2010 Urology Research Abstracts

A compilation of investigations made by Cleveland Clinic Glickman Urological & Kidney Institute physicians, research scientists and distinguished colleagues.

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Tacrolimus (FK506) as a Neuromodulator in the Radical Prostatectomy Population: A Multi-center, Double-blind, Randomized, Placebo-controlled Trial

John P. Mulhall, Eric Klein, Kevin Slawin, Peter T. Scardino

Introduction: Cavernous nerve injury is a major cause of long-term erectile dysfunction (ED) after radical prostatectomy (RP). Data from the rat cavernous nerve injury model suggest that tacrolimus (TAC), an immunosuppressant immunophilin ligand, facilitates neural recovery with improvement in erectile function recovery in this model. This clinical trial was undertaken to define the utility of TAC in men undergoing RP.

Methods: The study population consisted of men: ≤65 years of age; undergoing bilateral nerve sparing RP; with preoperative IIEF erectile function domain (EFD) scores ≥24. Patients were followed at weeks 1, 3, 5, 9 followed by months 3, 4, 6, 7, 12, 18 and 24. Patients were randomized pre-RP in a 1:1 ratio. Patients started placebo (PBO) or TAC 2mg daily seven days prior to surgery. At discharge, TAC patients were titrated to 3mg daily. Patients were administered the IIEF and had serum chemistries and TAC levels measured serially postoperatively. The primary efficacy end-point was the difference in EFD scores at 24 months between TAC and PBO groups. Secondary end-points included: other domain scores of the IIEF; % of patients with EFD ≥24 and the time to achieve this; % patients responding to PDE5 inhibitors (PDE5i) and the time to achieve this.

Results: 131 patients were enrolled with a mean age of 55±6 years. Baseline EFD score was 29±2 for both groups; 24 month scores were 20±10 and 17±11 for PBO and TAC groups respectively (p=0.2). 45% and 54% (p=0.4) had 24-month EFD scores ≥24. No differences existed in IIEF libido, orgasm or satisfaction domain scores between groups. At 24 months, there was no difference between groups in: % of men using PDE5i (96%), % responding to PDE5i (80%) or the time to PDE5i first response (182 days). No significant adverse events were experienced. At 1 week and 3 months, no differences in serum Cr, glucose, K or estimated creatinine clearance were seen between groups. Significant, but not clinically meaningful, reductions in serum Mg was seen at 1 week (p=0.05) and 3 months (p<0.01) post-RP.

Conclusions: These data demonstrate no significant benefit to TAC as used in this study. It is unclear at this time whether the dosing or timing strategies were inappropriate or whether the rat cavernous injury model fails to represent the human model.
Transrectal Ultrasound Probe Configuration and Repeat Prostate Cancer Detection Rates

Christina B. Ching, Ayman S. Moussa, Jianbo Li, J. Stephen Jones

Introduction and Objective: Type of transrectal ultrasound probe has previously been found to significantly influence prostate cancer detection rates in men undergoing initial prostate biopsy. It is still unknown, however, if it may affect cancer detection rates on repeat biopsy. We sought to determine if type of ultrasound probe affects prostate cancer detection rates in men undergoing a repeat prostate biopsy.

Methods: We retrospectively evaluated a total of 1190 patients undergoing a repeat prostate biopsy (PB) at our institution between 2000 and 2008. Patient age, prostate specific antigen (PSA), volume of prostate, number biopsy cores, abnormal DRE, and pathologic findings were all included in the analysis. There were 564 men whose repeat biopsy was with an end-fire probe and 626 men whose repeat biopsy was with a side-fire probe. We used multivariable logistic regression analysis to identify factors associated with cancer detection and the possible influence of the type of probe on repeat biopsy cancer detection rates.

Results: While we found that increasing age and decreasing volume of prostate correlated with increasing risk of cancer, we did not find that type of probe affected cancer detection on repeat biopsy. On multivariable logistic regression analysis, age, PSA, prostate volume, and presence of atypia were all significant factors predicting cancer with odds ratios of 1.45, 1.24, 0.66, and 1.75 respectively. The type of probe was not clinically significant in detecting cancer (p=0.8514).

Conclusions: While type of probe significantly affects overall prostate cancer detection rates on initial biopsy, it does not appear as significant on repeat biopsy. This is likely secondary to decreasing sensitivity overall of repetitive prostate biopsies. Increasing age, decreasing volume of prostate, higher PSA, and presence of atypia were multivariable factors that did predict presence of cancer.

continued
Prostate cancer detection rates in end-fire vs. side-fire probes stratified for different PSA values and number core biopsies

<table>
<thead>
<tr>
<th></th>
<th>Side-Fire</th>
<th>End-Fire</th>
<th>P-Value</th>
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<tr>
<td><strong>PSA &gt; 4 to ≤ 10</strong></td>
<td>Total: 662</td>
<td>Total: 986</td>
<td>&lt;0.004</td>
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<tr>
<td></td>
<td>Positive: 307</td>
<td>Positive: 384</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Percent: 46.4%</td>
<td>Percent: 38.9%</td>
<td></td>
</tr>
<tr>
<td><strong>PSA &gt; 10</strong></td>
<td>Total: 162</td>
<td>Total: 271</td>
<td>&lt;0.015</td>
</tr>
<tr>
<td></td>
<td>Positive: 100</td>
<td>Positive: 133</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Percent: 61.7%</td>
<td>Percent: 49.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Cores 8 to 12</strong></td>
<td>Total: 848</td>
<td>Total: 1140</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>Positive: 385</td>
<td>Positive: 434</td>
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<tr>
<td></td>
<td>Percent: 45.4%</td>
<td>Percent: 38.1%</td>
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</tr>
<tr>
<td><strong>Cores 13 to 19</strong></td>
<td>Total: 57</td>
<td>Total: 178</td>
<td>&lt;0.009</td>
</tr>
<tr>
<td></td>
<td>Positive: 34</td>
<td>Positive: 69</td>
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</tr>
<tr>
<td></td>
<td>Percent: 59.6%</td>
<td>Percent: 38.8%</td>
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Impact of Prostate Gland Volume on Cryoablation PSA Outcomes

David A. Levy, J. Stephen Jones

Objective: To assess the impact of prostate volume on outcomes following primary whole gland cryoablation.

Methods: Prognostic factors for favorable post cryo PSA were assessed in a risk stratified cohort from the COLD Registry. The cohort was substratified based on small (< 40 cm$^3$ group 1, n=2,315) and large (≥ 40 cm$^3$ group 2, n=881) prostate volume. Variables studied included patient age, PSA at diagnosis, Gleason score, risk category, and clinical T stage. The likelihood of reaching the favorable nadir of <0.6, as well as morbidity outcomes of incontinence, rectal fistula, and potency are reported.

Results: Pretreatment factors are detailed in table 1. **Nadir PSA difference here*** At 12 months, the large and small volume groups had statistically and clinically similar risks of incontinence (3.1% vs. 2.3%) retention (1.2% vs. 2.6%), potency (30.3% vs. 32.2%), and fistula (0.6% vs. 0.2%).

Conclusions: Larger prostate gland appears related to lower chance of reaching favorable PSA nadir, but not to higher risk of morbidity.

continued
<table>
<thead>
<tr>
<th>Variable</th>
<th>(n = 2,315)</th>
<th>P value Univariate</th>
<th>P value Multivariate</th>
<th>(n = 881)</th>
<th>P Value Univariate</th>
<th>P value Multivariate</th>
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<td>539</td>
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<td>10 - &lt; 20</td>
<td>362</td>
<td></td>
<td>192</td>
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<td></td>
<td>&gt; T2b</td>
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<td>Gl Score</td>
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<tr>
<td></td>
<td>&gt; 8</td>
<td>320</td>
<td></td>
<td>107</td>
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<td>(D’Amico)</td>
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<td>0.001</td>
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<td>0.003</td>
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<td>Intermediate</td>
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Statistical analysis for prognostic impact of demographic factors for initial post cryoablation PSA < 0.6 ng/ml based on prostate gland volume.
Impact of Disease Burden on Cryoablation PSA Outcomes

David A. Levy, Jianbo Li, J. Stephen Jones

Objective: To identify prognostic factors for favorable biochemical outcome (PSA < 0.6 ng/ml) following primary whole gland prostate cryoablation.

Methods: The charts from 122 cryoablation patients treated at Cleveland Clinic from 2004 through May 2009 were reviewed. Patient age, race, PSA at diagnosis, Gleason score, risk category, prostate gland volume, clinical T stage, number of cores positive, percent of core involved with disease, ratios of: number of cores positive to total cores biopsied and number of cores positive to prostate gland volume, and initial PSA results were studied. An initial post cryoablation PSA of < 0.6 was employed as the criterion for favorable outcome based on previously published data.

Results: 16.4% of patients had unfavorable postoperative PSA levels. On univariate analysis, number of cores positive (p= 0.031) and maximum percent core positive (p = 0.024) were prognostic of PSA outcome. On multivariate analysis, number of cores positive (p=0.010), maximum percent core positive (p = 0.034) and ratio of number of positive cores to prostate gland volume (cc’s) (p=0.023) were prognostic for favorable PSA outcomes based on an initial PSA < 0.6 ng/ml.

Conclusion: Favorable PSA outcomes following primary prostate cryoablation appear to be correlated with disease burden. The relative disease burden as defined by the number of and percent core positive, and the ratio of number of cores positive to prostate gland volume (cc’s) are highly prognostic for initial post cryoablation PSA < 0.6 ng/ml which is associated with favorable long term biochemical disease free survival regardless of risk stratification.
Primary Cryoablation Nadir PSA and Biochemical Failure

David A. Levy, Louis L. Pisters, J. Stephen Jones

**Purpose:** To correlate nadir post cryoablation prostate specific antigen (PSA) levels to long term biochemical disease free survival in a risk stratified cohort of prostate cancer cryoablation patients.

**Material and Methods:** The records of 2,427 cryoablation patients from the Cryo On-Line Data Registry were studied for biochemical disease free survival (bDFS) based on nadir + 2 criteria utilizing PSA determinations out to 60 months post cryoablation.

**Results:** Nadir PSA < 0.1 ng/ml, the 36, 48 and 60 month bDFS was: Low risk: 93%, 91.8% and 91.8%, respectively, intermediate risk: 88%, 81% and 76%, respectively, and high risk: 82%, 76% and 71%, respectively. PSA 0.1 – 0.5 ng/ml, the 36, 48 and 60 month bDFS rates were: Low risk: 92%, 91.5% and 86%, respectively, intermediate risk: 78%, 72% and 67%, respectively, and high risk: 64%, 61% and 51%, respectively. PSA 0.6 – 1.0 ng/ml, the 24 month bDFS for patients was: Low risk: 70.5%, intermediate risk: 56.1%, and high risk: 46.7%. PSA levels of 1.1 – 2.5 ng/ml were associated with 12 month failure rates of 29.6%, 38% and 74.8% for low, intermediate and high risk groups, respectively.

**Conclusion:** Nadir PSA following prostate cryoablation is prognostic for biochemical disease free survival, but by itself cannot be used as a definition of disease free survival since it has not been correlated with disease specific or metastasis free survival. A PSA of ≥ 0.6 ng/ml correlated with a 29.5% biochemical failure rate at 24 months, regardless of risk stratification therefore, these patients require close follow-up.
Disease Burden Predicts for Favorable Salvage Cryoablation PSA Outcome

David A. Levy, Jianbo Li, J. Stephen Jones

Objective: To identify prognostic factors for favorable biochemical outcome (PSA < 0.6 ng/ml) following salvage whole gland prostate cryoablation.

Methods: The charts from 58 salvage cryoablation patients treated at Cleveland Clinic from 2004 through July 2009 were reviewed. Patient age, race, PSA at diagnosis, Gleason score, risk category, prostate volume, clinical T stage, number of cores positive, percent of core involved with disease, ratios of: number of cores positive to total cores biopsied and number of cores positive to prostate gland volume, and initial PSA results were studied. Initial PSA levels measured at 6 – 12 weeks post treatment of < 0.6 ng/ml were employed as the criterion for a favorable outcome based on previously published data.

Results: 31% of patients had unfavorable postoperative PSA levels. The number of positive biopsy cores (p = 0.012), ratio of positive cores to prostate volume (cm³) (p = 0.004), and marginally the percent of cores positive divided by total number of cores biopsied (p = 0.060) were prognostic for favorable PSA outcomes. A higher ratio of number of cores positive to prostate volume (3rd quartile) had a lower (35%) chance of a favorable PSA than a lower ratio (1st quartile) (OR = 0.35, 95% CI: 0.14 – 0.84, p = 0.019).

Conclusion: Prostate gland disease burden as reflected by the number of cores positive and ratio of positive cores to gland volume (cm³), is prognostic for favorable biochemical outcome following salvage whole gland prostate cryoablation. Further study is warranted to better delineate this relationship.
Correlation of Thermocouple Data with Voiding Function following Prostate Cryoablation

David A. Levy, Jianbo Li, J. Stephen Jones

Objectives: To identify possible correlations of thermocouple recorded data with altered postoperative voiding function following prostate cryosurgery.

Methods: A retrospective analysis of the records of 58 patients treated with prostate cryoablation from October 2005 through April 2009 was conducted. Multivariable analysis of patient age, presenting prostate specific antigen (PSA) level, Gleason score, clinical T stage, prostate volume, maximum low temperature thermocouple recordings, prior history of radiation and/or hormonal therapy, were studied as possible correlative factors for altered post operative voiding function.

Results: Twenty-two of 58 (37.9%) patients manifested post cryoablation urgency and frequency (n= 13) requiring medical therapy, or retention (n=9). On multivariable analysis, age (p = 0.037) and an external sphincter temperature less than or equal to 23 degrees Celsius (p=0.012) were associated with voiding frequency / urgency or retention (odds ratio = 6.26, 95% CI: 1.62 – 24.16), while anterior rectal wall temperature (Denon) was weakly associated (p=0.079).

Conclusions: Thermocouple data provide an objective means of assessing cryosurgical outcomes. This is the first report of a correlation of such data to post treatment voiding function. 37.9% of patients experienced urgency / frequency or urinary retention following cryoablation of the prostate for localized disease. Older age and external sphincter temperature less than or equal to 23 degrees Celsius were statistically significant predictors of these events. The data suggest that limiting the degree of freezing at the external sphincter may decrease procedure related morbidity. Further study is warranted to better delineate temperature related data on treatment outcomes.
Comparison of Outcomes following Prostate Cryoablation with Liquid Nitrogen vs. Gas Driven Cryoprobes

John F. Ward, David A. Levy, J. Stephen Jones

Introduction and Objectives: Prostate cryoablation instrumentation and technique shifted dramatically with the introduction of gas driven cryoprobes (GDC) that employ the Joule-Thomson thermodynamic process to achieve cooling, effectively replacing the liquid nitrogen (LN2) direct cooling systems. While the instrumentation became more compact and user friendly with this conversion, no comparison of outcomes before and after this conversion to gas driven cryoprobes has been reported.

Methods: A retrospective analysis of the COLD Registry was examined to separately identify patients treated for prostate cancer (primary and salvage) with LN2 versus GDC systems. Reported rates of continence, biochemical freedom from disease, and rectourethral fistualization for each system were compared.

Results: Between 1990 and 2008, 604 men are reported treated with a LN2 system for localized prostate cancer (whole gland, 394; partial gland, 15; salvage, 195) while cryoablation with GDC system is reported in 4,665 men (whole gland 3283; partial gland 1033, salvage 349). A lower proportion of men undergoing cryoablation with a GDC system have highrisk disease than did men treated with a LN2 system (27% v 41%). Incontinence (any leakage of urine) following GDC cryoablation is significantly less than following LN2 therapy (6.6% v 1.9% whole gland; 12.7% v 10.2% salvage). A similar improvement in prolonged urinary retention (6 weeks to 12-months) is also seen following GDC cryoablation (8.6% v 6.8% whole gland; 16.4% v. 10.6% salvage). Fistula rates increased slightly with GDC cryoablation vs. LN2 system (0.5% v 0.3% whole gland; 2.0% v 0.5%). Biochemical freedom from disease following GDC primary and salvage cryoablation remained unchanged from LN2 systems (5 year freedom from BCR 74.4% v 70.2% whole gland).

Conclusions: Introduction of GDC cryoablation has maintained high cancer control rates while decreasing rates of urinary incontinence and retention. Increase in fistulas with salvage cryo may reflect more aggressive cryotherapy or the higher radiation doses in later years.
Assessing PSA Treatment Recommendation of the AUA Best Practice Policy Statement on Salvage Cryoablation: Report from the COLD Registry

John F. Ward, David A. Levy, J. Stephen Jones

Introduction and Objectives: The American Urologic Association Best Practice Policy Statement on Cryosurgery for the Treatment of Localized Prostate Cancer presented at the 2009 meeting of the annual AUA meeting recommends treatment when serum PSA is below 10ng/mL. This is based upon a report from a single institution and is without information regarding outcomes in patients with PSA < 4ng/ml or > 10ng/mL.

Methods: A retrospective analysis of the COLD Registry was examined to identify patients treated with cryoablation for biopsy proven persistent or recurrent prostate cancer following primary therapy with radiation (external beam and brachytherapy), had negative metastatic evaluation prior to salvage therapy, and at least 3 post-treatment PSA values available for analysis. Patients were stratified based upon pre-salvage treatment PSA of ≤ 4ng/mL (Group A), >4 to ≤10ng/mL (Group B), and >10ng/mL (Group C). Cancer specific outcomes based upon PSA levels were assessed. Date of treatment failure was the date of the PSA meeting the nadir PSA after salvage cryoablation + 2 ng/mL criteria. Log-Rank Analysis was performed comparing biochemical recurrence to the next closest group (A to B, B to C).

Results: A total of 590 patients met inclusion criteria for this analysis (Group A = 196; Group B = 245; Group C=149). The median time from cryoablation to this analysis is 38.5 months. A lower PSA was associated with improved odds of biochemical free survival. Median time to PSA recurrence for Group C was 24 months where as for Groups A and B median survival was not achieved at 48 months. Freedom from biochemical recurrence was significantly better for Group A than B (p=0.0032), and Group B than C (p=0.0539).

Conclusions: Greater therapeutic benefit is achieved with salvage cryoablation for radiorecurrent prostate cancer at lower pre-salvage PSA values. The study supports and adds greater guidance to that of the AUA Best Practice Policy Statement on Prostate Cryoablation. Early identification and treatment of radiorecurrent prostate cancer can result in improved biochemical outcome.
Classification Schema for Organ Preserving Prostate Cancer Treatments

John F. Ward, J. Stephen Jones

Introduction and Objectives: “Focal Therapy” for prostate cancer is now a rapidly growing practice. However, supporting evidence remains largely theoretical. Studies must be conducted and allowed to mature in order to judge its efficacy. Paramount to developing this field is a common nomenclature that conveys the volume and location of tissue both destroyed and preserved for investigators to report the ablative procedure. Here we introduce that common language for organ preserving prostate ablation.

Methods: Review of the published literature and institutional programs of organ preserving prostate cancer therapy.

Results: The following nomenclature and treatment templates are proposed for reporting results of prostate organ preserving ablation regardless of the energy employed for tissue destruction:

1. Nerve Sparing (unilateral or bilateral)
2. Hemi-Ablation
3. Anterior or Posterior Hockey Stick
4. Targeted Focal Therapy
5. Zonal Ablation

Conclusions: “Focal Therapy” has been use to report a wide range of destructive templates. This term should be abandoned for the more descriptive term “Organ Preserving Therapy”. Investigators in this field will do well to report results with the common classification scheme and terminology presented here.
Primary Full Gland and Salvage Prostate Cryoablation: Updated Results from 4693 Patients Tracked with the COLD Registry

Nivedita Dhar, Michael Cher, Zachary Liss, Aaron Katz, David A. Levy, J. Stephen Jones

Introduction: We report the updated outcomes of primary full gland and salvage prostate cryoablation at a large number of centers which have participated in the Cryo On-Line Database (COLD) Registry. The data on 4693 men presented herein comprise the largest series available for primary and salvage cryoablation.

Methods: Biochemical failure was defined according to the ASTRO and Phoenix definitions. Incontinence was defined as any leaking. Return to intercourse was the ability to penetrate and complete intercourse with or without assistance. Biopsy was performed at the physicians discretion, but most commonly if a patient had a rising or suspicious PSA.

Results: For the entire group of patients, mean age was 70 years and 46% had intermediate risk cancer (56% had a Gleason Score<7, 73% had PSA<10 ng/mL and 71% had Stage<T2b). Mean follow-up was 31.8 months for primary patients and 38.5 months for salvage patients. Actuarial survivals as determined by KM analysis are reported in the figures. Of the 4099 primary patients, 18 (0.4%) reported rectal fistulas postop and 65 (3.1%) reported incontinence at 12 months. Of the 639 primary patients potent prior to treatment, 207 (32%) were sexually active at 12 months postop. Biopsies were performed in 841 (20.6%) of primary patients and were positive in 125 (14.9%). Of the 594 salvage patients, 9 (1.5%) reported rectal fistulas postop and 33 (12%) reported incontinence at 12 months. Of the 60 salvage patients potent prior to treatment, 24 (40%) were sexually active 12 months postop. Biopsies were performed in 75 (12.6%) of salvage patients and positive in 18 (24.0%).

Conclusions: Cryoablation of the prostate, practiced over a wide range of users in a variety of case presentations, is a therapy with efficacy as demonstrated by biochemical survival and low morbidity with the exception of erectile dysfunction. Study supported by an unrestricted grant by Healthtronics.

continued
Primary Full Gland Cryoablation

Time to Failure * (ASTRO)

Time to Failure * (PHOENIX)
Salvage Cryoablation

Time to Failure *(ASTRO)*

Time to Failure *(PHOENIX)*
Repeat Cryoablation after Primary Full Gland Cryoablation: Results from 117 Patients Tracked with the COLD Registry

Franco Lugnani, J. Stephen Jones

**Introduction:** We report outcomes of a repeat cryoablation procedure after failure of primary full gland cryoablation at a large number of centers which have participated in the Cryo On-Line Database (COLD) Registry. The data on 117 men presented herein comprise the first series available for repeat cryoablation.

**Methods:** Biochemical failure was defined according to the ASTRO and Phoenix definitions. Incontinence was defined as any leaking. Return to intercourse was the ability to penetrate and complete intercourse with or without assistance.

**Results:** Mean age was 68 yrs and 53% had high cancer (26% had a Gleason Score>7 and 21% had PSA>20 ng/mL). Mean follow-up was 51 mos. Actuarial survivals as determined by KM analysis are reported in the figures. Of the 117 primary pts, 0 reported rectal fistulas within 12 months postop and 2 (2.6%) of the 77 reporting pts had incontinence. Of the 28 pts reporting potency prior to treatment, 8 (29%) were sexually active at 12 months postop.

**Conclusions:** Cryoablation after failure of primary full gland cryoablation is a therapy with reasonable efficacy as demonstrated by biochemical survival and low morbidity with the exception of erectile dysfunction.

continued
Prostate Cancer

**Time to Failure * (ASTRO)**

- **Note:** PercentSurviving is calculated from Kaplan-Meier product limit estimates. Deaths are censored at the last recorded visit.
- * Time to failure is defined as 3 rises in PSA (≥ 0.5 months after surgery). Failure occurs midpoint between NADE and the first rise.
- **Number Left:** Number of patients that have neither experienced an event nor been censored prior to the time point.

**Time to Failure * (PHOENIX)**

- **Note:** PercentSurviving is calculated from Kaplan-Meier product limit estimates. Deaths are censored at the last recorded visit.
- * Time to failure is defined as: Failure is defined as the change in PSA from NADE ≥ 2 ng/ml, (≥ 6 months after surgery).
- **Number Left:** Number of patients that have neither experienced an event nor been censored prior to the time point.
Does End Fire vs. Side Fire Probe Affect Anterior Zone Prostate Cancer Detection Rate?

Sara M. Falzarano, Adrian V. Hernandez, Ayman S. Moussa, J. Stephen Jones, Cristina Magi-Galluzzi

**Purpose:** End fire probes (EFP) have been reported to have a higher prostate cancer (PCA) detection rate than side fire probes (SFP). In addition, the EFP biopsy configuration allows a more accurate sampling of the anterior and lateral zones of the prostate gland. Detection of anterior zone (AZ) tumors, which are less likely to be palpable and not easily visualized by imaging, remains a challenge. The aim of this study was to determine whether there is any difference in the AZ PCA detection rate between EFP and SFP and if such difference might be attributable to factors other than the geometric configuration of the technique itself.

**Materials and Methods:** Our study group comprised 123 men who underwent prostate biopsy (66 SFP and 57 EFP) followed by radical prostatectomy (RP) for PCA at our institution. Assuming that biopsy cores from the apex sample the AZ of the prostate, the presence of apical involvement at biopsy (AI-Bx) was recorded and correlated with the presence or absence of AZ PCA on the RP specimen. The relationship with the number of biopsy cores (Bx #), prostate weight (PW), patient age, and preoperative PSA was also analyzed.

**Results:** Median age and preoperative serum PSA of patients was 60 years (range 38-75) and 5.4 ng/mL (range 0.4-51.6), respectively, with no difference between EFP and SFP. The median Bx # and PW was 12 (range 6-26) and 48.1 grams (range 25.7-274), respectively with no difference between type of probe. AI-Bx was found in 35 (61.4%) EFP and 45 (68.2%) SFP cases, respectively. AZ PCA was detected in 47/57 (82.5%) and 47/66 (71.2%) of the RP specimens corresponding to EFP and SFP, respectively. There was no difference in the negative predictive values (NPV) (27.3%, 95%CI [11.6%-60.4%] vs. 38.1%[19%-61.3%]) and positive predictive values (PPV) (88.6% [72.3%-96.3%] vs. 75.6% [60.1%-86.6%]) between EFP and SFP. No difference was found in the apical involvement between EFP and SFP, despite adjusting for PW (p=0.5), PSA (p=0.5), age (p=0.4), Bx # (0.4), or all variables together (p=0.4). The PW of patients with positive AI-Bx, was significantly smaller than for men with negative AI-Bx (p=0.04), even after adjusting for probe type, PSA, age and number of biopsy cores taken (p=0.03).

**Conclusions:** Although the configuration of EFP seems to be more suitable for AZ sampling, we found no difference in the detection rate of AZ PCA between EFP and SFP. The presence of a smaller prostate gland significantly affected AZ PCA detection independently of the probe and number of biopsy cores taken.
Predicting Prostate Cancer and High Grade Cancer among Men undergoing Initial Prostate Biopsy in the Extended Biopsy Era

Ayman S. Moussa, Yu Changhong, Michael Kattan, J. Stephen Jones

Introduction: Prostate cancer is associated with significant morbidity and mortality for men in the US. Traditional belief was that early and accurate diagnosis of the disease might improve survival in such patients. Despite the increase in prostate cancer detection with the advent of PSA testing, there is still no screening assay that predicts prostate cancer with perfect accuracy. Most existing prediction tools are based on sextant biopsies, and the PCPT Risk Calculator is limited to use in men age >55 years. As such, we developed a predictive model prostate cancer risk calculator to estimate the risk of cancer in an individual patient undergoing initial biopsy.

Methods: The study population included a total of 4720 consecutive patients who underwent initial prostate biopsy sessions between August 1999 and January 2008. All transrectal ultrasound-guided prostate biopsies were performed in our institution as an office-based setting under periprostatic block. Nomogram predictor variables were patient age, race, serum PSA, %free PSA, DRE findings. We calculated the nomogram predicted probability in each patient. Area under the ROC curve was calculated as a measure of discrimination. Calibration was assessed graphically.

Results: A total of 2200 men (46.6%) were diagnosed with prostate cancer. Mean age was 63.7y, mean PSA 7.3 ng/ml, %Free PSA 17.9% and mean number of cores taken 12.4. 85.6% were Caucasian and 8.4% of all men had abnormal DRE. All variables included in the study where highly significant predictors for prostate cancer (p value <0.001). A nomogram for predicting the possibility of having prostate cancer and high grade cancer was constructed that had a concordance index of 0.6. The nomogram was well calibrated.

Conclusions: This predictive model allows individualized assessment of prostate cancer risk and risk of high-grade disease for men who undergo an initial prostate biopsy without any limitation to the age to be above 55 years, and for current extended biopsy schemes instead of the sextant method prior prediction models were based on.

continued
Using a Saturation Biopsy Schema Increases Cancer Detection in Men with High Grade Prostatic Intraepithelial Neoplasia during Repeat Biopsy in the Contemporary Era

Ayman S. Moussa, Jianbo Li, Brian R. Lane, Michael C. Gong, Morgan R. Koepke, J. Stephen Jones

**Introduction and Objective:** High grade prostatic intraepithelial neoplasia (HG-PIN) was clearly associated with cancer risk in the sextant biopsy era, but this has not been clearly demonstrated in the extended biopsy era. We determined the role of saturation biopsy for cancer detection in men with HG-PIN diagnosed by extended biopsy.

**Methods:** From 1999 to 2007, 260 had at least 1 or more repeat biopsy due to the presence of exclusive HG-PIN (without any other pathological finding) in a previous extended biopsy. They were divided into two groups according to the follow up biopsy schema, 150 men were followed up using another extended biopsy schema and 110 were followed up using the saturation biopsy schema.

**Results:** In the extended repeat biopsy group 25 of 130 (19.2%) men had cancer on 1st repeat biopsy and 5 of 20 men had cancer on 2nd repeat biopsy (25%). In the saturation biopsy group 29 of 95 (30.5%) had cancer on 1st repeat biopsy, and 7 of 15 (46.6%) had cancer on 2nd repeat biopsy. (Overall p = 0.02)

**Conclusions:** Cancer detection in men with HG-PIN in the contemporary extended biopsy era is substantially improved using saturation technique.

<table>
<thead>
<tr>
<th>Follow up using</th>
<th>Initial repeated (Second over all)</th>
<th>Second repeated (3rd over all)</th>
<th>Overall P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-14 Extended Pattern</td>
<td>N = 130 Positive: 25 (19.2%)</td>
<td>N = 20 Positive: 5 (25%)</td>
<td>N = 150 Positive: 30 (20%)</td>
</tr>
<tr>
<td>≥ 20 Saturated Pattern</td>
<td>N = 95 Positive: 29 (30.5%)</td>
<td>N = 15 Positive: 7 (46.6%)</td>
<td>N = 110 Positive: 36 (32.7%)</td>
</tr>
</tbody>
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Saturation as a Repeat Biopsy Strategy after Negative Office Biopsy

Ayman S. Moussa, J. Stephen Jones, Tianming Gao, Yair Lotan, Claus G. Reohrborn, Shahrokh F. Shariat, Khaled Fareed

**Introduction and Objective:** Office biopsies have a high false negative rate as illustrated by an increasing yield of prostate cancer detected by strategies acquiring a higher number of cores. We evaluated the clinical utility of saturation biopsy in detecting clinically significant cancers missed on initial office biopsies.

**Methods:** We performed transrectal ultrasound (TRUS) guided biopsies on 328 consecutive patients, who had at least one but up to four prior negative office biopsies. We obtained a total of 20 cores. All slides were reviewed by pathologists from single institution. Biochemical and pathological variables including t-PSA, f-PSA, v-PSA, TV, TZ, the presence of High grade PIN, Atypia or inflammation on initial biopsy; were compared in men with and without CaP. For continuous variables, t-test was used; for categorical variables, association test (Chi-square or Fisher’s exact) was used as a Uni-variable analysis. Multivariable analysis (MVA) using Logistic regression of all the factors was done on the cancer detection status. \( p < 0.05 \) was considered to be statistically significant.

**Results:** There are 702 biopsies in total of 328 patients. Each patient has one final saturation biopsy. 87 patients were diagnosed with cancer by the saturation biopsy (26.52% cancer detection rate). Median age was 63.5 y, median t-PSA was 6.62 ng/ml. Men who were diagnosed with CaP had statistically comparable Age, t-PSA, f-PSA, v-PSA, TV, TZ, to those who were diagnosed with benign diseases at saturation biopsy. The associations between inflammation, HGPIN and atypia with cancer detection were strong. The cancer detection rate was much higher for men with HGPIN \((p= 0.004)\), Atypia \((p= 0.004)\) and without inflammation \((p< 0.001)\). On MVA the cancer detection rate is higher in men with higher PSA (OR 1.1; \(p=0.006\)), having Atypia (OR 2.9; \(p=0.005\)) and with inflammation the odd ratio was only 0.23 \((p<0.001)\).

**Conclusions:** Saturation biopsy detected up to 26.5% cancers in this select group of individuals who had previously underwent as many as 4 prior negative office biopsies. Saturation biopsy is effective in detecting cancer in men with persistently elevated PSA and prior negative biopsies.

**Summary of multi-variable analysis on cancer detection**

<table>
<thead>
<tr>
<th>Effect</th>
<th>Odds Ratio</th>
<th>95% Confidence Limits of OR</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA per one unit increase</td>
<td>1.072</td>
<td>1.020, 1.126</td>
<td>0.0062</td>
</tr>
<tr>
<td>Inflammation (Yes versus No)</td>
<td>0.234</td>
<td>0.135, 0.408</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atypia (Yes versus No)</td>
<td>2.927</td>
<td>1.380, 6.208</td>
<td>0.0051</td>
</tr>
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</table>
The Perception of Family History Risk and its Estimate Role of having Prostate Cancer in the Contemporary Era

Ayman S. Moussa, Shah Gaurang, Susan Luay, Changhong Yu, M. Kattan, J. Stephen Jones

Introduction and Objective: Prostate cancer (PCa) is the second leading cause of cancer death among US men. Earlier reports have shown increase risk of PCa in men with a family history (FH) of PCa. In addition, FH positive for prostate cancer has been stated to affect the likelihood of a positive prostate biopsy and is included in some prediction models, such as the PCPT risk calculator. We sought to assess the potential role of family history of PCa and its estimate risk of a positive prostate biopsy. Our hypothesis was that family history creates risk of PCa as suggested by elevated PSA, but that within men with elevated PSA, that family history does not affect the likelihood of a positive biopsy compared to men with no family history of PCa.

Methods: We evaluated 3840 men who underwent initial prostate biopsy between 2000-8 for elevated PSA. The FH was available in 1949 men. Multi-regressional analysis was used to analyze the data.

Results: The mean age was (64.4) y, PSA (7.57ng/ml), number of cores taken (12.1), prostate volume (47.98 cc) as shown in the table. The incidence of cancer detection was 50.4%. The percentage of positive cancer cases diagnosed among men with negative family history versus men with positive family history are (46.1 % vs. 51.1 %) respectively. On multivariate analysis, overall the family history was not an independent predicator for cancer detection (P value 0.59) in this large dataset. Also there was evidence indicating that patients with FH of cancer have lower level of PSA. (P value=0.009).

Conclusions: It appears that men with a family history of prostate cancer are more likely to undergo biopsy at a lower PSA than men without a family history based on our finding that men with family history positive for prostate cancer have a lower PSA than men biopsied without family history of prostate cancer. In our cohort of men with elevated PSA, FH did not increase the risk for prostate cancer when analyzed by multivariate analysis. We believe with more awareness for prostate cancer screening, better understanding of PSA level and strategy of extended-core prostate biopsy may have played a role.

continued
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<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Age</td>
<td>64.4 (38-94)</td>
<td></td>
</tr>
<tr>
<td>PSA</td>
<td>7.57 ng/ml (0.4-85.7)</td>
<td></td>
</tr>
<tr>
<td>Negative FH</td>
<td>7.08 ng/ml</td>
<td>0.009</td>
</tr>
<tr>
<td>Positive FH</td>
<td>5.94 ng/ml</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>C (84%)</td>
<td></td>
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<tr>
<td>African-American</td>
<td>AA (13%)</td>
<td></td>
</tr>
<tr>
<td>Prostate Volume</td>
<td>47.98 cc</td>
<td></td>
</tr>
<tr>
<td>Number of Cores</td>
<td>12.14</td>
<td></td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>50.44%</td>
<td></td>
</tr>
<tr>
<td>Negative FH</td>
<td>46.1%</td>
<td>0.59</td>
</tr>
<tr>
<td>Positive FH</td>
<td>51.1%</td>
<td></td>
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</tbody>
</table>
Initial Diagnosis of High-Grade Prostatic Intraepithelial Neoplasia is a Risk Factor for Subsequent Development of Prostate Cancer

Michael C. Lee, Ayman S. Moussa, Changhong Yu, Michael W. Kattan, J. Stephen Jones

Objectives: The management of patients diagnosed with high-grade prostatic intraepithelial neoplasia (HGPIN) on prostate biopsy remains controversial. Our aim was to evaluate the effect of HGPIN on initial biopsy toward future presence of prostate cancer.

Methods: From December 1997 to February 2008, 328 men had a second prostate biopsy after being initially diagnosed with HGPIN at the Cleveland Clinic. Men with concurrent prostate cancer (CaP) or atypia were excluded. Within the same time period, 225 men without HGPIN, CaP or atypia underwent a second prostate biopsy based on clinical suspicion. A total of 663 patients were included in the analysis. Data was prospectively obtained after IRB approval. A Cox proportional hazards model was used to estimate the effect of HGPIN on the subsequent diagnosis of CaP, after adjustment for PSA, age, presence of inflammation, abnormal DRE and number of cores taken at biopsy. Kaplan-Meier plots were generated to estimate the rates of CaP.

Results: HGPIN alone on initial prostate biopsy has a significant effect on the subsequent diagnosis of CaP. The hazard ratio is 1.89 (95% CI: 1.39, 2.55) for PIN versus no PIN with a \( p \)-value 0.00004. Kaplan-Meier curves are shown in Figure 1. The estimated cancer rates by year 1, 3 and 5 years are 9%, 30% and 49% for patients with PIN and 5%, 17% and 30% for patients without PIN.

Conclusions: HGPIN remains a risk factor for future development of CaP despite adjusting for other clinical indicators such as PSA and abnormal DRE. Repeat prostate biopsy should be considered in all patients with HGPIN.

continued
Figure 1. Kaplan-Meier Curves

- Patients with PIN
- Patients without PIN
The Relationship between Prostate-Specific Antigen and Prostate Cancer Risk: Findings from the Prostate Biopsy Collaborative Group


Introduction: Prostate specific antigen (PSA) is the only molecular marker widely used to screen for a common cancer. Yet more than 20 years after its discovery, the relationship between PSA level and prostate cancer risk remains subject to fundamental disagreements. We hypothesize that risk is affected by identifiable characteristics of the biopsy cohort under study. To test this hypothesis, we obtained raw data from a heterogeneous set of prostate biopsy cohorts.

Methods: We utilized data from 5 European and 3 US biopsy cohorts. Five data sets comprised screening studies (ERSPC Goteborg, ERSPC Rotterdam, ERSPC Tarn, SABOR, and ProtecT), while two were clinical cohorts (Cleveland Clinic, Durham VA). The Tyrol cohort was not expressly a screening trial, but involved PSA testing of a high proportion of the eligible population.

Results: The final data set included 25,773 biopsies and 8,504 cancers. There were gross disparities between cohorts with respect to both the prostate cancer risk at a given PSA level and the shape of the risk curve. These disparities were largely explicable in terms of identifiable differences between cohorts: for a given PSA level, extended biopsy increased risk of cancer (odds ratio 1.56; 95% C.I. 1.43, 1.71; p<0.0005); recent screening led to a smaller increase in risk per unit change in PSA (p=0.008 for interaction term) and US cohorts had higher risk than the European cohorts (1.49; 95% C.I. 1.40, 1.58; p<0.0005).

Discussion: Our results suggest that the relationship between PSA and prostate cancer risk differs between cohorts, both in terms of the probability of prostate cancer at a given PSA value and the shape of the risk curve. The difference between the US and European cohorts may result from patient selection (population-based in Europe vs. self-selection in US), differences in biopsy technique, or referral patterns (biopsy for elevated PSA in Europe vs. clinical work up in the US). PSA-based risk calculators are unlikely to have general applicability.

continued
Relationship between PSA and prostate cancer risk in DRE negative Caucasians

1) Cleveland Clinic; 2) SABOR; 3) PCPT (risks obtained from published formula); 4) Tyrol; 5) Goteborg rounds 2 to 6; 6) Rotterdam round 1; 7) Rotterdam rounds 2 to 3; 8) Goteborg round 1; 9) Tarn
Introduction and Objective: The 2000 AUA Best Practice statement on PSA considered serum PSA <4.0 ng/mL to be normal. However, the Prostate Cancer Prevention Trial (PCPT) reported a prostate cancer (CaP) biopsy rate of 6.6% even at PSA 0-0.5 ng/mL, increasing to 26.9% with PSA of 3.1-4.0. To reflect these findings our hospital initially ceased reporting PSA as normal or abnormal. We expected this to create increased, possibly unnecessary, referrals based on laboratory reports showing cancer risk at every PSA value. However, a paradoxical decrease in referrals prompted re-evaluation of this practice.

Methods: Traditionally, PSA values >4.0 in our health system were flagged as abnormal and reported to the physician electronically. In November 2007 we eliminated abnormal PSA flags and reported CaP prevalence with PSA ranges from PCPT. A significant decrease in consultations for elevated PSA (ePSA), including some with PSA >4.0, prompted reinstitution of flagging PSA >4.0 in March 2009 in addition to PCPT data.

Results: In the 14 months preceding the first change in PSA reporting, the mean of monthly ePSA consultations was 76. In 14 months following removal of the electronic flag, this mean decreased to 15 (P<0.001). In the months since the second change in reporting, this mean has increased to 33 (P<0.01). These differences were even more pronounced if a 2-month lag period for change in practice was accounted for. No other potential cause for these differences was identified.

Conclusions: Removing the reference range and electronic flags for laboratory reporting of PSA may have severely decreased referrals for evaluation of ePSA including high PSAs that the physician or patient would choose to evaluate. Our subsequent rise in referrals after reinstituting flags for PSA >4.0 is consistent with this. Therefore, simple flagging of PSA >4.0 may assist in decision-making between physician and patient.
Number of Consultations for Elevated PSA
Prostate-Specific Antigen Rises Faster in Patients with Multiple Negative Biopsies compared to Patients followed by Active Surveillance for Low-Risk Prostate Cancer

Akshat C. Pujara, Andrew J. Stephenson, Ranko Miocinovic, Ryan K. Berglund, J. Stephen Jones

Introduction and Objective: Prostate-specific antigen (PSA) is historically used as a marker of disease progression in most prostate cancer (PCa) active surveillance (AS) protocols without evidence of its utility. We compared PSA dynamics in AS patients to patients with similar clinical findings who had at least two prior negative biopsies and are unlikely to have prostate cancer.

Methods: Data were collected from a prospective database and chart review. AS patients were defined as those having favorable clinical features and biopsy parameters at diagnosis and repeat biopsy confirming low-risk disease. The control group consisted of patients considered to have no known disease by virtue of at least two prior negative biopsies. Patients were matched by age (5 year increments), PSA (1 ng/ml increments), BMI (increments of 5), gland volume (20 cm³ increments) at diagnostic or first negative biopsy, respectively, and race. PSA values were adjusted for 5-alpha reductase inhibitor use.

Results: From February 2000 to August 2009, 99 men were followed by AS for low-risk PCa. Of these, 46 could be matched to 53 of 434 men in the control group. At diagnostic biopsy (AS) and first negative biopsy (control), mean age was 68 ± 7 and 64 ± 6 years, mean PSA 5.84 ± 3.71 and 5.19 ± 1.67 ng/ml, mean BMI 28 ± 4 and 28 ± 4, and mean gland volume 47 ± 24 and 45 ± 13 cm³, respectively. Median interval from diagnosis to last PSA was 1.3 years (IQR 0.9 - 1.7) in AS patients and from first negative biopsy to last PSA 1.6 years (IQR 1.1 - 2.3) in the control group. Median PSA doubling time was 4.6 years (IQR 2.4 - 10.3) in AS patients and 4.31 years (IQR 2.8 - 7.0) in the control group. Median PSA velocity was 0.62 ng/ml/year (IQR 0.60 - 0.68) in AS patients and 1.63 ng/ml/year (IQR 0.79 - 2.59) in the control group (Figure 1).

Conclusions: PSA dynamics in patients with multiple negative PSA-triggered biopsies reflect a more rapidly rising PSA than in AS patients over short term-intervals. This finding calls into question the value of using PSA changes to follow patients on AS. Routine surveillance biopsy or magnetic resonance imaging may be warranted in AS patients regardless of PSA. Longer follow-up is required to further evaluate PSA dynamics in AS patients and implications for disease management.
Figure 1. Rise in PSA in patients on active surveillance and patients with at least 2 negative biopsies.
Prostate Specific Antigen/Solvent Interaction Analysis (PSA/SIA): Progress Report for a New Assay for Prostate Cancer

Mark Stovsky, Lee Ponsky, Srinivas Vourganti, Mike B. Siroky, Victor Kipnis, Olga Fedotoff, Larissa Mikheeva, Boris Zaslavsky, Arnon Chait, J. Stephen Jones

Background: We describe interim clinical data obtained during further assay development of a novel protein structural assay for CaP diagnosis. The assay uses PSA Solvent Interaction Analysis (SIA) to detect changes in PSA isoform composition that differentiate benign and malignant disease, independent of total PSA (tPSA).

Methods: We previously reported preliminary data. The prior SIA assay chemistry was cumbersome and expensive. In this study we focus on a newly developed SIA assay chemistry that could potentially reduce the cost and complexity of the assay by up to 5X. The current and prior studies include men undergoing prostate biopsy for accepted clinical criteria. Patients received systematic prostate massage followed by urine collection. The PSA/SIA assay determined relative partitioning of heterogeneous PSA isoform populations between two aqueous phases. A composite structural index, K, was calculated and is used to set a diagnostic threshold for CaP. We report preliminary data from a significantly simplified version of the urine assay.

Results: We report interim ROC AUC=0.89, and two different potential cutoff values of the composite structural index K=0.63 and 0.70 corresponding to sensitivities=91% and 71% and specificities=66% and 100%. We also demonstrate SIA’s ability to differentiate between free PSA (%fPSA) and PSA-ACT complex with K=4.37, 4.01, and 3.72 for 100% fPSA, 24.3% fPSA/75.7% PSA-ACT, and 100% PSA-ACT. However, in clinical serum samples we find no correlation between K values associated with fPSA levels specific to each sample, yet the K values provided for differentiation of samples based on clinical status.

Conclusions: PSA/SIA uniquely exploits the structural heterogeneity in PSA resulting in superior diagnostic performance over conventional biopsy selection criteria for the identification of CaP. Future trials will assess its utility in urine and serum for applications in CaP diagnosis and management.
High Patient Acceptance of Active Surveillance among Contemporary, Low-Risk Prostate Cancer Patients at a U.S. Tertiary Referral Center

Akshat C. Pujara, Ranko Miocinovic, Eric A. Klein, J. Stephen Jones, Andrew J. Stephenson

Introduction and Objective: Active surveillance (AS) for low-risk prostate cancer is under-utilized in patients who are candidates for definitive local therapy. We reviewed patient acceptance of AS, endurance of choice, and safety of triggers for intervention.

Methods: Between February 2000 and September 2009, patients were selected for AS based on favorable clinical features and biopsy parameters at the initial and repeat biopsy confirming low-risk disease. Patients were followed with routine clinical assessment, serum prostate-specific antigen (PSA), and a repeat biopsy every 1-2 years. Those with adverse biopsy parameters on either initial or repeat biopsy were recommended to undergo treatment. For the purpose of this study, progression on AS was defined as increase in Gleason score, increase in positive cores to \( \geq 33.3\% \), increase in maximum cancer in any core to \( \geq 50\% \), or rise in PSA to \( \geq 10\) ng/ml.

Results: A total of 273 men were referred for management of localized, low-risk prostate cancer to two urologic oncologists and were recommended to undergo repeat prostate biopsy for consideration of AS. Of the 273 men, 143 (52\%) agreed to consider AS and underwent repeat biopsy. After repeat biopsy, 27 (19\%) of these 143 men were recommended to undergo immediate treatment due to re-classification to higher risk disease and 116 were placed on AS. Median age at diagnosis among these 116 was 67 years (IQR 63 - 72); 12\% were younger than 60 and 27\% older than 70. Over a median follow-up of 26 months (IQR 17 - 42), 99 patients (85\%) remained on AS and 17 (15\%) were treated by radical prostatectomy (10 by choice, 7 for progression on AS). All treated patients had organ-confined cancer and none had specimen Gleason 8-10 disease. The 4-year freedom from treatment was 76\% (95\% CI 64 - 89) and 4-year freedom from progression was 87\% (95\% CI 76 - 98).

Conclusions: In urological oncology practice at a high-volume tertiary referral center, patient acceptance of AS as an initial management strategy and retention rate on AS is high. The majority of patients with adverse biopsy features are identified by initial repeat biopsy and the progression rate on AS in appropriately selected patients is low. The favorable pathological parameters of treated patients suggest the triggers for intervention on AS are safe. A repeat biopsy should be considered in all men with low-risk prostate cancer prior to definitive local therapy. Increasing acceptance of AS among patients and physicians may limit the treatment burden of screen-detected cancers.
The Epstein Criteria Predict for Organ Confined but not Insignificant Disease and a High Likelihood of Cure at Radical Prostatectomy


Background: Few reports attempt to validate the role of Epstein criteria in selecting patients for an active surveillance protocol.

Objective: To determine the performance of the Epstein biopsy criteria for predicting pathological endpoints and biochemical relapse free survival in men with early stage prostate cancer treated by radical prostatectomy (RP).

Design, Setting and Participants: Between October 1999 and January 2007, 746 consecutive patients were biopsied and then underwent radical prostatectomy (RP) at our tertiary care institution. 268 met the entry criteria of Gleason 6 disease only on initial biopsy with complete pathological information.

Measurements: Primary endpoint was insignificant disease. Insignificant disease was defined using a classical (organ-confined, Gleason score \( \leq 6 \), and tumor volume < 0.5 cm\(^3\)) and more liberal (organ confined Gleason \( \leq 6 \) tumor of any volume) formulation. Secondary endpoints included organ-confined disease and biochemical relapse free survival.

Results: One hundred thirty-six men (51%) met the Epstein biopsy criteria, 167 (62%) had organ-confined cancer. Insignificant disease by the classical and liberal definitions was present in 68 (25%) and 92 (34%) patients, respectively. Cases meeting Epstein’s biopsy criteria were more likely to have insignificant disease by either definition (\( p < .001 \)) and more likely to have organ confined tumors (\( p < .001 \)). Sensitivity, specificity, PPV, and NPV varied widely among the endpoints, with sensitivity (74%) and NPV (86%) best for the classical definition of insignificant disease and specificity (74%) and PPV (92%) best for organ confined disease. The estimated 5-year biochemical relapse-free survival was 100% for those meeting Epstein's biopsy criteria compared to 83% for those not meeting these criteria.

Conclusions: The Epstein biopsy criteria predict for a high likelihood of organ-confined disease and absence of biochemical failure up to 5 years after RP. These criteria are insufficiently robust to predict the presence of biologically insignificant disease.
Initial Diagnosis of High-Grade Prostatic Intraepithelial Neoplasia is a Risk Factor for Subsequent Development of Prostate Cancer

Michael C. Lee, Ayman S. Moussa, Changhong Yu, Michael W. Kattan, J. Stephen Jones

Objectives: The management of patients diagnosed with high-grade prostatic intraepithelial neoplasia (HGPIN) remains controversial. Our aim was to evaluate the effect of HGPIN on initial biopsy toward future presence of prostate cancer.

Methods: From December 1997 to February 2008, 328 men had a second prostate biopsy after being initially diagnosed with HGPIN. Men with prostate cancer (CaP) or atypia were excluded. 225 men without HGPIN, CaP or atypia underwent a second prostate biopsy based on clinical suspicion. A total of 663 patients were included in the analysis. Data were prospectively obtained after IRB approval. A Cox proportional hazards model was used to estimate the effect of HGPIN on the subsequent diagnosis of CaP, after adjustment for PSA, age, presence of inflammation, abnormal DRE and number of cores taken at biopsy. Kaplan-Meier plots were generated to estimate the rates of CaP.

Results: HGPIN alone on initial prostate biopsy has a significant effect on the subsequent diagnosis of CaP. The hazard ratio is 1.89 (95% CI: 1.39, 2.55) for PIN versus no PIN with a p-value 0.00004, increasing with time as shown in the Kaplan-Meier curves. The estimated cancer rates by year 1, 3 and 5 years are 9%, 30% and 49% for patients with PIN and 5%, 17% and 30% for patients without PIN.

Conclusions: HGPIN remains a risk factor for future development of CaP despite adjusting for other clinical indicators such as PSA and abnormal DRE.

continued
Figure 1. Kaplan-Meier Curves

- Patients with PIN
- Patients without PIN
Inhibition of Prostate Specific Membrane Antigen Gene-Expression is Mediated by TMPRSS2:ERG Gene Fusion in VCaP Prostate Cancer Cells

Lihong Yin, Pravin Rao, Jianghua Wang, Michael Ittmann, Warren D.W. Heston

Objective: Prostate specific membrane antigen (PSMA) is a type II transmembrane glycoprotein that is over-expressed in prostatic adenocarcinoma (CaP). Levels of PSMA expression have been correlated with aggressive disease and risk of early recurrence after radical prostatectomy (RP). Studies have shown that a significant fraction of CaP’s harbor a signature gene fusion between the androgen-responsive TMPRSS2 gene and transcription factors in the ETS family – most commonly ERG. The TMPRSS2-ERG fusion is likely the cause for over-expression of ERG in CaP. PSMA, unlike ERG, is negatively regulated by androgen. Elucidation of the relationship between TMPRSS2 gene fusions and PSMA expression could reveal mechanisms to alter PSMA expression and disease course. The purpose of this investigation was to determine whether PSMA gene expression could be regulated by the TMPRSS2-ERG fusion in prostate cancer cells.

Methods: VCaP cells (which harbor the TMPRSS2:ERG fusion) and LNCaP cells (which do not) were incubated with vehicle or the androgen-receptor antagonist flutamide prior to treatment with synthetic androgen R1881. In addition, transfection of siRNA against human ERG was performed to create ERG knockdown in VCaP cells. Reverse transcription (RT) PCR as well as real-time RT PCR were used to detect and quantify transcription of ERG, TMPRSS2:ERG, PSMA, and androgen receptor (AR) genes. Using the comparative threshold cycles method, the quantification of these transcripts was performed, and expression was compared in various androgen-treated and untreated VCaP and LNCaP cells.

Results: After 24-hour androgen treatment, ERG and TMPRSS2-ERG mRNA level were increased in VCaP cells and unchanged in LNCaP cells. PSMA and androgen receptor (AR) mRNA level were dramatically decreased in VCaP cells and modestly decreased in LNCaP cells. Treatment with the androgen antagonist flutamide partially restored PSMA and AR expression in androgen-treated VCaP cells. Knocking down ERG by siRNA in VCaP cells enhances PSMA mRNA expression both in the presence and absence of R1881, while it has minimal change of AR mRNA in VCaP-ERG knock down cells.

Conclusion: Down-regulation of PSMA in androgen-treated VCaP cells appears partially mediated by the TMPRSS2:ERG gene fusion. Since PSMA has been associated with aggressive disease and early biochemical failure after RP, further elucidation of the relationship between TMPRSS2 gene fusions and PSMA could reveal potential novel targets for treatment of prostate cancer.
Introduction: This is a description of the PSA kinetics > 5 years after definitive therapy for prostate cancer (CaP) with brachytherapy (PI) or external beam (RT).

Methods: The records of 960 patients treated for prostate cancer between 1996 and 2003 were reviewed. None of these patients had a biochemical failure (bF, using the Phoenix definition) within the first 5 years after therapy. Factors thought to influence bF were examined for correlation with the occurrence of bF >5 years after therapy. The PSA value at Year 5 (PSA5) was included as a covariate in these models. The sensitivity and specificity of different PSA5 cutpoint values to predict for bF were calculated.

Results: There were 341 patients who received PI and 619 who received RT. The median follow up time for PI patients was 6.9 years (range: 5.0-11.3 years) and was 7.5 years (range: 5.0-12.6 years) for the RT patients. The median D90 for the PI patients was 136.84 Gy and the median dose of RT was 80 Gy. For both modalities, the PSA gradually rose after 5 years whether they experience bF or not (slope of the PSA levels after 5 years for PI: 0.002 for non-bF and 0.77 for bF; for RT: non-bF 0.005 and bF 0.049). On univariable modeling only the PSA5 and the PSA testing frequency were significant (p < 0.0001 in both) for the PI patients. For the RT patients, the initial PSA, biopsy Gleason, clinical stage, PSA5 and PSA frequency were significant on univariable analysis (p < 0.0001, p = 0.0003, p = 0.0021, p= 0.0001, and p < 0.0001, respectively). On multivariable analysis, only PSA5 remained significant for PI (p < 0.0001) and for RT both PSA5 and PSA frequency persisted as being significant (p = 0.013 and p < 0.0001, respectively). For both PI and RT patients a PSA5 of >0.5 ng/mL optimizes the sensitivity and specificity for predicting bF. Accordingly, the sensitivity and specificity for PI are 90.9% and 94.4% while for RT they are 70.3% and 70.0%.

Conclusions: Patients 5 years or more after PI or RT, will experience a rise in PSA whether a patient experiences bF or not. Distinguishing between those patients likely to develop a late bF and those not likely to develop bF may be done by checking the PSA5 and tempering therapeutic recommendations appropriately.
Evaluation of Long-Term Bowel and Urinary Toxicity after Permanent Prostate Brachytherapy

Kevin L. Stephens, Chandana A. Reddy, Eric A. Klein, Kenneth W. Angermeier, James Ulchaker, Michael J. Burdick, Mohammad K. Khan, Lawrence Sheplan, Jay P. Ciezki

Purpose: To assess the late toxicity of permanent prostate brachytherapy (PI) monotherapy.

Methods and Materials: We reviewed 796 patients treated with $^{125}$I permanent PI (144 Gy) monotherapy between September 1996 and April 2003. Medical records were reviewed for objective measures of urinary and rectal toxicity. Other factors which might influence these endpoints including transurethral resection (TURP) and use of anticoagulants were scored. All colonoscopies done after PI were reviewed for evidence of radiation proctitis. Dosimetric data was gathered from post-implantation CT studies done one to thirty days after implant.

Results: Median follow up was 68 months (range 0-140 months). Median prostate volume was 34.1 cc (range 8-119) and median D90 139 Gy (range 66-223). Median V100% was 88% of prostate volume (range 16.5-100%). Prostate D100, V400%, V200% and V150% were also recorded. Median rectal V50 was 4.1 cc (range 0.01-15.8), rectal V100 0.25 cc (range 0-3.7), rectal V150 0 cc (range 0-1.2) and rectal V200 0 cc (range 0-0.3). Median rectal D5 was 73 Gy (range 22-180). Complete data on rectal bleeding were available for 646 patients. Rectal bleeding was noted in 113 patients (17.5%). Colonoscopies were performed for 317 patients including all patients with unknown cause of bleeding. The most common causes of bleeding were hemorrhoids (58%), radiation proctitis (10.6%), colorectal cancer (9.7%), diverticuli (7.1%), and polyps (7.1%). Seventeen patients were noted to have radiation proctitis on colonoscopy (five asymptomatic) representing 5.3% of colonoscopies and 2.6% of patients. Symptomatic radiation proctitis (twelve cases) was identified in 1.9% of patients. Patients on warfarin or clopidogrel were more likely to have rectal bleeding (16%, $p = 0.016$) and more likely to have symptomatic radiation proctitis (5.3%, $p = 0.03$). No other patient, prostate or rectal dosimetry parameter was correlated with risk of symptomatic radiation proctitis. 538 patients had complete data on urinary frequency. At a median 68 months after PI, daytime and nocturnal urinary frequency were unchanged from pre PI levels. The median pre and post-PI daytime frequency was 5 (mean 5.5 vs 5.6, $p = 0.86$) and the median pre and post-PI nocturnal frequency was 2 (mean 1.7 vs 1.9, $p = 0.07$). There was no change in percent differences of day ($p = 0.38$) or night-time ($p = 0.42$) frequencies for individual patients. Fifteen patients (2.3%) developed incontinence. Fifty-five patients (8.4%) under-
went a TURP (29 pre-PI, 30 post-PI). Incontinence was strongly correlated with a TURP (p<0.0001). Only one patient (0.2%) who never underwent a TURP developed incontinence compared with 29% of patients with a TURP. The correlation between a TURP and incontinence was noted regardless of the timing of the TURP (17% incontinence with pre-PIT, p = 0.0015; 46% incontinence with post-PI, p < 0.0001). Greater patient age (p = 0.0023) and higher activity seeds (median 0.458 vs median 0.430, p = 0.013) were associated with incontinence while no other dosimetric or volume related factors were correlated.

**Conclusions:** Rectal bleeding due to PI monotherapy is rare, occurring in approximately two percent of all patients. Radiation proctitis should not be assumed to be the cause of rectal bleeding in patients post-PI. Patients with rectal bleeding should receive a full work-up as not to miss a more serious diagnosis. Urinary frequency after PI returns to baseline long-term. Urinary incontinence after PI is strongly associated with TURP.
A Comparison of Cause-specific Mortality among Patients with Low or Intermediate-risk Prostate Cancer Treated with Brachytherapy, External Beam Radiotherapy or Radical Prostatectomy

Jay P. Ciezki, Chandana A. Reddy, C. Robinson, Kenneth Angermeier, James Ulchaker, Eric A. Klein, Nabil Chehade, A. Altman

Purpose and Objective: Biochemically defined outcomes suggest equivalent efficacy among brachytherapy (PI), external beam radiotherapy (RT), and radical prostatectomy (RP) in patients with low or intermediate-risk prostate cancer (CaP). Similar data on prostate cancer-specific mortality (PCSM) are lacking.

Materials and Methods: The records of 4222 consecutive patients with low or intermediate-risk disease treated between 9/96-9/05 were reviewed. Factors thought to influence mortality and PCSM were reviewed, including: age, Charlson score, initial PSA (iPSA), androgen deprivation (AD) duration, pack-years of smoking, income, body mass index (BMI), presence of coronary artery disease (CAD), presence of hypertension (HTN), alcohol use, race, biopsy Gleason score (bGS), and clinical stage. Univariate and multivariable analyses were done using competing risk methodology for Cox proportional hazards regression analysis.

Results: Fifty-two percent of patients were treated with RP, 30% with PI, and 18% with RT. The median follow up for all patients was 48 months (range: 0-126). More than 50% of patients were treated after 2001. At the time of analysis, 264 patients (6.3%) had died – 23 from CaP, 92 from CAD, 94 from other cancers, and 55 from other causes. The results of the PCSM multivariable analysis reveal that RT is associated with worse outcome relative to PI and RP (p < 0.0001).

Conclusions: Low and intermediate risk CaP patients treated with RT had a higher risk of death due to CaP than patients treated with RP or PI after adjusting for factors that influence overall and PCSM.
Dosimetric Analysis ofBiochemical Outcome following 125I Permanent Prostate Brachytherapy

Kevin L. Stephens, Chandana A. Reddy, Eric A. Klein, Kenneth W. Angermeier, James Ulchaker, Rahul D. Tendulkar, Jay P. Ciezki, Nabil Chehade, Andrew Aultman

Purpose: To assess the impact of D90 (dose received by 90% of prostate volume) and implant dosimetry on outcome in a large, uniformly treated patient population.

Methods and Materials: We reviewed 1,160 patients in an IRB approved prospectively maintained database treated with 125I permanent prostate brachytherapy as their sole form of definitive therapy between September 1996 and October 2005. Prostate volume and dimensions were measured intraoperatively. Dosimetric data was obtained by CT scan one to three after implantation. The Phoenix definition was used for biochemical free survival (bRFS). The primary endpoint was whether D90 was correlated with bRFS. D90 was analyzed as both a continuous and categorical variable using cutoffs of <130 Gy, 130-160 Gy (chosen to represent the 25th-75th percentile for D90’s in our population), and >160 Gy.

Results: Median follow up was 50 (range: 4-140) months and the median number of follow up PSAs was seven (range: 2-36). By NCCN definition 68% of patients had low-risk, 25% intermediate-, and 7% high-risk disease. Eighty-three percent of patients received no androgen deprivation, 15% received 1-6 months and 3% received >6 months. No patient received supplemental external beam radiation. The overall five-year bRFS rate was 91.5%. Median D90 was 143.4 Gy (range 66-227 Gy) with a standard deviation of 24.8 Gy. The 10th percentile for D90 was 113 Gy and the 90th 175 Gy. There was no association of NCCN risk group, Gleason score, or seed activity with D90. A smaller intra-operative prostate volume (p < 0.0001), shorter length (p < 0.0001), width (p < 0.0001) and height (p = 0.0058), and use of androgen deprivation (p < 0.0001) were associated with a lower D90. ON univariate analysis with Cox proportional hazards regression, D90 as a continuous variable was associated with better bRFS (p = 0.003) HR = 0.987). Patients with a D90 < 130 Gy had inferior bRFS (87.9%) compared to those with a D90 130-160 Gy (p = 0.019, HR = 1.75) or > 160 Gy (p = 0.042, HR = 1.86). However, patients with a D90 130-160 Gy had similar bRFS (94.0%) to those with D90 > 160 Gy (94.8%, p = 0.84). Twenty-nine (2.5%) patients experienced clinical failure and there was no association of D90 with clinical failure (p = 0.97). Additional variables predictive for bRFS in univariate analysis were initial PSA (p < 0.0001), Gleason score (p < 0.0001), V100% (p = 0.003), V150% (p = 0.002), V200% (p = 0.020), prostate vol-
ume (p < 0.0001, HR = 0.471). D100 (p = 0.31), V300% (p = 0.24), V400% (p = 0.40), seed activity (p = 0.75), Age (p = 0.78) and T-stage (T1, T2A vs T2B, T2C) (p = 0.47) were not associated with bRFS. On multivariate analysis D90 was no longer a significant predictor of bRFS as a categorical (p = 0.44) or continuous variable (p = 0.095). Patients with a D90 < 130 Gy had a similar bRFS to those with a D90 between 130-160 Gy (p = 0.20) or > 160 Gy (p = 0.39). There was no difference between patients with a D90 of 130-160 Gy and those > 160 Gy (p = 0.94). V100% (p = 0.96), prostate length (p = 0.59) and height (p = 0.50) were not associated with bRFS. In addition to initial PSA (p < 0.0001) and Gleason score (p = 0.0004) prostate width demonstrated a statistically significant association with improved bRFS (p = 0.0008, HR = 0.56).

Conclusions: Within the range of D90 examined in this study, there was no association between higher D90 and improved bRFS. However, improved bRFS was associated with lower initial PSA, lower bGS, and wider glands.
Section 2

Prostate Benign Disease
Single-Port Transvesical Enucleation of the Prostate (STEP): Clinical Experience


Introduction and Objective: We report our initial experience with a novel technique-single-port transvesical enucleation of the prostate (STEP) in 30 patients with symptomatic large volume BPH.

Methods: The STEP procedure was performed in 30 patients with symptomatic large volume BPH (TRUS volume > 80 grams). A novel single-port device (r-Port, Advanced Surgical Concepts, Ireland) was inserted percutaneously into the bladder through a 2.5 cm suprapubic incision under cystoscopic control. After establishing pneumovesiculc, a circumferential mucosal incision was made around the bladder neck and the plane between the adenoma and surgical capsule was identified and the entire adenoma enucleated using electrocautery and ultrasonic shears. Digital assistance was employed selectively through the port for completion of the enucleation. The adenoma was extracted through the single port device without the need for a specialized morcellation device.

Results: Mean age was 70 years, mean BMI was 26, mean prostate size was 97g (50-247) and mean PSA was 4.8 ng/ml. Mean operative time was 112 min. Mortality occurred in 1 patient who was a Jehovah’s witness from bleeding due to coagulopathy. Complications included bleeding (N=3), bowel injury (N=1). Mean hospital stay was 3 days and mean duration of catheterization was 6.8 days. All patients are voiding spontaneously (mean post op IPSS 3, Q max ml/sec) without significant post-void residual and are fully continent.

Conclusions: Single-port transvesical simple prostatectomy is technically feasible. Our initial experience demonstrates safety and efficacy in select patients with symptomatic large volume BPH.
Section 3

Kidney Cancer
Kidney Tumor Location Measurement Using the C-Index Method

Matthew N. Simmons, Christina B. Ching, Mary K. Samplaski, Chin Hyong Park, Inderbir S. Gill

Purpose: Tumor location assessment is essential for planning of nephron-sparing kidney surgery. This study describes a method to quantify proximity of kidney tumors to the renal central sinus for reporting and surgical management purposes.

Materials and Methods: C-index scoring was conducted using standard 2-dimensional cross-sectional CT images for 133 consecutive patients undergoing transperitoneal laparoscopic partial nephrectomy (LPN) between September 2003 and November 2005. The Pythagorean theorem was used to calculate c, the distance from the center of the tumor to the center of the kidney. The c distance was divided by the tumor radius to obtain the C-index. Correlation of C-index to LPN operative parameters and urologic complication rate was assessed. Accuracy and inter-observer variability of C-index were assessed.

Results: A C-index of 0 equates to a tumor that is concentric with the center of the kidney. A C-index of 1 equates to a tumor with its periphery touching the kidney center. As C-index increases the tumor periphery becomes located more distantly from the kidney center. Multivariate regression analysis revealed association of C-index with warm ischemia time (p=0.01), a surrogate for technical complexity. Inter-observer correlation of C-index values was >90%, with an estimated learning curve of 14 cases required for variability of measurements to decrease below 10% of the mean C-index value for 10 consecutive cases.

Conclusions: C-index scoring provides a clinically useful measure of tumor centrality. This system may allow for improved clinical and radiologic assessment of kidney tumors and improved quantitative tumor location reporting.
Bilateral Synchronous Kidney Tumors: Long-term Functional and Oncological Outcomes

Matthew N. Simmons, Ricardo Brandina, Adrian Hrnandez, Inderbir S. Gill

**Purpose:** Renal functional and oncologic outcomes after sequential radical (RN) and partial nephrectomy (PN) in patients with bilateral synchronous kidneys tumors were assessed.

**Materials and Methods:** Patients treated from June 1994-July 2008 were retrospectively analyzed. Study endpoints included MDRD2 eGFR <60ml/min/1.73m², overall survival (OS), cancer-specific survival (CSS), and recurrence-free survival (RFS).

**Results:** 220 patients were treated with sequential PN (PN-PN; n=134), PN followed by RN (PN-RN; n=60), or RN followed by PN (RN-PN; n=26). Postoperatively, cumulative eGFR decreased by 20ml/min/1.73m² in the PN-PN group compared to 37-38ml/min/1.73m² in the PN-RN and RN-PN groups (p<0.001). Tumor size >4cm and preoperative CKD stage ≥III correlated with postoperative progression to stage IV-V CKD. OS for the total cohort was 86% at 5y and 71% at 10y. CSS was 96% at 5y and 96% at 10y. RFS was 73% at 5y and 44% at 10y. Tumor size >7cm correlated with decreased OS 73% at 5y, 51% at 10y. Postoperative CKD stage ≥III correlated with decreased OS (80% at 5y, and 70% at 10y) vs. patients with stage I-II CKD (96% at 5y, and 93% at 10y; p=0.02).

**Conclusions:** Tumor size >4cm and preoperative CKD stage ≥III were risk factors for CKD stage progression. Postoperative stage ≥III CKD was strongly associated with decreased 5y and 10y OS. Nephron-sparing surgery should be compulsory for all amenable kidney masses given the impact of functional decline on OS.
Laparoscopic Radical vs. Partial Nephrectomy for Tumors >4cm: Intermediate-term Oncologic and Functional Outcomes

Matthew N. Simmons, Christopher J. Weight, Inderbir S. Gill

Objective: To compare oncologic and functional outcomes of laparoscopic radical (LRN) and LPN for clinical T1b-T3 RCC tumors >4cm in size.

Methods: This retrospective analysis compared patients undergoing LRN (n=75) or LPN (n=35) at a tertiary referral center from 04/2001 to 12/2005 for T1b-T3N0M0 RCC tumors. Endpoints included radiologically verified systemic and local recurrence, cancer-specific mortality, overall mortality, and CKD based on calculated GFR and K/DOQI diagnostic criteria.

Results: The LRN group had larger tumors (5.3cm vs. 4.9cm; p=0.03), more T3a tumors (33% vs. 9%; p=0.006), and more clear cell pathology (85% vs. 66%; p=0.03). There were no positive surgical margins in either group. Median follow-up was 57 months (range: 27-79) in the LRN group and 44 months (range: 27-85) in the LPN group (p=0.1). Overall mortality (11% vs. 11%), cancer-specific mortality (3% vs. 3%), and recurrence rates (3% vs. 6%; p=0.4) were equivalent. Postoperative decrease in eGFR was less in the LPN group than in the LRN group at 13ml/min and 24ml/min, respectively (p=0.03). Postoperatively, two-stage increases in CKD stage occurred in 12% vs. 0% of patients in the LRN vs. LPN groups, respectively (p<0.001).

Conclusions: Intermediate-term data indicate that in appropriate patients with T1b-T3 tumors >4cm, LPN provides equivalent oncologic efficacy and superior renal functional outcomes compared to LRN. Future studies are required to confirm these trends.
Active Treatment of Localized Renal Tumors May Not Impact Overall Survival in Patients 75 Years of Age or Older with Medical Comorbidity

Brian R. Lane, Robert Abouassaly, Andrew C. Novick, Inderbir S. Gill, Adrian V. Hernandez, Jihad H. Kaouk, Christopher J. Weight, Benjamin T. Larson, Steven C. Campbell

Introduction and Objective: Incidental renal tumors are increasingly being detected in patients of all ages. Nephrectomy cures localized renal cancer but worsens renal function. We investigated overall survival in ≥75 year-old patients managed with active surveillance, nephron-sparing surgery, or nephrectomy.

Methods: Pertinent data were recorded for all patients ≥75 years diagnosed with a renal mass and/or undergoing nephrectomy for any cause. Included were 557 patients with a clinical T1 renal tumor managed by surveillance, nephron-sparing surgery, or nephrectomy. Cox regression models evaluating overall survival were constructed based on age, comorbidity, management type, renal function, and other variables.

Results: Management of clinical stage T1 renal cancer in 557 patients included active surveillance (19%), nephron-sparing surgery (54%), or nephrectomy (27%). Median follow-up was 3.5 years, with death of any cause occurring in 124 patients (22%) and cancer progression in only 15 patients (2.7%). Kaplan-Meier analysis revealed differences in overall survival for patients undergoing surveillance, nephron-sparing surgery, or nephrectomy (p=0.01), but surveiled patients were older (p=0.002) and had greater comorbidity (p<0.0001). In multivariable analysis, significant predictors of overall survival included age (p=0.0004) and comorbidity (p<0.0001), but not management type (p=0.3). Neither preoperative nor change in renal function, nor pathologic tumor characteristics were significant after adjusting for all other variables. In a subset analysis of 75-80 year-old patients with Charlson score of 0-1, nephron-sparing surgery and nephrectomy were associated with improved survival compared with surveillance (p=0.05). A nomogram incorporating age and Charlson score was constructed to predict overall survival in patients with localized renal tumors.

Conclusions: Surgical management of localized renal tumors in older patients improves survival only in those predicted to have significant longevity (age<80 and minimal comorbidity). Patients with lesser predicted longevity appear to be safely managed with active surveillance.
Section 4

Kidney & Pancreas Transplant
Renal Artery Aneurysm Treated with Ex-vivo Reconstruction and Autotransplantation

Christina B. Ching, Una J. Lee, Ho Yee Tiong, Venkatesh Krishnamurthi, David A. Goldfarb

Introduction and Objective: Distally located renal artery aneurysms are a surgical difficulty. We performed a successful ex-vivo left renal artery aneurysm repair with autotransplantation in the distal left anterior segmental renal artery after determining this case was not amenable to endovascular or in situ repair. Computed tomographic arteriography (CTA) with 3-dimensional (3D) reconstruction helped to determine management of this patient.

Methods: A 64 year old man with gross hematuria was found to have a left renal artery aneurysm. The patient had a history of hypertension, peripheral vascular disease, and 70 pack years of smoking. A CTA with 3D reconstruction demonstrated a 2.2 cm saccular aneurysm arising from the distal left anterior segmental artery. Despite significant atherosclerosis of the aorta and iliac vessel, the aneurysm was non-calcified. Due to this fact as well as the aneurysm size and patient symptoms, surgical therapy was recommended. Given the distal location of the aneurysm and the possibility of branching arteries off the aneurysm, the decision was made for ex-vivo aneurysmal repair with autotransplantation in order to preserve as much renal parenchyma as possible.

Results: The patient underwent a successful autotransplant with ex-vivo aneurysmal repair without complications. Intraoperatively, we confirmed the presence of multiple arterial branches off the aneurysm which could only have been managed through an ex-vivo repair. The operative time was roughly 6.5 hours. The warm ischemia time was <3 minutes and the cold ischemia time was roughly 2.5 hours. The estimated blood loss was about 300ml. The discharge creatinine was 0.7.

Conclusions: Renal artery aneurysms, while uncommon, have been increasing in diagnosis likely secondary to improved imaging techniques. CT arteriography with 3-D rendering was instrumental in preoperative planning for this complex aneurysm.
The Use of SPECT/CT in Evaluating Suspected Urine Leaks Following Kidney Transplantation

N. Sezhian, A. Wee, C. Modlin, Stuart M. Flechner

Introduction: Renal transplantation provides the best quality of life for the patients with End stage renal disease (ESRD). While the majority of kidney transplant cases are uncomplicated, 5-10% result in urologic complications including urinary fistulae. We describe the usefulness of Single Photon Emission Tomography (SPECT CT) scan in identifying suspected urine leaks following renal transplants. SPECT uses tomographic scintigraphy, with computer generated three dimensional images of radioactive tracer produced by detection of single photons from acquired multiple planar images.

Materials and Methods: SPECT aided in the identification of urinary fistulae in complex cases, which were not detected with conventional CT scanning.

Case 1 A 52 year old male, seven foot tall and weighing 330lbs underwent Dual Disease Donor Kidney Transplant with bilateral polycystic Kidney disease nephrectomy. The upper kidney was anastomosed to the native ureter and the lower kidney ureter to the bladder. On post operative day six drain output and creatinine increased. A SPECT scan showed radioactive tracer in the drain coming from the upper kidney; and on exploration, the ureteroureterostomy anastomosis was necrotic and was revised.

Case 2 A 49 year old female underwent pediatric enbloc kidney transplant with a patch from donor bladder. She was discharged with an indwelling foley catheter. The creatinine rose following the removal of catheter and a SPECT scan showed a fluid collection with tracer activity in the pelvis. On exploration, the bladder patch was found to be necrotic and the donor ureters were anastomosed to the native ureter.

Case 3 A 38 year old male with a defunctionalized bladder was transplanted with a uretroureterostomy to the native ureter. Following removal of the foley catheter, there was sudden discharge from the transplant wound. The drain fluid and the serum creatinine were similar. A SPECT scan was diagnostic for a leak and identified a fluid collection with tracer activity. On exploration a leak from the ureteroureterostomy was repaired.

Conclusion: In complex renal transplants, especially using the pediatric en bloc or dual kidneys, a CT scan is likely to miss a small urine leak. SPECT, as we have demonstrated, is very sensitive and we recommend this imaging modality to diagnose urine leaks when there is a high index of suspicion.
Expanding Donor Pool in Kidney Transplants: Dealing With Capsular Injury

Natarajan Sezhian, Charles Modlin

**Introduction and Objectives:** End stage renal disease (ESRD) presents social, medical and financial problems for every country in the world. Kidney transplantation gives excellent quality of life and plays a crucial role in the treatment of ESRD. There continues to be a chronic shortage of available donor kidneys. Expanded criteria donor has addressed this issue to some extent. In some instances, procured kidneys may be considered unsuitable for transplantation for reasons such as significant capsular tear. We describe one such case of kidney with capsular injury which was successfully transplanted, with vicryl mesh reinforcement.

**Methods:** A 49 year old man with ESRD was admitted for a deceased donor kidney transplant. He was Jehovah's Witness. The allograft was from from a deceased donor of 45 years of age with cold ischemia time of 18 hours. While benching the allograft, we noticed more than two third of anterior surface of the kidney was devoid of capsule. The allograft otherwise looked fine with two renal arteries and a vein. We decided to reinforce the renal parenchyma with vicryl mesh covering the capsular defect (fig 1). The mesh was trimmed and sutured with catgut sutures. Evicel a fibrin sealant was applied over the mesh to provide further reinforcement. With the release of clamps and beginning of perfusion, there was no bleeding from the renal parenchyma.

**Results:** The patient had uneventful postoperative recovery with good graft function and was discharged on postoperative day five.

**Conclusions:** Number of patients waiting for a kidney transplant is ever increasing. In USA, nearly 82,000 pts are on the waiting list for kidney transplant. Expanded criteria donor has increased the donor pool. Minor degree of capsular injury of the allograft is unlikely to have an impact with respect to graft function and complication rate. Significant disruption, leads to non acceptance by the surgeon because of potential risk of hemorrhage. Rarely diffuse urine leak can occur from the denuded renal parenchyma. Reinforcing with vicryl mesh is a simple technique, which will avoid these potential complications and would enable proper use of renal allografts.
Comparison of Renal Autotransplantation and Ureteroileal Substitution for Management of Proximal Ureteral Obstruction

Alvin Wee, Ismael Saad, Ho Yee Tiong, Venkatesh Krishnamurthi

Introduction: Reconstructive options for proximal ureteral obstruction include renal autotransplantation (RA) or ureteroileal substitution (UI). These therapeutic options have been demonstrated to be successful in enabling normal urinary tract drainage with a low incidence of long term complications. What remains unknown however is the relative merit of each of these procedures.

Methods: From 1996 to 2007, 35 renal autotransplants and 15 ureteroileal substitutions were performed. A total of 12 patients were done for proximal ureteral obstruction (nonmalignant). These 12 patients who underwent RA (6 patients) and UI (6 patients) were identified in whom neither procedure was contraindicated. Patient charts were reviewed for renal function, new onset hypertension, metabolic disturbance, post-operative complications, and long term outcomes including need for reoperation, pain relief, readmission for urinary tract disorders.

Results: 4 men and 2 women underwent RA (mean age 44.6 years) and 3 men and 3 women underwent UI (mean age 46.6 years). Median follow up for the RA group is was 21 months (6-80 mos.) and for the UI group 12 months (6-20 mos.) p=0.08. Baseline serum creatinine (Scr) was 1.1 mg/dl with mean eGFR of 74.4 ml/min and for the UI group the Scr was 1.08 mg/dl and eGFR of 74.6ml/min. At 1, 6, 12, and 18 months post operatively the Scr was 1.14, 1.04, 1.06 and 1.06 mg/dl for RA and 1.03, 1.16, 1.15 and 1.15 mg/dl for the UI group. RA appeared to more effectively result in pain relief as 16% of patients required narcotics vs. 48% of UI patients. Additionally, although not statistically significant there tended to be a lower rate of urinary tract infections in RA patients 16% vs. 32%.

Conclusions: Both RA and UI are effective therapeutic options for patients with proximal ureteral obstruction. RA may have fewer long term complications due to the preservation of urinary tract integrity. Additional RA may enable more successful pain relief probably through renal denervation. RA also provides ease of access for future intervention. These differences may become more apparent with longer follow up and may be more relevant to younger patients.
Comparison Between Stapled vs Hand-Sewn Enteric Drainage in Pancreas Transplant

Ho Yee Tiong, Alvin Wee, John Rabets, Charlie Winans, Venkatesh Krishnamurthi

**Objective:** To compare post-operative surgical outcomes for stapled vs hand-sewn enteric drainage in pancreas transplant.

**Materials and Method:** All isolated pancreas and simultaneous kidney pancreas transplants from January of 2006 to Sept of 2008 were included. A total of 84 pancreas transplants were done, of which 69% (58/84) were hand sewn. The technique used was a single layer full thickness anastomosis using PDS 3-0 interrupted sutures, reinforced with Silk 3-0 Lembert seromuscular sutures. All anastomoses were fashioned as duodeno-jejunostomy. 31% (26/84) were stapled anastomosis, using an EEA circular staple size 21. 35% (9/26) were fashioned in a duodeno-duodenostomy while the remainder as duodeno-jejunosotmy. Primary outcome measure was the bowel anastomotic leak rate. Secondary outcome measures include rates of post-operative bleeding and small bowel obstruction.

**Results:** There were 2/56(3.4%) anastomotic leaks in the hand sewn group with no leaks in the stapler group (p=ns). There was one patient in each group who presented with bowel obstruction 1 month post-operatively (p=ns), both of which were manage conservatively. In the stapled group, there were 2/26(7%) who had an upper GI bleeding post operatively. Both of which were on a duodeno-duodenostomy type of enteric drainage. Bleeding were confirmed to be on the anastomotic site by endoscopy. One was managed conservatively, while the other was managed via angio- embolization. Short-term graft and patient survival was the same for both groups (p=ns).

**Conclusion:** Bowel anastomotic leak rate were slightly higher in the handsewn group compared to the stapled group although it did not reach statistical significance. Using the EEA stapler, both duodeno-duodenostomy and duodeno-jejunosotomy type of enteric drainage can be constructed with ease although the former may have a higher rate of anastomotic bleeding.
Living Donor Renal Transplantation Overcomes Racial Disparities in African American Recipients

Natarajan Sezhian, Charles Modlin, Joan Alster, Ho Yee Tiong, Barbra Mastroinni, Kathy Savas, Stuart M. Flechner

Introduction: End stage renal disease (ESRD) has a higher incidence and prevalence in African Americans (AA). In 2007, AAs accounted for 31% of wait list additions but only 22% of renal transplant recipients (RTR) with a longer mean waiting time. African Americans were less likely to present with a possible Living Donor (LD) and thus are less likely to receive a LD transplant. Studies of deceased (DD) renal transplants report 5 year survival of 60% for African Americans vs. 73% for non African Americans. We compared graft and patient survival in AA and non-AA patients who received a LD or DD renal transplant at our center.

Materials and Methods: Data were obtained retrospectively from the Uniform Transplant Database (UTD). Between 1995 and 2004, 772 patients underwent a primary kidney only or Kidney/Pancreas transplant at our center. Patients were grouped into Non-AA (n=604) and AA (n=168). We compared recipient, donor, transplant and immunologic parameters in both groups. Graft and patient survival with regards to donor type (LD vs. DD) were estimated using the Kaplan-Meier method.

Results: The mean follow up was 7.1 +/- 2.5 years. AAs received more deceased renal transplants (p<0.0001) and significantly less LD transplants (p<0.05). Graft survival was significantly worse in AA deceased Donor renal transplants when compared to non-AA DD –renal transplants (p=0.003) However graft survival of Living Donor kidney transplants were comparable in both the groups (p>0.05). Patient survival was similar in AA and Non AA RTRs of either LD or DD transplants (p=0.2) Table 1.

Conclusion: AA DD-renal transplant recipients are disadvantaged when compared to non-AA renal transplant recipients. Although AAs experience worst graft survival following DD kidney transplants, outcomes are virtually the same as non-AAs following LD transplants. LD transplantation in AA-RTRs seems to surmount suboptimal outcome of transplants in AA-RTRs. The merits of LD renal transplantation should be highlighted and encouraged for AA patients. More research is needed to gain understanding of, as well as attempt to modify, factors involved in this racial discrepancy in outcome of DD transplants.

continued
Table 1. Graft and Patient Survival

<table>
<thead>
<tr>
<th>Group</th>
<th>N=772</th>
<th>Graft Survival</th>
<th>Patient Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1-year</td>
<td>3-year</td>
</tr>
<tr>
<td>AA LD-RTR</td>
<td>50</td>
<td>96%</td>
<td>86%</td>
</tr>
<tr>
<td>Non AA LD-RTR</td>
<td>282</td>
<td>94%</td>
<td>85%</td>
</tr>
<tr>
<td>AA DD-RTR</td>
<td>118</td>
<td>80%</td>
<td>74%</td>
</tr>
<tr>
<td>Non AA-RTR</td>
<td>322</td>
<td>88%</td>
<td>81%</td>
</tr>
</tbody>
</table>
The Evolving Outcomes of Kidney Transplant Recipients Over 70 Years of Age

Islam A. Ghoneim, Ho Yee Tiong, Jesse D. Schold, Titte Srinivas, Charles Modlin, Stuart M. Flechner

Introduction: Prior to 2000 only 2 patients over age 70 years had received a kidney transplant at our center. This age limit restriction was based anecdotal reports of excess morbidity and mortality for this group. Since 2000, we have transplanted 47 such patients, representing about 3.5% of our recipients, up to 6.3% the past 2 years. The annual mortality of such patients on dialysis exceeds 20%. Nationally, the proportion of patients > 70 in the past three years is 6% (an increase from 2.7% in the prior decade). The 1, 3, and 5 yr overall and death censored graft loss rates are (87, 75, 66) and (94, 90, 88).

Methods: The Cleveland Clinic Unified Transplant Database was queried for all kidney-only transplant recipients age 70 years or older at transplant. There were 49 patients with a mean age of 72.5 (range 70-86) years including 34 males and 15 females. The cause of ESRD included GN 33%; HTN 22%; DM 12%, PKD 6%, Unknown 15%. The Donor Source included DD 67%; LRD 22%: and LUR 10%. The mean BMI was 27 kg/m2. Immunosuppression included myco-phenolate mofetil and steroids with a CNI drug in 53.1% or an mTOR in 38.7% of cases.

Results: The mean follow-up is 37.7 (range 1-92) months. K-M survivals (%) at 1, 3, 5 years, respectively are for Patient Survival (86, 72, and 56). For Graft Survival -uncensored (86, 72, 56) vs. Graft-death censored (97, 94, 88). Among 14 deaths the causes were CV 50%; Infectious 14%; Pulmonary 14%; and Unknown (out of hospital) 21%. One year biopsy confirmed acute rejection was 6%, and the mean creatinine was 1.25 mg/dL. There were 3 cases of de novo skin or solid organ cancers.

Conclusions: Patients over age 70 are seeking the option of kidney transplantation in greater numbers today. Their transplant outcomes are primarily driven by an increased rate of cardiovascular mortality the first 3 years. They exhibit relatively low rates of rejection, infection, and have excellent post transplant renal function. Pretransplant functional capacity and CV status are the best predictors of outcome.

continued
Patient Survival
70 year old Recipients

Graft Survivals 70 yo Recipients

100%
80%
60%
40%
20%
0%

Days Post Transplant

0 12 24 36 48 60 72 84 96

Percent survival

100%
80%
60%
40%
20%
0%

Months Post Transplant

0 12 24 36 48 60 72 84 96

Percent survival

Death Censored
Uncensored
Sirolimus Associated Alterations in Sex Hormone Profiles; Impact on Prostate Specific Antigen (PSA) Levels and Erectile Function among Adult Male Kidney Transplant Recipients


Introduction and Objectives: Hypogonadism has been reported among patients on mTOR inhibitors. Sirolimus use in transplantation created a unique patient population to study the effect of lowered sex hormones levels on PSA screening for prostate cancer. We analyzed a male renal transplant population on continuous sirolimus immunosuppression to identify possible correlations with both erectile dysfunction (ED) and screening serum PSA levels.

Methods: The study included 120 male kidney transplant recipients on an immunosuppression regimen containing sirolimus, mycophenolate mofetil and steroids, subgrouped by age; <50 and >50 years. Sera were analyzed for testosterone (T), PSA, follicle stimulating hormone (FSH), luteinizing hormone (LH), and prolactin levels pre-transplant, and at 12, 24, 36, 48, and 60 months post-transplant. Comparable controls comprised frozen sera from 40 male ESRD patients on the kidney transplant waiting list and analyzed for T, FSH, LH and prolactin on the date of listing, and at years 1, 3, and 5 on the wait list. PSA values were compared using historic controls adjusted for age and race. No cases or controls were diabetic, had prior history of ED or prostate cancer. Erectile function was evaluated using the International Index of Erectile Function Sexual Health Inventory for Men.

Results: Mean age was 48.7 years (20-75). Serum T levels declined at 12 months post transplant, becoming statistically significant at 40 months. Increase in FSH and LH levels occurred early, but was significant only in the >50 age group. PSA values exhibited a linear decline; no statistical significance was noted when compared to pretransplant values or to historical controls matched for age and race for both age groups. Summarized in Table 1. 27% of cases reported new onset ED. No correlation was found with decreased testosterone levels.

Conclusions: Sirolimus-based regimens have a significant effect on testosterone levels post transplant, with hypogonadism observed more frequently in patients over 50. Serum PSA levels decline in association with reduced testosterone. However, this decline is not significant and does not affect screening for prostate cancer in this population. Reduced sex hormones levels did not correlate with new onset ED. 

continued
Table 1: Patterns of change pre and post-transplant of testosterone (T), luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, prostate specific antigen (PSA) in the patients over and below 50 years of age. Mean follow-up is 46 months.

<table>
<thead>
<tr>
<th></th>
<th>&lt;50y</th>
<th></th>
<th></th>
<th>&gt;50y</th>
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<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
<td>N</td>
</tr>
<tr>
<td>T-pre</td>
<td>483.68</td>
<td>174</td>
<td>57</td>
<td>426**</td>
<td>185</td>
<td>61</td>
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<tr>
<td>T-post</td>
<td>324.52</td>
<td>124</td>
<td>33</td>
<td>261**</td>
<td>141</td>
<td>43</td>
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<tr>
<td>LH-pre</td>
<td>8.39*</td>
<td>4.1</td>
<td>57</td>
<td>12.7*</td>
<td>9.84</td>
<td>61</td>
</tr>
<tr>
<td>LH-post</td>
<td>13.57*</td>
<td>16.4</td>
<td>33</td>
<td>21.2*</td>
<td>21.1</td>
<td>43</td>
</tr>
<tr>
<td>FSH-pre</td>
<td>8.11**</td>
<td>10.3</td>
<td>57</td>
<td>12.1**</td>
<td>12.8</td>
<td>61</td>
</tr>
<tr>
<td>FSH-post</td>
<td>14.9**</td>
<td>19.6</td>
<td>33</td>
<td>25.4**</td>
<td>23.2</td>
<td>43</td>
</tr>
<tr>
<td>Prolactin pre</td>
<td>18.68</td>
<td>24.9</td>
<td>57</td>
<td>18.5</td>
<td>20.4</td>
<td>61</td>
</tr>
<tr>
<td>Prolactin-post</td>
<td>10.37</td>
<td>5.89</td>
<td>31</td>
<td>10.4</td>
<td>5.23</td>
<td>42</td>
</tr>
<tr>
<td>PSA-pre</td>
<td>1.03</td>
<td>0.73</td>
<td>19</td>
<td>1.59</td>
<td>1.3</td>
<td>55</td>
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<tr>
<td>PSA post</td>
<td>0.99</td>
<td>0.64</td>
<td>27</td>
<td>1.45</td>
<td>1.31</td>
<td>112</td>
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</tbody>
</table>

*P <0.05, **P <.01
Section 5

Laparoscopy
Predictors of Long-term Oncological Outcomes of Laparoscopic Nephroureterectomy for Upper Tract TCC

Michael Lee, Georges-Pascal Haber, Kazumi Kamoi, Sebastian Crouzet, Inderbir S. Gill

Introduction and Objectives: Laparoscopic nephroureterectomy (LNU) is now an accepted treatment alternative for patient with upper tract transitional cell carcinoma (UT-TCC). We analyzed factors which predict disease-specific and recurrence-free survival of patients following LNU.

Methods: 217 consecutive patients underwent with LNU for UT-TCC between 9/1997 and 2/2008. Data were collected prospectively and retrospectively when missing. Survival was determined from clinical follow up and the Social Security Death Index. Factors affecting disease-specific and recurrence-free survival were analyzed using Cox proportional hazard model.

Results: At 2, 5 and 8 years overall survival was 72%, 54% and 43%, disease-specific survival was 81%, 76% and 73%, and recurrence-free survival was 64%, 60% and 58%, respectively. In multivariate analysis T stage (muscle invasive) and positive surgical margin were independent predictors for disease-specific survival (P<0.01 for both, Table 1). Five-year disease-specific survival rate was 92% in the non-invasive diseases (127 patients) and 52% in the muscle invasive diseases (90 patients). Positive surgical margin occurred in 20 patients whose median survival was 17 months. In multivariate analysis grade 3 tumor in the pathological specimen was an independent predictor for recurrence-free survival (p<0.05, Table 2). Five-year recurrence-free survival rates were 79% in the patients without grade 3 tumor (71 patients) and 49% in the patients with grade 3 tumor (146 patients).

Conclusions: Long-term oncological outcomes for LNU appear comparable to those of open surgery. For patients undergoing LNU, T stage 2 or higher was an independent predictor for disease specific survival and tumor grade 3 was an independent predictor for recurrence-free survival. Patients with positive surgical margin had overall poor prognosis.
### Table 1: Univariate and multivariate analysis for disease-specific survival

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate p value</th>
<th>Multivariate p value</th>
<th>RR</th>
<th>95% CIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt;70 years)</td>
<td>0.29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson Comorbidity Index (&gt;0)</td>
<td>0.21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive History of Bladder Tumor</td>
<td>0.77</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Urine Cytology</td>
<td>0.83</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Bladder Cuff Removal</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location of Tumor (Kidney/Ureter/Both)</td>
<td>0.31</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Carcinoma in Situ</td>
<td>0.35</td>
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</tr>
<tr>
<td>Tumor Grade (&gt;2)</td>
<td>0.0041*</td>
<td>0.91</td>
<td>1.1</td>
<td>0.4 – 2.4</td>
</tr>
<tr>
<td>Tumor Stage (&gt;1)</td>
<td>&lt;0.0001*</td>
<td>&lt;0.0001</td>
<td>5.9</td>
<td>2.7 – 14.4</td>
</tr>
<tr>
<td>Positive Lymph Nodes</td>
<td>0.0032*</td>
<td>0.68</td>
<td>1.2</td>
<td>0.5 – 2.8</td>
</tr>
<tr>
<td>Positive Surgical Margins</td>
<td>&lt;0.0001*</td>
<td>0.0011</td>
<td>3.6</td>
<td>1.7 – 7.0</td>
</tr>
<tr>
<td>Lymphovascular Invasion</td>
<td>&lt;0.0001*</td>
<td>0.19</td>
<td>1.6</td>
<td>0.8 – 3.0</td>
</tr>
</tbody>
</table>

* Variables with p value < 0.10 by univariate analysis are selected for multivariate variables

### Table 2: Univariate and multivariate analysis for recurrence-free survival

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate p value</th>
<th>Multivariate p value</th>
<th>RR</th>
<th>95% CIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt;70 years)</td>
<td>0.15</td>
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<td></td>
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<tr>
<td>Charlson Comorbidity Index (&gt;0)</td>
<td>0.63</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Positive History of Bladder Tumor</td>
<td>0.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Urine Cytology</td>
<td>0.073*</td>
<td>0.30</td>
<td>1.3</td>
<td>0.8 – 2.1</td>
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<tr>
<td>Bladder Cuff Removal</td>
<td>0.88</td>
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<td></td>
<td></td>
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<tr>
<td>Location of Tumor (Kidney/Ureter/Both)</td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma in Situ</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Grade (&gt;2)</td>
<td>0.0003*</td>
<td>0.055</td>
<td>2.0</td>
<td>1.1 – 3.8</td>
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<tr>
<td>Tumor Stage (&gt;1)</td>
<td>0.0003*</td>
<td>0.29</td>
<td>1.4</td>
<td>0.8 – 2.4</td>
</tr>
<tr>
<td>Positive Lymph Nodes</td>
<td>0.22</td>
<td></td>
<td></td>
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<tr>
<td>Positive Surgical Margins</td>
<td>0.066*</td>
<td>0.26</td>
<td>1.5</td>
<td>0.7 – 2.9</td>
</tr>
<tr>
<td>Lymphovascular Invasion</td>
<td>0.0045*</td>
<td>0.21</td>
<td>1.5</td>
<td>0.8 – 2.7</td>
</tr>
</tbody>
</table>

* Variables with p value < 0.10 by univariate analysis are selected for multivariate variables
Tumor in Solitary Kidney: Laparoscopic Partial Nephrectomy vs. Laparoscopic Cryoablation

Michael Lee, Georges-Pascal Haber, Sebastian Crouzet, Kazumi Kamoi, Inderbir S. Gill

Introduction and Objectives: We compare peri-operative, functional and intermediate term oncological outcomes of laparoscopic partial nephrectomy (LPN) versus laparoscopic cryoablation (LCA) for small renal tumor in patients with a solitary kidney.

Methods: Between 2/1998 and 9/2008, 48 patients underwent LPN and 30 patients underwent LCA for small renal tumor in a functionally solitary kidney. Baseline, peri-operative, and follow-up data were collected prospectively. Data analysis was retrospective.

Results: There were no significant differences between the LPN and LCA group with respect to mean patient age, BMI, and Charlson Comorbidity Index. Tumor size was larger (3.2 vs. 2.6cm; p= 0.23) in the LPN group. LPN was associated with greater blood loss (391 vs 162 mL; p=0.003), and more intra-operative (6% vs. 3.5%; p= 0.23) and post-operative complications (22.9% vs. 6.7%; p= 0.07). By 3 months after LPN and LCA, eGFR decreased by 14.5% and 7.3%, respectively (p=0.02). Post-operative temporary dialysis was required after 3 LPN (6.2% vs 0%, p = 0.16). Local recurrence was detected after 0 LPN and 4 (13.3%) LCA (p=0.02). Median follow-up time for LPN and LCA was 42.7 and 60.2 months respectively. Overall survival was comparable between LPN and LCA at 3 years (93% vs. 93%) and 5 years (93% vs. 88%), respectively (p=0.74). Cancer-specific survival in the LPN and LCA group was 100% vs. 93% and 100% vs. 92% at 3 years, and recurrence-free survival was 100% vs 88% and 100% vs. 86% at 5 years, respectively (p<0.05, for all comparisons).

Conclusions: Both LPN and LCA are viable nephron-sparing options for patients with tumor in a solitary kidney. Although LCA is technically easier and has superior functional outcomes, oncologic outcomes are superior after LPN.

continued
### Table 1. Comparison of perioperative, functional and oncological outcomes in LPN versus LCA

<table>
<thead>
<tr>
<th></th>
<th>Lap Partial Nephrectomy (n=48)</th>
<th>Lap Renal Cryoablation (n=30)</th>
<th>p</th>
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<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td>60.8±13.7</td>
<td>60.9±11.4</td>
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<tr>
<td><strong>Male (%)</strong></td>
<td>25 (52.1)</td>
<td>22 (73.3)</td>
<td>0.06</td>
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<tr>
<td><strong>Body mass index</strong></td>
<td>30.1±6.2</td>
<td>31.5±5.8</td>
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<tr>
<td><strong>Charlson comorbidities index</strong></td>
<td>1.7±1.3</td>
<td>2.0±1.1</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>ASA score</strong></td>
<td>2.7±0.5</td>
<td>2.7±0.8</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Comorbidities (%)</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>6 (12.5)</td>
<td>3 (12)</td>
<td>0.95</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20 (41.7)</td>
<td>16 (64)</td>
<td>0.07</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6 (12.5)</td>
<td>3 (12)</td>
<td>0.95</td>
</tr>
<tr>
<td>CRI</td>
<td>13 (27.1)</td>
<td>13 (50)</td>
<td>0.07</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>3.2±1.0</td>
<td>2.6±1.0</td>
<td>0.23</td>
</tr>
<tr>
<td>Estimated blood loss (mL)</td>
<td>391.3±692.0</td>
<td>162.4±163.2</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>Transfusion (%)</td>
<td>8 (16.7)</td>
<td>1 (3.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Total operating time (min)</td>
<td>227.7±73.1</td>
<td>197.4±52.6</td>
<td>0.14</td>
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<tr>
<td>Hospital stay (days)</td>
<td>4.6±2.9</td>
<td>2.4±2.2</td>
<td><strong>0.0001</strong></td>
</tr>
<tr>
<td>Intra operative complication (%)</td>
<td>6 (12.5)</td>
<td>1 (3.5)</td>
<td>0.23</td>
</tr>
<tr>
<td>Urter injury (%)</td>
<td>3 (6.2)</td>
<td>0</td>
<td>0.28</td>
</tr>
<tr>
<td>Hemorrhage (%)</td>
<td>3 (6.2)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Open conversion (%)</td>
<td>3 (6.2)</td>
<td>0</td>
<td>0.28</td>
</tr>
<tr>
<td>Post operative complication (%)</td>
<td>11 (22.9)</td>
<td>2 (6.7)</td>
<td>0.07</td>
</tr>
<tr>
<td>Urine leak (%)</td>
<td>2 (4.2)</td>
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<td>0.5</td>
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<td>Pulmonary (%)</td>
<td>1 (2.1)</td>
<td>1 (3.3)</td>
<td>1</td>
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<tr>
<td>Hemorrhage (%)</td>
<td>4 (8.3)</td>
<td>0</td>
<td>0.16</td>
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<tr>
<td>Myocardial infarction (%)</td>
<td>1 (2.1)</td>
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<td>1</td>
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<tr>
<td>Infection (%)</td>
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<td>1 (3.3)</td>
<td>0.4</td>
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<td>Thrombo-embolic (%)</td>
<td>3 (6.3)</td>
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<td>0.28</td>
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<td>Nadir SCr increase (mg/dl)</td>
<td>0.4±0.5</td>
<td>0.2±0.3</td>
<td><strong>0.04</strong></td>
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<td>Percent creatinine increase after surgery (%)</td>
<td>35.1±42.0</td>
<td>14.4±21.0</td>
<td><strong>0.013</strong></td>
</tr>
<tr>
<td>eGFR decrease after surgery (mL/min/1.73m²)</td>
<td>14.5±16.4</td>
<td>7.3±12.2</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Percent eGFR decrease after surgery (%)</td>
<td>21.4±21.9</td>
<td>11.0±16.1</td>
<td><strong>0.018</strong></td>
</tr>
<tr>
<td>Local Recurrence (%)</td>
<td>0</td>
<td>4 (13.3)</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Metastasis (%)</td>
<td>1 (2.1)</td>
<td>4 (3.3)</td>
<td><strong>0.05</strong></td>
</tr>
<tr>
<td>Overall survival - 5 years (%)</td>
<td>93</td>
<td>88</td>
<td>0.74</td>
</tr>
<tr>
<td>Disease specific survival - 5 years (%)</td>
<td>100</td>
<td>88</td>
<td><strong>0.027</strong></td>
</tr>
<tr>
<td>Disease free survival - 5 years (%)</td>
<td>96</td>
<td>64</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>Local recurrence free survival -5 years (%)</td>
<td>100</td>
<td>86</td>
<td><strong>0.05</strong></td>
</tr>
</tbody>
</table>
Single Port Transumbilical Robotic Surgery

Raj K. Goel, Wesley M. White, Robert J. Stein, Sebastien Crouzet, Georges Pascal-Haber, Jihad H. Kaouk

Introduction and Objectives: The technical constraints of single port laparoscopic surgery have generated concerns regarding its feasibility and pragmatism. Robotics has greatly facilitated the surgeon’s ability to complete complex extirpative and reconstructive procedures laparoscopically. We present our institution’s experience employing the robotic surgical platform during single port laparoscopic surgery was performed. Patient demographics, peri-operative data, pain assessment and operative times were obtained. Single port robotic surgery was performed in patients suitable for standard laparoscopy. Exclusion criteria included patients with advanced malignancy, multiple abdominal or renal surgeries and those with a solitary kidney. Single port access was achieved via a commercially available multi-channel port. The daVinci-S® surgical platform using pediatric instruments were used.

Results: Nine single port robotic procedures were completed without complications or use of additional ports. Surgeries included radical prostatectomy (n = 1), radical nephrectomy (n = 1), ureteral reimplantation (n = 1), dismembered pyeloplasty (n = 2), partial nephrectomy (n = 2), sacrocolpopexy (n = 1), and nephroureterectomy (n = 1). Control of the renal artery and vein during radical nephrectomy was achieved using Hem-O-Lok clips. Suture ligation of the dorsal venous complex was completed intracorporeally. The urethral-vesical and uretero-pelvic anastamoses were completed without additional ports using a running suture technique. During partial nephrectomy under normal renal perfusion, renal tumor excision was performed using a Harmonic scalpel. Surgical margins for all cancer-related procedures were negative. No evidence of pelvic organ prolapse has been noted at 4 month follow up.

Conclusions: Application of the robotic platform during single port surgery may represent the next step in its evolution. The improved articulation offered by robotics may expand and disseminate the role and reproducibility of single port surgery.
Introduction and Objectives: Laparoendoscopic Single-site Surgery (LESS) has been used to perform a variety of urologic reconstructive and extirpative procedures through a single umbilical incision. We present complications and rates of conversion from LESS to conventional laparoscopy (CL) as well as the factors leading to those conversions at three high-volume centers pioneering urologic LESS procedures.

Methods: All patients undergoing laparoscopic nephrectomy, adrenalectomy and pyeloplasty were identified at each institution. From these patients, those undergoing planned LESS procedures and those requiring conversion to CL with the placement of additional ports were identified. Conversion was defined as the placement of additional 5 or 10/12 mm ports beyond the single incision site. A planned 2 mm needle port was not considered as conversion. In each case the operative reports were reviewed, the reason for conversion was determined, and number and types of additional ports were noted.

Results: A combined total of 1271 laparoscopic nephrectomies (n=978), pyeloplasties (n=204) and adrenalectomies (n=89) were performed at the participating institutions. Of these, a total of 145 were attempted with LESS techniques through an umbilical incision representing 11.4% of the overall experience. Of these, 10 (6.8%) required conversion to CL techniques to safely complete the procedure. Reasons for conversion included: facilitate dissection in 5 (50%), facilitate reconstruction in 3 (30%), and control of bleeding in 2 (20%). A range of 1-5 (mode=2) additional ports were added during conversions. No patient required conversion for repair of inadvertent organ/visceral injury or other intra-abdominal complication. Complications occurred in 10.3% of LESS cases. Three of the 10 (30%) patients requiring conversion developed post-operative complications (1 urine leak, 1 post-operative hemorrhage requiring transfusion, and 1 deep venous thrombosis requiring anticoagulation).

Conclusions: While careful patient selection and realistic surgeon expectations remain paramount for the safe performance of LESS procedures, it is clear that these can be completed with a low rate of conversion to CL. It should be emphasized that conversion to CL should in no way be seen as a failure of the surgeon or the single port technique. In fact, the ability to place only the required number and size of additional ports remains a strength of the technique.
E-NOTES Ureteral Reimplantation


Introduction and Objective: Distal ureteral obstruction can be secondary to multiple etiologies and has historically been treated by primary ureteral reimplantation through a large, often painful open incision. We demonstrate the first virtually scar-free E-NOTES (Embryonic Natural Orifice Transumbilical Endoscopic Surgery) ureteral reimplantation with psoas hitch.

Methods: The patient is a 43 year old woman who was found to have a complete left distal ureteral stricture 2 weeks following laparoscopic assisted vaginal hysterectomy. Left ureteral reimplantation was performed through a novel multi-channel single port (R-port, Advanced Surgical Concepts) with the addition of one 2mm needle access. The procedure begins with dissection of the left ureter and complete mobilization of the bladder. The ureter is divided just proximal to the point of obstruction and then spatulated widely. The bladder is hitched cranially with interrupted sutures to the psoas muscle and a small cystotomy is created. A ureteral stent is placed and interrupted sutures are used to create the ureterovesical anastomosis.

Results: Operative time was 210 minutes and estimated blood loss was 120cc. Hospital stay was 1.5 days and postoperative IVP demonstrated resolution of obstruction. Virtually no scar was noted at 10 weeks following the E-NOTES procedure.

Conclusions: E-NOTES techniques can provide scar-free results for major urologic reconstruction procedures.
Single Port – Single Surgeon Robotic Assisted Laparoscopic Urologic Surgery

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Introduction and Objectives: We present our initial operative experience in which single port robotic-assisted reconstructive and extirpative urologic surgery was performed by a single surgeon.

Methods: A pilot study was performed on male farm pigs to determine the feasibility and safety of single port, single-surgeon urologic surgery. Under general anesthesia, all pigs were placed in the flank position and a 2cm umbilical incision was made through which a single port was placed and pneumoperitoneum achieved. An operative laparoscope was introduced and securely held employing a novel small robot with foot and/or voice control. Using articulating instruments, each pig underwent bilateral reconstructive and extirpative renal surgery. Salient intraoperative and postmortem data were recorded. Results were analyzed statistically to determine if outcomes improved with surgeon experience.

Results: Five male farm pigs underwent bilateral partial nephrectomy and bilateral pyeloplasty prior to undergoing completion bilateral radical nephrectomy. No intraoperative complications were encountered and there was no need for additional port placement. Mean operative times for partial nephrectomy, pyeloplasty, and nephrectomy were 120 minutes (100-150 minutes), 110 minutes (range 95-130 minutes), and 20 minutes (15-30 minutes), respectively. Mean estimated blood loss for all procedures was 240mL (range 200-280mL). When analyzed statistically, there was a trend towards improved outcomes with increasing surgeon experience (p = 0.08).

Conclusions: Use of a novel minirobot attached to the operating table as a camera holder may facilitate single port surgery and enable one surgeon to perform an entire procedure with flexibility and ease of movement.
E-NOTES Management of Proximal Ureteral Pathology-Ileal Interposition


Introduction and Objectives: Proximal ureteral pathology can be one of the most complicated Urologic dilemmas and ileal ureteral replacement one of the most difficult reconstructive procedures performed. E-NOTES (Embryonic Natural Orifice Transumbilical Endoscopic Surgery) allows this procedure to be performed through an extremely small incision compared to its open or even laparoscopic counterpart.

Methods: The patient is a 72 year old man who has developed 2 ureteral strictures from chronic stone impaction. Other forms of ureteral reconstruction including reimplantation or ureteroureterostomy were not feasible due to stricture location and length. Ileal interposition was performed through a novel multi-channel, transumbilical, single port (R-port, Advanced Surgical Concepts) with 2 additional 2mm needle ports. Initially the ureter is identified and dissected distally to the area of obstruction. The bladder is then completely mobilized. The umbilical incision is enlarged slightly in order to deliver the bowel for extracorporeal ileal harvest. A stent is secured within an isolated ileal segment and bowel continuity is reestablished. The bowel contents are returned to the abdomen and E-NOTES technique is used to create a 2 layer ileovesical anastomosis with the ileal segment in an iso-peristaltic configuration. The proximal portion of the ileal segment is led through the sigmoid mesentery and anastomosed in 2 layers to the dilated ureter cranial to the site of obstruction.

Results: Operative time was 5 hours and hospital stay was 2.5 days. The patient did not require any postoperative narcotic analgesics. Our initial experience includes 2 patients who underwent E-NOTES ileal ureter with symptomatic and radiographic relief of obstruction in both cases.

Conclusions: E-NOTES ileal interposition allows for an especially complex procedure to be performed through a remarkably small incision.
Stereotactic Percutaneous Cryoablation for Renal Tumor: Initial Experience

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Introduction and Objectives: Percutaneous needle ablation is assuming an increasingly prominent role in the minimally invasive treatment of renal tumors. Precise needle placement is essential for successful ablation. CT-Nav® (Koelis, France) is a novel stereotactic surgical navigation system that has the potential to achieve precise percutaneous needle placement while reducing radiation exposure compared to conventional CT-guided procedures. We present our initial experience using the CT-Nav® system to perform percutaneous renal cryoablation.

Methods: After IRB-approval, a prospective observational pilot study was performed to evaluate the technical feasibility, safety, and accuracy of the CT-Nav® system during renal cryoablation. Patients with enhancing renal masses amenable to renal cryoablation underwent preoperative CT scan with a pre-placed tracking sensor. These images were sent to the navigation platform for 3-D volume rendering. Using a stereoscopic infrared camera, the tracking sensor was located threedimensionally and a tracking handle used to navigate and guide the needle percutaneously to the targeted tumor. The optimal trajectory was subsequently saved by the CT-Nav® system. Local anesthesia was administered and needle biopsy performed. Two cycles of cryoablation were sequentially completed. Demographic and perioperative data were obtained. Needle placement accuracy was measured in 3 axes.

Results: A total of 13 tumors in 10 patients (6 males, 4 females) successfully underwent cryoablation using the novel navigational system. Mean age was 65.7 years. Four patients presented with solitary renal units and 7 patients had a history of prior ipsilateral renal surgery. Mean tumor size was 2.2 cm (1.2-3.5 cm). Tumors were located at the upper (n = 3), mid (n = 5), and lower poles (n = 5). Preoperative biopsy demonstrated renal cell carcinoma in 6 cases. Mean operative time was 155 min. Conscious sedation was used in 8 cases and elective general anesthesia was employed in 2 cases. No intraoperative or postoperative complications were noted. Mean length of stay was 9.5hrs. A mean decrease in fluoroscopy duration of 18 secs (range 15 - 20 secs) was noted for each probe placed. Mean targeting registration error was 4.2mm with the largest range of error in the vertical (head-foot) axis.

Conclusions: Based on our experience, stereotactic percutaneous cryoablation of renal tumors offers the potential for safe and precise needle placement while reducing radiation exposure compared to traditional CT guidance.
Introduction and Objectives: Laparoendoscopic single site surgery (LESS) can be used to perform reconstructive Urologic procedures with an essentially scar-free technique. Comparison of results with standard laparoscopic methods is vital to ensure that functional and symptomatic outcomes are not compromised and to identify any differences in perioperative variables. We present our experience with LESS reconstructive procedures and compare LESS pyeloplasty patients with those using standard laparoscopic technique.

Methods: We reviewed our prospectively maintained, IRB approved, minimally invasive surgery database and identified 27 patients who underwent LESS reconstructive procedures. LESS pyeloplasty patients were compared to a matched cohort of those undergoing standard laparoscopic (lap) pyeloplasty. Matching criteria included age, gender, BMI, and ipsilateral renal function. Criteria for comparison included operative time, estimated blood loss, visual analog score at discharge, symptomatic relief, and radiographic success.

Results: LESS reconstructive procedures performed included pyeloplasty (n=17), robotic pyeloplasty (n=4), ureteroneocystotomy (n=3), robotic ureteroneocystotomy (n=1), and ileal interposition (n=3). All cases other than pyeloplasty demonstrated symptomatic and radiographic success. No significant differences were noted between LESS and lap pyeloplasty with respect to operative time (214min. vs 212min., p= 0.9), estimated blood loss (81.5ml vs 95ml, p= 0.56), visual analog score at discharge (2.2 vs. 2.3, p=0.95), and radiographic success (86% vs 88%, p= 0.56). All patients were asymptomatic after surgery in both cohorts.

Conclusions: LESS reconstructive surgery provides nearly scar-free results for reconstructive Urologic procedures. Preliminary evidence suggests that the LESS approach does not compromise perioperative variables and clinical success rates when compared to lap pyeloplasty.
Introduction and Objective: To report the technical feasibility of performing transvesical robotic radical prostatectomy.

Methods: Transvesical robotic radical prostatectomy was performed in 2 fresh male cadavers (prostate volume 46 and 30 cc) and in 1 live patient (61 years, PSA 4.6, Gleason 6 in 2 cores). The first procedure was performed using 4 laparoscopic transvesical trocars and the 2 following procedures using one single port device placed percutaneously into the bladder. Pneumovesicum was established in both cases and the Da Vinci-S robotic System (Intuitive Surgical, Sunnyvale, CA) was used to perform transvesical radical prostatectomy. All steps of the procedure including dissection of the seminal vesicles and vas deferens, ligation of prostatic pedicles, release of neurovascular bundles, apical dissection, urethral transection, and urethro-vesical anastomosis were performed transvesically and robotically. Real time trans-rectal ultrasound (TRUS) monitoring was performed in case #1.

Results: All procedures were technically successful transvesically without need for additional ports or conversion to standard laparoscopy. In the cadaver, operative time for the multi-port procedure was 3 hours and the single-port procedure was 4.2 hours. Operative time in the live patient was 8 hours, estimated blood loss 50 cc, hospital stay 2 days. Pathological report confirmed a Gleason 6 prostate cancer. Clashing of the Da Vinci arms was the primary technical difficulty with the single port procedure.

Conclusions: Transvesical radical robotic prostatectomy under pneumovesicum is technically feasible using multiple ports or using a single port approach. Further refinement of technique and instruments may lead to an increasing role of percutaneous transvisceral surgery in various surgical disciplines.
LESS (Laparo Endoscopic Single-Site) Robotic Surgery

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Introduction and Objectives: Single port laparoscopy has expanded over the last year although technical constraints still hinder its routine application. Herein, we present our video illustrating single port robotic surgery.

Methods: Through a multi-channel single port and using 5 mm robotic trocars, single port robotic surgery was performed for various urological pathologies. Patients are positioned in lithotomy and flank position for pelvic and renal procedures, respectively. The da Vinci-S robotic surgical platform was utilized for all procedures. The fourth arm was available but not employed.

Results: Five single port robotic procedures were successfully completed without conversion or complication. No additional ports were utilized. Single port robotic surgeries included radical prostatectomy, partial nephrectomy, ureteral reimplantation, dismembered pyeloplasty and radical nephrectomy. Oncologically, negative margins were obtained for radical prostatectomy and both radical and partial nephrectomy. Nuclear renography following dismembered pyeloplasty and ureteral reimplantation demonstrated excellent drainage of the obstructed system with no evidence of anastomotic leak.

Conclusions: Robotic LESS can provide a platform to further advance single port laparoscopy. Initial experience demonstrates safety, efficiency and acceptable oncological and functional outcomes. While early results are promising, long term evaluation of this approach is warranted.
Laparoendoscopic Single Site (LESS) Donor Nephrectomy: Alternative Use of the Gelport Access

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**Introduction and Objective:** Laparoscopic live donor nephrectomy is recognized as a safe, feasible and less morbid alternative to open allograft procurement. In an attempt to further reduce postoperative pain and shorten convalescence, single port donor nephrectomy has been reported. While outcomes with this approach have been favorable, the currently employed multichannel port limits triangulation of instrumentation and may result in difficulties during allograft extraction. Given these limitations, we report our experience with LESS donor nephrectomy using GelPort access.

**Methods:** We assessed perioperative outcomes of laparoscopic live donor nephrectomy with use of a standard GelPort. Patients underwent a preoperative computed tomography of the abdomen with 3-D reconstruction. Appropriate candidates were placed in the flank position and an approximate 5cm periumbilical incision made. A commercially available GelPort was deployed and the abdomen insufflated. Standard laparoscopic ports were placed through the GelPort and the donor nephrectomy performed. The allografts were then extracted through the existing incision. Demographic and peri-operative data were obtained.

**Results:** From October 2008 to November 2008, 2 patients underwent laparoscopic live donor nephrectomy as described. Mean age was 37.5 years. Mean BMI was 24. One patient demonstrated 2 renal arteries and 1 vein with the remaining patient having 1 artery and 1 vein. Mean operative time was 240 minutes. Mean blood loss was 50mL. Mean length of the incision was 6.65cm. Mean warm ischemia time was 6 minutes, 40 seconds. There were no intraoperative or immediate postoperative complications. Mean length of hospitalization was 3 days. Mean visual analog pain scale score at discharge was 0/10. Mean recipient creatinine at discharge was 1.2 mg/dL.

**Conclusions:** As is demonstrated in our video, use of a GelPort during LESS donor nephrectomy offers versatility and improved spacing of instruments as compared to standard multichannel single ports and allows for the preparation of the extraction incision prior to renal hilar control. In addition, the design of the GelPort is more accommodating for allograft extraction and may avoid possible compression of the kidney.
Pure NOTES Transvaginal Nephrectomy in the Porcine Model

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Introduction and Objectives: To determine the feasibility, reproducibility and technical aspect of pure NOTES transvaginal nephrectomy.

Methods: We performed in 5 female pigs with a mean weight of 45 Kg, 5 right side radical nephrectomies. The animal is placed in lateral flank position, pneumoperitoneum was obtained using a Veress® needle. A needle/knife is introduced in the posterior fornix of the vagina, followed by balloon dilation and introduction of the gastroscope (single channel in initial 3 cases and dual channel in the remaining 2 cases). Kidney is localized we started by dropping the colon. The ureter is individualized laterally and followed toward the hilum. Then, we introduced an XL articulated 60 cm endo-GIA to retract the ureter medially and start dissecting the posterior side of the kidney close to the psoas. The vessels are dissected until we identified the upper limit of the renal vein. The hilum is then clamped en bloc and endo-GIA is fired. Upper pole is freed followed by the lateral attachments. Once the dissection is finished, we replace the endo-GIA by a 15 cm endo-Catch to entrap the kidney and extract it.

Results: All procedures were performed successfully without any addition of laparoscopic port or open conversion. Mean operative time was 113.2 min and estimated total blood loss was 50cc. No intraoperative complication was observed.

Conclusions: Pure NOTES transvaginal nephrectomy is feasible and safe in the porcine model. It has the potential of a less morbid approach with scarless surgery. Further development of the instrumentation is necessary.
Postoperative Renal Function Decrease After Laparoscopic Partial Nephrectomy: Predicting Factors

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Introduction and Objective: Renal function after laparoscopic partial nephrectomy (LPN) is a major concern. Herein, we studied the predictive factors of postoperative renal function after LPN.

Methods: A total of 840 patients underwent a partial nephrectomy between September 1999 and October 2007. Demographic, operative indication, intraoperative, peri-operative, and renal functional follow-up data were collected prospectively. We used uni and multivariate analysis with logistic fit regression for each data to identify predicting factor of post operative renal function decrease. To evaluate the renal function variation we used the percentage eGFR variation.

Results: Three factors appear to be significant predictor of post-operative eGFR decrease: The operative indication (elective or imperative), the warm ischemia time (WIT) and the tumor size (> 2cm/µ2.4cm) (p<0.01). OR time, estimated blood loss, patient with a solitary kidney, and the sex also influence the post operative eGFR but did not reach significance. The following factor did not appear to affect the post-operative eGFR: BMI, ASA score, HTN, Diabetes, coronary artery disease. The decrease of eGFR is more pronounced after 30 min of WIT (table 1).

Conclusions: Pre-operative surgical indication (elective or imperative), the warm ischemia time and the tumor size are the most predictive factors of post-operative eGFR decrease after laparoscopic partial nephrectomy.
Retroperitoneal Single Port Renal Surgery: Initial Operative Experience and Comparative Outcomes

Wesley M. White, Raj K. Goel, Georges-Pascal Haber, Jihad H. Kaouk

**Introduction and Objectives:** We present initial operative outcomes and comparative data among patients undergoing retroperitoneal single port surgery (RSPS).

**Methods:** A prospective, observational study of all patients who underwent RSPS was performed. Salient demographic and operative data including age, BMI, operative indications, operative time, estimated blood loss (EBL), complications, and post-operative visual analog pain scale (VAPS) scores were recorded. Patients who underwent cryoablation were then retrospectively compared to a contemporary, matched cohort of patients undergoing traditional laparoscopic retroperitoneal cryosurgery. Statistical analyses were performed.

**Results:** Between September 25, 2007 and July 15, 2008, 8 patients underwent RSPS. Five patients underwent RSP cryoablation and 1 patient underwent RSP partial nephrectomy for radiographic evidence of an enhancing renal mass. One patient underwent RSP metastectomy for isolated recurrence of renal cell carcinoma. The remaining patient underwent RSP cyst decortication for unrelenting pain. Mean patient age was 63.5 years. Mean BMI was 28.9kg/m2. Mean operative time and EBL were 165 minutes (+/- 23 minutes) and 134mL (+/- 152mL), respectively. No intra-operative or postoperative complications were noted. Mean length of hospitalization was 1.4 days. Mean VAPS score at discharge was 0.4/10 (range 0 - 2). No significant difference was noted between the single port and standard retroperitoneal cryotherapy cohorts with respect to age, BMI, EBL, and length of hospitalization (p > .05). Patients who underwent RSP cryoablation reported lower VAPS scores (p = 0.023).

**Conclusions:** Retroperitoneal single port surgery is feasible and offers comparable surgical outcomes and superior cosmesis and pain control when compared to traditional retroperitoneoscopy.
Robotic-NOTES: Video Presentation in Reconstructive Urology

Georges-Pascal Haber, Sebastien Crouzet, Kazumi Kamoi, Raj K. Goel, Wesley M. White, Jihad H. Kaouk

Introduction and Objectives: This video presents our initial experience using the da Vinci® surgical system to perform R-NOTES (Robotic Natural Orifice Transluminal Surgery) reconstructive urological procedures.

Methods: In 10 female farm pigs we performed 10 pyeloplasties (right 5; Left 5), 10 partial nephrectomies (right 5; Left 5) and 10 radical nephrectomies (right 5; Left 5). The animal is placed in the lateral flank position and pneumoperitoneum is obtained using a Veress® needle. The scope and the 1st robotic arm are placed through a single 2 cm umbilical incision and the 2nd robotic arm is placed through the vagina.

Results: A total of 30 procedures were performed successfully without the addition of additional laparoscopic ports or open conversion. The mean incision size after closure was 2.6 cm (range 2.4 to 2.9 cm). Mean total operative time was 153.7min (range 140 to 187) and mean estimated total blood loss was 72.3 cc (range 55 to 100). Mean warm ischemia time in the partial nephrectomy group was 25.4 min (range 22 to 30). After completion of the procedure, autopsy was performed that demonstrated no visceral complications.

Conclusions: R-NOTES pyeloplasty, partial nephrectomy and radical nephrectomy are feasible and safe in the animal model. This approach may offer less morbidity and superior cosmesis. Further development of an R-NOTES vaginal port is ongoing.
Renal Cryoablation: A Comparative Analysis Between Laparoscopic and Percutaneous Approaches

Georges Pascal-Haber, Sebastien Crouzet, Kazumi Kamoi, Wesley M. White, Raj K. Goel, Inderbir S. Gill, Jihad H. Kaouk

Introduction and Objectives: The widespread use and refinement of computed tomography has led to a dramatic increase in the number of incidentally discovered and localized renal lesions. This trend has allowed urologists to explore alternative and less invasive forms of therapy. Among patients with significant co-morbidities or compromised renal function, renal cryoablation is viewed as an efficacious treatment option. However, the optimal approach for cryoablation is as yet unproven. We present our institution’s cumulative experience and comparative outcomes with laparoscopic (LRC) and percutaneous renal cryoablation (PRC).

Methods: A retrospective cohort study was performed to assess perioperative outcomes and treatment efficacy among patients with radiographically enhancing renal masses treated with LRC or PRC. Demographic, radiographic, and perioperative data were obtained for all patients. Patients were followed post-operatively for evidence of immediate and remote complications and treatment success. Renal function was assessed using absolute creatinine and estimated glomerular filtration rate (eGFR). Statistical analysis was performed.

Results: Between 1997 and 2008, 307 patients underwent LRC (n = 244) or PRC (n = 63) for the management of a radiographically enhancing renal mass. Patient demographics, tumor characteristics and baseline renal function were similar between the 2 groups (p > 0.05). Patients who underwent PRC were significantly more likely to have a solitary kidney (19 vs. 30, p = .0012) or a prior history of kidney surgery (35 vs. 54, p < .001) compared to LRC. Mean pre- and post-operative creatinine for all patients was 1.5 and 1.4mg/dL, respectively (p = 0.97). Mean pre- and post-operative eGFR was 59.2 and 57.3mL/min/1.73m2, respectively (p = 0.94). Mean number of probes used for LRC and PRC was 1.4 and 2.2, respectively (p < .0001). Length of hospitalization was significantly shorter in the PRC cohort (22 hours) as compared to the LRC cohort (59.1 hours) (p < .0001). PRC demonstrated a significantly higher incomplete treatment rate (7.6%) compared to LRC (1.6%) (p = 0.0055). Two-year overall, disease-specific, and recurrence-free survival was similar between the 2 groups.

Conclusions: Based on our experience, LRC and PRC offer encouraging short-term efficacy with excellent preservation of renal function. While PRC is associated with a higher incomplete treatment rate compared to LRC, PRC is associated with less morbidity.
E-NOTES Pyeloplasty with Pyelolitotomy and Renal Pelvis Reduction


Introduction and Objective: Ureteropelvic junction obstruction (UPJO) is a congenital abnormality marked by obstruction of the flow of urine from the renal pelvis to the proximal ureter. We demonstrate the first E-NOTES (Embryonic Natural Orifice Transumbilical Endoscopic Surgery) pyeloplasty, stone removal, and renal pelvis reduction for treatment of UPJO.

Methods: Dismembered pyeloplasty was performed through a novel multi-channel single port (R-port, Advanced Surgical Concepts) with the addition of one 2mm needle access. The procedure begins with ureteral and renal pelvic dissection. A small renal pelvotomy is created and a flexible nephroscope is introduced into the collecting system for stone identification and removal. The ureter is completely detached and the area of UPJO is excised. The ureter is reanastomosed to the renal pelvis at its most dependent point. A large portion of the redundant renal pelvis is then excised to improve the efficiency of urinary drainage. The renal pelvis is then suture closed primarily.

Results: Our initial experience with E-NOTES pyeloplasty includes 8 patients and 10 renal units (2 cases bilateral). Mean operative time is 197.2 minutes and mean estimated blood loss is 55cc with no transfusions yet required. At 4 month mean follow-up there have been no clinical or radiographic failures. Post-operative scarring is largely imperceptible.

Conclusions: Despite only preliminary experience with this new technique, E-NOTES pyeloplasty appears to hold great promise for scar-free results after major reconstructive procedures.
Standard vs. Single Port Laparoscopic Partial Nephrectomy: Comparative Outcomes

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Objectives: To evaluate perioperative outcomes among patients who underwent single port or conventional laparoscopic partial nephrectomy.

Methods: A prospective, observational study was performed to evaluate perioperative outcomes among patients who underwent single port laparoscopic partial nephrectomy (SPLPN). Salient demographic and operative data were obtained. These patients were next retrospectively compared to a contemporary, matched-cohort of patients who underwent conventional LPN (CLPN). End-points including age, BMI, operative time, estimated blood loss (EBL), complications, conversion, and post-operative Visual Analog Pain Scale (VAPS) scores were examined. Statistical analysis was performed.

Results: Fifteen SPLPN and 15 CLPN patients were evaluated. There was no significant difference between the SPLPN and CLPN cohorts with respect to mean age (66 vs. 59 years, p = 0.149), mean BMI (26.7 vs. 28.0, p = 0.422), mean operative time (196 vs. 245 minutes, p = 0.08), mean EBL (422 vs. 337mL, p = 0.67), and mean length of hospitalization (4.5 vs. 3.5 days, p = 0.494). Mean VAPS score at discharge was significantly less in the SPLPN cohort (0.67/10 vs. 3/10, p = 0.009). One patient in the SPLPN cohort required conversion to standard laparoscopy. Four patients in the SPLPN cohort required post-operative blood transfusions, one of which required angioembolization. Three patients in the CLPN cohort received blood transfusions.

Conclusions: Based on our experience, single port LPN demonstrates equivalent comparative outcomes to conventional LPN with significantly less pain and superior cosmesis in the single port cohort. Prospective, randomized studies are needed to confirm these findings.
Robotic Partial Nephrectomy: Cumulative Single Center Experience

W.M. White, G.P. Haber, R.K. Goel, Sebastien Crouzet, J.H. Kaouk

Objectives: We present perioperative outcomes in an observational cohort of patients who underwent Robotic Partial Nephrectomy (RPNx) at a single academic institution.

Methods: A prospective study was performed to evaluate operative outcomes following RPNx. Salient demographic and radiographic data were obtained. Operative data including estimated blood loss (EBL), operative time, and warm ischemia time (WIT), where applicable, were recorded. Pathology was reviewed and classified according to the AJCC staging system. Patients were followed post-operatively for evidence of immediate and delayed complications. Renal functional outcomes were obtained and estimated creatinine clearance calculated using the MDRD formula. Statistical analysis was performed.

Results: Between June 2006 and June 2009, a total of 72 patients underwent right (n = 35) or left (n = 37) RPNx for radiographic evidence of an enhancing renal mass. Mean age of the cohort was 64 years. Mean BMI was 27.9 kg/m². Mean operative time was 203 minutes. Mean EBL was 325mL. Ten patients underwent RPNx without hilar clamping. The remaining 62 patients underwent hilar clamping with a mean WIT of 23 minutes. Mean pathologic tumor size was 2.7cm (range 1 – 7.5cm). Pathology confirmed renal cell carcinoma in 63 patients, angiomyolipoma in 4 patients, and oncocyto in 5 patients. All margins were negative. Complications occurred in 6 patients. Three patients required blood transfusions, 1 patient developed a renal fluid collection, and 2 patients required post-operative angioembolization.

Conclusions: Robotic Partial Nephrectomy offers excellent perioperative outcomes with promising short-term oncologic control. Prospective, comparative study to conventional laparoscopic partial nephrectomy is needed.
Single Port Laparoscopic Surgery: Cumulative Outcomes with Over 100 Cases

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Objectives: To present perioperative outcomes in an observational cohort of patients who underwent LaparoEndoscopic Single Site (LESS) surgery at a single academic center.

Methods: A prospective study was performed to evaluate patient outcomes following LESS urologic surgery. Demographic data including age, BMI, operative time, estimated blood loss (EBL), operative indications, complications, and post-operative Visual Analog Pain Scale (VAPS) scores were accrued. Patients were followed post-operatively for evidence of adverse events.

Results: Between September 2007 and June 2009, 105 patients underwent LESS urologic surgery. Specifically, 78 patients underwent LESS renal surgery (cryoablation – 9, partial nephrectomy – 15, metastectomy – 1, renal biopsy – 1, simple nephrectomy – 7, radical nephrectomy – 8, cyst decortication – 2, nephroureterectomy – 7, donor nephrectomy – 20, and dismembered pyeloplasty – 8) and 27 patients underwent LESS pelvic surgery (varicocelectomy – 3, radical prostatectomy – 7, radical cystectomy – 3, sacral colpopexy – 13, and ureteral reimplant – 1). Mean patient age was 55 years. Mean BMI was 26.1 kg/m². Mean operative time was 198 minutes. Mean EBL was 132mL. No intraoperative complications occurred. Six patients required conversion to standard laparoscopy. One patient required open conversion. Mean length of hospitalization was 3 days. Mean VAPS score at discharge was 1.5/10. At a mean follow-up of 11 months, 10 Clavien Grade II (transfusion – 8, UTI – 1, DVT – 1) and 2 Clavien Grade IIIb (recto-urethral fistula – 1, angioembolization – 1) surgical complications occurred.

Conclusions: Based on our experience, LESS urologic surgery is feasible, offers improved cosmesis, and may offer decreased pain. Its superiority compared to standard laparoscopy is currently speculative.
Single Port Laparoscopic Surgery in the Obese Population: Feasibility and Comparative Outcomes

M. White, G.P. Haber, R.K. Goel, Sebastien Crouzet, J.H. Kaouk

Objectives: To evaluate outcomes among obese patients who underwent Laparo-Endoscopic Single Site (LESS) surgery at a single academic center.

Methods: A retrospective cohort study was performed to evaluate comparative outcomes between obese and non-obese patients undergoing LESS urologic surgery. Obesity was defined as a Body Mass Index (BMI) ≥ 30 kg/m². Demographic and perioperative data including age, BMI, operative time, estimated blood loss (EBL), operative indications, complications, conversion to standard laparoscopy, and post-operative Visual Analog Pain Scale (VAPS) scores were examined. Statistical analysis was performed.

Results: Between September 2007 and June 2009, 19 obese and 86 non-obese patients underwent LESS urologic surgery. Mean BMI of the obese and non-obese cohorts was 34kg/m² and 24.6kg/m², respectively (p < 0.01). There was no significant difference between the obese and non-obese cohorts with respect to age (60 years vs. 53.4 years, p = 0.16), operative time (209 minutes vs. 196 minutes, p = 0.42), EBL (252mL vs. 175mL, p = 0.33), length of hospitalization (3.3 days vs. 2.9 days, p = 0.52), or VAPS score (1.9/10 vs. 1.4/10, p = 0.20). Conversion to standard laparoscopy was required in 2 obese patients and 5 non-obese patients. There was no significant difference in perioperative adverse events between the 2 groups (p = 0.89).

Conclusions: Based on our experience, LESS surgery in obese patients is technically challenging but is not associated with a disproportionate risk of operative conversion or perioperative adverse events. Therefore, BMI should not be an explicit contraindication to LESS urologic surgery.
Single Port Laparoscopic Sacral Colpopexy: Initial Operative Experience and Comparative Outcomes

W.M. White, R.K. Goel, G.P. Haber, Sebastien Crouzet, M.A. Swartz, R.R. Rackley, J.H. Kaouk

Objectives: To determine the efficacy and safety of single port laparoscopic abdominal sacral colpopexy (ASC) for the treatment of female pelvic organ prolapse (POP).

Methods: A retrospective cohort study was performed to assess perioperative outcomes among women who underwent treatment of symptomatic pelvic organ prolapse with laparoscopic, robotic, or single port laparoscopic ASC. All patients underwent pre-operative history and physical examination including pelvic organ prolapse quantification (POP-Q) staging and urodynamics. ASC with or without anti-incontinence surgery was performed via the aforementioned approaches. Demographic and peri-operative data were obtained. Patients were followed postoperatively for a minimum of 12 months with POP-Q evaluation. Statistical analysis was performed.

Results: From October 2005 to July 2008, 30 females with symptomatic Stage II (6 patients), Stage III (23 patients), or Stage IV (1 patient) POP were treated with laparoscopic (10), robotic (10), or single port laparoscopic (10) ASC. Mean age of the entire cohort was 61.1 years. Mean BMI was 26.7kg/m². Seventeen patients demonstrated stress urinary incontinence and underwent concomitant sling placement. No intraoperative complications were encountered. There was no significant difference in the 3 cohorts with respect to operative time, blood loss, mean visual analog pain score at discharge, or duration of hospitalization. At 12 months following surgery, 27 patients underwent follow-up POP-Q with all patients demonstrating excellent apical support and prolapse reduction.

Conclusions: Single port laparoscopic ASC offers comparable efficacy, decreased pain, and superior cosmesis compared to alternative approaches. Long-term follow-up is needed to confirm durability of repair.
Factors Leading to Conversion from Single Port to Conventional Laparoscopy: A Multi-Institutional Study

Brian H. Irwin, Andre Berger, Ricardo Brandina, Raj K. Goel, Wesley M. White, Georges-Pascal Haber, Kamoi Kazumi, Sebastien Krouzet, Aron Monish, Robert J. Stein, Jihad H. Kaouk, Mihir M. Desai

Introduction and Objectives: Laparoendoscopic Single-site Surgery (LESS) has been used to perform a variety of urologic reconstructive and extirpative procedures through a single umbilical incision. We present complications and rates of conversion from LESS to conventional laparoscopy (CL) as well as the factors leading to those conversions at three high-volume centers pioneering urologic LESS procedures.

Methods: All patients undergoing laparoscopic nephrectomy, adrenalectomy and pyeloplasty were identified at each institution. From these patients, those undergoing planned LESS procedures and those requiring conversion to CL with the placement of additional ports were identified. Conversion was defined as the placement of additional 5 or 10/12 mm ports beyond the single incision site. A planned 2 mm needle port was not considered as conversion. In each case the operative reports were reviewed, the reason for conversion was determined, and number and types of additional ports were noted.

Results: A combined total of 1271 laparoscopic nephrectomies (n=978), pyeloplasties (n=204) and adrenalectomies (n=89) were performed at the participating institutions. Of these, a total of 145 were attempted with LESS techniques through an umbilical incision representing 11.4% of the overall experience. Of these, 10 (6.8%) required conversion to CL techniques to safely complete the procedure. Reasons for conversion included: facilitate dissection in 5 (50%), facilitate reconstruction in 3 (30%), and control of bleeding in 2 (20%). A range of 1-5 (mode=2) additional ports were added during conversions. No patient required conversion for repair of inadvertent organ/visceral injury or other intra-abdominal complication. Complications occurred in 10.3% of LESS cases. Three of the 10 (30%) patients requiring conversion developed post-operative complications (1 urine leak, 1 post-operative hemorrhage requiring transfusion, and 1 deep venous thrombosis requiring anticoagulation).

Conclusions: While careful patient selection and realistic surgeon expectations remain paramount for the safe performance of LESS procedures, it is clear that these can be completed with a low rate of conversion to CL. It should be emphasized that conversion to CL should in no way be seen as a failure of the surgeon or the single port technique. In fact, the ability to place only the required number and size of additional ports remains a strength of the technique.
Prediction of Complications in Laparoscopic Partial Nephrectomy

Kazumi Kamoi, Georges-Pascal Haber, Sebastien Crouzet, Inderbir S. Gill

Introduction and Objective: We evaluate our experience with laparoscopic partial nephrectomy (LPN) to determine risk factors for postoperative complications.

Methods: A prospectively maintained database of 1000 LPN procedures since September 1999 was retrospectively analyzed with emphasis on postoperative complications. Various baseline patient and tumor characteristics were assessed using multivariate analysis in order to identify risk factors associated with postoperative urological and nonurological complications. Complication rates were also compared among the 1999-2003, 2004-2006 and 2007-2008 eras.

Results: In 1000 LPN procedures, a total of 200 including 68 urologic and 132 non-urologic postoperative complications occurred in 138 patients (13.8%). Of 200 complication, 20% were grade I, 45% were grade II, 30% were grade III, 4.5% were grade IV and 0.5% was grade V. Risk factor analysis with baseline patient characteristics demonstrated that body mass index more than 30 was associated with postoperative urine leak with 3.0 of odds ratio (p=0.011), Charlson comorbidity index greater than or equal to 1 was associated with nonurological complications with 2.0 of odds ratio (p=0.019). Tumor size was significantly associated with postoperative hemorrhage (requiring interventional treatment) with 5.8 (p=0.0002) of odds ratio. The tumor abutting renal hilum was associated with intraoperative complications with 3.4 of odds ratio (p=0.037). Surgery eras was also significantly associated with urine leak, hemorrhage and non-urological complications (p<0.01 for all). These urological and non-urological complications were significantly lower in the recent era (10.2%, 4.9% and 4.4%, p=0.0044 and 22.8%, 11.4% and 8.8%, p<0.0001, respectively) despite increased technical difficulty to treat more complicated renal tumors.

Conclusions: Tumor characteristics including size and location as well as baseline comorbidities are associated with intra and postoperative complications. Infrequent urological and non-urological complications are currently achieved by a laparoscopic expertise. Uni and multivariate logistic regression analysis to predict complications are currently achieved by a laparoscopic expertise.
Single-Port Transumbilical Live Donor Nephrectomy

Sebastien Crouzet, David A. Goldfarb, Georges-Pascal Haber, Inderbir S. Gill

**Introduction and Objective:** We present our initial experience of single port transumbilical live donor nephrectomy which provide a virtually scar free procedure.

**Methods:** We used an intra-umbilical single-access multichannel laparoscopic port, the R-port (Advanced Surgical Concepts, Dublin, Ireland) which provide 3 inlet channels (one 12 mm and two 5 mm) that allows simultaneous passage of a laparoscope and 2 laparoscopic instruments. Inserted through a 2 to 3 cm incision, the port is secured in position by 2 plastic rings, 1 inserted within the peritoneum and the other remaining outside the skin, both connected by a sliding plastic sleeve. Pulling up on the sleeve removes its slack, thereby tightly approximating the 2 rings against each other and creating an airtight seal for pneumoperitoneum. A 2 mm Veress needle port, inserted via skin needle puncture to establish pneumoperitoneum, was used to selectively insert a needlescopic grasper for tissue retraction. The surgical technique of single-port Live Donor Nephrectomy duplicates standard Laparoscopic procedure. Donor kidney was pre-entrapped and extracted transumbilically.

**Results:** We successfully performed 17 single port live donor nephrectomies without need for any extra umbilical skin incisions or conversion to standard laparoscopy. A matched pair comparison of 9 regular laparoscopic and 9 single port live donor has been done. Operative time and estimated blood loss did not differ between the 2 groups but Warm ischemia time was longer in the single-port group (3 vs 6 minutes) as this report includes the learning curve for the single-port procedure. Median length of the intra-umbilical incision was 4 cm in the single-port group Hospital stay was 3.3 days in each group. The single port group trended towards requiring less morphine equivalents and had lower discharge visual analog pain scores, however these differences did not achieve statistical significance. Patients undergoing single-port Laparoscopic Donor Nephrectomy required oral pain medication for a shorter duration, returned to work on average 1 month sooner, and reported 100% postoperative physical recuperation on average almost 2 months sooner.

**Conclusions:** This initial experience with Single-Port Transumbilical Live donor nephrectomy is encouraging. Preliminary data suggest that single-port Laparoscopic Donor Nephrectomy shortens convalescence, as measured by pain medication requirement after discharge, time off work, and time to resolution of physical symptoms.
Risk Factors to Predict Positive Surgical Margins during TRUS-Guided Laparoscopic Radical Prostatectomy

Kazumi Kamoi, Georges-Pascal Haber, Inderbir S. Gill

Introduction and Objective: Real-time transrectal ultrasound (TRUS) guidance has significantly decreased our incidence of positive surgical margins (PSM) during LRP, yet considerable number of patients still have PSM. Herein, we sought to identify risk factors to predict PSM in patients undergoing TRUS-guided LRP.

Methods: TRUS measurements were documented during LRP in 215 consecutive patients with prostate cancer. TRUS findings and various clinical parameters were compared with pathological outcomes.

Results: Twenty nine PSM (13%) occurred in 215 LRP specimens. Commonest locations of positive surgical margins were apical and postero-lateral aspects of the prostate (45% and 38%, respectively). Intra-operative TRUS demonstrated hypoechoic lesion (HEL) in 120 (56%) of the patients in those 60 (28%) were suspicious for ECE. Multivariate logistic regression analysis demonstrated that the appearance of HEL was the only significant variable to predict PSM. In patients with HEL, the chance of PSM was 23%, while only 1% without HEL (p <0.0001). In 61 patients with suspicion of extracapsular extension by TRUS, 14 (23%) unilateral and 16 (27%) bilateral dissection of neurovascular bundles were performed to avoid PSM and successfully achieved negative surgical margin in 43 (70%) of these high risk patients.

Conclusions: Negative ultrasound findings at LRP enable us to ensure the safe postero-lateral and apical dissection of the prostate. Since most of PSM arose in patients with abnormal findings on TRUS, site-specific wider excision at the high risk area of ECE should be considered to secure negative margins.
Diaphragmatic Reconstruction of the Diaphragm with GORE-TEX™ Graft

Ricardo Brandina, Monish Aron, Andre Berger, Roberto Colombo, Burak Turna, Robert J. Stein, David Canes, Kazumi Kamoi, Georges-Pascal Haber, Sebastien Crouzet, Brian H. Irwin, Marcelo Miranda, Denilson C. Santos, Gauarang Shah, Mihir M. Desai, Inderbir S. Gill

Introduction and Objectives: In a 10-year (1997 to 2006) review of 1,850 upper abdominal renal and/or adrenal laparoscopic procedures at our institution 13 patients (0.7%) sustained diaphragmatic entry. We present our experience with and the technique of laparoscopic mesh reconstruction or suture repair of intentional resection or intraoperative injury of the diaphragm.

Methods: In this video, we present a 66 year-old male with history of left open radical nephrectomy for RCC in 2001. During followup he presented with a metastatic 1.6-cm left diaphragm nodule and a 3-cm right adrenal nodule. He underwent a right adrenalectomy and excision of the diaphragmatic nodule in the same procedure.

Results: The excision of the diaphragmatic nodule was completed in 3.5 hours. Total operative time was 5 hours. Estimated blood loss was 150 ml. Post-operative course was uneventful. No chest tube was required. Hospital stay was 3 days. Final pathology revealed metastatic RCC for both adrenal and diaphragm nodules. After 1 year follow-up, there was no evidence of recurrence. In our experience, laparoscopic repair techniques involved primary suture repair in 11 cases and primary reconstruction with a synthetic graft in 2. A rubber catheter and water seal system were used to primarily evacuate the pneumothorax. Inadvertent diaphragmatic injury in 7 cases occurred during transperitoneal (6) and retroperitoneal (1) laparoscopy, including partial nephrectomy in 4, radical nephrectomy in 2 and adrenalectomy in 1. A diaphragmatic breach occurred due to hook electrocautery in 5 cases, trocar insertion in 1 and liver retraction in 1. Deliberate diaphragmatic excision and mesh reconstruction in 2 cases were performed after en bloc excision of the diaphragm during radical nephrectomy in 1 and during excision of a metastatic diaphragmatic nodule in 1. Four transthoracic transdiaphragmatic adrenalectomies were completed successfully without any intraoperative complications. All cases were completed laparoscopically without open conversion. A chest tube was placed prophylactically in the initial 2 patients undergoing transthoracic transdiaphragmatic adrenalectomy.

Conclusions: Laparoscopic and transthoracic repair/reconstruction of the diaphragm is safe and effective. It requires advanced laparoscopic skills.
Initial Use of Body-GPS for 4-D Augmented Reality Surgical Navigation System

Osamu Ukimura, Tsuneharu Miki, Arul Mahadevan, Masahiko Nakamoto, Yoshinobu Sato, Makoto Hashizume, Geroges-Pascal Haber, Brian Herts, Inderbir S. Gill

Introduction and Objective: Recently, we first introduced augmented reality (AR) in urology as novel 3D image navigation system beyond the surgical view. AR can superimpose 3D model of the surgical target onto the surgeon's endoscopic surgical view. In order to achieve the 4D (3D plus real-time) navigation system, we integrated the 4D localization system in the body, named by body-GPS (Global Positioning System), to achieve continuous organ tracking during surgical manipulation in minimally invasive urology.

Methods: First, the 3 Beacon® electromagnetic transponders (1.8mm x 8.6mm) (Calypso Medical, Seattle, WA) were implanted on the surface of a calf kidney within 0-5 mm margin of the experimentally created renal mimic tumor; then, pre-operative CT was acquired to develop 3D surgical model with our concept of 4 color-coded zonal navigation (tumor zone shown by red, 0-5 mm zone from the margin of the tumor by yellow, 5-10 mm zone by green, over 10 mm zone by blue). In this system, ideal surgical dissection was designed to keep advancing within the green zone, resulting in achieving the 5-10 mm safe margin with maximizing preservation of the normal renal tissues. The real-time electromagnetic localization system was integrated with our developed AR navigation system in order to achieve the continuous tracking of the organ motion and dynamic superimposing of the 3D surgical model onto the surgical endoscopic view.

Results: The implanted electromagnetic transponders could real-timely provide the dynamic co-ordinates of the movable surgical target in the space, allowing real-time registration of the developed 3D surgical model onto the real surgical field. Provided real-time digital information was computerized to achieve real-time superimposition of 3D surgical model even during advancing surgical dissection. The surgical margins was successfully achieved within 5-10 mm (n=10). In this experimental study, the spacial error in the given digital co-ordinates was maintained within 1.0 mm, even when the metallic surgical instruments were close to the body-GPS in the magnetic field.

Conclusions: By integration of Body-GPS with our developed AR navigation system, accurate continuous superimposing 3D surgical model of the target onto the real surgical view was technically feasible during advancing surgical procedure. This study suggested that 4D AR surgical navigation is a reality with the body-GPS system.
Internal Validation for Computer-Aided Diagnosis to Predict Histology of Solid Renal Mass Using CT Images

Kazumi Kamoi, Brian Herts, Georges-Pascal Haber, Inderbir S. Gill

**Introduction and Objective:** Currently, thin slice renal CT scanning is the single most important radiographic test for delineating the nature of renal mass. We examined if the histology of solid renal cortical tumors can be predicted using computer-aided analysis of the morphologic and enhancement patterns on helical triphasic CT scan images.

**Methods:** Between May 2003 and December 2006, 340 consecutive patients (age range, 17-84 years; 214 men, 126 women) with renal masses underwent partial nephrectomy and preoperative renal CT. Inclusion criteria were an enhancing solid renal mass, less than 7 cm, and 1mm slice thickness CT scans available for review (n = 300). We used Oncocare software (Siemens Medical Solutions, Malvern, PA) for making tumor volumetric measurements, and assessing the various tumor characteristics on non-contrast (NC), vascular phase (VP), and parenchymal phase (PP) of the CT scans. Tumor volume, largest transverse diameter (RECIST diameter), largest orthogonal diameter, and a maximum ratio of intraparenchymal extension to total diameter were calculated on PP. Means and standard deviations (SDs) of attenuation in the entire tumor, abdominal aorta and normal renal parenchyma were calculated on all phases. Final pathology of the 300 renal tumors (mean size, 3.0 cm; range, 0.9-6.7 cm) included, 157 (52%) clear cell renal cell carcinoma (RCC), 56 (19%) papillary RCC, 27 (9%) chromophobe RCC, 28 (9%) angiomyolipoma, and 32 (11%) oncocytoma. Using randomly selected records of 200 patients (training set) we constructed 3 different models, based on discrimination analysis, artificial neural network, and classification-regression tree (CART) analysis, to predict 5 histological subtypes of renal tumor and applied each model to the remaining 100 patients (validation set).

**Results:** CART analysis appeared to be performing best in the validation set to predict 5 subtypes of renal tumor on final pathology. Hierarchical divisions by gender, BMI, tumor volume, RECIST/orthogonal diameter ratio, attenuation of tumor, aorta and normal parenchyma correctly identified renal malignancy with 90% sensitivity and 73% specificity in overall patients. Pathological subtype analysis showed that hierarchy of divisions by these same parameters correctly identified 72% of 5 subtypes of renal tumor with moderate agreement (kappa = 0.57).

**Conclusions:** Computer-aided models based on certain demographics and advanced CT image analyses may allow preoperative prediction of renal tumor histology.
Risk Analysis of Chronic Kidney Disease After Laparoscopic Partial, Radical and Donor Nephrectomy

Kazumi Kamoi, Georges-Pascal Haber, Sebastien Crouzet, Philippe Koenig, Inderbir S. Gill

Introduction and Objective: We evaluate baseline demographic and renal functional data as well as followup renal function data in kidney cancer patients and donors in order to evaluate risk factors for and prevalence of chronic kidney disease (CKD) after kidney ablative surgery.

Methods: Prospectively-collected data of 1325 patients with healthy contralateral kidney undergoing partial (n=512), radical (n=380) and donor (n=433) nephrectomy were evaluated retrospectively. Nonmatched analysis and matched-pair analysis (n=100 in each group) correcting for age, sex, and ethnicity were performed to evaluate demographic data as regards general medical condition and comorbidities as well as baseline and postoperative renal function.

Results: Non-matched analysis revealed kidney patients were older and less healthy, with higher incidence of hypertension, diabetes mellitus, and coronary artery, pulmonary, gastrointestinal, hematological, and endocrine diseases (p<0.0001 for all). Matched pair analysis also confirmed these disparities as significant. Cancer patients had poorer renal function in the non-matched and matched-pair analyses (serum creatinine higher by 29 % and 19%, Modification of Diet in Renal Disease (MDRD) estimated GFR lower by 23% and 16%, respectively (p<0.0001 for all)). Follow up of renal function demonstrated that kidney cancer patients who underwent radical nephrectomy had significantly lower MDRDeGFR than other treatment groups throughout the time after surgery. Contrarily, kidney cancer patients who underwent partial nephrectomy had comparable renal function with kidney donor patients from 12 months after surgery (p>0.05 for all). For 1165 (88%) patients with preoperative eGFR ≥ 60 mL/min/1.73m2 in the entire cohort, multivariate analysis identified age more than 60 years, preoperative eGFR, and type of surgery as independent predictors of postoperative eGFR <60 mL/min/1.73m2.

Conclusions: For patients with healthy contralateral kidney undergoing laparoscopic nephron ablative surgery, higher age, poorer baseline renal function and undergoing nephrectomy were the risk factors for developing CKD. These data underscore the importance of nephron-sparing surgery for appropriate patients with kidney cancer.
Experience with Complex Percutaneous Resections for Upper Tract Urothelial Carcinoma

Brian H. Irwin, Andre Berger, Ricardo Brandina, David Canes, Armine K. Smith, Sebastien Crouzet, Georges-Pascal Haber, Kazumi Kamoi, Robert J. Stein, Mihir M. Desai

Introduction and Objective: Percutaneous endoscopic resection is a viable treatment option for upper tract urothelial carcinomas (UC) in carefully selected patients. We present our experience with patients who have undergone percutaneous endoscopic therapy for complex tumors.

Methods: Patients undergoing endoscopic treatment for UC were identified within a prospectively maintained patient database at a single institution. Charts were reviewed to identify complex patients who met at least one of the following criteria: (a) tumor size >2.5cm, (b) preoperative creatinine level >3.0, or (c) anatomical variant such as autotransplanted kidneys, prior partial nephrectomy of effected kidney or prior cystectomy/urinary diversion. Demographic, operative, and oncologic data were captured. Recurrence free, disease specific and overall survivals were calculated for both the complex and the non-complex cases.

Results: A total of 48 patients were identified who underwent endoscopic treatment for upper tract UC since 1985. Of these, 17 patients met the criteria for complex resections (tumors >2.5cm (N=9), pre-op creatinine>3.0 (N=3), prior partial nephrectomy (N=2), prior cystectomy (N=2), prior distal ureterectomy (N=1), auto-transplanted kidney (N=1)) with a median follow-up of 22 months. No difference was found between the two groups with regard to mean age (70.3±10.3 years in noncomplex cases versus 69.5±10.9 years in complex cases), complication rate (4% versus 6%) or change in creatinine (1.30 to 1.25 versus 1.40 to 1.38). The incidences of high grade tumors (40% in non-complex cases versus 60% in complex cases), invasive tumors (18% versus 18%), prior contralateral nephroureterectomy (46% versus 56%) and history of prior bladder cancers (52% versus 42%) were similar between the two groups. Patients in the non-complex group were less likely to have solitary kidneys (32% versus 92%) and larger tumors (1.48 ± 0.65cm versus 3.13 ± 0.79cm). No difference was seen cancer specific survival (P=0.97). Improved trends in overall survival (P=0.14) and recurrence free survival (P=0.08) were seen in the non-complex groups when compared to the complex group.

Conclusions: These findings suggest that patients with large tumors, poor renal function and significant anatomical variations may be well served by endoscopic treatment for upper tract UC. These resections may be both safe and feasible even in patients who might be thought to be at high risk for technical and physiologic complications.
Long Term Oncological Outcomes for Upper Tract Urothelial Carcinoma: Endoscopic Treatment vs. Nephroureterectomy

Andre Berger, Ricardo Brandina, Brian H. Irwin, Kazumi Kamoi, Sebastien Crouzet, Georges-Pascal Haber, David Canes, Robert J. Stein, Monish Aron, Inderbir S. Gill, Mihir M. Desai

Introduction and Objective: To compare longterm oncological outcomes following endoscopic treatment and nephroureterectomy (NU) either open or laparoscopic for upper tract transitional cell carcinoma (TCC).

Methods: Between April 1992 and January 2008, 45 patients (76% with solitary kidneys) underwent endoscopic treatment (percutaneous or ureteroscopic) with curative intent and 402 underwent NU (216 laparoscopic and 186 open) for upper tract TCC at our institution. Data were obtained from a prospectively maintained database, patient charts, telephone follow-up and a review of the Social Security Death Index.

Results: There were no significant differences between the endoscopic and NU groups as regards mean patient age (70vs. 70 yrs), ASA class and comorbidities. Mean follow-up was 44 and 43 months, respectively. Most patients presented with high grade disease (56% vs. 74% p= 0.01). Five-year overall, cancer specific survival and recurrence free survival in the endoscopic group and NU group were, respectively, 56%, 78% and 55% vs. 56%, 78% and 59% (p > 0.05 for all). Tumor grade was the only independent prognostic factor for both cancer-specific (p=0.02) and recurrence-free survival on a multivariate analysis (p = 0.03). Even after analyzing survival by grade, no statically significant difference was found between the groups.

Conclusions: Long-term oncological outcomes after endoscopic treatment for upper tract TCC comparable to extirpative procedure either in low grade or high grade disease. It can be recommended as an alternative to nephroureterectomy in selected patients.
Laparoscopic Partial Nephrectomy – 1000 Patients

Kazumi Kamoi, Georges-Pascal Haber, Andre Berger, Monish Aron, Inderbir S. Gill

Introduction and Objectives: We hypothesized that the indications, perioperative parameters and complication rates of laparoscopic partial nephrectomy (LPN) may have changed significantly during a 9-year period. 1000 LPNs were compared during 2 to 4-year periods.

Methods: Contemporary series of 320 LPNs performed from Jan 2007 to Sep 2008 (group III) were compared with 294 LPNs from Sep 1999 to Dec 2003 (group I) and 386 LPNs performed from Jan 2004 to Dec 2006 (group II) with regard to indications, perioperative parameters and complication rates.

Results: There were no significant differences among groups I, II and III with regard to age (61, 58 and 60 years), gender (60%, 62% and 61% male) and tumor size (2.9, 2.9 and 3.0 cm). Tumors removed in the recent era were more often centrally located (34%, 47%, and 58%, p<0.0001), and more often abutting renal hilum (0.3%, 3% and 15%, p<0.0001). Despite increased technical difficulty warm ischemia time in the more recent era was shorter (31.6, 31.0 and 15.3 min, p<0.0001), and the urological and overall complication rates were significantly lower (10.2%, 4.9% and 4.4%, p=0.0044 and 22.8%, 11.4% and 8.8%, p<0.0001, respectively). Positive surgical margins were documented 3 (1.4%), 3 (1.1%) and 2 (0.8%) cases in each era (p=0.92). Percent decrease of MDRDeGFR was significantly lower in the recent era (17.5%, 18% and 10.8%, p<0.0001).

Conclusions: At a referral center increasing number of complicated renal tumors has been treated by LPN. With experience these more difficult tumors are being successfully treated, preserving more renal function with shorter warm ischemia time, while maintaining low complication rates and excellent short-term oncological outcome.
Development and Evaluation of a Transrectal Ultrasound Robot for Prostate Biopsy and Focal Therapy

Georges-Pascal Haber, Kazumi Kamoi, Sebastien Crouzet, Inderbir S. Gill

Introduction and Objectives: Prostate biopsies and focal treatment such as cryotherapy are generally performed under transrectal ultrasound (TRUS). However, manual needle insertion is not reproducible. Robotic platform may allow targeting and reproducibility. Herein we present a novel robotic platform for prostate biopsy and focal therapy of prostate cancer.

Methods: Initial testing was performed on a phantom model. The test was conducted to evaluate targeting accuracy of a tumor mimic. After adjusting the fiducial point (A0) as an intra-prostatic target, the probe was randomly and remotely commanded to move to another point (X), and then the robot was asked to “go back” to the fiducial point (A1). The distance between points A0 and A1 was measured three-dimensionally (∂x, ∂y, ∂z) and registration error was calculated as √(∂x² + ∂y² + ∂z²). We next used a fresh cadaver to test (1) safety, (2) visualization, (3) 3-D ultrasound acquisition, and (4) targeting accuracy.

Results: In a total of 140 trials on the prostate phantom model, the fiducial point registration errors on the prostate phantom ranged from 0.1mm to 0.9mm (mean 0.5mm). Three consecutive biopsy procedures successfully sampled tumor mimic. In the cadaver, the robot successfully moved within its full range of motion in all degrees of freedom. Automated 3-D image acquisition was successful. The fiducial point registration error ranged from 0.2mm to 0.9mm (mean 0.6mm). There were no unexpected robotic movements or any rectal injury.

Conclusions: This new robotic platform is safe and preliminary results are encouraging. Its accuracy and reproducibility offers the potential for automated targeted biopsy and focal therapy.
Predicting Oncological Outcomes in Patients Undergoing Laparoscopic Nephroureterectomy

Michael C. Lee, Georges-Pascal Haber, K. Kamoi, D. Snow, Jihad Kaouk, Inderbir S. Gill

**Background:** In the last decade, laparoscopic nephroureterectomy (LNU) has emerged as an alternative treatment for urothelial carcinoma of the upper urinary tract (UC-UUT). We analyzed the factors to predict overall, disease-specific and recurrence-free survival of patients treated by LNU.

**Methods:** 217 consecutive patients who were treated with LNU for UC-UUT between 9/1997 and 2/2008 at the Cleveland Clinic (Cleveland, OH, USA) were identified. Data was collected prospectively and retrospectively when missing. Survival was determined from clinical follow up and the Social Security Death Index. The factors affecting overall, disease-specific and disease-free survival were analyzed using Cox proportional hazard model.

**Results:** The median age at the time of surgery was 75 years (IQR 65–80). Median follow up was 35 months (IQR 18–64). Kaplan-Meier estimate revealed that 5-years overall, disease-specific and recurrence-free survival was 54%, 76% and 60%, respectively. In multivariate analysis T stage (muscle invasive) and positive surgical margin were independent predictors for disease-specific survival (P<0.01 for all). Five-year disease-specific survival rate was 92% in the non-invasive diseases (127 patients) and 52% in the muscle invasive diseases (90 patients). Positive surgical margin was documented in 20 patients whose median survival was 17 months. In multivariate analysis grade 3 tumor in the pathological specimen was an independent predictor for recurrence-free survival (p<0.05). Five-year disease-free survival rates were 79% in the patients without grade 3 tumor (71 patients) and 49% in the patients with grade 3 tumor (146 patients).

**Conclusion:** For patients undergoing LNU, T stage 2 or higher was an independent predictor for disease-specific survival and tumor grade 3 was an independent predictor for recurrence-free survival. Patients with positive surgical margin had overall poor prognosis.

continued
Table 1 Univariate and multivariate analysis for disease-specific survival

<table>
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<th>Univariate p value</th>
<th>Multivariate p value</th>
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<td>Tumor Grade (&gt;2)</td>
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<td>0.91</td>
<td>1.1</td>
<td>0.4 – 2.4</td>
</tr>
<tr>
<td>Tumor Stage (&gt;1)</td>
<td>&lt;0.0001*</td>
<td>&lt;0.0001</td>
<td>5.9</td>
<td>2.7 – 14.4</td>
</tr>
<tr>
<td>Positive Lymph Nodes</td>
<td>0.0032*</td>
<td>0.66</td>
<td>1.2</td>
<td>0.5 – 2.8</td>
</tr>
<tr>
<td>Positive Surgical Margins</td>
<td>&lt;0.0001*</td>
<td>0.0011</td>
<td>3.6</td>
<td>1.7 – 7.0</td>
</tr>
<tr>
<td>Lymphovascular Invasion</td>
<td>&lt;0.0001*</td>
<td>0.19</td>
<td>1.6</td>
<td>0.8 – 3.0</td>
</tr>
</tbody>
</table>

*: Variables with p value < 0.10 by univariate analysis are selected for multivariate variables

Table 2 Univariate and multivariate analysis for recurrence-free survival

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate p value</th>
<th>Multivariate p value</th>
<th>RR</th>
<th>95% CIs</th>
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</thead>
<tbody>
<tr>
<td>Age (&gt;70 years)</td>
<td>0.15</td>
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<td></td>
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<tr>
<td>Charlson Comorbidity Index (&gt;0)</td>
<td>0.63</td>
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<tr>
<td>Positive History of Bladder Tumor</td>
<td>0.81</td>
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<tr>
<td>Positive Urine Cytology</td>
<td>0.073*</td>
<td>0.30</td>
<td>1.3</td>
<td>0.8 – 2.1</td>
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<tr>
<td>Bladder Cuff Removal</td>
<td>0.88</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Location of Tumor (Kidney/Ureter/Both)</td>
<td>0.19</td>
<td></td>
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<tr>
<td>Carcinoma in Situ</td>
<td>0.13</td>
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<tr>
<td>Tumor Grade (&gt;2)</td>
<td>0.0003*</td>
<td>0.035</td>
<td>2.0</td>
<td>1.1 – 3.8</td>
</tr>
<tr>
<td>Tumor Stage (&gt;1)</td>
<td>0.0003*</td>
<td>0.29</td>
<td>1.4</td>
<td>0.8 – 2.4</td>
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<tr>
<td>Positive Lymph Nodes</td>
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<td>Positive Surgical Margins</td>
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<td>0.28</td>
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<td>Lymphovascular Invasion</td>
<td>0.0045*</td>
<td>0.21</td>
<td>1.5</td>
<td>0.8 – 2.7</td>
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</tbody>
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*: Variables with p value < 0.10 by univariate analysis are selected for multivariate variables
Robotic Partial Nephrectomy: Cumulative Single Center Experience

Wesley M. White, Georges-Pascal Haber, Raj K. Goel, Sebastien Crouzet, Jihad Kaouk

Background: We present perioperative outcomes in an observational cohort of patients who underwent Robotic Partial Nephrectomy (RPNx) at a single academic institution.

Methods: A prospective study was performed to evaluate operative outcomes following RPNx. Salient demographic and radiographic data were obtained. Operative data including estimated blood loss (EBL), operative time, and warm ischemia time (WIT), where applicable, were recorded. Pathology was reviewed and classified according to the AJCC staging system. Patients were followed post-operatively for evidence of immediate and delayed complications. Renal functional outcomes were obtained and estimated creatinine clearance calculated using the MDRD formula. Statistical analysis was performed.

Results: Between June 2006 and June 2009, a total of 72 patients underwent right (n=35) or left (n=37) RPNx for radiographic evidence of an enhancing renal mass. Mean age of the cohort was 64 years. Mean BMI was 27.9 kg/m2. Mean operative time was 203 minutes. Mean EBL was 325 mL. Ten patients underwent RPNx without hilar clamping. The remaining 62 patients underwent hilar clamping with a mean WIT of 23 minutes. Mean pathologic tumor size was 2.7 cm (range 1–7.5 cm). Patholog confirmed renal cell carcinoma in 63 patients, angiomyolipoma in 4 patients, and oncocytoma in 5 patients. All margins were negative. Complications occurred in 6 patients. Three patients required blood transfusions, 1 patient developed a renal fluid collection, and 2 patients required post-operative angioembolization.

Conclusion: Robotic Partial Nephrectomy offers excellent perioperative outcomes with promising short-term oncologic control. Prospective, comparative study to conventional laparoscopic partial nephrectomy is needed.
Predicting Factor for Renal Function Decrease After Laparoscopic Partial Nephrectomy

K. Kamoi, Sebastien Crouzet, Georges-Pascal Haber, A. Kawauchi, T. Miki, Inderbir S. Gill

**Background:** Renal function after laparoscopic partial nephrectomy (LPN) is a major concern. Herein, we studied the predictive factors of postoperative renal function after LPN.

**Methods:** A total of 953 patients underwent a LPN between September 1999 and September 2008. Demographic, operative indication, intra-operative, peri-operative, and renal function follow-up data were collected prospectively. We used univariate and multivariate analysis with logistic fit regression model for each data to identify predicting factors of post operative percent change in eGFR at the highest postoperative values between 1 to 24 months after surgery.

**Results:** The mean nadir eGFR was reached at postoperative day 1 and the plateau at 6 month. Three factors appear to be significant predictor for the post-operative percent eGFR decrease >20, >25 and >30 points: the imperative surgical indications, the warm ischemia time and a tumor size (p <0.01 for all). Sex, ASA score, Carlson Comorbidities Index, patient with a solitary kidney, coronary artery disease or hypertension also influence the post operative eGFR change in the univariate analysis but did not reach statistical significance on the multivariate analysis. With ROC curve analysis to predict >30% decrease in plateau eGFR, warm ischemia time >30 min and a tumor size >2.0 cm were the optimal threshold value.

**Conclusion:** Pre-operative imperative surgical indication, warm ischemia time and the tumor size are the most predictive factors of post-operative eGFR decrease after LPN.
Open vs. Laparoscopic Partial Nephrectomy for Hilar Tumors

D. Snow, Georges-Pascal Haber, K. Kamoi, Michael C. Lee, Sebastien Crouzet, Inderbir S. Gill

Objectives: Although laparoscopic surgery for hilar renal tumors is a relatively recent addition to the laparoscopic repertoire, over 63 patients have undergone the procedure at the Cleveland Clinic since 2001. With the recent advent of early unclamping technique, laparoscopic partial nephrectomy has evolved. Therefore, we have analyzed a contemporary cohort to compare the perioperative outcomes of open partial nephrectomy (OPN) and laparoscopic partial nephrectomy (LPN) for hilar tumors.

Methods: We evaluated patients who, between 1/2006 and 8/2008, underwent planned LPN or OPN for hilar tumor. Hilar tumor was defined as those located in renal hilum and demonstrated to be in actual physical contact with renal vasculature on preoperative 3D CT. Baseline, perioperative, and follow-up data were collected prospectively and data was analyzed retrospectively.

Results: Of the 378 OPN and the 477 LPN cases, 43 LPN for hilar tumor and 89 OPN for hilar tumor were attempted. 5 patients in the laparoscopic group were converted from LPN to laparoscopic radical nephrectomy; no patients were converted to open. Similar data is not available for the OPN analysis. Significant differences were present between the average preoperative estimated glomerular filtration rate (54, 78 p = 0.03) and the percentage decline at last follow up (26%, 6% p = 0.01) between OPN and LPN respectively. There were no significant differences between operative time (3.95 vs 4.08 hours p = 0.7), estimated blood loss (508 vs 338 ml p=0.3), intra-operative complications (5.6% vs 2.6% p=0.7 ), or % with positive margins (3.4% vs 2.6% p=0.5). A significantly increased length of hospital stay was seen in the open group (6 vs 4 days p=0.001).

Conclusions: While hilar tumors represent a great technical challenge for partial nephrectomy, in experienced hands both OPN and LPN deliver comparable outcomes. This data further advances the applicability of laparoscopic partial nephrectomy.
Natural Orifice Translumenal Endoscopic Surgery (NOTES) Toolbox: Instruments, Scopes, and Ports

Georges-Pascal Haber, Sebastien Crouzet, Wesley M. White, J. Talarico, Stacy Brethauer, Jihad Kaouk

**Background:** Natural orifice surgery currently involves gaining access to the peritoneum via natural body orifices (transgastric, transcolonic, transvaginal, and transvesicular). There are several major limits to NOTES; however, at our institution we have successfully performed several procedures. We offer a practical summary of the necessary tools used during NOTES.

**Methods:** Instruments used during access in transcolonic and transgastric cases include an over tube with dilator, Olympus dual (160/180) and single channel (T130) endoscopes, needle knife cautery, and an Olympus SWIFT balloon dilator. During the procedure, the previous instruments are used in addition to endoscopic graspers, Olympus Endojaw biopsy forceps, and Olympus surgical scissors. For closure we are using a t-tag based system available under approved protocols (Ethicon’s Tissue Apposition System (TAS) or Bard’s EndoStitch). Alternatively, there are several other closure devices available (PARE surgical based on endoluminal knot tying) or the H-type by USGI. For transvaginal procedures single port techniques were employed. This included extended length Novare RealHand as well as Cambridge Endo instruments (articulating graspers, Horgan dissectors, and hook cautery). Our visualization came via Olympus EndoEye flexible and traditional Olympus 0o and 30o laparoscopes.

**Results:** Transcolonic and transgastric access and closure is reliable in the canine model using this set of instruments. Procedures such as peritonoscopy, drainage of intrabdominal abscess, cholecystectomy, and appendectomy are feasible. Transvaginal experience is limited to nephrectomy using single port techniques and extended length instruments.

**Conclusion:** Industry support and physician acceptance are required to continue developing new dedicated NOTES instruments. Although there are ever expanding possibilities, there exists a continued and pressing need for an entirely new platform dedicated to NOTES. We continue to practice cautious optimism.
A Non-Randomized Comparison of Overall Survival in Patients with Clinical T1B Renal Tumors treated with Radical Nephrectomy (RN) or Partial Nephrectomy (PN)

Christopher J. Weight, Benjamin T. Larson, Amr F. Fergany, Steven C. Campbell, Jihad H. Kaouk, Tianming Gao, Inderbir S. Gill, Andrew C. Novick

Introduction and Objective: PN is preferred to RN for most clinical T1a (>4 cm) renal masses. For larger tumors, 4 to 7 cm tumors, there is still debate regarding the best management. RN is perceived to offer the best oncologic control, whereas PN best preserves the glomerular filtration rate (GFR) which would hypothetically prevent the morbidity and mortality associated with renal insufficiency. We compared overall survival (OS) in patients undergoing PN or RN for cT1b tumors.

Methods: From 1998-06, 1004 patients with renal masses between 4-7 cms underwent extirpative surgery. We calculated the propensity to undergo PN vs. RN using multivariable logistic regression model and pre-operative patient characteristics including age, tumor size, eGRF, presence of contralateral disease, solitary kidney status, surgery type (laparoscopic vs. open) and Charlson comorbidity index. We compared overall and cancer specific survival in a subset of patients (n=510) who were potential candidates for both RN and PN, i.e. ‘elective’ PN, with sporadic, unilateral renal masses and a GFR>60, and a normal contralateral kidney.

Results: Median follow up for the entire cohort was 48 months. Selection of RN vs. PN was not random, with those undergoing RN more likely to be older, have larger tumors, higher pathologic stage, and a higher burden of comorbid diseases, whereas those getting a PN were more likely to have a solitary kidney, the presence of contralateral disease and a decreased eGFR. In the ‘elective’ cohort, multivariate analysis demonstrated that when controlling for both the propensity to undergo a PN and pathologic stage, PN continued to be associated with better overall survival (Hazard ratio=0.48(95%CI=0.25-0.93). However, when drop in eGFR was included in the model, PN was no longer a significant predictor of survival.

Conclusions: PN in patients with cT1b tumors is an oncologically safe and viable alternative to RN and was associated with a significantly better overall survival in this cohort, even when controlling for age, tumor size, preoperative eGFR, solitary kidney status, presence of contralateral disease, pathologic stage and burden of comorbid diseases. This difference in survival appears to be attributable to the better preservation of GFR for those undergoing PN.
Standard vs. Single Port Laparoscopic Partial Nephrectomy: Comparative Outcomes

Wesley M. White, Georges-Pascal Haber, Raj K. Goel, Sebastien Crouzet, M. White, Jihad Kaouk

Background: To evaluate perioperative outcomes among patients who underwent single port or conventional laparoscopic partial nephrectomy.

Methods: A prospective, observational study was performed to evaluate perioperative outcomes among patients who underwent single port laparoscopic partial nephrectomy (SPLPN). Salient demographic and operative data were obtained. These patients were next retrospectively compared to a contemporary, matched-cohort of patients who underwent conventional LPN (CLPN). Endpoints including age, BMI, operative time, estimated blood loss (EBL), complications, conversion, and post-operative Visual Analog Pain Scale (VAPS) scores were examined. Statistical analysis was performed.

Results: Fifteen SPLPN and 15 CLPN patients were evaluated. There was no significant difference between the SPLPN and CLPN cohorts with respect to mean age (66 vs. 59 years, p=0.149), mean BMI (26.7 vs. 28.0, p=0.422), mean operative time (196 vs. 245 minutes, p=0.08), mean EBL (422 vs. 337 mL, p=0.67), and mean length of hospitalization (4.5 vs. 3.5 days, p=0.494). Mean VAPS score at discharge was significantly less in the SPLPN cohort (0.67/10 vs. 3/10, p=0.009). One patient in the SPLPN cohort required conversion to standard laparoscopy. Four patients in the SPLPN cohort required post-operative blood transfusions, one of which required angioembolization. Three patients in the CLPN cohort received blood transfusions.

Conclusion: Based on our experience, single port LPN demonstrates equivalent comparative outcomes to conventional LPN with significantly less pain and superior cosmesis in the single port cohort. Prospective, randomized studies are needed to confirm these findings.
Single Port Laparoscopic Surgery: Cumulative Outcomes with Over 100 Cases

Wesley M. White, Raj K. Goel, Georges-Pascal Haber, Sebastien Crouzet, M. White, Jihad Kaouk

Background: To present perioperative outcomes in an observational cohort of patients who underwent Laparo Endoscopic Single Site (LESS) surgery at a single academic center.

Methods: A prospective study was performed to evaluate patient outcomes following LESS urologic surgery. Demographic data including age, BMI, operative time, estimated blood loss (EBL), operative indications, complications, and postoperative Visual Analog Pain Scale (VAPS) scores were accrued. Patients were followed post-operatively for evidence of adverse events.

Results: Between September 2007 and June 2009, 105 patients underwent LESS urologic surgery. Specifically, 78 patients underwent LESS renal surgery (cryoablation -9, partial nephrectomy -15, metastectomy -1, renal biopsy -1, simple nephrectomy -7, radical nephrectomy -8, cyst decortication -2, nephroureterectomy -7, donor nephrectomy -20, and dismembered pyeloplasty -8) and 27 patients underwent LESS pelvic surgery (varicocelectomy -3, radical prostatectomy -7, radical cystectomy -3, sacral colpopexy -13, and ureteral reimplant -1). Mean patient age was 55 years. Mean BMI was 26.1 kg/m2. Mean operative time was 198 minutes. Mean EBL was 132 mL. No intraoperative complications occurred. Six patients required conversion to standard laparoscopy. One patient required open conversion. Mean length of hospitalization was 3 days. Mean VAPS score at discharge was 1.5/10. At a mean follow-up of 11 months, 10 Clavien Grade II (transfusion - 8, UTI - 1, DVT -1) and 2 Clavien Grade IIIb (recto-urethral fistula -1, angioembolization -1) surgical complications occurred.

Conclusion: Based on our experience, LESS urologic surgery is feasible, offers improved cosmesis, and may offer decreased pain. Its superiority compared to standard laparoscopy is currently speculative.
NOTES Transvaginal Nephrectomy: Initial Clinical Experience

Wesley M. White, Georges-Pascal Haber, Raj K. Goel, Sebastien Crouzet, Stacy Brethauer, Jihad Kaouk

Background: To present the first clinical experience of Natural Orifice Transluminal Endoscopic Surgery (NOTES) transvaginal nephrectomy.

Methods: A prospective, IRB-approved study was performed to evaluate the feasibility and safety of NOTES transvaginal nephrectomy. Operative candidates included females with a nonfunctioning kidney and a compelling indication for removal. All patients underwent complete history/physical examination, serologic testing, and appropriate imaging studies. Following consent, a 3 cm posterior colpotomy was made to access the peritoneal cavity. Standard and articulating instruments were employed to perform pelvic adhesiolysis, reflect the colon, and expose the renal hilum. An endovascular stapler was deployed transvaginally to divide the renal hilum. Upper pole attachments were divided using a 65 cm articulating monopolar hook. The kidney was entrapped in a laparoscopic retrieval bag and removed.

Results: NOTES transvaginal nephrectomy was successfully completed in 2 patients. Mean patient age was 57.5 years. Mean BMI was 30.57 kg/m2. Mean operative time was 405 minutes. Mean EBL was 75 mL. Mean length of hospitalization was 18.5 hours. Mean visual analog pain scale score at discharge was 1/10. No perioperative complications occurred. A 5mm umbilical port was placed in one patient who had undergone prior pelvic surgery to direct safe vaginal entry. The second case was completed transvaginally without any abdominal instruments or ports.

Conclusion: NOTES transvaginal nephrectomy is safe and technically feasible. In patients with prior pelvic surgery, access to the peritoneal cavity should be performed under visual guidance. Future study is needed to better define patient selection criteria and indications for NOTES transvaginal urologic surgery.
Single Port Robotic Radical Prostatectomy

Raj K. Goel, Wesley M. White, Georges-Pascal Haber, Sebastien Crouzet, Jihad Kaouk

Background: Single port laparoscopy has gained momentum in achieving a virtually scarless minimally invasive approach. Technical hindrances currently prevent the widespread adoption of this evolving technique. Recent application of the robotic platform to radical prostatectomy has demonstrated excellent results. Herein, we evaluate our experience with single port robotic surgery during radical prostatectomy.

Methods: A retrospective analysis of single port robotic (SPR) radical prostatectomies performed at a single institution was reviewed. Patients eligible for the SPR approach included patients with low risk, organ confined disease, baseline impotency and the absence of previous abdominal or pelvic surgery. The daVinci-S system was positioned through a commercially available single port. Perioperative variables including operative time, blood loss and surgical technique were assessed. Postoperative visual analog pain scores (VAPS); oncological and functional outcomes were also evaluated.

Results: Three single port robotic radical prostatectomies were performed without use of additional laparoscopic ports. Mean operative time was 217 minutes with estimated blood loss of 133 ml. All patients were discharged on postoperative day two. Standard robotic dissection was performed throughout the case with note of a continuous urethral-vesical anastomotic suture in all three cases. Mean VAPS at discharge was 1.3 ± 0.8. Pathology revealed T2b disease with Gleason 7 (2) and Gleason 6 (1) disease. One patient demonstrated margin positivity however no evidence of biochemical relapse has been detected. Given the brevity of follow up, evaluation of continence is premature.

Conclusion: Robotic application to single port laparoscopic surgery has the potential to further evolve this technique. Improved imaging, range of motion and robotic ergonomics assist the surgeon during complex reconstructive procedures. Further evaluation of the single port robotic technique requires extended evaluation, however, early functional outcomes show promise.
Robotic Single Port Suprapubric Transvesical Enucleation of the Prostate (R-STEP): Initial Experience

K. Fareed, Wesley M. White, Georges-Pascal Haber, Raj K. Goel, Sebastien Crouzet, Jihad Kaouk

**Background:** We present perioperative outcomes in an observational cohort of patients who underwent Robotic Single Port Suprapubic Transvesical Enucleation of the Prostate (R-STEP).

**Methods:** A prospective study was performed to evaluate operative outcomes following R-STEP for symptomatic benign prostatic hyperplasia (BPH). All patients underwent preoperative transrectal ultrasound (TRUS) of the prostate and urodynamics prior to intervention. Appropriate candidates underwent transurethral incision of the prostate apex, were repositioned in the supine position, and an approximate 3 cm lower midline incision made. A cystotomy was created and a GelPort laparoscopic system positioned in the bladder. The da Vinci S robotic operating system was docked through the GelPort platform and prostate enucleation performed in a standard fashion. Perioperative outcomes were obtained for all patients.

**Results:** Between March 2009 and June 2009, 3 patients underwent R-STEP. Mean preoperative prostate volume by TRUS was 131 grams. Preoperatively, 2 patients were in urinary retention and one patient had bladder stones and a $Q_{\text{max}}=5.2$ mL/second. Mean operative time was 3.8 hours. Mean EBL was 233 mL. No intraoperative complications occurred. Post-operatively, one patient developed clot retention and required evacuation and fulguration. The same patient required a blood transfusion. No other postoperative complications occurred. Cystogram was negative in all patients. Mean volume of resected tissue was 42 grams. Postoperative mean $Q_{\text{max}}=26.8$ mL/second.

**Conclusion:** R-STEP is a technically challenging procedure with a brief yet pronounced learning curve. Use of the robot during STEP procedures may ultimately offer improved outcomes as compared to standard laparoscopic STEP.
Natural Orifice Translumenal Endoscopic Surgery (NOTES) Access: Transvesical, Transvaginal, Transcolonic, and Transgastric

Georges-Pascal Haber, J. Talarico, Sebastien Crouzet, K. Litwak, Stacy Brethauer, Jihad Kaouk

**Background:** One of the biggest challenges of NOTES is the access technique and the closure of the port of entry. In this video we present the technical requirements and specifications to reproducibly enter and close each access site in the animal model.

**Methods:** Transvesical access was performed at the dome using a flexible cystoscope, needle knife cautery and a coronary dilator. For transvaginal procedures, a posterior colpotomy is created and the endoscope is advanced over the SWIFT balloon dilator. Instruments used during access in transcolonic and transgastric cases include an over tube with dilator, dual (160/180) and single channel (T130) endoscopes, needle knife cautery, and balloon dilator. Similar techniques are employed to enter the peritoneum after balloon dilation.

**Results:** Transvesical approach is safe, feasible and reproducible. Complete peritonoscopy is possible through this approach. Specimen extraction is limited to the size of the urethra. Transvaginal access is feasible and reproducible with a theoretical risk of rectal/bowel injury. Transgastric and transcolonic access are technically challenging with an average time for access greater than 90 minutes. Closure of entry point is necessary and not reliable with current instrumentation.

**Conclusion:** Industry support and physician acceptance are required to continue developing new dedicated NOTES instruments. All four types of access are feasible. From our experience and for urological applications we believe that the transvaginal approach is the route of choice in the female patient. However, the transvesical approach is a safe route, but specimen extraction is limited to the size of the urethra.
NOTES Transvaginal Nephrectomy: Initial Clinical Experience

Jihad Kaouk, Wesley M. White, Raj K. Goel, Sebastien Crouzet, Stacy Brethauer, Georges-Pascal Haber

Background: To present the first clinical experience with Natural Orifice Translumenal Endoscopic Surgery (NOTES) transvaginal nephrectomy.

Methods: A prospective, IRB-approved study was performed to evaluate the feasibility and safety of NOTES transvaginal nephrectomy. Operative candidates included females with a nonfunctioning kidney and a compelling indication for removal. All patients underwent complete history/physical examination, serologic testing, and appropriate imaging studies. Following consent, a 3 cm posterior colpotomy was made to access the peritoneal cavity. Standard and articulating instruments were employed to perform pelvic adhesiolysis, reflect the colon, and expose the renal hilum. An endovascular stapler was deployed transvaginally to divide the renal hilum. Upper pole attachments were divided using a 65 cm articulating monopolar hook. The kidney was entrapped in a laparoscopic retrieval bag and removed.

Results: NOTES transvaginal nephrectomy was successfully completed in 2 patients. Mean patient age was 57.5 years. Mean BMI was 30.57 kg/m2. Mean operative time was 405 minutes. Mean EBL was 75 mL. Mean length of hospitalization was 18.5 hours. Mean visual analog pain scale score at discharge was 1/10. No perioperative complications occurred. A 5mm umbilical port was placed in one patient who had undergone prior pelvic surgery to direct safe vaginal entry. The second case was completed transvaginally without any abdominal instruments or ports.

Conclusion: NOTES transvaginal nephrectomy is safe and technically feasible. In patients with prior pelvic surgery, access to the peritoneal cavity should be performed under visual guidance. Future study is needed to better define patient selection criteria and indications for NOTES transvaginal urologic surgery.
Steriotactic Percutaneous Cryoablation for Renal Tumors (Video)

Georges-Pascal Haber, Sebastien Crouzet, E. Remer, K. Kamoi, Wesley M. White, Jihad Kaouk

**Background:** Precise cryoprobe placement is essential for successful ablation. CT-Nav_ (Koelis, France) is a novel stereotactic surgical navigation system that has the potential to achieve precise percutaneous cryoprobe placement while reducing radiation exposure compared to conventional CT-guided procedures.

**Methods:** A prospective pilot study was performed to evaluate the technical feasibility, safety, and accuracy of the CT-Nav_ system during renal cryoablation. Patients with enhancing renal masses amenable to renal cryoablation underwent preoperative CT scan with a pre-placed tracking sensor taped to the body of the patient. Using a stereoscopic infrared camera, the tracking sensor is located three-dimensionally and a tracking handle used to guide the cryoprobe percutaneously based on the preoperative preloaded CT-scan. Demographic and perioperative data were obtained prospectively into an IRB approved database. Immediately following cryoprobe placement, a CT-scan is repeated to confirm cryoprobe placement accuracy.

**Results:** A total of 13 tumors in 10 patients successfully underwent cryoablation using the novel navigational system. Mean tumor size was 2.2 cm. Preoperative biopsy demonstrated renal cell carcinoma in 9 cases. Mean operative time was 155 min. No intraoperative or postoperative complications were noted. Mean length of stay was 9.5 hrs. A mean decrease in CT fluoroscopy duration of 18.3 sec was noted for each cryoprobe placed. Mean targeting registration error was 4.2 mm.

**Conclusion:** Stereotactic percutaneous cryoablation of renal tumors offers the potential for safe and precise needle placement while reducing radiation exposure compared to traditional CT-guided probe placement.
Robotic Assisted Extended Lymph Node Dissection

Raj K. Goel, C. Sebastien, Wesley M. White, Georges-Pascal Haber, Stephen C. Campbell, Jihad Kaouk

Background: Minimally invasive approaches to urothelial carcinoma of the bladder is gaining momentum. Early results indicate reduced blood loss, pain and shortened convalescence. The extent of lymphadectomy is crucial for both prognostic and therapeutic variables. The robotic application offers a new paradigm in the treatment of bladder cancer. Its ability to safely and effectively perform an extended lymphadectomy has been scrutinized. Here we present a case of a robotic assisted extended lymph node dissection for urothelial carcinoma of the bladder.

Methods: A 70 year old gentleman with refractory T1 high grade urothelial carcinoma presented for definitive treatment. Preoperative evaluation reveals no evidence of locally advanced or disseminated disease. A robotic assisted radical cystoprostatectomy was performed followed by lymphadenectomy as shown.

Results: A total of 26 lymph nodes were successfully cleared in the patient. The lymph node dissection was carried to the level of the inferior mesenteric artery thereby skeletonizing the external, internal, common iliac arteries and aorta. Presacral nodal tissue were also removed with robotic assistance. Estimated blood loss during robotic lymph adenectomy was 200 cc, with operative time of 90 minutes.

Conclusion: Robotic assistend extended lymph node dissection for urothelial carcinoma of the bladder is safe and effective in select patients. Operative time and blood loss are minimal while offering extensive clearance of nodal tissue following extirpative surgery. Proper patient selection for any minimally invasive approach to urothelial carcinoma is paramount.
Robotic Assisted Radical Cystectomy (Video)
Raj K. Goel, Sebastien Crouzet, Wesley M. White, Georges-Pascal Haber, Jihad Kaouk

Background: Radical cystectomy for muscle invasive urothelial carcinoma of the bladder remains the gold standard therapeutic option. However, open technique can be associated with significant perioperative morbidity. New minimally invasive procedures are evolving to provide sound oncological outcomes while minimizing postoperative sequelae. Use of the robotic platform has improved laparoscopic ergonomics during various challenging laparoscopic procedures. Its application to radical cystectomy is highlighted here in this video.

Methods: A 70 year old male with refractory T1 high grade urothelial carcinoma who failed BCG was selected to undergo radical cystectomy, bilateral pelvic lymphadenopathy and urinary diversion. Preoperative investigations reveal no evidence of locally advanced or metastatic disease. Upon gaining intra-abdominal access and patient in steep trendellenburg, a 5-port configuration was utilized for the cystectomy. Key steps of the procedure are highlighted in the video.

Results: Time to complete the radical cystectomy was 1 hour and 30 minutes. Estimated blood loss was 200 cc. The entire procedure was performed robotically without complication or conversion to an open technique. Following cystectomy, an extended lymph node dissection was completed followed by urinary diversion in the form of an ileal conduit via a mini-laparotomy incision. Post operatively, the patient was ambulating on POD#1, tolerating a full diet on POD#3 was was eventually discharged on POD#5. Pathology confirmed his preoperative diagnosis of T1 high grade urothelial carcinoma. Ureteral and urethral margins for urothelial carcinoma were negative. The prostate contained foci of high grade pin and all lymph nodes removed during surgery were negative.

Conclusion: Robotic assisted radical cystectomy in select patients can offer sound oncological outcomes while minimizing perioperative morbidity. A minimally invasive approach can minimize blood loss, expedite early ambulation and offer quicker return of bowel function. Proper patient selection is paramount when a minimally invasive approach is considered.
Laparoendoscopic Single Site (LESS) Donor Nephrectomy: Alternative Use of the Gelport Device

A. Patel, Wesley M. White, Georges-Pascal Haber, Raj K. Goel, Sebastien Crouzet, Jihad Kaouk

Background: To present our institution’s experience with LESS donor nephrectomy using the GelPort_ laparoscopic system as an access platform.

Methods: A prospective observational study was performed to assess perioperative outcomes among patients undergoing LESS donor nephrectomy with use of a standard GelPort_ as the operative platform. Appropriate candidates were placed in the flank position and an approximate 5 cm periumbilical incision made. A commercially available GelPort_ was deployed and the abdomen insufflated. Standard laparoscopic ports were placed through the GelPort_ and the donor nephrectomy performed. The allografts were then extracted through the existing incision. Demographic and peri-operative data were obtained.

Results: From October 2008 to November 2008, 2 patients underwent laparoscopic live donor nephrectomy as described. Mean age was 37.5 years. Mean BMI was 24. One patient demonstrated 2 renal arteries and 1 vein with the remaining patient having 1 artery and 1 vein. Mean operative time was 240 minutes. Mean blood loss was 50 mL. Mean length of the incision was 6.65 cm. Mean warm ischemia time was 6 minutes, 40 seconds. There were no perioperative complications. Mean length of hospitalization was 3 days. Mean visual analog pain scale score at discharge was 0/10. Mean recipient creatinine at discharge was 1.2.

Conclusion: Use of the GelPort_ during LESS donor nephrectomy offers versatility and improved spacing of instruments as compared to standard multichannel single ports. In addition, the design of the GelPort_ is more accommodating for allograft extraction and requires neither use of a laparoscopic retrieval bag nor unnecessary compression of the kidney.
NOTES (Natural Orifice Translumenal Endoscopic Surgery) Renal Cryoablation in the Porcine Model

Sebastien Crouzet, Georges-Pascal Haber, Kazumi Kamoi, Stacy Brethauer, Patrick Gatmaitan, Jihad Kaouk

Introduction: We present our initial laboratory experience with natural orifice translumenal endoscopic surgery (NOTES) renal cryoablation.

Methods: In 2 female farm pigs, we performed 4 NOTES renal cryoablation. In each animal we performed 1 transgastric approach and 1 transvaginal approach. The animal is placed in the flank position and pneumoperitoneum obtained using a transabdominal Veress® needle. In the first animal, we started on the left kidney with a transgastric approach: a dual-channel video gastroscope (Olympus, Tokyo, Japan) was used, the stomach wall was punctured using a needle-knife, a guide wire was passed into the abdominal cavity and the access dilated using a controlled radial expansion balloon. The bowel was mobilized medially and the Gerota’s fascia overlying the upper pole was dissected. Under direct endoscopic vision, a cryoablation probe was introduced percutaneously into the anterior upper pole of the kidney. Then the animal is flipped and a transvaginal approach is used for the right side: the gastroscope is introduced through the posterior fornix of the vagina in a similar transgastric fashion and the procedure was performed. For the second animal, we performed initially a transgastric right side cryoablation then a transvaginal left side cryoablation: as described in the first animal.

Results: All 4 procedures were performed successfully. No intraoperative complication was observed. No additional laparoscopic port or open conversions were necessary. The vision of the kidney and the ice-ball were excellent. Mean operative time was 82.75 min. The stomach closure was watertight, and no abdominal or pelvic injuries were found at autopsy.

Conclusion: NOTES can provide adequate minimal surgical dissection for safe and effective percutaneous renal cryoablation under direct videoscopic monitoring at kidney locations otherwise not accessible percutaneously. Both transgastric and transvaginal approaches can be used effectively to perform renal cryoablation providing a minimally-invasive scarless surgery.

continued
Figure 1. Endoscopic instruments

Figure 2. First freezing cycle

Figure 3. Dilatation with a controlled radial expansion balloon
A Novel Proximity-Sensing Stent to Assist Non-Urological Surgeons with Intraoperative Identification of the Ureter

John C. Kefer, Mihir M. Desai, Monish Aron, Georges Pascal-Haber, Inderbir S. Gill

Introduction: Inadvertent ureteric injury by non-urological surgeons remains a significant concern. Temporary ureteric stents may be placed preoperatively to assist in the identification of a difficult ureter, but these stents may not be palpable during laparoscopic surgery, nor visible if surrounded by a bulky mass. Here, we report our design and laboratory experience with a novel intraoperative device incorporating a flexible, magnetic, 7 Fr J-J stent (Fig. 1), combined with a portable, battery-powered, magnetic field-detecting intraoperative wand utilizing a linear output Hall effect transducer (Honeywell Intl. Inc., Morristown, NJ) (Fig. 2). When the detector wand nears the stent, an audible warning tone is emitted. As proximity to the stent increases, the frequency of the audible tone increases proportionally.

Methods: Our stent design utilizes rare-earth neodymium-iron-boron cylindrical magnets (OR 0.975 mm, IR 0.53 mm) incorporated into a silicone JJ stent. The cylindrical magnet shape was required to allow guidewire placement and luminal urinary drainage. Detection of the magnetic stent within the ureter was quantified using a portable, battery-powered voltmeter. The stent was placed in 4 pigs (8 renal units), and laparotomy was subsequently performed. The sensor wand was placed near the ureter at varying distances before and after releasing the colon. The magnetic field strength was recorded in all positions.

Results: The intraoperative detector wand reliably registered increasing magnetic field strength from a distance of 2 cm to 0.1 cm from the stent, and also precisely detected the position of the ureter behind the colon. The detected magnetic signal increased proportionally with increasing proximity to the stent from all angles of attack, including perpendicular and parallel to the stent, and reliably produced an audible warning tone when near the ureter.

Conclusion: Our novel stent design allows precise, predictable proximity detection of the ureter during intra-abdominal and pelvic surgeries. This magnetic stent and portable sensor system may serve to decrease the rate of inadvertent ureteral injury, and allows non-urologic surgeons the ability to actively identify the difficult ureter intraoperatively.
NOTES and Single Port Surgery: What Do Patients Want?

David Canes, Andre Berger, Monish Aron, Kazumi Kamo, Georges-Pascal Haber, Robert J. Stein, Stephen C. Campbell, Jihad H. Kaouk, Mihir M. Desai, Inderbir S. Gill

Background: Enthusiasm for Natural orifice translumenal endoscopic surgery (NOTES) and Laparo-endoscopic single-site (LESS) surgery continues to escalate. Notably absent are specific insights into patient attitudes towards these techniques, and surgical scars. Our aim was to evaluate patient perceptions of various approaches, determine how scarring impacts patient decision making, determine the preferred orifice-of-entry for NOTES, and understand the demographics of patients interested in these novel approaches.

Materials and Methods: After IRB exemption, beginning July 2008, 608 consecutive patients presenting to urologic, general surgical, and obstetrics/gynecology clinics were asked to complete a 25-item questionnaire. The survey included baseline demographics, medical history, presence and attitudes about preexisting scars, decision making for hypothetical surgeries for benign/malignant indications.

Results: Mean age was 58 and 51% were male. Forty percent were presenting to Cleveland Clinic for surgical indications, and 73%, 46%, 10% had prior open, laparoscopic, or robotic surgery respectively. Fourteen percent were unhappy about the scars. When presented the hypothetical need for nephrectomy for benign and malignant indication, or cholecystectomy, surgical scars ranked 11th amongst considerations for surgical approach, with reputation of hospital, reputation of doctor and doctor’s recommendation accounting for the top three considerations. Majority of patients preferred standard laparoscopic approach for cholecystectomy (34%) and benign nephrectomy (31%). However the preferred approach for nephrectomy for malignancy was open surgery (24%), followed by laparoscopy (21%). LESS was chosen by 13%, 11% and 8%, and NOTES by 2%, 2.5%, and 2%, respectively. When asked to choose between NOTES and LESS, 70% preferred LESS for kidney cancer and 75% preferred LESS for non-kidney cancer surgery. The preferred orifice for NOTES was rectum in males (38%) and vagina in females (43%). On multivariate analysis, only female was an independent predictor for choosing NOTES or LESS for benign indications.

Conclusions: Postoperative scarring ranks low in the hierarchy of patient concerns when given hypothetical surgical scenarios. Patients currently prefer LESS over NOTES. Further research is warranted to determine how best to communicate these novel approaches, which at face value may not be appealing to patients.
Robotic vs. Laparoscopic Nephrectomy: 
A Single Surgeon Matched Comparison of 100 Cases

Georges-Pascal Haber, Wesley M. White, Raj K. Goel, Sebastien Crouzet, 
Kazumi Kamoi, Jihad Kaouk

Objective: To compare a single-surgeon experience of Laparoscopic Partial Nephrectomy (LPN) and Robotic Partial Nephrectomy (RPN) in matched populations.

Materials and Methods: Between 06/2006 and 02/2009, 50 patients underwent RPN for radiographic evidence of an enhancing renal mass. Outcomes were then compared retrospectively to 50 matched patients who underwent LPN. Patients were matched for demographics, comorbidities, tumor specifications, and clamping technique. Preoperative, intraoperative and postoperative data were measured and compared. A learning curve for the RPN group was formulated.

Results:

<table>
<thead>
<tr>
<th></th>
<th>LPN (n=50)</th>
<th>RPN (n=50)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative Data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male/ Female</td>
<td>26/24</td>
<td>28/22</td>
<td>0.84</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>48</td>
<td>52</td>
<td>0.57</td>
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<tr>
<td>BMI(Kg/m2)</td>
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<td>29</td>
<td>0.64</td>
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<tr>
<td>ASA</td>
<td>2.4</td>
<td>2.4</td>
<td>0.89</td>
</tr>
<tr>
<td>CCI</td>
<td>0.68</td>
<td>0.74</td>
<td>0.7</td>
</tr>
<tr>
<td>Side R/L</td>
<td>30/20</td>
<td>23/27</td>
<td>0.16</td>
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<tr>
<td>Tumor size (cm)</td>
<td>2.3</td>
<td>2.6</td>
<td>0.24</td>
</tr>
<tr>
<td>Inter/Lower/Upper Pole (n)</td>
<td>10/18/22</td>
<td>13/20/17</td>
<td>0.56</td>
</tr>
<tr>
<td>Preoperative eGFR (ml/mn)</td>
<td>78</td>
<td>83</td>
<td>0.33</td>
</tr>
<tr>
<td>Early/Conventional/Unclamped(n)</td>
<td>26/14/10</td>
<td>26/12/12</td>
<td>0.84</td>
</tr>
</tbody>
</table>

|                |            |            |       |
| **Intraoperative Data** |        |            |       |
| OR time (mn)    | 184        | 202        | 0.04  |
| EBL (cc)        | 218        | 334        | 0.09  |
| WI time (mn)    | 19.1       | 16.5       | 0.25  |
| LOS (days)      | 4.3        | 4          | 0.54  |
| Intraoperative Complications (n) | 0     | 0         | -     |
| Conversion to laparoscopy (n)     | -         | 2         | -     |
| Conversion to open          | 1         | 0         | 0.31  |

|                |            |            |       |
| **Postoperative Data** |        |            |       |
| % eGFR Change    | -8.51%     | -8.91%     | 0.98  |
| Postoperative Complications (n) | 6     | 8         | 0.56  |
| RCC (n)          | 43         | 46         | 0.34  |
| Positive Surgical Margin (n) | 0     | 0         | -     |

continued
**Conclusion:** Based on our experience, RPN offers comparable outcomes to LPN with an acceptable learning curve. With improved technique and burgeoning robotic experience, we expect RPN to assume a prominent role in the management of small renal masses.
Single-Port vs. Standard Laparoscopic Donor Nephrectomy: Matched-Pair Comparison

David Canes, Andre Berger, Ricardo Brandina, Monish Aron, Georges-Pascal Haber, Jihad H. Kaouk, David A. Goldfarb, Mihir M. Desai, Inderbir S. Gill

**Purpose:** To present the initial experience with laparoendoscopic single site (LESS) donor nephrectomy (LESS-DN), retrospectively comparing perioperative outcomes with patients undergoing standard LDN.

**Materials and Methods:** Between 11/07 and 11/08, 18 consecutive patients underwent LESS-DN through an intra-umbilical novel multi-channel port. The kidney was extracted through a slightly extended umbilical incision in all cases. A contemporary matched-pair cohort of 18 patients undergoing standard LDN was selected for comparison.

**Results:** Baseline demographics, operating time, blood loss, and hospital stay were comparable between groups. No patient in the LESS group was converted to standard laparoscopy. Mean warm ischemia time was longer in the single-port group (3.2 vs 6 minutes, p=0.0001); however, allograft function was immediate and comparable between groups. Analgesic requirements (102 vs 100 mg) and mean visual analog score at discharge (1.5 vs 2.6) were statistically equivalent. Patient-reported convalescence was faster in the single-port group, including days on oral pain medication (18 vs 4, p=0.009), days off work (40 vs 14, p=0.003), and days to 100% physical recovery (85 vs 25, p=0.005). Regardless of laparoscopic approach, patient global satisfaction with kidney donation and willingness to recommend their procedure to others were favorable and equivalent between groups.

**Conclusions:** Matched-pair comparison between LESS and standard LDN suggests the single-port approach is associated with quicker convalescence. Early allograft outcomes are comparable. Although single-port LDN is associated with longer warm ischemia times in this initial series, this is expected to decrease with experience.
Section 6

Female Urology/
Voiding Dysfunction
Long-term Follow Up of Voiding Parameters and Surgical Recurrence after Urethral Diverticulectomy

Michael Ingber, Farzeen Firoozi, Kamran Sajadi, Christina B. Ching, Howard B. Goldman, Courtenay Moore, Sandip Vasavada, Raymond Rackley

Introduction and Objectives: Studies evaluating outcomes after urethral diverticulectomy are limited by small numbers and short-term follow-up. We present the largest reported cohort of women with urethral diverticula (UD) and evaluate both surgical outcome and long-term voiding parameters after this surgery.

Methods: All women who underwent surgery for UD at our institution over a twelve year period (1996-2008) were mailed surveys. These included a one-page health questionnaire detailing any further surgeries on their urethra or bladder, as well as number of urinary tract infections (UTI), and dysuria. Additionally, these women were sent the Urogenital Distress Inventory (UDI-6). Women not responding to the mailed survey were telephoned. For purposes of determining surgical recurrence, charts of women not responding to the mailing or telephone survey were reviewed. Women having an eventual diagnosis of carcinoma associated with the UD were excluded.

Results: 123 women were identified as having a urethral diverticulectomy during the study period. Of these, 13 (10.5%) had an eventual recurrence requiring repeat surgical excision. On univariate analysis, patients with a proximal UD, multiple UD, or prior pelvic or vaginal surgery (excluding prior urethral diverticulectomy) were more likely to have a failure (p=0.02, 0.03, <0.001, respectively). On multivariate analysis, only prior pelvic or vaginal surgery predicted surgical failure (Odds Ratio 9.54, p<0.001).

Sixty-two women (50.4%) responded to our survey. Mean follow-up in this group was 50.4 months. Twenty-five (40.3%) had a UTI within the last year, with 15 (24.2%) women having 3 or more UTIs over the past year. 17 (27.4%) had persistent pain or discomfort with urination. Mean (standard deviation) total UDI-6 was 5.2 (4.5) in patients with a surgical success, vs. 8.5 (5.2) in failures, p<0.05.

Conclusions: To our knowledge this represents the largest study with the longest follow-up after surgery for UD. Patients with prior pelvic surgery must be counseled appropriately with regards to recurrence risk. Additionally, over the long-term, many of these women have persistent voiding dysfunction and persistent symptoms, including UTI and dysuria.
Introduction and Objective: Patients with neurogenic bladders due to multiple sclerosis, spinal cord injury, or other neurologic disease are often dependent on intermittent catheterization to empty their bladders completely. Over time many of these patients lose their fine motor skills and are no longer able to catheterize per urethra. Some of these patients undergo urinary diversion and are prone to a multitude of complications. A suprapubic tube may be an alternative; however, the chronic indwelling catheter may lead to infections, stone formation or leakage due to bladder spasm.

Methods: We present our experience with the Rackley Continent Neo-Urachus™ for urinary diversion. An overview of the procedure is given. The procedure is described in detail, including creation of a bladder flap similar to a Boari flap. This flap is rotated anteriorly and tubularized around a catheter which will exit the skin surface. The continence mechanism is created by a rectus crossover technique which is also shown.

Results: This procedure provides patients with a conduit for suprapubic catheterization that remains continent due to the rectus crossover. Additionally, the procedure is completely extraperitoneal and therefore avoids bowel complications commonly seen after traditional intraperitoneal urinary diversion procedures.

Conclusions: The Rackley Continent Neo-Urachus™ for urinary diversion is a safe and effective procedure for urinary diversion in the neurogenic patient. A multi-center trial is currently underway to study this technique with respect to patient outcomes and satisfaction.
Force of Stream After Sling Therapy (FAST): Midterm Analysis of Safety and Efficacy of Rapid Discharge based on Subjective Report

Michael Ingber, Farzeen Firoozi, Courtenay Moore, Raymond Rackley, Sandip Vasavada, Howard B. Goldman

Introduction and Objectives: Currently there are no data to support recommendations on when to discharge patients after midurethral sling surgery (MUS). Many physicians continue to base discharge timing on post-void residual volumes (PVR) and some routinely leave catheters in overnight. Our objective was to evaluate the safety of a protocol using patient subjective reporting of force of stream (FOS) to minimize both length of stay (LOS) and need for catheter placement.

Methods: Fifty-six consecutive women undergoing MUS without concomitant pelvic surgery were prospectively enrolled. Within one hour of arrival to the recovery area, the bladder was filled with 300mL of saline and the catheter removed. Patients were prompted to void within 15 minutes of filling, and, if unable, were given one hour to try to void. Patients rated their post-operative FOS on a visual analog scale (VAS) compared to their baseline. If their subjective report of FOS was greater than 50% compared to their baseline FOS they were discharged immediately. Only women who were unable to void, or who rated FOS <50% and had a PVR>500mL had a catheter placed. Patients were telephoned within one week of surgery and all women completed follow-up at 4-6 weeks, where any visits to the emergency room (ER) or office for acute voiding dysfunction or UTI were noted. LOS was defined as the time from the completion of surgery to discharge.

Results: 56 women completed the study protocol. Three (5.4%) women were unable to void and had a catheter placed. These women all passed a subsequent voiding trial within 48-72 hours. Per protocol all other women were discharged without a catheter. PVRs ranged from 0-427 mL in these women and 11 (19.6%) voided less than half of what had been instilled. Despite our large number of women who were sent home without a catheter (94.6%), none returned to the ER or office for acute voiding dysfunction. Mean LOS was 152 minutes for the entire group.

Conclusions: All patients who report a post-op FOS of >50% can be safely and rapidly discharged after uncomplicated MUS. Scanned PVRs do not add much value in women who are able to void postoperatively, and excessive LOS due to multiple PVR checks after sling surgery may only delay discharge. Following our protocol, all patients can be discharged home within 3 hours after surgery.
Obstructive Symptoms with Concomitant Stress Incontinence: Improvement in Symptoms After Midurethral Slings

Michael S. Ingber, Farzeen Firoozi, Sandip P. Vasavada, Courtenay K. Moore, Raymond R. Rackley, Howard B. Goldman

Introduction and Objective: The midurethral synthetic sling is commonly utilized to treat stress urinary incontinence (SUI) in women. However, some women may have additional symptoms which complicate the decision on whether or not to offer this type of therapy to patients. Specifically, women with obstructive-type complaints (weak stream and incomplete emptying) with concomitant incontinence represent a challenging subset to treat. Many are hesitant to place a sling in these women, as it might exacerbate their obstructive symptoms. We present our prospective data on women with obstructive symptoms based on the American Urological Association Symptom Score (AUA-SS) and Quality of Life (AUA-QOL) questionnaire undergoing sling surgery for stress urinary incontinence (SUI).

Methods: Women undergoing isolated midurethral sling surgery for SUI were enrolled. Women had a post-void residual (PVR) checked and completed an AUA-SS, Urogenital Distress Inventory (UDI-6), and Incontinence Impact Questionnaire (IIQ-7) preoperatively and at a follow-up visit at one month. Women with an AUA-SS of 20 or more represented the “severe” symptom group. Any episodes of acute urinary retention were noted within the first month.

Results: Twenty-six women with severe symptoms based on the AUA-SS underwent sling surgery and were seen at follow-up. Mean AUA-SS in this group was 24.6 (range 20-33). Twenty-three women had urodynamic data available. Of these, 9 (39%) were obstructed based on urodynamic criteria. Thirteen (50%) had a retropubic sling and 13 (50%) had a transobturator sling. Three (11.5%) required catheter drainage for 3 days for failed voiding trials. Mean PVR was 25mL (range 0-199mL) preoperatively, 132mL (range 2-425mL) at the time of voiding trial, and 47mL (range 0-244mL) at the postoperative visit. The postoperative AUA-SS decreased by a mean of 15.8 (p<0.0001) with individual improvements in each of the seven questions (p<0.01 for each). Mean AUA-QOL was 5.0 (unhappy) preoperatively and 1.7 (pleased - mostly satisfied) postoperatively (p<0.0001). After sling surgery total UDI-6 decreased by a mean of 9.2 (p<0.0001) and total IIQ-7 decreased by 10.9 (p<0.0001).

Conclusions: Women with SUI and concomitant obstructive-type symptoms can have midurethral synthetic slings placed in the transobturator or retropubic approach safely. Interestingly, many of these obstructive symptoms disappeared after placement of the sling.
Percutaneous Tibial Nerve Stimulation

Michael Ingber, Farzeen Firoozi, Howard B. Goldman, Courtenay Moore, Raymond Rackley, Sandip Vasavada

Introduction and Objective: Percutaneous Tibial Nerve Stimulation (PTNS) has been utilized as an office-based procedure for the treatment of urinary urgency, frequency, and urge incontinence throughout the past decade. Safety and efficacy of this therapy has been shown in multiple clinical studies. Nevertheless, many practitioners are not familiar with the procedure and its applications.

Methods: We provide the viewer an opportunity to see how the technology is applied at our institution. An overview of PTNS is presented. The placement of the 34-Gauge needle electrode at the posterior tibial nerve is shown, and stimulation parameters are described.

Results: We utilize PTNS as first and second-line therapy in men and women with refractory overactive bladder symptoms. Adverse events are rare and typically are related to insertion of the needle electrode. Typically, patients undergo weekly 30-minute sessions for twelve weeks. Subsequent sessions are determined by the physician.

Conclusion: Percutaneous Tibial Nerve Stimulation is easy to perform in the outpatient setting. This technology is an alternative to more traditional sacral neuro-modulation, with no need for anesthesia and less risk of complications.
Single-Port Transvesical Excision of Foreign Body

Michael Ingber, Farzeen Firoozi, Mihir Desai, Robert Stein, Courtenay Moore, Howard Goldman, Sandip Vasavada, Raymond Rackley

Introduction and Objective: Managing foreign bodies of the bladder can be technically challenging. Often times, these foreign bodies are a result of trocar passage through the bladder during midurethral sling and prolapse procedures. Attempts at cystoscopic removal of mesh from midurethral slings may leave residual mesh within the detrusor, which may cause future stone formation, infections or irritable voiding symptoms. Traditionally, removal involves opening the bladder, removing the mesh under direct vision, and placement of a suprapubic tube. We present a novel technique of foreign body removal of the bladder through a single laparoscopic port placed directly into the bladder.

Methods: The Triport (Advanced Surgical Concepts, Bray, Ireland) allows simultaneous passage of three instruments through a single laparoscopic port. The port is placed directly into the bladder after it is maximally filled. Using flexible instruments designed for use with the single-port system, mesh material is grasped and dissected through the detrusor. Once all foreign material is removed, hemostasis is confirmed and the port is removed. The small cystotomy is less than 2cm and can be closed under direct vision.

Results: Patients treated with this novel approach can be managed in the outpatient setting. No suprapubic catheter is necessary, and foley drainage for 1 week is sufficient.

Conclusions: Removal of foreign bodies of the bladder through a single transvesical laparoscopic port is a technically feasible procedure and offers excellent visualization especially near the bladder neck, where mid-urethral sling material is often found. This approach offers patients a minimally invasive approach through a single small incision.
Risk of Infection after Mid-Urethral Sling Surgery: Are Postoperative Antibiotics Necessary?

Mia Swartz, Bradley Gill, Jianbo Li, Raymond Rackley, Sandip Vasavada, Howard Goldman

**Introduction:** We reviewed our infection experience using single-dose preoperative antibiotics during mid-urethral sling surgery.

**Methods:** A retrospective study was performed of all mid-urethral sling surgery from 2004-2008 performed by one surgeon (HG) who uses single-dose preoperative antibiotics only (controls), and two surgeons (RR and SV) who also prescribe three days of postoperative antibiotics (cases). A chart review and telephone survey were performed to evaluate postoperative infections and adverse events related to antibiotic use.

**Results:** We identified 103 cases and 116 controls; the telephone survey response rate was 80.6% and 81.9%, respectively. The occurrence of postoperative urinary tract infection in cases and controls was 6.8% and 9.5%, respectively (p>0.05). There were no vaginal or skin infections in either group. Adverse events related to antibiotic use were more common among those that received postoperative antibiotics (7.8% vs 0.9%, p=0.01).

**Conclusion:** The occurrence of UTI does not appear to be lower when postoperative antibiotics are prescribed. However, adverse events associated with antibiotic use are increased. These findings do not support continued use of postoperative antibiotics, and as such, we have abandoned this practice.
Decrease in Radiation Exposure during Fluoro Urodynamics (FUDS)

Courtney Lee, Kevin Wunderle, Sandip Vasavada, Raymond Rackley, Courtenay Moore, Howard B. Goldman

Introduction and Objectives: In accordance with the As Low As Reasonably Achievable (ALARA) principle for radiation, our institution initiated a quality assurance protocol to decrease the amount of fluoroscopy during FUDS. We compare the radiation emitted from the fluoroscopic unit before and after the protocol to evaluate whether the decrease in fluoroscopic images translates into a significant reduction in radiation.

Methods: The quality assurance protocol defined 5 points for fluoroscopic images: a scout image prior to the exam, during the filling phase, during a valsalva maneuver or cough, during voiding, and an optional image while voiding without catheter (if patient was unable to void with catheter). Additional imaging was allowed according to the discretion of the physician performing the FUDS. All fluoroscopic images were performed using the Seimens Arcadis Avantic fluoroscopic unit with the patient seated in the anterior-posterior position. The number of spot films, fluoroscopy time, cumulative dose area product (DAP), and cumulative air kerma (AK) from FUDS performed by our division during the 3 months prior to the conceptualization of the quality assurance protocol were compared to FUDS performed by our division after the initiation of the protocol.

Results: Fifty-four FUDS performed in the 3 months prior to the conceptualization of the protocol were compared to 24 FUDS that were performed after the initiation of the protocol. There was no significant difference in age, sex, body mass index, and diagnosis. The mean number of spot films recorded before and after the quality assurance protocol was 11.19 and 4.92 respectively (p<0.001). The mean fluoroscopy time decreased from 40.94 seconds to 9.21 seconds per procedure (p<0.001). The mean DAP decreased from 518.90 mGycm2 to 105.60 mGycm2, and the mean AK decreased from 15.48 mGy to 2.95 mGy (p=0.001 and p = 0.001 respectively).

Conclusions: Our quality assurance protocol significantly decreased the amount of fluoroscopy time, DAP, and AK during each FUDS. This may be secondary to adherence to the protocol or staff awareness of radiation exposure during FUDS. Further study using a phantom will be required to determine the decrease in actual radiation exposure using our protocol.
Sacral Neuromodulation for Refractory Overactive Bladder: Initial Insight into Effects on Female Sexual Function

Bradley C. Gill, Mia A. Swartz, Courtenay K. Moore, Howard B. Goldman, Raymond R. Rackley, Sandip P. Vasavada

Introduction and Objectives: Sexual function (SF) has been hypothesized to improve following sacral neuromodulation (SNM). A comprehensive description of baseline sexual and relationship characteristics in a sample of refractory overactive bladder-wet (OAB-w) patients undergoing SNM was described previously. This study investigates the changes seen in SF at the first office visit following device implantation.

Methods: Patients undergoing SNM for OAB-w were prospectively enrolled from 2008 to present. Baseline SF was determined using 2 validated questionnaires, the Sexual Health Questionnaire (SHQ) and Female Sexual Function Index (FSFI). Follow-up visits utilized the same surveys to assess changes with treatment. Results from the SHQ were used to determine relationship status, impact of incontinence on SF, sexual activity status (inactive versus active), and reasons for sexual inactivity. Patients who reported sexual inactivity due to disability, partner problems, or age were excluded from analyses due to the need for repeated measures.

Results: A total of 33 women, median age 60[Q1-Q3: 48-69] years, underwent stage 2 implantation. Of a total 31 follow-ups, 8 women, age 54[47-63] years, were sexually active and completed both baseline and follow-up surveys at 3.2[3.0-3.7] months. Results from the SHQ showed an increase from 2(25%) to 7(88%) in the number of women who were “seldom” or “never” incontinent during intercourse. Likewise, an increase from 3(38%) to 7(88%) patients felt their incontinence “seldom” or “never” restricted sexual activity. Lastly, an increase from 3(38%) to 7(88%) women felt their orgasms were the “same” or “more” intense than before, with a reduction from 5(63%) to 1(13%) noting orgasms were “less” or “much less” intense than before. FSFI results also showed improvement. Total FSFI score improved significantly from 21.9 to 24.7 (p<0.03). The arousal sub-score improved significantly from 3.7 to 4.5 (p<0.05) and satisfaction sub-score improved from 3.8 to 4.6 (p<0.04). None of the sexually inactive women became sexually active after implantation, but 2 women became inactive following implantation.

Conclusions: As evidenced by improvements on both the SHQ and FSFI, the effects of SNS on OAB-w women support the clinical hypothesis that SNS improves SF. However, this conclusion is applicable only to those who are sexually active at baseline.
Section 7

Male Voiding Dysfunction
Patient-Perceived Effectiveness of the AdVance Sling in Post-Prostatectomy Incontinence

Bradley C. Gill, Mia A. Swartz, John B. Klein, Raymond R. Rackley, Sandip P. Vasavada, Drogo K. Montague, Kenneth W. Angermeier

Introduction and Objective: Various options exist for treating post-prostatectomy incontinence (PPI), including the recently introduced AdVance transobturator sling. Our primary aim was to assess the patient-perceived effectiveness of this procedure using a validated global response instrument. Our secondary objective was to describe perioperative complications.

Methods: Medical records of all patients who received an AdVance sling at our institution were reviewed. Data collected included demographics, urologic history, and pad use. A follow-up telephone survey included the Patient Global Index of Severity (PGI-S) and previously validated Patient Global Index of Improvement (PGI-I). The survey also included questions regarding pad use, recommending the surgery, and postoperative complications. A PGI-I response of “very much better” or “much better” without subsequent PPI treatment was classified a subjective success. In keeping with prior studies, we defined objective success as dry or a reduction to 1-2 pads daily.

Results: A total of 27 patients (mean age 64) received the sling at a mean of 55 months post-prostatectomy. PPI severity ranged from 1 to 12 pads daily and etiology consisted of 26 radical retropubic and 1 laser prostatectomy. Prior PPI treatments included penile clamp (15%), collagen injection (11%), artificial sphincter (7%), and electrostimulation (7%). According to the chart review, there were 18 (66%) objective successes. Follow-up calls were placed at a mean of 9.5 months post-sling; 25 (93%) patients were contacted. The survey data showed a mean reduction from 4.3 to 1.7 (p<0.0001) pads daily and 13 (48%) subjective successes. Of the subjective failures, 7 (50 %) were “a little better”, 3 (21%) had “no change”, and 1 (7%) was “a little worse.” Six patients (86%) that were “a little better” stated they would “maybe” recommend the sling and 3 (75%) that answered “no change” or “a little worse” would not. Patient perceived improvement (PGI-I) correlated highly with PGI-S response (p<0.0001). There were no major perioperative complications. Two patients (7%) developed urinary retention that resolved at 13.9 and 21.7 weeks. Three (11%) cases pursued further treatment with bulking agents.

Conclusions: The AdVance sling is a minimally invasive PPI treatment with low complication risk. As with many treatments for incontinence, there can be lack of agreement between objective measures of improvement and patient-perceived efficacy. Therefore, patients should be carefully counseled prior to pursuing this procedure.
Single-Port Transvesical Enucleation of the Prostate (STEP)

Mihir M. Desai, Rene J. Sotelo, Oswaldo J. Carmona, David Canes, Aron Monish, Juan C. Astigueta, Robert J. De Andrade, Calkins Herrera, James Ulchaker, Mahesh Desai, Daniel A. Shoskes, Khaled Fareed, Inderbir S. Gill

Introduction and Objective: We present the initial series of single port transvesical enucleation of the prostate (STEP) in 22 patients with large volume benign prostatic hypertrophy.

Methods: Between April and September 2008, 22 men underwent STEP using a transvesical approach under pneumovesicum. A multichannel single trocar was introduced percutaneously into the bladder through a 2.5 cm skin, fascial and bladder incision under simultaneous cystoscopic vision. The adenoma was enucleated in its entirety transvesically under laparoscopic visualization using standard and articulating laparoscopic instrumentation. The adenoma was extracted through the vesicotomy.

Results: The surgery was technically feasible in all cases. The average age was 69 years old (57–89 years-old); the operative time was 106 minutes (45 - 360 min); estimated blood loss was 422 cc. (50–1500 cc). Digital assistance for enucleation was required in 42%. Complications included postoperative bleeding requiring reoperation in 2 cases, and bowel injury in one case from trocar injury. The hospital stays averaged 3.2 days (range 1–10), and the Foley catheter was removed on day 7 (range 4–12). The size of the incision was not more than 3 cm. The average adenoma specimen weight was 61.4 grams (range 36.5–212 g). AUA symptom score decreased on average from 19 to 3, and maximum flow rate from 8 to 40.

Conclusions: Our initial series of transvesical single port laparoscopy for simple prostatectomy is encouraging, and the technical problems are progressively being solved. The procedure is technically feasible and reproducible. Longer follow up and experience in larger series will help determine the role of STEP in the treatment of BPH.
Section 8

Infertility
Correlation of Testis Pathology and Maturation Arrest Subgroups with Follicle Stimulating Hormone Levels

Kashif Siddiqi, John Kefer, Lynn Schoenfield, Howard Levin, Ahmed Ragheb, Kamran P. Sajadi, Edmund S. Sabanegh

**Introduction and Objective:** Patients with azoospermia present a difficult diagnostic and therapeutic challenge for the urologist. In particular, those men with testis failure are often beset with both psychological stress from their diagnosis, as well as the financial burden of numerous diagnostic tests and repeated biopsies in an effort to find sperm. Studies analyzing results of micro-tese and testicular sperm extraction suffer from small sample size, and a lack of standardization. Often, patients need to undergo a diagnostic biopsy as well as a separate fresh and timed micro-tese depending upon the pathology results. In this study, we sought to correlate testis pathology, particularly subgroups of maturation arrest (MA), with levels of follicle stimulating hormone (FSH).

**Methods:** Institutional review board approval was obtained for this retrospective analysis. A total of 155 consecutive patients with testis biopsies from 1995 to date was the initial cohort. Of these, 109 patients underwent diagnostic biopsy for infertility, and were included in the study. Of these, 78 patients were reviewed by our pathologist to confirm and sub-classify the categories of maturation arrest. Developmental arrest at the level of the primary spermatocyte was deemed early maturation arrest, whereas arrest at secondary spermatocytes was called late maturation arrest. These groups were further subdivided into complete and incomplete arrest based upon the presence of elongated spermatids in the specimen. Patients with active spermatogenesis on biopsy were used as controls.

**Results:** A total of 32 patients had a pathologic diagnosis of germ cell aplasia, and the mean FSH levels were 22.0, significantly higher than the FSH levels of all other pathologies (p <0.0001). Although the mean FSH for early complete maturation arrest (n = 15) was elevated compared to early incomplete (n = 5; 11.3 vs. 10.9) this difference did not reach statistical significance (p = 0.57). Similarly, no significance was found in the difference between late, complete MA (n = 3) compared with late, incomplete MA (n = 6, p = 0.87). In comparing early and late maturation arrest, there was again a difference in the mean FSH levels (11.2 vs. 8.15) however, this did not achieve statistical significance (p = 0.37). Finally, although a difference was noted between early maturation arrest and the control group (11.2 vs. 7.42), this also did not reach statistical significance (p = 0.23).
Conclusions: In our study, although there was a difference noted in mean FSH levels between early and late maturation arrest, this difference did not reach statistical significance. Our very small study group is likely a significant contributor to the lack of significance, although the wide ranges in FSH levels also contribute to this finding. Moreover, contrary to published dogma, there was no observed difference in the FSH levels of early maturation arrest compared to controls, although this difference did not reach statistical significance. We conclude that based upon this study, FSH levels are not useful in predicting the classification of maturation.
Pretreatment Sperm DNA Fragmentation Index (DFI) in Cancer Patients and its Relationship to Postcryopreservation Motile Sperm Concentration (PCMSC) and Sperm Motility (PCSM)

Ahmed M. Ragheb, Reda Z. Mahfouz, Islam A. Ghoneim, Edmund S. Sabanegh

Introduction and Objective: Fertility is an area of particular concern to young cancer survivors owing to the substantial improvement in cancer survival rates rendering characterization of semen quality of paramount importance. While the data on the pretreatment effect of cancer on sperm genomic integrity remains scarce and inconsistent, we studied the impact of various types of cancer on sperm function and sperm DNA integrity.

Methods: 66 cryopreserved samples of 34 cancer patients: testicular cancer (n=25), Hodgkin’s disease (n=14), non-Hodgkin’s disease (n=8) and other neoplasm (n=19) were analyzed. We examined both the general impact of malignancy as well as the specific influence of tumor type on semen quality (concentration and motility), and sperm DFI using terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay. In addition to the effect of cryopreservation on sperm motility, we analyzed the relationship between semen sperm quality and DNA damage. Results were ultimately compared to the results of 10 healthy donors as controls.

Results: Average age was 28.3 years (15-53). Mean PCMSC and PCSM of cancer group (7.4 ± 8.1 M/mL and 25.1 ± 14.3 % respectively) were not significantly distinct from those of controls (6.8 ± 6 M/mL and 24.1 ± 11.8 % respectively) (p= 0.78 and 0.8 respectively). In contrast, different tumor types showed significant differences among both parameters (p= 0.004 and 0.01 respectively). Testicular cancer patients demonstrated an exclusively significant decline in PCMSC compared to other tumors (p=0.0004) as opposed to sperm PCSM and DFI. Cancer patients had a significantly higher mean for DNA fragmentation levels (39.3 ± 16.8 %) compared to controls (26.9 ± 10.9 %) (p= 0.007). DFIs were comparable among the various cancer types (p= 0.2). Mean sperm motility declined significantly after cryopreservation in all population (>50%, p<0.001). DFIs, PCMSC and PCSM demonstrated a weak inverse correlation.

Conclusions: Cancer causes a significant increase in levels of sperm DNA damage regardless of type of tumor. PCMSC and PCSM are significantly affected by tumor type. Testicular cancer has an exclusive adverse effect on sperm concentration. Cryopreservation similarly decreases sperm motility in cancer versus healthy donors as controls.

continued
males. Sperm DNA damage infirmly correlates with low sperm motility. Our findings derive importance from the potential hazardous effects of impaired sperm chromatin on male fertility and offspring welfare.
Section 9

Bladder Cancer
Gender Differences in Bladder Cancer Survival Between African-American Men and Women

Kripa Kavasseri, B. Dimmer, S.J. Jones, N. Dhar

Introduction: Our study evaluates the gender differences and trend in urothelial bladder cancer (BC) survival between African American women and men compared over two decades.

Methods: Using Surveillance, Epidemiology, and End Results data, trends in 5 year BC survival between 273 patients (67 women, 206 men) with localized BC diagnosed between 1985–1987 were compared to 255 patients (76 women, 176 men) diagnosed between 1995–1997. Log rank analysis was used to make these comparisons.

Results: Between 1985–1987, women had a 5 year BC survival of 67% compared to 66% for men (p = 0.8560). Between 1995–1997, women had a 5 year BC survival of 55% compared to 71% for men (p = 0.0117).

Conclusions: This study demonstrates that although between 1985–1987, there was no significant difference in BC survival between African American men and women, a decade later a significant difference was observed. Our findings with regards to African American women are important and necessary to appropriately direct BC detection and education efforts, especially with the finding that prognosis in those diagnosed with bladder cancer appears to have worsened in that duration while prognosis in African American men appears to have improved slightly.
Management of Superficial Bladder Cancer Recurrence

Lauren Marquette, J.S. Jones, Krishnan Venkatesan, Amarnath Rhambhatla, Nivedita Dhar

Objective: In 2007, the AUA published revised practice guidelines for the management of Non-Muscle-Invasive (NMI) Bladder cancer (BC). The purpose of the current study is to get insight into urologists’ compliance with the guidelines when managing patients with Ta-T1G3 or High Grade Bladder BC w & w/o CIS.

Methods: We surveyed 400 urologists using a specially designed survey instrument. Information gathered included type of practice, size of practice, volume of bladder cancer patients being managed, and treatment patterns as they relate to following AUA Guidelines.

Results: Of 400 urologists contacted, 186 (47%) completed a questionnaire and their characteristics are shown in table 1. Treatment preferences for each patient population are shown in table 2. Chi-squared analysis demonstrated no significant difference in practice patterns amongst academic and community urologists for recurrent T1G3 BC w/ and w/o CIS. In addition, contrary to previous publications following the prior guidelines ( Joudi, UROLOGY 62:1083-1088, 2003) there was no significant difference in practice patterns between those who graduated before (23%) and after (77%) 1985.

Conclusions: Studies prior to publication of the 2007 AUA Non-Muscle-Invasive Bladder Cancer Guidelines demonstrated different practice patterns and compliance with the guidelines between academic and nonacademic urologists, as well as between older and younger urologists. In the present era we found no difference between these groups, suggesting improved overall compliance with AUA BC Guidelines.

Table 1. Characteristics of surveyed urologists and their practice

<table>
<thead>
<tr>
<th>Practice Type</th>
<th>Group Size</th>
<th>Annual Vol. of Pts. With Bladder Cancer Seen by Entire Practice</th>
<th>Annual Vol. of Pts. Receiving Intravesical Therapy Treated by Entire Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>13% Academic</td>
<td>21% Small</td>
<td>15% Low (&lt;50)</td>
<td>28% Small (&lt;10)</td>
</tr>
<tr>
<td>(1-3 urologists)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45% Academic</td>
<td>29% Medium</td>
<td>58% Medium (51-100)</td>
<td>60% Medium (10-25)</td>
</tr>
<tr>
<td>affiliated</td>
<td>(4-6 urologists)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>43% Community</td>
<td>49% Large</td>
<td>27% Large (&gt;100)</td>
<td>12% Large (&gt;25)</td>
</tr>
<tr>
<td>Practice</td>
<td>(&gt;6 urologists)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

continued
Table 2. Treatment preference for different subcategories of superficial bladder cancer as determined from urologists responding to survey

<table>
<thead>
<tr>
<th>Subcategory</th>
<th>TUR (%)</th>
<th>TUR + Chemotherapy (%)</th>
<th>TUR + BCG (%)</th>
<th>Cystectomy or Radiotherapy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newly Diagnosed Tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ta-T1 HG</td>
<td>3</td>
<td>16</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Ta HG + CIS</td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Failed Intravesical Chemotherapy x 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ta-T1 HG</td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>T1 HG + CIS</td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Failed Intravesical BCG x 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ta-T1 HG</td>
<td></td>
<td>47</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>T1 HG + CIS</td>
<td></td>
<td>47</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Failed Intravesical BCG x 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ta-T1 HG</td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>T1 HG + CIS</td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

*KEY: TUR = transurethral resection; TUR + Chemotherapy = TUR with intravesical chemotherapy; TUR + BCG = TUR with Intravesical BCG; BCG = Bacille Calmette-Guérin; HG = high grade; CIS = carcinoma in situ*
The Role of Pathology Review of TURBT Specimens in the Modern Era

Michael C. Lee, Howard S. Levin, J. Stephen Jones

Purpose: The value of pathological reinterpretation of tissue slides has long been questioned. At the Cleveland Clinic (CC), subspecialization in genitourinary (GU) pathology began in 2003 and has continued. We evaluate the role of second review on TURBT pathology slides pre- and post- subspecialization and potential impact on patient management.

Materials and Methods: TURBT specimens from 78 bladder cancer patients in 2002 and 116 in 2004 were reviewed. Initial surgical pathology reports from institutions outside CC were compared with review report by a pathologist with GU pathology specialization (HSL). Those cases with differences in diagnosis or staging were then evaluated by a urologist (JSJ) considering current standards of care.

Results: Reinterpretation differed substantially from the initial report in 26/78 (33.3%) in 2002 and in 31/116 (26.7%) in 2004 (p=0.3), resulting in possible impact on patient management in 28.2% (22/78) in 2002 and 23.3% (27/116) in 2004 (p=0.54). In each year, four cases diagnosed with bladder cancer elsewhere were determined to have no malignancy. The majority of discrepancies related to the presence of carcinoma in situ (CIS) in 2002 and to the presence or absence of muscularis propria and/or muscle involvement by carcinoma in 2004.

Conclusions: Second review of TURBT specimens shows differences of interpretation in 26.7-33.3% of the cases sufficient to alter case management. There was no significant difference in the rate of discrepancies pre- and post- GU pathology subspecialization. Referral centers must assume responsibility for establishing their own diagnosis prior to consultation and/or therapy.
Early Outcomes of Radical Cystectomy in Patients with Human Immunodeficiency Virus (HIV) Infection

Islam Ghoneim, Brian Lane, Amr Fergany

Introduction and Objective: Only 15 cases of bladder cancer in the setting of human immunodeficiency virus (HIV) infection have been reported in the literature to date, only one case underwent radical cystectomy. We present a small series of radical cystectomy for urothelial carcinoma in HIV patients.

Methods: A review of our database between 2007-2009 revealed three cases of muscle invasive urothelial carcinoma of the urinary bladder in patients with HIV-AIDS. The cohort comprised one female and two males, with a mean age of 52.6 years. All patients were on highly active antiretroviral treatment (HAART) perioperatively, and all underwent open radical cystectomy with orthotopic neobladder (patient choice) reconstruction.

Results: Patients have been HIV positive for an average of 17 years (14-20y). CD4 counts were low in 2 cases preoperatively; all cases had low counts during first three months postoperatively. HIV viral loads were undetectable in one case preoperatively, with low levels in remaining cases. Mean hospital stay was 7 days. Only minor complications were encountered during the postoperative period: urine leak in one case, vancomycin resistant enterococcal urinary tract infection (1 case), small intra-abdominal collection (1 case), and superficial wound infection in one case. No major complication, reoperation, or perioperative mortality was encountered. At a mean follow-up duration was 17.6 months (9-31m) no patients developed local or distant recurrence.

Conclusions: Muscle invasive bladder cancer in the setting of HIV-AIDS presents a unique medical challenge that urologists may face. HIV positive patients with muscle invasive disease can be safely treated with radical cystectomy and continent diversion. In our small experience underlying HIV disease does not predispose to perioperative complications or early cancer recurrence.
Section 10

Pediatric
Holmium: YAG Laser to Incise Anterior Urethral Valves

Christina B. Ching, Jeffrey S. Palmer

Objectives: Anterior urethral valves (AUV) are rare obstructing lesions of the urethra. Traditionally urethral valves have been incised by an electrocautery and cold knife incision. We report on the use of lasers to perform transurethral incision of AUV.

Methods: All children with AUV incision with a holmium:YAG laser were evaluated. The valves were incised at the points of maximum obstruction. Postoperatively, radiographic confirmation of complete valve ablation was performed. Patients were also monitored for complications including urinary extravasation.

Results: Three children underwent laser incision of AUV. The ages ranged from 1 month to 15.9 years. The patients did not have any intraoperative or postoperative complications, including urethral injury, urine extravasation, or reincision of residual valves.

Conclusions: These cases demonstrate that the holmium:YAG laser can be used safely and efficaciously to incise AUV. Further experience is necessary using this technique for this rare condition.
Lymphatic-sparing Laparoscopic Varicocelectomy: Safe and Effective

Christina B. Ching, Jeffrey S. Palmer

Objectives: Complications associated with open and laparoscopic varicocelectomy techniques include varicocele recurrence and hydrocele formation. We determined the effectiveness and safety of lymphatic-sparing laparoscopic varicocelectomy in the pediatric population.

Methods: We evaluated all children less than 18 years of age undergoing laparoscopic varicocelectomy for grade 3 varicoceles. A three-port technique is used with one infraumbilical port and one port in the midclavicular line bilaterally at the level of the umbilicus. An incision is made in the posterior peritoneum over the spermatic cord vessels. The vessels are dissected away from the lymphatics with minimal manipulation, and then the artery/veins are double ligated with clips and transected. Patients are monitored postoperatively for varicocele recurrence and hydrocele formation. A successful varicocelectomy is defined as no varicoceles palpable in the standing position with Valsalva.

Results: Forty-eight boys between the ages of 10.0 and 17.6 years of age underwent laparoscopic varicocelectomy. No patient needed to be converted to an open varicocelectomy. All patients underwent successful varicocelectomy. No postoperative complications occurred including varicocele recurrence, hydrocele formation, infection, or testicular atrophy after at least 6 months of follow-up.

Conclusions: Lymphatic-sparing laparoscopic varicocelectomy is a safe and effective technique to treat varicoceles. Postoperative varicocele recurrence and hydrocele formation were not noted.
Section 11

Reconstructive Surgery
The Cleveland Clinic Experience with Adult Hypospadias Patients Undergoing Repair: Their Presentation and a New Classification System

Christina B. Ching, Hadley M. Wood, Jonathan H. Ross, Kenneth W. Angermeier

**Introduction and Objective:** While hypospadias is one of the most common genital urinary congenital anomalies, little is known about long-term outcomes both after childhood hypospadias repair and for uncorrected hypospadias. We reviewed our experience with adult hypospadiacs to better clarify their presentation, history, and intraoperative findings. In so doing, we identified a means of categorizing this group to better describe the natural history of this anomaly in adulthood.

**Methods:** A retrospective chart review was performed on adults with hypospadias who underwent urethroplasty at Cleveland Clinic between 1985 and 2009. The charts were reviewed for site of hypospadias, presenting complaint, overall symptoms, history of repair, and type of surgery performed.

**Results:** 55 adult patients between 18 and 72 years of age were identified (mean age 37.8). The majority (90.9%) of patients had an anterior urethral hypospadias (glanular/subcoronal 10.9%, penile/shaft 45.5%, bulbar 34.5%) (Figure 1a). Obstructive or irritative voiding symptoms were the most common presenting complaint (50.9%) and overall symptom (81.8%). Based on their history of repair, we found that patients fit into 3 categories: Category I: true hypospadias cripples; Category II: delayed complications after an initially successful childhood repair; and Category III: no previous repair. The majority of patients were Category I (41.8%); however, 7 patients (12.7%) were Category III (Figure 1b). Balanitis xerotica obliterans (BXO) was more common in this subgroup (42.9% vs. 12.7% overall). The length of strictures among Category III patients with BXO were 3.5, 7, and 8 cm.

**Conclusions:** Adults with hypospadias represent a heterogeneous group. About half of adults with hypospadias have had multiple surgeries (Category I). Interestingly, the majority of adult hypospadiacs presenting with complications have anterior hypospadias and not more proximal disease. Unrepaired hypospadiacs may be at risk for severe stricture disease in adulthood due to BXO.
Renal Auto Transplantation and Pyelovesicostomy for Intractable Metabolic Stone Disease

Alvin Wee, Stuart M. Flechner, Ho Yee Tiong, Rey Littleton, Mark Noble

Introduction: Auto transplantation with pyelovesicostomy is an alternative solution for patients with a heavy metabolic stone burden who may be dependent on narcotics, and need frequent urologic interventions. The natural history of these metabolic stone problems is associated with frequent urinary tract infections and a decline in renal function over time.

Methods: Auto transplantation and pyelovesicostomy were done for six kidneys in four patients with cystinuria (n=5) and uric acid stones (n=1). 5 kidneys with stone burden at the time of surgery that needed bench extraction of residual stones. All patients had a nephrostomy and Foley placed after the procedure. Mean age of 29.6 years old. There were 3 female and 1 male patients. 2 of the female patients have both kidneys treated. All were Caucasians. All patients have prior stone treatments with a mean treatment (which include ESWL and J insertion) of 3-4/year. 2 of the patients have 2-3 episodes of UTI per year which doesn't require hospitalization. All patients have been on narcotics, number with prior ESWL and tubes. Preoperatively the patients had a Serum creatinine mean of 1.08ug/ml (0.7-1.4) and eGFR (aMDRD) 69.75ml/min (59.2-100).

Results: All six kidneys were successfully auto transplanted through 1 midline incisions. Mean follow up of 26 months (12-60 mos) with mean cold ischemia time of 4 hours and 7 minutes. 5 kidneys had a single artery and single vein. Mean hospital stay was 6.3 days. All patients continued to pass stone debris. Only 1 patient on one kidney needed one intervention in one year. All patients were weaned off narcotics by 8 weeks. The same 2 patients continue to experienced UTI but with decrease episode to about 1 per year, of which none require hospitalization. There was no new onset Hypertension. There were no post-operative complications. Serum creatinine were 1, 0.9, and 1.1 mg/dl at 6, 12, 24 months respectively. Mean eGFR were 77.3, 75.1 and 63.25 ml/min at 6, 12, 24 months.

Conclusion: With careful selection, renal auto transplantation with pyelovesicostomy is a reasonable option for patients with metabolic stone burden; which preserves renal function and improves the quality of life by reducing the frequency of subsequent clinical stone events and the requirement for narcotics. Stone Passage continues to occur after pyelovesicostomy. However, it often consists of small granules that are passed spontaneously and cause few symptoms.
Section 12

Basic Science
Effects of Neurotrophin Supplementation on Functional Recovery of the Pudendal Nerve following Simulated Childbirth Injury

Bradley C. Gill, Hai-Hong Jiang, Brian M. Balog, Amy S. Nowacki, Margot S. Damaser

**Introduction and Objective:** Pudendal nerve (PN) injury in childbirth is associated with the development of stress urinary incontinence (SUI). The external urethral sphincter (EUS) upregulates BDNF after pudendal nerve crush (PNC) to facilitate neuroregeneration and functional recovery, but downregulates expression after vaginal distension (VD). Thus, expression following simulated childbirth consisting of VD+PNC is lower than PNC alone. This study investigates the effects of BDNF treatment on PN recovery following simulated childbirth.

**Methods:** Female, virgin, Sprague-Dawley rats weighing 225g underwent 2, 30-second, bilateral PNC. Two osmotic pumps were implanted on the back, containing a saline and rat albumin solution, with or without BDNF (1ug/6ul), in 7 animals each. A catheter was run from the pump and secured at the site of PNC. Additional rats underwent identical PNC and treatment after 4 hours of VD. Lastly, 7 rats underwent sham PNC. After 2 weeks of treatment rats were analyzed with leak point pressure (LPP), EUS electromyography (EMG), and PN electroneurography (ENG). Briefly, the bladder was filled and intravesical pressure recorded by urethral catheter while PN motor branch and EUS potentials were recorded at rest and while the exposed bladder was compressed to induce leakage. Cross sections of the EUS were stained with Masson's trichrome for histological analysis.

**Results:** Compared to sham injury, VD+PNC and PNC had significantly lower EMG amplitude and frequency at baseline and EMG amplitude in the guarding reflex during LPP. LPP after VD+PNC showed a trend toward significance (p = 0.07) with the saline group leaking at a lower pressure than BDNF, while both leaked at a lower pressure than sham. Following VD+PNC, the saline group had significantly lower baseline EMG amplitude and frequency compared to sham while BDNF treatment did not. EMG amplitude and frequency during guarding reflex showed a similar pattern with a trend toward significance (p = 0.06 & 0.08, respectively). EUS histology showed less atrophy and deterioration with BDNF than saline, compared to sham. After PNC only, there were no significant LPP differences with treatment. PNC animals given BDNF showed a small, significant decrease in EMG frequency at baseline compared to sham, while those given saline did not. A similar trend toward significance was observed in PNC baseline EMG amplitude (p = 0.07). Histology showed atrophy and degeneration in PNC compared to sham.

**Conclusions:** BDNF treatment after PNC+VD improves PN functional and structural recovery, but does not after PNC only. BDNF may provide a means of reducing SUI development after childbirth injury.
Effects of Obesity and Type 2 Diabetes on Recovery from Pudendal Nerve Injury in Female Zucker Rats

Hai-Hong Jiang, Bradley C. Gill, Dan Li Lin, Jonathan B. Glaab, Bruce I. Kinley, Margot S. Damaser

Introduction and Objective: Along with childbirth, obesity and Type 2 Diabetes (DM) are risk factors for Stress Urinary Incontinence (SUI). Diabetic peripheral neuropathy and pre-diabetes are also associated with SUI. The ongoing obesity epidemic and related increase in DM incidence highlight the value of understanding their effects on SUI after childbirth. Using a rat model, this study investigated the impact of obesity and DM on pudendal nerve (PN) recovery after crush injury.

Methods: For 10 weeks, female, leptin-resistant, Zucker Diabetic Fatty (ZDF) rats were given low-fat [N=12] or high-fat [N=6] diets and Zucker Lean (ZL) rats received standard feed [N=11]. ZDF rats naturally become obese and only develop DM when given a high-fat diet. Approximately half of each group then underwent 2 consecutive 30 second bilateral PN crushes. Recovery was assessed 4 weeks later with urinary leak point pressure (LPP), PN electroneurography (ENG), and external urethral sphincter (EUS) electromyography (EMG). Specifically, the bladder was filled and intravesical pressure recorded via a supra-pubic catheter while electrodes recorded PN motor branch and EUS potentials at rest and while the exposed bladder was compressed with a cotton swab to induce leakage. Histology was analyzed in additional rats with the same injuries and diets.

Results: At injury, ZL rats weighed 210g on average and had a mean blood glucose (BG) of 104mg/dl, obese rats weighed 392g with 114mg/dl BG, and obese+DM rats weighed 388g with 345mg/dl BG. Uninjured obese+DM rats showed significantly lower ENG amplitude at rest and in the bladder-to-EUS guarding response during LPP than uninjured ZL rats. Trends in ENG frequency were similar. Obese rats had significantly impaired PN recovery compared to ZL rats at rest and with guarding during LPP. All uninjured ZDF rats had significantly lower EMG amplitude at rest compared to uninjured ZL rats. EMG amplitude during guarding with LPP and the magnitude of change from rest to guarding was significantly lower in injured obese+DM rats compared to injured ZL rats. Trends in EMG frequency were similar. There were no significant differences in bladder pressures between any groups. Obese rats showed increased EUS fibrosis compared to lean rats.

Conclusions: A combination of obesity and Type 2 DM was associated with significantly lower PN activity in uninjured animals and impaired EUS guarding response recovery after PN injury. Obesity alone was associated with lower EUS activity and impaired PN recovery. These results suggest obesity may impact sphincter function and nerve recovery, while Type 2 DM may contribute to pudendal nerve dysfunction.
Effects of Electrical Stimulation of the Pudendal Nerve on Expression of Neurotrophins in Onuf’s Nucleus Following Simulated Childbirth Injury

Hai-Hong Jiang, Bradley C. Gill, Levilester B. Salcedo, Paul J. Zaszczurynski, Brian M. Balog, Dan Li Lin, Margot S. Damaser

Introduction and Objective: During childbirth, a combinatorial injury occurs, involving both the urethra and pudendal nerve, which can result in stress urinary incontinence (SUI). We have previously demonstrated that dual simulated childbirth injury, consisting of pudendal nerve crush (PNC) and vaginal distension (VD), results in slowed recovery of both continence function & pudendal nerve function, as well as decreased expression of brain derived neurotrophic factor (BDNF). Electrical stimulation has been shown to upregulate BDNF in motor neurons and facilitate nerve regeneration after injury. In this study, we electrically stimulated the pudendal nerve proximal to the crush site to determine if this upregulates BDNF in Onuf’s nucleus (dorsolateral motoneurons) as a potential treatment to facilitate nerve recovery after childbirth.

Methods: Sprague-Dawley female rats were assigned to 3 groups; dual injury (n=5), sham injury (n=5), and intact control (n=5), respectively. Rats in the dual injury group received 4 hours of VD immediately followed by bilateral PNC. Rats in the sham injury group underwent sham procedures. All rats received 1 hour of electrical stimulation (20 Hz, 0.3mA, 0.1 ms duration) of the left pudendal nerve and sham stimulation of the right pudendal nerve immediately after dual or sham injury. The lumbosacral spinal cord was harvested 2 days after stimulation and was flash frozen, sectioned at L6/S1, and laser dissected to isolate Onuf’s nucleus. BDNF mRNA expression in Onuf’s nucleus was determined by real-time RT-PCR and was normalized to expression of S-18.

Results: Two days after dual injury, BNDP expression in Onuf’s nucleus was significantly decreased in both stimulated and sham stimulated groups compared to that of intact or sham injury. BNDP expression was significantly increased on the stimulated side compared to the sham stimulated side 2 days after dual injury, indicating that electrical stimulation upregulates BDNF expression.

Conclusions: BDNF expression appears to be deficient in Onuf’s nucleus after a dual childbirth simulation injury. Electrical stimulation of the pudendal nerve proximal to the Crush immediately after dual injury upregulated BDNF expression in Onuf’s nucleus, suggesting that it will improve recovery after injury. Future work will be aimed at optimizing and developing electrical stimulation to facilitate recovery of the pudendal nerve after childbirth as a preventative paradigm for SUI.
Increased Apoptosis and Ganglioside GM2 Positivity of Peripheral T Lymphocytes in Patients with Conventional Renal Cell Carcinoma

Matthew N. Simmons, Amy Richmond, Soumika Biswas, Stephen C. Campbell, Brian Rini, Andrew C. Novick, Charles Tannenbaum, James H. Finke

Introduction: Renal cell carcinomas (RCC) produce gangliosides that induce reactive T lymphocyte apoptosis and inappropriate type-1 T cell suppression. This study measured GM2 content and apoptosis in peripheral CD3+ T lymphocytes obtained from patients with conventional clear cell RCC to determine association with disease severity.

Methods: Control subjects (n=10) and patients (localized n=6; disseminated n= 26) with clear cell RCC were included in the study. Peripheral CD3+ T lymphocytes were purified using magnetic bead negative selection. Cells were then stained with anti-CD3 and anti-GM2 antibodies, annexinV, and 7-AAD. Flow cytometric analyses were conducted to quantify annexinV and 7-AAD positivity as well as GM2 positivity and fluorescence intensity. Flow cytometric data were statistically correlated with patient clinical data.

Results: Compared to age-matched healthy controls, patients with both localized and disseminated RCC had higher levels of annexinV+ CD3+ T cells in circulation (5% vs. 20% vs. 29%, respectively; p<0.001). GM2 MFI in the annexinV+ CD3+ T cells from patients with disseminated RCC was 124 compared to 11.5 and 37 in controls and patients with localized disease, respectively (p<0.001). Both elevated annexinV and GM2 positivity correlated with both calculated and observed risk of disease progression (p<0.001).

Conclusions: Levels of GM2 and apoptosis are significantly elevated in circulating CD3+ T lymphocytes, and the magnitude of positivity is directly correlated with RCC disease severity. This suggests that RCC tumors with increased GM2 levels have a more aggressive clinical course, and that measurement of GM2 and annexinV may serve as useful biomarkers to detect high risk disease.
Alpha Melanocyte Stimulating Hormone Analog AP214 Protects Against Ischemia-induced Acute Kidney Injury in a Porcine Surgical Model

Matthew N. Simmons, Vairavan Subramanian, Sebastien Crouzet, Georges-Pascal Haber, Jose R. Colombo Jr., Osamu Ukimura, Søren Neilsen, Inderbir S. Gill

**Purpose:** Alpha-melanocyte stimulating hormone (α-MSH) protects kidneys against ischemic and sepsis-induced acute kidney injury (AKI) in rodents. This study examined efficacy of α-MSH analog AP214 to protect against AKI in higher vertebrates.

**Materials and Methods:** The study was conducted as a prospective blinded randomized placebo-controlled study in 26 pigs. Laparoscopic technique was employed to conduct left nephrectomy, and to induce complete warm ischemia in the right kidney for 120 minutes. AP214 (200μg/kg IV) was administered daily on the day of surgery and for 5 days thereafter, and kidney function was measured for 9 days. Changes in serum creatinine (Scr), estimated GFR, serum C-reactive protein (CRP), and urine IL-18 levels were measured.

**Results:** Mean peak Scr was 10.2 mg/dL and 3.92 mg/dL in the placebo control and AP214 groups, respectively (p< 0.001). Estimated GFR (eGFR) nadir was 22.9ml/min/kg and 62.6 ml/min/kg in control and AP214 groups, respectively (p=0.001). Functional nadir occurred at 72h and 24h in the control and AP214 groups, respectively. eGFR outcome on postoperative day 9 was 118 ml/min/kg in controls vs. 156 ml/min/kg in the AP214 group (p=0.04).

**Conclusions:** A robust renoprotective effect of AP214 was observed. It is anticipated that a similar effect of AP214 may be observed in humans. Future research includes mechanistic studies in pigs and a phase II human clinical trial of AP214 in kidney transplant and partial nephrectomy patient populations.
Successful Intravesical Therapy for Bladder Cancer Utilizing Paclitaxel Containing Nanoparticles

Mary K. Samplaski, Armine Smith, William Larchian, Vinod Labhasetwar, Warren Heston

Introduction: Approximately 70% of bladder cancers are non-muscle invasive and amenable to intravesical therapy. Nanoparticles (NPs) provide an ideal vehicle for localized drug delivery. They achieve rapid intracellular penetration and provide slow, regional release of encapsulated drug. The transferrin receptor (TfR) is overexpressed in bladder cancer cells. Paclitaxel (Tx) has activity against human metastatic bladder cancer and intravesically inhibits superficial murine bladder cancer growth. To optimize NP preparation, we evaluated Tf and poly-L-lysine (PLL) conjugated NP penetration. We then tested Tf conjugated NPs as a vehicle for Tx delivery to bladder cancer cells in a murine model.

Methods: After bladder pretreatment with PLL, orthotopic MBT-2 bladder tumors were induced in C3H/HeJ female mice. Tumors were confirmed sonographically after 14 days. Coumarin-conjugated NPs were instilled intravesically in several groups: with & without PLL pretreatment, conjugated and unconjugated to PLL, and conjugated and unconjugated to Tf. Confocal microscopy of bladders was performed after 1.5 hours of incubation. All subsequent experiments used Tf-conjugated NPs without PLL pretreatment. Cremophor (solvent for Tx) and Tx, Cremophor and saline, saline, and Tx loaded NPs (8 mg/kg) were instilled intravesically for 1.5 hours. Ultrasound was performed every 2 days starting on post-instillation day (PID) 5. Bladders were histologically examined on PID 15.

Results: Tf conjugation led to NP accumulation in the tumors at a higher concentration than normal bladder. PLL conjugation and PLL pre-wash enhanced overall penetration but negated the selective tumor binding.

By PID 5 the Cremophor, Cremophor and saline, and saline groups had developed bladder tumors > 1mm, which progressively enlarged. On PID 5 and 7, tumors in the Tx-NP group were comparatively smaller, 0.682mm and 0.878mm, respectively. By PID 9 tumors in the Tx-NP group were also enlarging (Fig 1). Histology confirmed invasive tumors in all groups on PID 15.

Conclusion: NP conjugation to Tf allows for selective and enhanced uptake of the NP by cancerous cells. A single dose of NP encapsulated Tx suppresses murine superficial bladder tumor growth for up to 7 days. Further studies will focus on repeated instillation of Tx-NPs and increasing the dose of Tx in each NP.

continued
Effect of Taxol-NPs on MBT-2 Cell Growth

Tumor size (mm)

Post-implantation day

-1
0
1
2
3
4
5
6

PID #6
PID #7
PID #9
PID #15

NS
Cremaphor
Taxol-Cr
Taxol-NP
Characterization of XMRV in Prostate Cancer

Eric Klein, Francois Villinger, Jaydip Das Gupta, Cristina Magi-Galluzzi, Seunghee Hong, Beihua Dong, Carvell Nguyen, Christopher Weight, Gerald Schochetman, John Hackett Jr, Robert Silverman

Introduction: Xenotropic Murine Leukemia Related Virus (XMRV) is a novel gammaretrovirus discovered in prostate tissue of men genetically predisposed to prostate cancer. A growing body of evidence suggests a potential causative role in prostate cancer.

Methods: XMRV was isolated and cloned from prostate tissue of unselected men with prostate cancer who underwent radical prostatectomy, with initial identification accomplished by hybridization to a DNA microarray containing conserved sequences of known viruses. Live virus was injected intravenously into rhesus macaques for acute and chronic infection studies. Tissue distribution of XMRV was studied by immunohistochemistry (using a rhesus-derived monoclonal to ENV protein) and RT-PCR based assays. Effect of androgen on XMRV growth was assessed by infection of LnCap and DU145 cells using virus mutated in the androgen response element (ARE) promoter region as control. Chromosomal integration sites were mapped from human prostates using a PCR-based approach that produced biotinylated-ds DNA and isolated by binding to streptavidin-agarose Dynabeads. Expressed prostatic secretions (EPS) were obtained by milking radical prostatectomy specimens. The presence of XMRV in EPS was assessed by qRT-PCR.

Results: 1) preliminary observations suggest that XMRV is detectable by immunohistochemistry in prostate epithelium; 2) XMRV preferentially integrates into host chromosomes at transcriptionally active sites 3) IV injection of XMRV produces viremia and persistent infection in rhesus macaques with a robust immune response; 4) the XMRV promoter contains a consensus ARE; 5) androgen stimulates transcription and replication of XMRV independent of cell growth; 6) XMRV is present in 15% of EPS from unselected cases of prostate cancer; 7) human semen and semen-derived enhancers substantially increase XMRV in both prostate stroma and epithelium.

Conclusions: XMRV is infective in primates and produces an immune response. The presence of XMRV in EPS and effect of semen on infectivity suggest sexual transmission. The presence of an ARE and the stimulatory effect of androgen suggests that XMRV integration into host DNA could impart androgen stimulation on cellular genes, serving as a potential oncogenic mechanism.
Correlation between HER2 Gene Amplification and Protein Expression in Micropapillary Urothelial Cell Carcinoma

Christina B. Ching, Donna E. Hansel

Introduction: HER2 is a well known growth promoting factor in oncogenesis and has been found to be up-regulated in urothelial cell carcinoma, both in regards to gene amplification and protein over-expression. In particular, it has been previously found to be upregulated in a small sampling of micropapillary bladder carcinomas, a rare but highly aggressive variant of urothelial carcinoma (UC). We looked at an expanded number of micropapillary UC samples to confirm these previous findings and directly compare HER2 gene amplification with HER2 protein expression.

Methods and Materials: We evaluated 20 patients who after radical cystectomy were found to have micropapillary UC. Each cystectomy specimen was processed as a tissue microarray (TMA) of 3-4 1.0-mm cores. HER2 gene amplification was determined by chromogenic in situ hybridization (CISH). The centromeric probe CEP17 served as a control and was used to evaluate ploidy. A single reviewer (CBC) evaluated each TMA to determine ploidy as well as HER2 gene expression. Only cells with evidence of at least 2 chromosomes were included upon review. A ratio of HER2 to normal genomic expression of >2.2 was considered evident of increased gene amplification. HER2 protein expression was evaluated after immunohistochemical (IHC) staining by a single reviewer (DEH), and scored according to standard criteria as 0 (no staining), 1+ (faint partial staining in >10% of cells), 2+ (weak staining in >10% of cancer cells), and 3+ (intense staining in >10% of cancer cells). Protein over-expression was considered to be present at IHC scores of 2+ and 3+.

Results: Of the 20 samples, we found that 13 samples demonstrated HER2 protein over-expression (65%). HER2 gene amplification was found in 11/20 (55%) of samples with all 11 samples also demonstrating increased protein expression for a 100% correlation between gene amplification and protein expression. We found 2 samples with protein over-expression without gene amplification although one of the samples had a ratio of 3:2 of HER2 and CEP17 expression. We found that polyploidy was demonstrated in 9/20 (45%) of samples, with 5 of the 9 samples demonstrating increased gene amplification.

Conclusion: We found a positive correlation between HER2 gene amplification and protein over-expression in micropapillary UC. Direct correlation between gene amplification and protein over-expression suggests that HER2-targeted therapy may be successful on the genomic level in patients with this aggressive variant of UC for which there is currently limited therapy. We also found that polyploidy
is found in a little less than half of micropapillary cases with about half of those patients showing evidence of HER2 gene amplification suggesting an inherent genomic instability in these patients.
Section 13

History of Urology
**The History of Urology in Cleveland**

*Kamran P. Sajadi, Howard B. Goldman*

**Introduction and Objective:** Urology in Cleveland, as in the rest of the country, has evolved greatly over the past century. The recent passing of Martin Resnick and Andrew Novick warrants a review of Cleveland’s rich urological history.

**Methods:** We reviewed historical references, the scientific literature, and performed personal interviews with long-standing Cleveland urologists.

**Results:** Frank Weed and George Crile performed the first nephrectomy in Cleveland in 1890 and the first prostatectomies in the early 1900s. Crile’s cousin, William Lower, studied Urology abroad and joined him as professor at Case Western Reserve University (CWRU) before they became two of the four founders of the Cleveland Clinic (CC) in 1921. Harry Goldblatt’s animal experiments in the late ‘30s at CWRU led to our modern understanding of renal hypertension and the development of renal arteriography and renovascular bypass surgery by CC urologist Eugene Poutasse. Both CC and CWRU began training urology residents in 1939, and CC’s first graduate, Charles Higgins, later chaired the department and gained national fame for his “acid-ash” diet for nephrolithiasis. Willem Kolff developed the first “artificial kidney”, and brought dialysis to the United States when he joined CC in 1950. Ralph Straffon initiated CC’s renal transplant program in 1963, and his success with deceased donor transplants popularized this approach nationwide. George Austen, Jr at CWRU had the first successful series of radical prostatectomies in Cleveland, a legacy upheld by his successor Lester Persky. Persky chaired urology at CWRU for nearly 30 years and trained six future university department chairpersons. Resnick succeeded him in 1981, and became one of the eminent figures in urology; an authority on prostate disease, stone surgery, and an advocate of urologic ultrasound. Nationally, he served in many capacities, notably as president of the American Urological Association and Editor of the *Journal of Urology*. Novick trained at CC and became chairman in 1985. He was the consummate renal surgeon; he was adept at renal revascularization and transplantation, but his greatest surgical innovation was the partial nephrectomy. Novick greatly expanded the department, hiring subspecialists, expanding the role of basic science research, and built one of the top resident training programs in the country.

**Conclusions:** Cleveland urology has been not only a microcosm of American urology, but one of the major driving forces for the evolution of the field in the 20th and early 21st centuries. In particular, Resnick and Novick led a golden age of urology for several decades until their untimely passing in 2007 and 2008, respectfully.
Andrew C. Novick, MD: Surgeon, Scholar, and Mentor

Drogo K. Montague, Eric A. Klein, J. Stephen Jones

Introduction and Objectives: Andrew C. Novick died at the age of 60 on October 18, 2008 from complications of lymphoma. This review was undertaken to highlight his contributions to urology.

Methods: Interviews of patients and colleagues as well as a review of his publications form the basis of this review.

Results: Andrew Novick received his medical degree from McGill University in 1972. After 2 years of general surgery training there, he came to the Cleveland Clinic in 1974 for his urology training. He remained at the Cleveland Clinic ever since becoming chairman of the department of urology in 1985. Andy initially specialized in renal transplantation and renovascular surgery, however, he later became best known internationally for his pioneering work in nephron-sparing surgery. Under Andy’s leadership the department became an institute expanding from 7 staff urologists and no research laboratories to 74 staff with 8 research laboratories. The residency changed from 3 residents per year for 5 years of training to 5 residents per year for 6 years of training including a full year dedicated to laboratory research. More than 150 residents and fellows completed their training under Andy’s leadership. Andy was Professor of Surgery and Associate Dean for Faculty Affairs at the Cleveland Clinic Lerner College of Medicine. Andy was the only individual to serve in 3 key positions: President of the American Board of Urology, Chair of its Examination Committee, and Chair of the Residency Review Committee for Urology. He authored 591 peer-reviewed research articles, 104 book chapters, and he edited or co-edited 14 textbooks. The most notable of his many honors are the Ramon Guiteras Award from the AUA, the Barringer Medal from the American Association of Genito-Urinary Surgeons, Honorary Fellowships in the Royal College of Surgeons of Ireland and the Canadian Urological Association, and the St. Paul’s Medal from the British Association of Urological Surgeons. Andy lived to see the fulfillment of his dreams, the dedication on September 12, 2008 of the Glickman Tower, the new $128 million 10 story outpatient facility for the Glickman Urological and Kidney Institute.

Conclusions: Andrew C. Novick was a giant on whose shoulders many stand.
Andrew C. Novick – The Legend in Urology

Gaurang Shah, Luay P. Susan

Introduction and Objective: To outline the life and career of Andrew C. Novick (1948 - 2008), a presetting pioneer in nephron sparing surgery and extracorporeal kidney surgery.

Methods: The historical literature review including papers published by Dr. Novick.

Results: Andrew C. Novick was born in 1948 in Montreal, Canada. He attended McGill University Medical School at Royal Victoria Hospital in Montreal. In the 1974, he left Canada and joined as urology resident at the Cleveland Clinic (CC). After finishing his training, he joined as staff urologist at CC in 1977. He pioneered reconstructive renal surgery and extracorporeal kidney surgery for repairing complex kidney disorders. He accumulated the largest experience in nephron sparing surgery and popularized it throughout the world. In 1985, he was appointed as Chairman of the Department of Urology at CC. Dr. Novick’s goal was to achieve excellence in patient care, education and research (Three pronged approach). Under his leadership, the urology department grew to 40 residents/ fellows, 74 physicians and scientists and 7 research labs (e.g. transplant biology, prostate cancer, kidney cancer, andrology, urothelial biology, neurology and minimally invasive therapy). He established Glickman Urological and Kidney Institute to better serve its growing patient population, teach the next generation of urologists and promote world-class research at CC. He edited or co-edited 14 urological textbooks including Campbell-Walsh Urology. He served as a Visiting Professor at 136 academic medical centers throughout the world. He authored 591 scientific papers, 104 book chapters. Dr. Novick served as President of American Urological Association (AUA), President of American Board of Urology/Examination Committee, Chairman of the National Urology Resident Review Committee and Associate Dean for Faculty Affairs at Cleveland Clinic Lerner College of Medicine. He received numerous career-achievement awards, including the Ramon Guiteras Award from AUA in 2008.

Conclusions: Andrew C. Novick was a visionary, pioneer and legend of modern urology.
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