermis Papillary Dermis &lt;100 micron s</td>
<td>1-2</td>
<td>3-4 days</td>
<td>4-6</td>
<td>3-4 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate to Deep Wrinkles and Scars</td>
<td>Reticular Dermis 300 – 800 micron s</td>
<td>1</td>
<td>30 days</td>
<td>1-2</td>
<td>5-7 days</td>
<td>Fractional Ablative-Downtime and healing are best</td>
<td>Pearl Fractional</td>
</tr>
</tbody>
</table>
Absorption (Water)

Water Absorption by Wavelength

Absorption (1/cm)

Wavelength (nm)
Pearl’s Mechanism of Action

Top Down:
• **Full Epidermal Treatment** through Ablation and Coagulation
  - **Ablation**: up to 1/3 of the epidermis ablated during treatment
  - **Coagulation**: Up to 2/3 of the epidermis coagulated during treatment
    • Provides a natural dressing that peels off in 3-5 days

Bottom Up: **Collagen Stimulation**
• **Collagen Remodeling**: Residual heat in dermis stimulates new collagen