Clinical Applications of Lasers in Urology: a Review

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PGY 5
UBC Department of Urological Sciences Grand Rounds
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Objectives

• Review basic laser physics and design
• Outline standard of care applications of lasers in urology
• Describe emerging laser technology and techniques in urology
Laser Physics

- LASER: Light Amplification by Stimulated Emission of Radiation
- Basic design: excitable gain medium in an optical resonant cavity
- Energy source (electrical, mechanical, chemical) used to stimulated medium
Result: collimated, in phase, uniform beam of light

Laser design

- Gain media
  - Solid
  - Liquid
  - Gas
- Input energy
  - Chemical
  - Electrical
  - Light
- Output energy
  - Continuous (CW mode)
  - Pulsed
Laser tissue interactions

- Photochemical
  - Photodynamic therapy for TCC
- Photothermal
  - Ho:YAG lithotripsy
  - KTP prostate photovaporisation
- Photomechanical
  - FREDDY, dye laser lithotripsy

Jacques LSM 1996
photochemical

- Administration of photosensitive dye preferentially taken up by certain tissues
- Administer light of appropriate wavelength absorbed by dye to cause tissue damage/ablation
- Eg. Photodynamic therapy for superficial TCC


photothermal

- Direct irradiation of material/tissue with light energy causes vaporization
- Primary mechanism of long pulse, near infrared laser lithotripsy

Photomechanical/acoustic

- Three mechanisms
  - Spallation
  - Recoil pressure wave from ablated material (conservation of momentum)
  - Phase change induced pressure transients
    - cavitation bubbles
    - Plasma formation


Phase change induced pressure transients

- Plasma formation
  - Considered a fourth state of matter consisting of atoms sharing free electrons
  - Phase change to a gas releases energy = pressure waves
  - Pressure waves = ablate tissue/stones
  - Requires large amounts of energy
Phase change induced pressure transients

• Cavitation bubbles
  – Vaporization of water causes microscopic water vapor bubble formation with rapid expansion in non-compressible liquid environment
  – Rapid, violent collapse releases ++ energy as pressure waves, causing lithotripsy

Fast flash photography of cavitation bubble collapse in H2O at room temp

Jansen LSM 1996
Energy Confinement

- Refers to the temporal or spatial density of laser light when applied to a material/tissue
- Based on the wavelength and energy of the laser and the optical properties of the media

confinement

- Temporal
  - Same energy in a shorter pulse = higher power ($P = \frac{E}{t}$)
- Spatial confinement
  - Optical scattering of media
  - Beam width
  - Medium pigmentation
Pulse duration

- Recall: cavitation bubble and plasma formation require +++ energy
- Short pulse = ↑ temporal confinement of E, thus ↑ PEAK energy
- Longer pulse = irregular bubble ≠ photomechanical lithotripsy

Jansen LSM 1996
Photoacoustic lithotripsy

- Safe for tissues
- Propogates in all directions (no need to be “right on the stone”)

- Produces large fragments
- Can’t ablate hard stones (COM, brushite, cystine)

Teichman, J Urol 1998
Tissue pigmentation

- Pigmentations such as hemoglobin, melanin, can be used as chromophobes to absorb a particular wavelength of light sparing other structures

Teichmann WJU 2007
Photothermal ablation

- Direct irradiation by laser light energy
- Little to no acoustic transients
- Small, irregular, cavitation bubbles
- Primary mechanism of Ho:YAG, Er:YAG, Th:YAG, Nd:YAG lasers
- Produces smaller, powderized fragments
- lithotripsy of all stone types


Ho:YAG photothermal mechanism

  - Ho:YAG lithotripsy better in air
  - Time course: immediate ablation
  - Max lithotripsy at 90 degrees
  - Thermal breakdown products measured
  - Max lithotripsy at higher temperatures
  - Minimal pressure transients
Chan LSM 1999

Short pulse laser pressure transient signature
45° parallel

Chan LSM 1999

Teichman, J Urol, 1998
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Photothermal</th>
<th>Photomechanical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lasers</td>
<td>Holmium, erbium, thulium, diode, Nd:YAG, KTP</td>
<td>FREDDY, dye lasers</td>
</tr>
<tr>
<td>+</td>
<td>Small fragments</td>
<td>Cheap</td>
</tr>
<tr>
<td></td>
<td>All stone types</td>
<td>No direct contact needed</td>
</tr>
<tr>
<td></td>
<td>Minimal retropulsion</td>
<td>Effective</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Safe for tissues</td>
</tr>
<tr>
<td>-</td>
<td>Collateral damage</td>
<td>Ineffective for hard stones</td>
</tr>
<tr>
<td></td>
<td>Longer litho times</td>
<td>Large frags</td>
</tr>
<tr>
<td></td>
<td>Requires direct contact</td>
<td>More retropulsion</td>
</tr>
</tbody>
</table>

Lasers used in urology

- CO2
- FREDDY
- Holmium:YAG
- KTP (green light)
- Thulium/diode lasers
CO2

- 10,600 nm wavelength
- Continuous mode only
- High peak power, but low efficiency
- Highly absorbed by water
- Used in treating skin/genital lesions with some success (Rosemberg, Urol 1985, 1986)

Frequency Doubled double-pulsed Nd:YAG laser (FREDDY)

- Incorporating a KTP crystal into the resonator of a Nd:YAG laser halves the wavelength (double frequency)
- Produces light at 532 nm and 1064 nm
- Light at 532 nm forms plasma, light at 1064 nm adds further E
- Photoacoustic mechanism

FREDDY laser

- In vitro: capable of photomechanical lithotripsy
  - Zorcher, LSM, 1999
- safe for tissues
  - 300 pulses to human ureter in vivo pre cystectomy failed to perforate (Santa Cruz J EndoU 1998)
  - 2000 pulses ex vivo failed to perforate human ureter (2 pulses for Ho) (Bazo BAUS 2001)

FREDDY: clinical data

<table>
<thead>
<tr>
<th></th>
<th>95% stone free, no complications, ureteric stones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schafhauser DGU 2000</td>
<td></td>
</tr>
<tr>
<td>Stark ICSD 2001</td>
<td>87% combined stone free, ureteric/bladder stones</td>
</tr>
<tr>
<td>Bazo BAUS 2001</td>
<td>100% stone free kidney/ureteric stones</td>
</tr>
<tr>
<td>Dubosque J Endo 2006</td>
<td>69% stone free No litho 1 COM, 2 cystine</td>
</tr>
<tr>
<td>Yates LSM 2007</td>
<td>Ho:YAG vs FREDDY: trend favors Holmium</td>
</tr>
</tbody>
</table>
FREDDY

- Safe, effective, cheap
- Ineffective against hard stones (cystine, COM, brushite)
- Role continues to evolve

Holmium:YAG

- Wavelength 2.1 microns, pulse duration average 350 microseconds
- Industry standard laser lithotrite
- Applications in lithotripsy, tissue ablation
- Primary photothermal mechanism
- Well absorbed by water (safety margin)
- Uses cheap, flexible, low OH silica fibers
Ho:YAG endopyelotomy

- Giddens J Urol 2000
  - 83% success when combined with intraluminal U/S
  - 50% of failures successfully treated with repeat laser endopyelotomy
- El Nahas J Urol 2006
  - RCT accucise vs. Ho:YAG: fewer complications/better success in laser arm (not statistically significant)
- Ponsky J Endo 2007
  - Laser endopyelotomy/accucise equivalent
  - Two episodes of transfusion in accucise group (n = 27)

Ho:YAG endoureterotomy

- Singal 1997 Urology
  - Ureteric stricture incision: 76% success at minimum 9 months F/U
- Waterson 2002 J Urol
  - Ho:YAG incision of uretero-intestinal stricture
  - Success at 1, 2, 3 years: 85%, 72%, 56%
  - Compares with 76% long term with open repair (DiMarco Urol 2001)
Ho:YAG urethrotomy

- Kamp J Endo 2006:
  - Ho:YAG urethrotomy equivalent to DVIU
- Lagerveld J Endo 2005:
  - post RRP stricture at VU anastamosis
  - All pts voiding post op, no retreatment

HoLEP

- = or > TURP in outcomes/complications, more tissue resected
- = results to simple retropubic for large glands
- Can be done in fully anticoagulated patients (14% transfusion vs 30% with TURP)
- Steep learning curve, up to 50+ cases
  - Seki J Urol 2003
Ho:YAG lithotripsy

- Most series > 95% stone free rates
- Slightly less effective in renal stones, especially large (> 1cm) or lower pole stones
- Main drawbacks
  - Collateral damage
  - Long lithotripsy times
  - Some retropulsion issues

Potassium titanyl phosphate (KTP/green light) laser

- Wavelength 532 nm
- Highly absorbed by hemoglobin, poorly absorbed by water
- 0.8 mm penetration depth in tissues
- 1-2 mm coagulation zones in tissues
KTP “green light” PVP

- Absorption of hemoglobin advantageous for hemostasis and focusing of laser on vascular tissue
- Can use H2O or N/S
- Can use in anticoagulated patients
- Theoretically “bloodless”

KTP PVP: 1990’s

- Hybrid KTP/Nd:YAG laser PVP
- Nd:YAG coagulation zones > KTP = prostate slough
- Unacceptably high rates of complication/irritative LUTS
- Limited tissue ablated
- Long OR times

KTP PVP: 2000

- 60 W KTP laser alone studied
- Most studies showed reasonable results and acceptable complication rates
- Some studies showed decreased hospital stay, less (or no) catheterization time, less (or no) CBI, and less retrograde ejaculation (9%)

60W KTP PVP

- Malek, Urology 98
  - AUASS ↓ 77%
  - Q max ↑ 166%
  - PVR ↓ 82%
- Malek J Urol 2000
  - 4% post op hematuria
  - 7% mild dysuria
  - Q max improvement at 2 years ↑ 278%
  - 9% retrograde ejaculation
**KTP PVP: 2005-2008**

- 80 W high power laser
- 70 degree side firing fiber
- Uses 21-23 scope (less strictures?)

**High power 80 W KTP PVP**

- Bachmann, Eur Urol 2005
  - Review of several studies on 80W KTP PVP
  - Mean prostate volume 49.6 cc
  - Mean OR time 53.7 minutes
  - Volume reduction 37-53% (similar to TURP)
  - Foley 6-69 hours
  - No significant bleeding, no transfusions
  - Q max, IPSS improvements similar to published data on TURP
High power 80 W KTP PVP

- Te, BJU, 2006
  - Long term results up to 3 years comparable to TURP results
  - Less improvement in pts with PSA > 6ng/dL (less effective for larger prostates?)

High power KTP PVP

- Adverse events
  - Retention: 1-15.4%
  - Dysuria: 6.2-30%
  - Minor bleeding: up to 18%
  - Retrograde ejaculation: 36-50%

Sulser, J Endo 2004, Volkan, Eur Urol 2005
PVP vs. TURP

- Non-randomized trial PVP vs TURP
  - Decreased foley time in PVP
  - Decreased hospital stay in PVP
  - Longer OR time for PVP
  - No bleeding in PVP
  - PVP Comparable results to TURP group at 6 months

Bachmann, Eur Urol 2005

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PVP vs. TURP

- Bouchier Hayes, J Endourol 2006
  - RCT of PVP vs TURP
  - Similar results at 6 weeks and 1 year
  - PVP had shorter foley time, hospital stay
  - Fewer early complications in PVP group
  - TURP: better re-operative rates
  - N = only 59
Cost?

- TURP = $3,874 to $8,608
- Meds for a year = $73 to $974
- Cost analysis for all MIS BPH treatments: PVP least costly
- TURP vs PVP cost analysis
  - TURP: AUS$ 4,291
  - PVP: AUS$ 3,368

High power KTP PVP: high risk patients

- Safe for ASA III patients
  - Reich J Urol 2005
- Anticoagulated: good results, no transfusions
  - Ruszat, Eur Urol 2007
- Large prostates: good results, short stay/cath time
  - Sandhu, Urol 2004
- Pts in retention: similar outcomes for BPH vs BPH and AUR
  - Ruszat, Eur Urol 2006
HPS

- 20-120W tunable diode pumped laser
- Delivers energy in 10W instead of 5W increments
- Maximum focus capability up to 3-5 mm (consistent ablation, even with laser a bit away from tissue)
- Enthusiasm: 4
- Results: no studies with this model...yet

Table 1. Major Advantages and Disadvantages of PVP Compared to TURP

<table>
<thead>
<tr>
<th>Advantage</th>
<th>PVP</th>
<th>TURP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safer for larger prostates (&gt;100 mL) with no risk of dilutional hypotension</td>
<td>Risk of fluid absorption-TURP syndrome when resection time &gt; 90 min</td>
<td></td>
</tr>
<tr>
<td>Lengthier procedure-slower vaporization speed (~0.5 gr/min)</td>
<td>Shorter operation time-higher resection speed (up to 1 gr/min)</td>
<td></td>
</tr>
<tr>
<td>Minimal to no catheterization time &amp; reduced hospital stay (day-case procedure)</td>
<td>Catheterization time of at least 2-3 days, resulting to prolonged hospital stay</td>
<td></td>
</tr>
<tr>
<td>Reduced risk of retrograde ejaculation (35-55%)</td>
<td>Significant risk of retrograde ejaculation (53-75%)</td>
<td></td>
</tr>
<tr>
<td>Absence of histological evaluation of removed prostatic tissue</td>
<td>Ability to detect (incidental) prostate cancer</td>
<td></td>
</tr>
<tr>
<td>Higher reoperation rate</td>
<td>More durable results over time</td>
<td></td>
</tr>
</tbody>
</table>

PVP: photoselective vaporization of the prostate, TURP: transurethral resection of the prostate.

*Journal Med J Vol. 49, No. 3, 2008*
Thulium lasers

- Wavelength 2 microns
- Well absorbed by water (safety profile)
- Theoretically optimal for hard/soft tissue ablation
- Most clinically available lasers are diode pumped, continuous wave lasers

Thulium laser resection of prostate-Tangerine Technique

- 100 patients randomized to TmLRP-TT or TURP (52 TmLRP-TT, 48 TURP)
- All patients underwent IPSS, IIEF, full urodynamics
- F/U: 1, 6, 12 months
- All complications recorded

Xia et al, Eur Urol, 2008
Follow up data: TmLRP-TT vs. TURP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean preop ± SD (range)</th>
<th>Mean 1 mo postop ± SD (range)</th>
<th>Mean 6 mo postop ± SD (range)</th>
<th>Mean 12 mo postop ± SD (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS</td>
<td>23.9 ± 6.7 (0-30)</td>
<td>6.8 ± 3.6 (0-15)</td>
<td>4.0 ± 2.4 (0-10)</td>
<td>3.5 ± 2.9 (0-12)</td>
</tr>
<tr>
<td>p value</td>
<td>0.38</td>
<td>0.83</td>
<td>0.64</td>
<td>0.46</td>
</tr>
<tr>
<td>QoL</td>
<td>4.7 ± 0.9 (0-6)</td>
<td>1.6 ± 1.4 (0-9)</td>
<td>1.1 ± 1.1 (0-4)</td>
<td>1.0 ± 0.9 (0-3)</td>
</tr>
<tr>
<td>p value</td>
<td>0.32</td>
<td>0.89</td>
<td>0.80</td>
<td>0.68</td>
</tr>
<tr>
<td>Qmax (ml/s)</td>
<td>8.0 ± 2.6 (0.2-14)</td>
<td>23.8 ± 9.6 (6.6-45.9)</td>
<td>24.5 ± 9.2 (7.8-48.7)</td>
<td>23.7 ± 6.0 (10.3-40.4)</td>
</tr>
<tr>
<td>p value</td>
<td>0.63</td>
<td>0.47</td>
<td>0.54</td>
<td>0.77</td>
</tr>
<tr>
<td>PVR (ml)</td>
<td>93.1 ± 32.1 (30-150)</td>
<td>9.7 ± 3.1 (0-40)</td>
<td>7.1 ± 6.6 (0-35)</td>
<td>5.2 ± 4.8 (0-27)</td>
</tr>
<tr>
<td>p value</td>
<td>0.24</td>
<td>0.72</td>
<td>0.76</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Preop, preoperative; postop, postoperative; SD, standard deviation; IPSS, International Prostate Symptom Score; TmLRP-TT, transurethral resection of the prostate-laser technique; TURP, transurethral resection of the prostate; QoL, quality of life; Qmax, maximum flow rate; PVR, postvoid residual; vol, volume.

Xia et al, Eur Urol, 2008
### Table 2 – Perioperative data

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD (range)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TmLRF-T</td>
<td>TURP</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>46.3 ± 16.2 (20–88)</td>
<td>50.4 ± 20.7 (40–92)</td>
</tr>
<tr>
<td>Resected weight (g)</td>
<td>23.2 ± 10.3 (10–55)</td>
<td>30.8 ± 14.4 (12–68)</td>
</tr>
<tr>
<td>Vaporization weight (g)</td>
<td>---</td>
<td>29.8 ± 7.3 (0–39.6)</td>
</tr>
<tr>
<td>Estimated resection weight (g)</td>
<td>62.0 ± 16.2 (35–98)</td>
<td>38.8 ± 14.4 (12–66)</td>
</tr>
<tr>
<td>Retrival rate (g/min)</td>
<td>0.91 ± 0.34 (0.68–1.27)</td>
<td>0.79 ± 0.36 (0.56–1.37)</td>
</tr>
<tr>
<td>Preop hemoglobin (g/dl)</td>
<td>14.01 ± 1.62 (10.1–17.3)</td>
<td>13.91 ± 1.84 (10.3–17.6)</td>
</tr>
<tr>
<td>Hemoglobin decrease (g/dl)</td>
<td>0.92 ± 0.52 (0.2–5.9)</td>
<td>1.96 ± 0.65 (0.7–3.1)</td>
</tr>
<tr>
<td>Serum sodium decrease (mmol/l)</td>
<td>1.36 ± 0.27 (0–3)</td>
<td>4.46 ± 1.47 (1.5–34)</td>
</tr>
<tr>
<td>Catheterization time (h)</td>
<td>45.7 ± 25.8 (20–95)</td>
<td>87.4 ± 33.8 (21–165)</td>
</tr>
<tr>
<td>Hospital stay (d)</td>
<td>115.1 ± 25.5 (87–165)</td>
<td>103.1 ± 33.8 (75–246)</td>
</tr>
</tbody>
</table>

SD, standard deviation; TmLRF-T, thulium laser resection of the prostate–tangerine technique; TURP, transurethral resection of the prostate; preop, preoperative.

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**Revolix laser**

- 110 W diode pumped, continuous wave thulium:YAG laser

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Xia et al, Eur Urol, 2008
Revolix laser

- 70 W continuous wave diode pumped Th:YAG laser
- 1 retrospective review of “vapor-resection” in 54 patients at one year F/U

Revolix PVP: results

![Functional results table]

Bach, WJU, 2007
results

- Average OR time: 52 minutes
- Average catheterization time: 1.7 days
- Q max: average 4.2 to 20.1 cc/min
- PVR: average 86 to 12 cc
- IPSS: 19.8 to 6.9
- QoL: 4 to 1

Bach, WJU, 2007

980 nm diode laser

- New laser technology
- Good absorption by hemoglobin AND water
- Theoretically good hemostasis AND tissue ablation
- Small, portable, easy to maintain, 110V power source
980 nm diode laser

Teichmann, WJU, 2007
980 nm diode laser

• Ex vivo porcine kidney: Wendt-Nordahl Eur Urol 2007
  – Greater tissue ablation than KTP
  – Less bleeding than TURP
  – Smaller coagulation zones than KTP

980 nm diode laser

• Ruszat et al (unpublished)
  – Retrospective review of diode prostate ablation vs KTP PVP
  – Similar outcomes (IPSS, PVR, Qmax)
  – Hemostasis diode > KTP
  – Slightly more irritative LUTS with diode
980 diode laser vs TURP

- Lucan et al (unpublished)
  - Retrospective review 980 diode laser vs TURP with 6 months F/U
  - TURP superior in AUASS improvement, PVR reduction
  - Diode laser: shorter OR time, less irrigation, shorter bed rest

Thulium/diode lasers?

- CW mode
- Fiber laser technology
- No RCT’s vs KTP, HoLEP, TURP
- Early results only
- Other endoscopic procedures?
Summary

- Basic understanding of laser physics will help guide technique and application of lasers
- Lasers are safe and effective for many tissue ablation and lithotripsy procedures
- Ho:YAG laser is the industry standard for lithotripsy
- Emerging laser technologies such as KTP laser, Th:YAG and diode lasers require further study

“Thank you”