Society of Urologic Oncology, Inc.

Board of Directors
2005-2006

OFFICERS

President
W. Marston Linehan, MD

Past President
Robert C. Flanigan, MD

President Elect
Ralph W. deVere White, MD

Secretary
Eric A. Klein, MD

Treasurer
Laurence H. Klotz, MD

STANDING COMMITTEE CHAIRS

Bylaws Committee Chair
Jeffrey Maxwell Holzbeierlein, MD

Fellowship Committee Chair
J. Brantley Thrasher, MD

Fellowship Representative
Shomik Sengupta, MBBS, Msurg

Long Range Planning Chair
Paul Henry Lange, MD

Membership Chair
Leonard G. Gomella, MD

NCI Liaison
W. Marston Linehan, MD

Nominating Committee Chair
Judd W. Moul, MD

Publications Committee Co-Chairs
Michael J. Droller, MD
James E. Montie, MD

Scientific Program Chair
Robert Evan Reiter, MD

AUA Representative
Martin E. Gleave, MD

EXECUTIVE COMMITTEE

Members at Large
Gerald L. Andriole Jr., MD
Steven Charles Campbell, MD
Christopher Paul Evans, MD

Liaison Chair
Colin P.N. Dinney, MD

AJCC Representative
Sam S. Chang, MD

EXECUTIVE OFFICE

Executive Director
Wendy J. Weiser

Associate Director
Kelly Cushing

Society of Urologic Oncology, Inc.
Program Committee
2005

Steering Committee
Eric Klein, MD
W. Marston Linehan, MD

Prostate Cancer
Eric Klein, MD*
Ian Thompson, MD
Peter Scardino, MD
Bill Shipley, MD

Bladder Cancer
Colin Dinney, MD*
Yves Fradet, MD
Eila Skinner, MD
Rob Dreicer, MD
Bernie Bochner, MD

Kidney Cancer
W. Marston Linehan, MD*
Arie Belldegrun, MD
Nick Vogelzang, MD
Steve Campbell, MD

Testis Cancer
Joel Sheinfeld, MD*

Y.U.O.
John Davis, MD*

*Topic Coordinators
PLATINUM

Bayer Healthcare Pharmaceuticals Corporation
Oncology Division

Dendreon Corporation

Sanofi Aventis

GOLD

Abbott Laboratories

Antigenics Inc.

SILVER

Valera Pharmaceuticals
Meeting Objectives and Needs
The goal of this meeting is to increase communication among urologic oncology researchers and forge a strong relationship between the National Cancer Institute and the Society of Urologic Oncology, as well as the Society’s members and others interested in urologic oncology.

Following participation in this program, attendees will be able to:

- Identify and describe new methods for neo-adjuvant therapies in prostate cancer.
- Understand and explain advances in molecular therapeutic approaches for the treatment of cancer of the kidney.
- Name and compare methods for treatment of patients with advanced, hormone refractory prostate cancer.
- Identify and assess new biomarkers for screening for bladder cancer.
- Evaluate and depict the advances in radiation therapy of localized and locally advanced prostate cancer.
- Describe the recent advances in minimally invasive therapies for prostate and kidney cancer.
- Become familiar with the molecular genetic basis of kidney, bladder and prostate cancer and how these findings lead to the development of better methods for diagnosis, prevention and treatment of genitourinary malignancies.
- Become informed about and compare the recent advances in surgical treatment of patients with localized bladder cancer.
- Identify and evaluate the role of neo-adjuvant and adjuvant therapies for patients with bladder cancer as well as chemotherapies for patients with advanced bladder cancer.

Joint Sponsorship Accreditation Statement
This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the National Institutes of Health/Foundation for Advanced Education in the Sciences (NIH/FAES) and the Society of Urologic Oncology. The NIH/FAES is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation Statement
The NIH/FAES designates this educational activity for a maximum of 11.25 category 1 credits toward the AMA Physician’s Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Meals
A continental breakfast, lunch, and mid-morning snack on both days of the meeting, and an afternoon snack on the first day are included in the registration fee.

**SUO Dinner at the Hyatt Regency Bethesda**
Friday, December 2, 2005
7:00 p.m. – 10:00 p.m.
Enjoy dinner with friends and colleagues at the Hyatt Regency Bethesda. Registration for this is an additional cost of $60.00 per person ($30.00 for fellows, nurses and residents). You may register for this event and select your choice of entrée at the registration desk. *Business casual attire is appropriate.*
THURSDAY, DECEMBER 1, 2005

6:30 p.m. – 9:30 p.m.  Young Urologic Oncologists’ Dinner: The Surgeon Scientist – Is it Feasible?
Balancing the Academic with the Clinical
Speaker: Robert Uzzo, MD, Fox Chase Cancer Center
Location: Hyatt Regency Bethesda

FRIDAY, DECEMBER 2, 2005

7:00 a.m. – 8:00 a.m.  Continental Breakfast and Registration

8:00 a.m. – 8:05 a.m.  Introduction
W. Marston Linehan, MD
President, Society of Urologic Oncology
Eric Klein, MD
Program Co-Director

8:05 a.m. – 9:05 a.m.  Bladder Cancer I: New Paradigms for Invasive Bladder Cancer
Moderator: Colin P. N. Dinney, MD – The University of Texas MD Anderson Cancer Center

8:05 a.m. – 8:20 a.m.  Lessons Learned from Targeted Therapy: Applicability to Bladder Cancer
Colin P. N. Dinney, MD – The University of Texas MD Anderson Cancer Center

8:20 a.m. – 8:35 a.m.  New Prognostic Tools Following Cystectomy: International Bladder Cancer Nomogram Project
Bernard H. Bochner, MD – Memorial Sloan-Kettering Cancer Center

8:35 a.m. – 8:50 a.m.  Neoadjuvant Chemotherapy for Muscle-Invasive Bladder Cancer: State of the Art?
Robert Dreicer, MD – The Cleveland Clinic

8:50 a.m. – 9:05 a.m.  Case Presentation
Moderator: Eila Skinner, MD – USC
Panelists: Bernard H. Bochner, MD – Memorial Sloan-Kettering Cancer Center
Colin P. N. Dinney, MD – The University of Texas MD Anderson Cancer Center
Yves Fradet, MD, FRCSC – University Laval/Chirurgie
Robert Dreicer, MD – The Cleveland Clinic
William Shipley, MD – Harvard Medical School

9:05 a.m. – 10:05 a.m.  Testis Cancer
Moderator: Joel Sheinfeld, MD – Memorial Sloan-Kettering Cancer Center

9:05 a.m. – 9:20 a.m.  Serum Tumor Markers and Clinical Decision Making in Low Stage and Advanced Germ Cell Tumors: Current Concepts
James McKiernan, MD – Columbia University

9:20 a.m. – 9:35 a.m.  Mapping Studies, Modified Templates and the Under Treated Retroperitoneum
Joel Sheinfeld, MD – Memorial Sloan-Kettering Cancer Center
9:35 a.m. – 9:50 a.m.  
**Late Relapse of Testicular Cancer**  
Richard S. Foster, MD – Indiana University

9:50 a.m. – 10:05 a.m.  
**Acute and Long-Term Morbidity of Chemotherapy in the Management of Testicular Cancer**  
David Vaughn, MD – University of Pennsylvania

10:05 a.m. – 10:20 a.m.  
**Break**

10:20 a.m. – 10:35 a.m.  
**State of the Art Talk: A Novel Virus Associated With Genetic Susceptibility to Prostate Cancer**  
Eric Klein, MD – The Cleveland Clinic

10:35 a.m. – 12:00 p.m.  
**Prostate Cancer I: Management of Localized Prostate Cancer**  
Moderator: Eric Klein, MD – The Cleveland Clinic

10:35 a.m. – 10:50 a.m.  
**The Case for Intervention – Results and Implications of the Scandinavian Randomized Trial**  
Patrick C. Walsh, MD – Johns Hopkins Hospital Brady Urological Institute

10:50 a.m. – 11:05 a.m.  
**The Case for Active Surveillance with Delayed Intervention – START and the Quarter Million Man Trial**  
Laurence H. Klotz, MD – University of Toronto

11:05 a.m. – 11:15 a.m.  
**Dynamic Contrast Enhanced Magnetic Resonance Scanning (DCE MR) and Magnetic Resonance Spectroscopy (MRS)**  
Daniel Vigneron, PhD – UCSF

11:15 a.m. – 11:25 a.m.  
**Lymphotrophic Nanoparticle Enhanced MRI for Staging of Lymph Nodes in Genito-Urinary Malignancies**  
Shanin Tabatabeai, MD – Massachusetts General Hospital

11:25 a.m. – 11:35 a.m.  
**PET Imaging of the Androgen Receptor**  
Pradeep Garg, PhD – Wake Forest University Medical Center

11:35 a.m. – 11:45 a.m.  
**Does Fluorescence Cystoscopy Improve the Outcome of Patients with Bladder Cancer?**  
H. Barton Grossman, MD – The University of Texas MD Anderson Cancer Center

11:45 a.m. – 12:00 p.m.  
**Discussion**

12:00 p.m. – 1:00 p.m.  
**Lunch**

1:00 p.m. – 1:10 p.m.  
**Huggins Medal Presentation**  
Robert Flanigan, MD – Loyola University Medical School

1:10 p.m. – 1:30 p.m.  
**Huggins Award Lecture: The PSA Dilemma in the Overdiagnosis and Underdiagnosis of Prostate Cancer**  
William Catalona, MD – Northwestern University Medical Center

1:30 p.m. – 2:30 p.m.  
**Prostate Cancer II: Role of Radiation Therapy in the Management of Prostate Cancer**  
Moderator: William Shipley, MD – Massachusetts General Hospital

1:30 p.m. – 1:50 p.m.  
**Definitions of Biochemical Failure after Radiation: Past Problems and Future Solutions**  
Howard M. Sandler, MD – University of Michigan

Continues on next page
1:50 p.m. – 2:10 p.m.  What is the Evidence for Benefit from Radiation After Prostatectomy: The EORTC Phase III Adjuvant Trial  
Hendrik Van Poppel, MD – Katholieke Universiteit Leuven

2:10 p.m. – 2:30 p.m.  Surgical Management of Radiation-Induced Rectourethral Fistulas  
Kenneth Angermeier, MD – The Cleveland Clinic

2:30 p.m. – 3:00 p.m.  Young Urologic Oncologists (Y.U.O.) Podium Presentations  
Moderator: John Davis, MD – Eastern Virginia Medical School

3:00 p.m. – 3:15 p.m.  Break

3:15 p.m. – 4:00 p.m.  Late Breaking Developments I  
Moderator: Ralph W. deVere White, MD – UC Davis School of Medicine

3:15 p.m.  MEASURING HEALTH-RELATED QUALITY OF LIFE OUTCOMES IN BLADDER CANCER PATIENTS USING THE NEWLY VALIDATED BLADDER CANCER INDEX (BCI)  
Scott Gilbert, MD, David Wood, MD, Alon Weizer, MD, Rodney Dunn, MS and John Wei, MD, MS (Presented By: Scott Gilbert, MD)

3:22 p.m.  EFFICACY OF SUUNITINIB-MALATE (SU11248) IN RENAL CELL CARCINOMA (RCC)  
Daniel J. George, MD, R.J. Motzer, B.I. Rini, M.D. Michaelson, B.G Redman, G.R. Hudes, G. Wilding, R.M. Bukowski, S.T. Kim and C.M. Baum (Presented By: Daniel J. George, MD)

3:29 p.m.  RENAL CELL CARCINOMA SUB-TYPING BY REAL-TIME PCR ON NEEDLE BIOPSY  
Daniel Barocas, MD, Yao-Tseng Chen, MD, PhD, Stephen Rohan, MD, Jean Kao, BS, Joseph DelPizzo, MD, E. Darracott Vaughan, MD, Ronnie Gurevich, BS, Mohammed Akhtar, MD and Douglas Scherr, MD (Presented By: Daniel Barocas, MD)

3:36 p.m.  RELATIONSHIP OF PSA VELOCITY AND GLEASON SCORE IN THE PLCO CANCER SCREENING TRIAL  
Gerald Andriole, MD, David Levin, MD, Paul Pinsky, PhD, Thomas Riley, Jerome Mabie, Douglas Reding, MD, E. David Crawford, MD and Robert Grubb, MD (Presented By: Gerald Andriole, MD)

3:43 p.m.  25-YEAR OUTCOMES OF RADICAL PROSTATECTOMY FOR THE TREATMENT OF ALL STAGES OF NON-METASTATIC PROSTATE CANCER  
Brant A. Inman, MD, FRCS, Robert P. Myers, MD, Bradley C. Leibovich, MD, Eugene D. Kwon, MD, Michael L. Blute, MD and Horst Zincke, MD, PhD (Presented By: Brant A. Inman, MD, FRCS)

3:50 p.m.  25 YEAR CANCER SPECIFIC AND OVERALL SURVIVAL FOR CLINICALLY LOCALIZED PROSTATE CANCER TREATED IN A SINGLE INSTITUTION BY RADICAL PROSTATECTOMY  
Christopher Porter, MD, Koiichi Kodama, MD, Robert Gibbons, MD, Roy Correa, MD, Paul Perrotte, MD and Pierre Karakiewicz, MD (Presented By: Christopher Porter, MD)

4:00 p.m. – 6:00 p.m.  Poster Session/Reception

7:00 p.m. – 7:30 p.m.  SUO Reception at the Hyatt Regency Bethesda

7:30 p.m.  SUO Dinner at the Hyatt Regency Bethesda
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:45 a.m. – 8:30 a.m.</td>
<td>Continental Breakfast</td>
</tr>
<tr>
<td>8:30 a.m. – 9:30 a.m.</td>
<td><strong>Bladder Cancer II: Contemporary Management of Superficial Bladder Cancer</strong>&lt;br&gt;Moderator: Bernard H. Bochner, MD – Memorial Sloan-Kettering Cancer Center</td>
</tr>
<tr>
<td>8:30 a.m. – 8:45 a.m.</td>
<td><strong>T1 Bladder Cancer</strong>&lt;br&gt;Guido Dalbagni, MD – Memorial Sloan-Kettering Cancer Center</td>
</tr>
<tr>
<td>8:45 a.m. – 9:00 a.m.</td>
<td><strong>Beyond BCG: The Next Generation of Intravesical Therapy</strong>&lt;br&gt;Yves Fradet, MD, FRCSC – University Laval/Chirurgie</td>
</tr>
<tr>
<td>9:00 a.m. – 9:30 a.m.</td>
<td><strong>Therapy of Superficial Bladder Cancer: Discussion</strong>&lt;br&gt;Moderator: Bernard H. Bochner, MD – Memorial Sloan-Kettering Cancer Center&lt;br&gt;Panelists: Ashish Kamat, MD – The University of Texas MD Anderson Cancer Center&lt;br&gt;Yves Fradet, MD, FRCSC – University Laval/Chirurgie&lt;br&gt;Eila Skinner, MD – USC</td>
</tr>
<tr>
<td>9:30 a.m. – 9:45 a.m.</td>
<td><strong>State of the Art: Targeted Therapy for Kidney Cancer</strong>&lt;br&gt;Nicholas Vogelzang, MD – Nevada Cancer Institute</td>
</tr>
<tr>
<td>9:45 a.m. – 10:00 a.m.</td>
<td><strong>Fellow/Resident Poster Session Awards</strong></td>
</tr>
<tr>
<td>10:00 a.m. – 11:00 a.m.</td>
<td><strong>Radical Prostatectomy – What’s the Best Surgical Approach?</strong>&lt;br&gt;Moderator: James E. Montie, MD – University of Michigan</td>
</tr>
<tr>
<td>10:00 a.m. – 10:15 a.m.</td>
<td><strong>Laparoscopic Prostatectomy</strong>&lt;br&gt;Bertrand Guillonneau, MD – Memorial Sloan-Kettering Cancer Center</td>
</tr>
<tr>
<td>10:15 a.m. – 10:30 a.m.</td>
<td><strong>Robotic Prostatectomy</strong>&lt;br&gt;Joseph Smith, Jr., MD – Vanderbilt University</td>
</tr>
<tr>
<td>10:30 a.m. – 10:45 a.m.</td>
<td><strong>Open Prostatectomy</strong>&lt;br&gt;William Catalona, MD – Northwestern University Medical Center</td>
</tr>
<tr>
<td>10:45 a.m. – 11:00 a.m.</td>
<td><strong>Summary and Overview</strong>&lt;br&gt;James E. Montie, MD – University of Michigan</td>
</tr>
<tr>
<td>11:00 a.m. – 11:20 a.m.</td>
<td><strong>State of the Art: PCPT</strong>&lt;br&gt;Ian Thompson, MD – UTHSCSA</td>
</tr>
<tr>
<td>11:20 a.m. – 12:20 p.m.</td>
<td>Lunch</td>
</tr>
<tr>
<td>12:20 p.m. – 1:05 p.m.</td>
<td><strong>Prostate Cancer III: Markers in Prostate Cancer</strong>&lt;br&gt;Moderator: Georg Bartsch, MD – University of Innsbruck</td>
</tr>
<tr>
<td>12:20 p.m. – 12:35 p.m.</td>
<td><strong>Clinical Applications of PSA Kinetics</strong>&lt;br&gt;Christopher Lee Amling, MD – University of Alabama at Birmingham</td>
</tr>
<tr>
<td>12:35 p.m. – 12:50 p.m.</td>
<td><strong>BPSA and proPSA</strong>&lt;br&gt;Kevin Slawin, MD – Baylor</td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------</td>
</tr>
</tbody>
</table>
| 12:50 p.m. – 1:05 p.m. | Beyond PSA: What Markers are Useful in Prostate Cancer for Diagnosis and Clinical Management?  
Mark Rubin, MD – Brigham & Women’s Hospital |
| 1:05 p.m. – 2:05 p.m. | Late Breaking Developments II  
Moderator: J. Brantley Thrasher, MD – University of Kansas Medical Center |
| 1:05 p.m. | THE INFLUENCE OF SURGICAL MANIPULATION ON PROSTATE GENE EXPRESSION: IMPLICATIONS FOR MOLECULAR CORRELATES OF TREATMENT EFFECTS AND DISEASE PROGNOSIS  
Daniel Lin, MD, Ilsa Coleman, BA, Sarah Hawley, MS, Ruth Dumpit, BA, David Gifford, BS, Phil Kezele, PhD, Hau Hung, MS, Beatrice Knudsen, MD, PhD, Alan Kristal, PhD and Peter Nelson, MD (Presented By: Daniel Lin, MD) |
| 1:15 p.m. | WITHDRAWN |
| 1:25 p.m. | PROSTATE CANCER DIAGNOSIS: DEVELOPMENT OF A MULTIPLEXED, SCORPIONS-BASED, QUANTITATIVE PCR ASSAY FOR DNA HYPERMETHYLATION  
Tatiana Vener, PhD (Presented By: Tatiana Vener, PhD) |
| 1:35 p.m. | VALIDATION OF GENE EXPRESSION ANALYSIS OF MICRODISSECTED HUMAN PROSTATE CANCER  
Heidi Erickson, PhD, Gillespie John, MD, Carolyn Best, PhD, Yajun Yi, PhD, W. Marston Linehan, MD, Gallya Gannot, DMD, PhD, Michael Tangrea, PhD, Rodrigo Chuaqui, MD and Michael Emmert-Buck, MD, PhD (Presented By: Heidi Erickson, PhD) |
| 1:45 p.m. | ANDROGEN-SENSITIVE PROSTATE CANCER SURVIVAL AND PROGRESSION IS SUPPORTED BY ANDROGEN-INSENSITIVE CELL PARACRINE FACTORS IN THE CASTRATED ENVIRONMENT  
Christopher Evans, MD, Erik Busby, MD, Hsing-Jien Kung, PhD and Joy Yang, PhD (Presented By: Christopher Evans, MD) |
| 1:55 p.m. | MEASUREMENT OF PROSTATE BIOPSY NUCLEAR STRUCTURE AND TISSUE MORPHOMETRY FROM A DOUBLE BLINDED, PLACEBO CONTROLLED TRIAL OF TESTOSTERONE REPLACEMENT  
Danil Makarov, MD, Cameron Marlow, BS, Leonard Marks, MD, M. Craig Miller, BS, Jonathan Epstein, MD, Alan Partin, MD, PhD and Robert Veltri, PhD (Presented By: Danil Makarov, MD) |
| 2:15 p.m. | Adjourn |
THURSDAY, DECEMBER 1, 2005

6:30 p.m. – 9:30 p.m.
Young Urologic Oncologists’ Dinner: The Surgeon Scientist – Is it Feasible?
Balancing the Academic with the Clinical
Speaker: Robert Uzzo, MD, Fox Chase Cancer Center
Location: Hyatt Regency Bethesda

Objectives
At the end of this discussion, the participants should be able to:
1. Identify barriers to the surgeon scientist and strategies to overcome them.
2. Identify developmental schemes for the aspiring young urologic oncologist interested in clinical and scientific pursuits.

7:00 p.m. – 8:30 p.m.
Young Urologic Oncologists (Y.U.O.) Podium Presentations
Moderator: John Davis, MD, Eastern Virginia Medical School

7:00 p.m.
BODY MASS INDEX AND IMPACT ON PSA SCREENING AND PROSTATE CANCER DETECTION IN THE PLCO TRIAL
Robert Grubb, MD, David Levin, MD, Paul Pinsky, PhD, Jerome Mabie, Thomas Riley, Robert Greenlee, PhD, Donald Urban, MD, Lawrence Ragard, MD, E. David Crawford, MD and Gerald Andriole, MD (Presented By: Robert Grubb, MD)

7:10 p.m.
A PHASE I/II PROSPECTIVE DOSE ESCALATING TRIAL OF LYCOPENE IN PATIENTS WITH BIOCHEMICAL RELAPSE OF PROSTATE CANCER FOLLOWING DEFINITIVE LOCAL THERAPY
Peter Clark, MD, M. Craig Hall, MD, Lester Borden, MD, Antonius Miller, MD, Jennifer Hu, PhD, W. Robert Lee, MD, Ralph D’Agostino, PhD, James Lovato, Michelle Harmon and Frank Torti, MD (Presented By: Peter Clark, MD)

7:20 p.m.
QUANTIFYING THE PUBLIC HEALTH IMPACT OF LOW HOSPITAL VOLUME ON OUTCOMES FOLLOWING CANCER SURGERY
Brent Hollenbeck, MD, MS, David Miller, MD, David Taub, MD, Rodney Dunn, MS and John Wei, MD, MS (Presented By: Brent Hollenbeck, MD, MS)

7:30 p.m.
BRANCHING PHENOTYPE OF RENAL CELL CARCINOMA IS ABROGATED BY NOX4 SILENCING
Jodi Maranchie, MD and Ye Zhan (Presented By: Jodi Maranchie, MD)

7:40 p.m.
RISK OF DEATH DUE TO PROSTATE CANCER AND COMPETING CAUSES AMONGST AFRICAN AMERICAN MEN CHOOSING WATCHFUL WAITING
Ash K Tewari, George Divine and Mani Menon (Presented By: Ash K Tewari)
7:50 p.m.  
**EXTENDED VS. LIMITED Laparoscopic PELVIC LYMPH NODE DISSECTION FOR PROSTATE CANCER: THE VALUE OF PARTIN TABLES IN SELECTION OF THE NEED FOR AND THE EXTENT OF DISSECTION**  
Karim Touijer, MD, Farhang Rabbani, MD, Javier Romero, MD and Bertrand Guillonneau, MD (Presented By: Karim Touijer, MD)

8:00 p.m.  
**RISK OF DIABETES MELLITUS IN MEN UNDERGOING ANDROGEN DEPRIVATION THERAPY FOR PROSTATE CANCER**  
Ithaar Derweesh, MD, Matt Kincade, MD, John Malcolm, MD, Kimberly Lamar, PhD, Anthony Patterson, MD, Abbas Kitabchi, MD, PhD and Robert Wake, MD (Presented By: Ithaar Derweesh, MD)

8:10 p.m.  
**REDOX REGULATION OF INVASION AND MIGRATION IN BLADDER CANCER**  
Badar Mian, MD, James Belarmino, MD, Xiao Fang Ha and J. Andre Melendez, PhD (Presented By: Badar Mian, MD)

8:20 p.m.  
**IMPACT OF FLOURESCENT IN SITU HYBRIDIZATION OF RENAL TUMORS AND HISTOPATHOLOGIC DIAGNOSIS**  
Michael Franks, MD (Presented By: Michael Franks, MD)

8:30 p.m.  
**PATTERNS OF CARE FOR MEN WITH PROSTATE CANCER FOLLOWING FAILURE OF PRIMARY TREATMENT**  
Tracey Krupski, MD, MPH, Christopher Saigal, MD, MPH, Janet Hanley, MS and Mark Litwin, MD, MPH (Presented By: Tracey Krupski, MD, MPH)

8:45 p.m. – 9:00 p.m.  
**The Surgeon Scientist – Is It Feasible? Balancing the Academic with the Clinical**  
Invited Speaker: Robert Guy Uzzo, MD – Fox Chase Cancer Center, Philadelphia, PA

FRIDAY, DECEMBER 2, 2005

2:30 p.m. – 3:00 p.m.  
**Young Urologic Oncologists (Y.U.O.) Podium Presentations**  
Moderator: John Davis, MD – Eastern Virginia Medical School

2:30 p.m.  
**THE NATURAL HISTORY OF RESIDUAL AND RECURRENT DISEASE FOLLOWING RENAL ABLATIVE THERAPY: A MULTI-INSTITUTIONAL STUDY**  
Surena Matin, MD, Kamran Ahrar, MD, Jeffrey Cadeddu, MD, Debra Gervais, MD, Francis McGovern, MD, Ronald Zagonia, MD, Robert Uzzo, MD, John Haaga, MD, Martin Resnick, MD and Jihad Kaouk Inderbir Gill, MD (Presented By: Surena Matin, MD)

2:40 p.m.  
**PERIOPERATIVE QUALITY CARE INDICATORS OF RETROPUBLIC, LAPAROSCOPIC, AND ROBOTIC PROSTATECTOMY: RESULTS FROM A NATIONAL, MULTI-CENTER, PROSPECTIVE COHORT**  
Jim Hu, MD, MPH, David Wood, MD, Gerald Andriole, MD, Rodney Dunn, PhD, Mark Litwin, MD, MPH, Louis Pisters, MD, Eric Klein, MD, James Montie, MD, John Wei, MD, MPH and Martin Sanda, MD (Presented By: Jim Hu, MD, MPH)

2:50 p.m.  
**GENOME-WIDE ASSOCIATION STUDY FOR PROSTATE CANCER USING THE AFFYMETRIX 10K GENECHIP AND EVALUATION OF SUSCEPTIBILITY GENES FOR PROSTATE CANCER IN A CLINICAL SETTING**  
Robert Nam, MD, MSc, William Zhang, MD, PhD, Laurence Klotz, MD, John Trachtenberg, MD, Michael Jewett, MD, Steven Narod, MD, Robert Nam, MD, MSc, William Zhang, MD, PhD, Laurence Klotz, MD, John Trachtenberg, MD, Michael Jewett, MD and Steven Narod, MD (Presented by Robert Nam, MD, MSc)
MEASURING HEALTH-RELATED QUALITY OF LIFE OUTCOMES IN BLADDER CANCER PATIENTS USING THE NEWLY VALIDATED BLADDER CANCER INDEX (BCI)
Scott M Gilbert, David Wood, Alon Weizer, Rodney Dunn, John T Wei
Department of Urology, University of Michigan, Ann Arbor, MI

Introduction: As cancer therapies have improved and patients have experienced greater survival, health-related quality of life (HRQOL) has become an important outcome measure. Few groups have attempted to quantitatively measure QOL in bladder cancer patients, and a standardized reliable instrument is currently lacking. Without a validated instrument, assessing the impact of treatment on QOL is challenging, and commonly held perceptions regarding QOL issues related to bladder cancer, such as continent vs. incontinent urinary diversion, cannot be confirmed. We developed and validated a quality of life instrument (Bladder Cancer Index) designed to measure urinary, sexual and bowel function and bother domains in patients with bladder cancer, and compared these QOL-specific domains between different standard treatments in a cohort of patients with bladder cancer.

Methods: Following Institutional Review Board approval, patients with bladder cancer were identified from a prospective bladder cancer outcomes database and contacted for study participation. The BCI questionnaire, consent form and instructions were mailed to willing participants and data from returned questionnaires was entered into a central database. Cases were stratified according to treatment (cystectomy/neobladder, cystectomy/ileal conduit, cystoscopy/intravesical therapy, and cystoscopy/no intravesical therapy) for analysis. Bivariate analysis using Analysis of Variance (ANOVA) and multivariable analysis using Analysis of Covariance (ANCOVA) adjusted for age, gender, income, education, relationship status, catheter use and follow-up time were performed for comparison of BCI urinary, bowel and sexual domains, as well as function and bother sub-domains within each category, between treatment groups. Final models were selected using backwards model-building technique. In the BCI, a higher score represents a better health state. All analyses were performed with a significance threshold of 0.05 using the SAS system (Cary, NC).

Results: A total of 316 bladder cancer patients treated at the University of Michigan completed the Bladder Cancer Index in 2004. The median age was 69 years (range 41-89). The median follow-up period was 2.9 years (range 0.2-9.8). Differences in treatment groups were found for each of the BCI domains (all ANCOVA p<0.001). Urinary domain scores were significantly lower in the cystectomy/neobladder group compared to the other treatment groups (p<0.001). The cystoscopy/intravesical therapy group had a significantly higher bowel score than either cystectomy group (p<0.005). Finally, both the cystoscopy and the cystoscopy/intravesical therapy groups had significantly higher sexual scores than either cystectomy group (p<0.01).

Conclusions: The Bladder Cancer Index is a reliable validated instrument designed to measure HRQOL in patients with bladder cancer. These results clearly demonstrate significant differences between common therapy groups for bladder cancer in each of the urinary, bowel, and sexual domains. Despite the common perception that neobladder urinary diversion offers patients superior QOL, our findings suggest that urinary function related-quality of life is inferior in neobladder patients compared to patients with ileal conduit urinary diversion.

Table  Adjusted BCI Domain Scores by Localized Bladder Cancer Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Urinary Domain</th>
<th>Bowel Domain</th>
<th>Sexual Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystoscopy/No IV Rx</td>
<td>90.7</td>
<td>87.3</td>
<td>53.9</td>
</tr>
<tr>
<td>Cystoscopy/IV Rx</td>
<td>89.7</td>
<td>90.4</td>
<td>53.6</td>
</tr>
<tr>
<td>Cystectomy/Neobladder</td>
<td>76.2</td>
<td>82.8</td>
<td>35.8</td>
</tr>
<tr>
<td>Cystectomy/Ileal Conduit</td>
<td>87.6</td>
<td>79.8</td>
<td>35.0</td>
</tr>
</tbody>
</table>
3:22 p.m.

**EFFICACY OF SUNITINIB MALATE (SU11248) IN RENAL CELL CARCINOMA (RCC)**

D.J. George, R.J. Motzer, B. I. Rini, M. D. Michaelson, B. G. Redman, G. R. Hudes, G. Wilding, R. M. Bukowski, S. T. Kim, C. M. Baum, the SU11248 Study Group; Duke University, Durham, NC; Memorial Sloan-Kettering Cancer Center, New York, NY; UCSF, San Francisco, CA; Dana Farber Harvard Cancer Center, Boston, MA; University of Michigan, Ann Arbor, MI; Fox Chase Cancer Center, Philadelphia, PA; University of Wisconsin, Madison, WI; Cleveland Clinic Foundation, Cleveland, OH; Pfizer Inc., San Diego, CA.

**Introduction and objectives:** Metastatic RCC (mRCC) is associated with a 5-year survival rate of ≤10%, is highly resistant to chemotherapy, and only a limited subset of patients benefit from cytokine therapy (high-dose interleukin-2 and/or interferon-α). Historical data from 251 patients receiving conventional second-line therapies have reported a response rate of 4% and progression-free survival (PFS) of 2.4 months. Sunitinib is an oral multi-targeted receptor tyrosine kinase inhibitor that exhibits both antitumor and antiangiogenic activity through its inhibition of VEGF receptors (types 1–3), PDGF receptors (α and β) and other tyrosine protein kinases. We performed two multicenter, single arm phase II studies to demonstrate and confirm the overall response rate (ORR), PFS, overall survival (OS) and tolerability associated with sunitinib treatment in patients with cytokine-refractory mRCC.

**Patients and methods:** Eligibility for both trials included measurable disease, failure of one prior cytokine therapy, ECOG PS of 0/1, and adequate organ function. Patients received sunitinib 50 mg q.d. orally for 4 weeks, followed by 2 weeks off treatment to comprise a cyclical 6-week regimen. Best response was assessed using RECIST.

**Results:** Results from the two phase II studies (trial 1: 014 and trial 2: 1006; total N=168) of sunitinib in patients with mRCC demonstrated an ORR of 42%. PFS correlated with tumor response: median PFS was 14.8 months in responders (n=71), 7.9 months in those with stable disease ≥ 3 months (n=41), and 2.1 months in patients with stable disease <3 months or progressive disease (n=56). In the first study, median OS was 16.4 months; median OS in the second study has not yet been reached. Overall, the majority of treatment-related adverse events and hematological abnormalities were grade 1 and 2. These included the following treatment-related adverse events (grade 3 only as 0% for grade 4 severity) and laboratory abnormalities (grade 3/4) reported in trial 1 and trial 2, respectively: fatigue (11%, 11%), diarrhea (3%, 3%), stomatitis (2%, 5%), neutropenia (13%, 16%), anemia (10%, 6%), and thrombocytopenia (0%, 6%). Other targeted therapies as single agents for second-line treatment of mRCC have been associated with response rates of 2–10% and PFS/TTP of 5–6 months.

**Conclusions:** In summary, sunitinib has demonstrated substantial single-agent antitumor activity in mRCC, with both durable ORR and prolonged median PFS comparing positively with those observed for other second-line therapies. Sunitinib is currently under investigation in a randomized phase III study as a first-line therapy versus interferon-α.

**References:**

3:29 p.m.

**RENAL CELL CARCINOMA SUB-TYPING BY REAL-TIME PCR ON NEEDLE BIOPSY**

Departments of Urology and Pathology of New York Presbyterian Hospital – Weill Cornell Medical Center, New York, NY

**Objectives:** We set out to determine the sub-type of renal cell carcinoma (RCC) on needle core biopsies of renal masses, using a combination of histopathology (HP) and a molecular diagnostic algorithm (MDA) developed at our institution. Stage migration, decrease in the proportion of aggressive tumors, and the expanding options for treating and observing renal masses are likely to increase the role of preoperative diagnostic
modalities. We hypothesized that the MDA would enhance the diagnostic accuracy of the needle core biopsy. The MDA is based on the differences in expression profiles among the different tumor types, as identified on cDNA arrays.

Methods: Fifty-one consecutive patients with renal masses of undetermined histology underwent nephrectomy or partial nephrectomy, yielding a total of 54 tumors. Fourteen-gauge needle core biopsies were taken of the mass immediately following surgery. RNA was extracted from one core and quantitative real time PCR was performed for carbonic anhydrase IX, alpha-methylacyl coenzyme A racemase, parvalbumin and a kidney-specific chloride channel. Ratios of expression were used to differentiate among RCC sub-types. HP was performed on a second core. A pathologist, blinded to final pathology, read the HP without the MDA results and subsequently with the MDA results. MDA prediction and HP were compared with final pathology.

Results: Adequate material was obtained for HP diagnosis in 47 cases (87.0%). Forty-one of these cases were a sub-type of RCC or oncocytoma. HP alone correctly identified the histologic sub-type in 37 (90.2%) of cases. Addition of the MDA improved the pathologist’s accuracy to 97.6%, p=0.12. MDA was evaluable in 39 of these cases. MDA prediction was concordant with final pathology in 34/39 cases (87.2%). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for HP alone and HP plus MDA on the 41 evaluable RCC/oncocytomas were calculated. Adding the MDA to HP improved the sensitivity for clear cell (n=24) from 87.5% to 95.8% (p=0.19) and improved the NPV from 87.5% to 95.5% (p=0.20). With papillary RCC (n=8), sensitivity improved from 75.0% to 87.5% (p=0.37) and NPV improved from 95.0% to 97.4% (p=0.34). For chromophobe (n=3), specificity improved from 93.0% to 100% (p=0.07) and PPV improved from 50% to 100% (p=0.10). Diagnostic accuracy for oncocytoma (n=6) and unclassified (n=1) RCC was 100% on both HP and HP plus MDA.

Table: Cases improperly sub-typed on histopathology of biopsy

<table>
<thead>
<tr>
<th>Case</th>
<th>Problem with Histopathology</th>
<th>MDA Prediction</th>
<th>Biopsy Re-read with MDA</th>
<th>Final Pathologic Sub-type</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>Equivocal reading</td>
<td>Clear cell</td>
<td>Clear cell</td>
<td>Clear cell</td>
</tr>
<tr>
<td>22</td>
<td>Equivocal reading</td>
<td>Clear cell</td>
<td>Clear cell</td>
<td>Clear cell</td>
</tr>
<tr>
<td>27</td>
<td>Mistaken for chromophobe</td>
<td>Papillary</td>
<td>Papillary</td>
<td>Papillary</td>
</tr>
<tr>
<td>49</td>
<td>Mistaken for clear cell</td>
<td>Clear cell</td>
<td>Clear cell</td>
<td>Papillary</td>
</tr>
</tbody>
</table>

Conclusion: Needle core biopsy of renal tumors provides adequate material for evaluation of histologic sub-type, providing important prognostic information. Adding the MDA improved the overall accuracy of the pathologic assessment. This method of determining the histologic sub-type of RCC may have applications for preoperative diagnosis, guiding therapeutic options.

3:36 p.m.

RELATIONSHIP OF PSA VELOCITY AND GLEASON SCORE IN THE PLCO CANCER SCREENING TRIAL

Robert L. Grubb*, David L. Levin+, Paul F. Pinsky†, Jerome Mabie†, Thomas L. Riley†, Douglas J. Reding‡, Donald A. Urban‡, Lawrence R. Ragard‡, E. David Crawford§, and Gerald L. Andriole†
*St. Louis, MO, †Rockville, MD, ‡Marshfield, WI, §Denver, CO

Introduction and Objective: Recent studies have suggested that men whose PSA rises by more than 2.0 ng/mL in the year before diagnosis of prostate cancer (CaP) may have a high risk of dying of prostate cancer. Among men diagnosed with CaP in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, we examined the distribution of PSA velocity in the year prior to cancer diagnosis and the relationship of PSA change in the year prior to diagnosis to Gleason score.

Methods: Between 1993 and 2001, 38,350 men aged 55-74 were randomized to the intervention arm of the PLCO trial and underwent annual PSA and DRE screening. Of these men, 1694 men were diagnosed with cancer; 1284 men had complete demographic information, recorded Gleason score and the results of the 2 PSA levels preceding diagnosis available. Mean age was 64.1 years. 90% of the subjects were white. There was a family history of CaP in 11.5% of the subjects.

Results: Mean PSA at the time of diagnosis in the study population was 6.55 ng/mL. Mean PSA the year prior to diagnosis was 4.85 ng/mL. The mean change in PSA was 1.70 ng/mL. PSA increased by more than 2 ng/mL in 302 (23.5%) of men diagnosed with cancer; 164 (12.8%) had a change of more than 3 ng/mL in the year prior to diagnosis. The proportion of men whose PSA changed by >2 ng/mL varied with each screening year (range 16.2-27.2%) but did not decrease with time.

Continues on next page
Among men whose PSA increased > 2 ng/mL, 30.8% had Gleason scores of 7 and 12.9% had Gleason scores > 8 compared to 25.9% and 5.9%, respectively of men whose PSA increased by < 2 ng/mL (see table). For multiple PSA levels, a higher percentage of men whose PSA had changed by > 2 ng/mL had Gleason > 8 cancers. In a multivariate model, PSA change > 2 ng/mL was predictive of biopsy Gleason score of > 8 (Odds Ratio 2.36). Other variables such as PSA at diagnosis, race and family history were not predictive in this model.

**Conclusions:** In the PLCO Screening Trial, 24% of men diagnosed with CaP had PSA increases of > 2 ng/mL in the year prior to CaP diagnosis. This increase was associated with high grade (Gleason score > 8) tumors on biopsy. Further study is needed to see the effect of PSA velocity on outcomes for surgical and radiation therapy and overall survival and to determine the optimal PSA velocity level for predicting outcomes.

<table>
<thead>
<tr>
<th>PSA change in year prior to diagnosis</th>
<th>&lt; 2 ng/mL</th>
<th>&gt;2 ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gleason score</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>2-6</td>
<td>670 68.2</td>
<td>170 56.3</td>
</tr>
<tr>
<td>7</td>
<td>254 25.9</td>
<td>93 30.8</td>
</tr>
<tr>
<td>8-10</td>
<td>58 5.9</td>
<td>39 12.9</td>
</tr>
<tr>
<td>All</td>
<td>982 100.0</td>
<td>302 100.0</td>
</tr>
</tbody>
</table>

\[ p = 0.0052 \ (\text{test for trend}) \]

### 25-YEAR OUTCOMES OF RADICAL PROSTATECTOMY FOR THE TREATMENT OF ALL STAGES OF NON-METASTATIC PROSTATE CANCER

Brant Inman, Eugene Kwon, Robert Myers, Bradley Leibovich, Michael Blute, and Horst Zincke
Mayo Clinic College of Medicine, Rochester, MN

**Introduction:** A recently published watchful waiting (WW) study (Albertsen PC *et al*. JAMA. 2005.) has suggested that many patients with prostate cancer (PCa) may not require treatment. In the current study, we examine the extended long-term survival outcomes of a similar cohort of patients selected from the same Prostate Patient Outcomes Research Team (PORT) II study as the WW series who underwent radical retropubic prostatectomy (RRP) as primary treatment for their disease.

**Methods:** Institutional IRB approval was obtained prior to commencing this study. The cohort consisted of 849 men selected from the PORT II study who underwent bilateral pelvic lymphadenectomy and radical retropubic prostatectomy between 1971 and 1984. Study entry criteria were age 55 to 74 years at PCa diagnosis and RRP performed within 6 months of diagnosis. Before surgery all patients underwent digital rectal examination and radiological testing for metastasis (bone scan or plain x-ray). Biopsy specimens were graded using the Gleason system by the same pathologist that analyzed the biopsies in the WW study. Follow-up data were obtained from medical records and death certificates and additional information was obtained by contacting patients, family members or referring physicians. The Kaplan-Meier method was used to calculate survival estimates and the impact of covariates (Gleason score, age, Charlson score, and clinical stage) were estimated using the Cox proportional hazards model. The overall and prostate cancer-specific cumulative death rates were stratified by age and Gleason score groups, using a competing risk strategy.

**Results:** Median patient age at surgery was 65 years (IQR: 61-68) and median follow-up was 22 years. Clinical stage (TNM 1997) was cT1 in 69 patients, cT2A in 529 patients, cT2B in 110 patients, and cT3/T4 in 140 patients. Preoperative Charlson score was 0 in 523 cases, 1 in 232 cases, 2 in 75 cases, and 3+ in 19 cases. Biopsy Gleason score was 2-4 in 39 patients, 5 in 94 patients, 6 in 410 patients, 7 in 166 patients, and 8-10 in 140 patients. The estimated 25-year death rates are given below.

<table>
<thead>
<tr>
<th>Age</th>
<th>2-4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>PCA</td>
<td>PCA</td>
<td>PCA</td>
<td>PCA</td>
<td>PCA</td>
<td>PCA</td>
</tr>
<tr>
<td>55-59</td>
<td>59.4</td>
<td>18.7</td>
<td>62.2</td>
<td>12.3</td>
<td>66.6</td>
</tr>
<tr>
<td>60-64</td>
<td>75.0</td>
<td>20.6</td>
<td>78.4</td>
<td>13.4</td>
<td>81.8</td>
</tr>
<tr>
<td>65-69</td>
<td>86.7</td>
<td>18.8</td>
<td>90.1</td>
<td>12.0</td>
<td>91.9</td>
</tr>
<tr>
<td>70-74</td>
<td>91.9</td>
<td>15.8</td>
<td>94.7</td>
<td>9.9</td>
<td>95.7</td>
</tr>
</tbody>
</table>
**Conclusion:** When compared to the patients in the WW study, our very similar cohort of patients treated by RRP experienced a lower cancer-specific death rate. The RRP advantage was seen in tumors with biopsy Gleason scores > 6 regardless of age grouping but became most pronounced in poorly differentiated tumors. These data suggest that many men with moderately or poorly differentiated PCa managed conservatively will die needlessly of their disease.

### 3:50 p.m.

**25 YEAR CANCER SPECIFIC AND OVERALL SURVIVAL FOR CLINICALLY LOCALIZED PROSTATE CANCER TREATED IN A SINGLE INSTITUTION BY RADICAL PROSTATECTOMY**

Christopher Porter, Koichi Kodama, Robert Gibbons and RJ Correa  
Virginia Mason Medical Center, Seattle, Washington.  
Paul Perrotte and Pierre Karakiewicz  
Cancer Prognostics and Health Outcomes Unit, University of Montreal, Montreal, Canada.

**Introduction and Objectives:** Prostate cancer (CAP) is recognized as the most common non-cutaneous malignancy in men in the United States. Twenty-year cancer specific survival for patients treated conservatively is available; unfortunately similar long-term cancer specific survival outcome data from definitive surgical therapy is not available. We report 10, 15, 20 and 25-year CAP specific survival, overall survival, local and distant progression-free survival and freedom from biochemical progression in a large single center series.

**Methods:** Between 12/1954 and 5/1994, 787 consecutive patients underwent Radical Prostatectomy (RP) at Virginia Mason Medical Center, Seattle Washington. No patient received neoadjuvant therapy. The data was managed by one of the authors (RG) from 1969 to 1999 and later was updated by detailed chart review. Clinical and Pathological parameters evaluated by actuarial analyses included: patient age at RP, year of RP, 1992 pathological stage, surgical margin status, RP Gleason sum, type of surgery (radical perineal prostatectomy (RPP) vs. radical retropubic (RRP), lymph node dissection (LND) status, use of hormonal therapy, administration of radiotherapy and cause as well as date of death. RP was performed in 428 (56.9%) patients, while 324 (43.1%) underwent RRP. A total of 328 patients (45.5%) had LND. Patients were followed quarterly for 2 years, then semi-annually for 2 years and then annually. 118 patients received adjuvant radiation therapy (6270cGy). 74 patients received salvage radiation therapy at 6270cGy. 118 patients received adjuvant hormonal therapy and 75 patients received salvage hormonal therapy. Univariable and multivariable Cox regression models addressed time to recurrence RP.

**Results:** Average patient age was 63.6 years. In 411 patients (54.7%), the pathological stages were T2a to T2c. Extra capsular extension and/or seminal vesicle invasion were recorded in 341 patients (45.3%) and a positive surgical margin was recorded in 283 specimens (37.6%). The majority of specimens demonstrated a Gleason sum of 6 (39.8%). Gleason sum of 7 was recorded in 170 men (22.6%) and sum of 8-10 was recorded in 63 specimens (8.4%). Overall, PSA recurrence was noted in 189 patients (31.4% of 601 patients), local recurrence was noted in 63 patients (8.4%) and distant recurrence was noted in 85 patients (11.3%). Overall, 298 men died (39.6%). Of these, 50 men died of prostate cancer (6.6%) and the remaining 248 (33.0%) died of other causes. Follow-up ranged from 0.1 to 40.5 years (mean 11.7, median 11.4). Organ confined disease demonstrated improved survival probability, when compared to non-organ confined disease (pT3). The presence of negative surgical margins was a strong predictor of improved survival (p<0.001). Patients with poorly differentiated disease (Gleason 8-10) had significantly worse survival outcomes than those with either well or intermediate grade disease.

Actuarial estimates of PCa-specific survival range from 99.0% at 5 years to 81.5% at 25 years, whereas estimates of overall survival ranged from 93.5% at 5 years to 19.3% at 25 years. PSA progression-free survival ranged from 84.8% to 54.5%, at 5 and 25 years respectively. Local progression-free estimates range from 95.3% to 87.8% at 5 and 25 years respectively. Finally, distant recurrence-free estimates range from 95.9% to 78.2% at 5 and 25 years respectively.

Univariate and multivariate analyses of models predicting PSA progression, local progression, distant progression and of PCa-specific mortality. In univariate analyses of PCa-specific mortality, pathological stage (p<0.001), surgical margin status (p=0.001), Gleason sum (p<0.001), delivery of radiotherapy (p<0.001) and delivery of hormonal therapy represented statistically significant predictors. In multivariate analyses, all variables, except delivery of radiotherapy remained statistically significant predictors of PCa-specific mortality.

**Conclusion:** Excellent long-term survival outcomes may be expected after RP for clinically localized prostate cancer. Further maturation of contemporary surgical series will be necessary to evaluate the applicability of these outcomes to men undergoing surgery in the PSA screening era.
THE INFLUENCE OF SURGICAL MANIPULATION ON PROSTATE GENE EXPRESSION: IMPLICATIONS FOR MOLECULAR CORRELATES OF TREATMENT EFFECTS AND DISEASE PROGNOSIS

Daniel W. Lin,1,3 Ilsa M. Coleman,1 Sarah Hawley,2 Ruth Dumpit,1 David Gifford,1 Philip Kezele,1 Hau Hung,1 Beatrice S. Knudsen,2 Alan R. Kristal,2 Peter S. Nelson1

1Divisions of Human Biology and 2Public Health Sciences, Fred Hutchinson Cancer Research Center and 3Department of Urology, University of Washington

Seattle, Washington

Introduction and Objective: Measurements of tissue gene expression are increasingly used for disease stratification, clinical trial entry, and assessments of neoadjuvant therapy response. However, surgical manipulation could significantly influence the expression of specific transcripts or proteins. This study was designed specifically to assess gene expression changes associated with the process of surgical resection.

Materials and Methods: Immediately after induction of anesthesia for radical prostatectomy, 12 prostate cancer patients underwent in situ prostate biopsy. Ex vivo prostate biopsies were performed immediately after surgical removal. Prostate epithelium was acquired by laser-capture microdissection, and transcript abundance levels quantitated by cDNA microarray hybridization. Data were analyzed by paired, two-sample gene expression using Statistical Analysis of Microarray algorithms fit linear models using Generalized Estimating Equations and confirmed with quantitative polymerase-chain reaction.

Results: Median prostate volume was 43cc (range 31-149), median patient age was 64.4 yrs (range 52.6-69.4), median ischemia time was 33.5 minutes (range 24-42), and median preoperative serum PSA was 5.2 ng/ml (range 2.5-16.0). Of 5,753 clones with measurable expression in prostate epithelium, 88 (1.5%) were altered due to surgery (FDR<10%), representing 62 unique genes. These included transcripts encoding acute phase response proteins, IER2 and JUNB, and regulators of cell proliferation, p21Cip1 and KLF6. Of several clinical characteristics examined, such as patient age, prostate volume, serum PSA, blood loss, and operative time, only gland volume was significantly and negatively associated with the magnitude of gene expression difference between pre- and post-surgical specimens.

Conclusions: Surgical manipulation results in significant and reproducible gene expression changes. Molecular analyses of surgical samples should recognize that transcript, and potentially protein, alterations occur rapidly, and these changes may be associated with the method of tissue acquisition and be mistaken for markers of disease severity or disease response to treatment.

Funding sources: DK65083 (DWL), Pacific Northwest Prostate Cancer SPORE CA97186 (DWL, PSN), and CA85859 (PSN).

1:15 p.m.

WITHDRAWN
PROSTATE CANCER DIAGNOSIS: DEVELOPMENT OF A MULTIPLEXED, SCORPIONS-BASED, QUANTITATIVE PCR ASSAY FOR DNA HYPERMETHYLATION

Jyoti Mehrotra, Tatiana Vener, Hsiling Chiu, Carlo Derecho, Shobha Varde, and Abhijit Mazumder
Veridex, LLC, a Johnson and Johnson Company, Warren, NJ

Introduction: Prostate cancer is the second leading cause of cancer-related deaths among men in the United States. The known 25-30% false negative rate of initial biopsy calls into question which patients should undergo a follow up biopsy. Complicating the scenario is the debate regarding whether patients having a diagnosis of atypical small acinar proliferation and high-grade prostatic intraepithelial neoplasia (HG-PIN) should undergo a second biopsy. Novel approaches for diagnosis and prognosis in prostate cancer are needed. Detection of DNA hypermethylation is one such approach.

Methods: We have developed a novel, multiplexed assay using Scorpion amplification and detection reagents for the quantification of methylation levels for Glutathione-S-Transferase P1 (GSTP1), Adenomatous Polyposis Coli (APC), and Retinoic Acid Receptor 2 (RAR2) with the Cepheid SmartCycler™ II as the readout platform. Singlex assays were also run with the ABI 7900 as the readout platform. A sample preparation protocol using the QiaAmp DNA Mini Kit (Qiagen) was used to extract genomic DNA. Both singlex and multiplexed assays were run with an internal control (housekeeping gene).

Results: We present data demonstrating the analytical performance of these Scorpion assays using 142 formalin-fixed, paraffin-embedded prostatectomies and biopsies. Comparison of resulting data with pathology shows that GSTP1 alone can generate an analytical sensitivity of 87% at a specificity of 100%, consistent with the literature. We also demonstrate the impact of other markers in our multiplexed assay on these samples and the relationship of a quantitative methylation index to Gleason Score and/or recurrence.

Conclusions: A prototype quantitative Methylation Specific PCR (MSP) assay was developed for the detection of DNA hypermethylation of candidate genes that can discriminate between clinically relevant and clinically benign disease. Feasibility potential of this multiplexed assay as a novel application in prostate cancer has been demonstrated.

VALIDATION OF GENE EXPRESSION ANALYSIS OF MICRODISSECTED HUMAN PROSTATE CANCER

Heidi S. Erickson, Ph.D.1, John W. Gillespie, M.D.2, Carolyn J.M. Best, Ph.D.1, Yajun Yi, Ph.D.3, W. Marston Linehan, M.D.4, Gallya Gannot, D.M.D., Ph.D.1, Michael A. Tangrea, Ph.D.1, Rodrigo F. Chuaqui, M.D.1, and Michael R. Emmert-Buck, M.D., Ph.D.1

1Pathogenetics Unit, Laboratory of Pathology and Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD.
2SAIC-Frederick, Inc., National Cancer Institute at Frederick, Frederick, MD 21702-1201
3Vanderbilt Prostate Cancer Center, Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN.
4Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD.

Using microarray analysis of frozen microdissected (MD) prostate tissue specimens, we previously identified genes whose expression profiles segregated moderate- versus high-grade tumors, and androgen dependent (AD) versus androgen independent tumors (AI). To complete the validation process, we are both utilizing standard techniques (quantitative reverse transcription polymerase chain reaction (qRT-PCR) and immunohistochemistry (IHC), as well as developing novel approaches, (Differential Gene locus MAPping (DIGMAP) comparison, expression microdissection (xMD), and indirect Layered Peptide Arrays (iLPA)). Numerous housekeeping genes have been used as endogenous controls for qRT-PCR, even though it is known that environmental conditions can change their expression in certain model systems. This issue has not been rigorously examined in MD cell populations, and it is not known if any single gene has stable transcript levels across different patients’ specimens. To facilitate accurate validation of array-based expression findings by qRT-PCR, we determined the stably expressed gene or gene pairs and developed an accurate normalization strategy for frozen MD human prostate normal (N) and cancer (T) tissues. Samples were normalized using the gold standard of cell counting (10,000 microdissected cells per tissue type) and quantitation of total RNA was conducted using Bioanalyzer and NanoDrop techniques. Via rigorous examination: 1) stable endogenous controls were identified, 2) one gene (ACTB or PGK1) or a pair of genes (CYP1A1 & TFRC or CYP1A1 & PGK1) were found to work just as well as using the average of all ten genes, and 3) a normalization strategy allowing differentially expressed candidate genes to be identified and rigorously validated was identified. From the list
Continued from previous page

of differentially expressed genes for both the moderate- versus high-grade and the AD versus AI tumors, genes for validation were selected based upon known differences, novel differences, genes highly differentiated, genes only slightly differentiated, availability of commercial monoclonal antibodies, and detection p-values, with genes showing detection p-values <0.0009 given the highest priority. The initial gene set for validation includes: STAT5B, JAK-1, SOD2, MTR, CD69, and LAMP2. These data suggest that each of the standard and novel validation approaches can uniquely contribute to validation of large-scale gene expression data sets. This research was supported by the Intramural Research Program of the NIH, National Cancer Institute, Center for Cancer Research.

1:45 p.m.

ANDROGEN-SENSITIVE PROSTATE CANCER SURVIVAL AND PROGRESSION IS SUPPORTED BY ANDROGEN-INSENSITIVE CELL PARACRINE FACTORS IN THE CASTRATED ENVIRONMENT

Christopher P. Evans, J. Erik Busby, Hsing-Jien Kung, Joy C. Yang. Univ. of California, Davis, Sacramento, CA, and MD Anderson Cancer Center, Univ. of Texas, Houston, TX

Introduction: Neuroendocrine (NE) cells are present in all developing and adult prostates. We believe that androgen withdrawal (castration) is an early propagation factor, facilitating androgen independence through NE progression. We hypothesize that NE cells are androgen independent (AI) and secrete neuropeptides that support androgen sensitive cell proliferation in the absence of androgens. This study demonstrates that expression of the neuropeptide gastrin-releasing peptide (GRP) in LNCaP cells not only renders the cells AI, but also supports the growth and migration of the coexistent LNCaP cells under castrated conditions.

Methods: GRP overexpressing LNCaP cells (LNCaP-GRP) were developed in our lab through transfection and selection. Xenograft tumors grown in nude mice with the LNCaP-GRP cells were re-cultured and termed GRP-Pro cells. Soft agar growth under androgen-depleted conditions was performed to illustrate in vitro chimeric AI growth of both AI and coexistent LNCaP cells. Scratch migration assay was performed to demonstrate chemotactic migration in both AI and androgen sensitive cells. Castrated SCID mice were orthotopically co-implanted with GRP-Pro and LNCaP cells tagged with red and green fluorescent proteins, respectively. Frozen sections of the resulted tumor were viewed under fluorescence microscopy for color appearance and distribution.

Results: GRP-Pro cells grew aggressively in androgen depleted soft agar by forming greater than 100 fold more colonies than the control LNCaP cells. When the LNCaP cells were co-plated with GRP-Pro cells, the colony formation of the former increased by more than 10 fold, suggesting paracrine support from the GRP-Pro cells. Migratory activity of LNCaP cells was enhanced 2 fold when plated with GRP-Pro cells. Tumors harvested from SCID mice co-implanted with the two cell lines showed both green and red fluorescence, compared to no tumor growth in mice implanted with only green LNCaP cells.

Conclusions: Neuropeptide expressing LNCaP cells are AI and can support the AI survival and growth of parental LNCaP cells in a paracrine fashion. This supports a role for NE cells in the early post-castration transition to AI.

Supported by NIH Grants KO8 DK60748-01, 2RO1 DK/AG52659-04, and Department of Defense PC10520.
MEASUREMENT OF PROSTATE BIOPSY NUCLEAR STRUCTURE AND TISSUE MORPHOMETRY FROM A DOUBLE BLINDED, PLACEBO CONTROLLED TRIAL OF TESTOSTERONE REPLACEMENT

Danil V. Makarov, Cameron Marlow, Leonard S. Marks, M. Craig Miller, Jonathan I. Epstein, Alan W. Partin, Robert W. Veltri
The James Buchanan Brady Urological Institute and the Departments of Urology and Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD

Introduction and Objective: Androgen deficiency of the aging male (ADAM) is a syndrome associated with depressed mood, decreased bone and muscle mass, and increased adiposity which is treatable with exogenous testosterone (T). We examined the effects of T replacement on tissue architecture and nuclear structure of human prostate tissue.

Methods: 48 men with low serum T and ADAM were enrolled in a 6 month, double-blind, placebo-controlled trial testing biweekly injections of 150mg T. Prostate needle biopsies were performed at 0 and 6 months. 37 men biopsies’ were analyzable. Consecutive histologic tissue sections were stained with Masson trichrome and CAM-5.2 cytokeratin marker for analysis of stromal-epithelial (S-E) ratio and also Feulgen stained nuclei for quantitative nuclear morphometry (QNM). The Wilcoxon test for paired variables was applied for analysis of S-E ratios. Logistic regression was used to build cell nuclei models starting with 60 variables to differentiate pre- and post-treatment cohorts in both groups.

Results: 4 men in the placebo vs. 3 men in the T group had prostate cancer (CaP). The mean S-E ratios between groups was not significantly different pre- and post-treatment with T, 2.15 ± 0.79 vs. 2.41 ± 1.64 (P = 0.59), but showed a significant difference in the placebo treated group, 2.161 ± 1.28 vs. 3.396 ± 1.87 (P = 0.82). There was no significant difference in either group when CaP cases were removed from the analysis. A training set of cell nuclei from both T (n=3657) and placebo (n= 3681) groups were calculated using QNM. The T training model used 5 significant variables and had a ROC-AUC = 0.63 and a placebo model used 7 variable to produce a ROC-AUC = 0.63. Three similarly sized nuclei sets from both test groups were created and cross-validated based on these training models. Similar results were obtained performing analyses excluding all CaP cases and then again when further excluding an outlying placebo case.

Conclusions: While the S-E ratios were similar, QNM modeling detected a statistically significant difference in nuclei from human prostate tissue after treatment either with T or placebo, as compared to cells pre-treatment. These alterations may represent; possible biologic phenomena (effects of inflammation, occult cancer), placebo effect (diet/lifestyle modification) or statistical artifact. Further evaluation to determine both the etiology and the long term clinical significance of these observations is warranted.

Supported by a grant from the NIH/NCI SPORE Grant No. P50CA58236

Continues on next page
Poster #1

IMPACT OF PATIENT AGE AT TREATMENT ON OUTCOME FOLLOWING RADICAL RETROPUBIC PROSTATECTOMY FOR PROSTATE CANCER
Sameer Siddiqui, Shomik Sengupta, Jeffrey Slezak, Eric Bergstralh, Bradley Leibovich, Robert Myers, Horst Zincke, Michael Blute
Funding provided by Mayo Clinic, Rochester, MN

Purpose: Historically, young patients with prostate cancer were found to have poorer outcomes. Recent studies suggest both favorable pathology and improved survival for younger patients undergoing radical retropubic prostatectomy (RRP). The aim of this study was to assess age at treatment as a predictor of post-RRP survival.

Methods: We identified 5509 patients treated by RRP for prostate cancer at the Mayo Clinic, between 1987 and 1995. Age at treatment was classified into categories of <55y, 55-59y, 60-64y, 65-69y and > 70y. Cancer-specific survival (CSS), systemic progression-free survival (sPFS) and biochemical progression-free survival (bPFS) were estimated by the Kaplan-Meier method and analyzed using Cox proportional hazard models.

Results: Younger patients had lower pre-operative PSA, grade and stage of tumor. CSS, sPFS and bPFS were similar across age-groups, but overall survival decreased with older age at treatment. After multivariate adjustment, the risk of cancer death was lower (RR=0.53, 95% CI 0.30-0.90) for patients > 70y, while the risk of progression was lower (RR=0.57 to 0.62) for all age groups, compared to men <55y. On stratified subset analysis, sPFS was progressively worse with younger age among patients with high risk pathology. However, the addition of age to multivariate models incorporating pre-operative PSA, pathological features and adjuvant therapy failed to improve their predictive value for CSS and sPFS.

Conclusions: Despite more favorable clinico-pathological features, younger patients undergoing RRP for prostate cancer have similar survival as older counterparts. Given the greater proportionate impact of prostate cancer on survival, it is particularly important to pursue aggressive treatment for younger patients.

Poster #2

THREE YEAR OUTCOMES AFTER RADIOFREQUENCY ABLATION ASSISTED LAPAROSCOPIC PARTIAL NEPHRECTOMY
Michael Oefelein, MD, FACS (Presented By: Michael Oefelein, MD, FACS)

Introduction/Objectives: The report, herein, examines outcomes and complications after thermal ablation assisted laparoscopic partial nephrectomy.

Materials and Methods: Radiofrequency Ablation (RFA) assisted laparoscopic partial nephrectomy was employed in 24 consecutive renal masses over 36 months. Indications for laparoscopic directed RFA primarily included adjacent bowel and or hilar location. After RFA, the renal mass was laparoscopically excised and pathologically examined.

Results: For the 24 renal tumors, the mean tumor size was 3.0 cm with an operative treatment time of 99 minutes. The estimated blood loss was 121 ml and no patient required a blood transfusion. Urinoma was diagnosed in 3 patients at an average of 13 days post-operatively. Kaplan-Meier disease-free survival is 85 % at a mean follow-up of 20 months.

Conclusions: RFA assisted LPN provides effective hemostasis and, in the short term, cancer control. In this setting, urinoma presents with ipsilateral flank pain 1-2 weeks after surgery. The proposed mechanism for the delayed presentation is thermal injury to the urinary collecting system. Conservative management and or ureteral stent placement resolved all the urinomas.

Poster #3

WITHDRAWN
POSTER SESSION

Poster #4

PATTERNS OF CARE FOR MEN WITH PROSTATE CANCER FOLLOWING FAILURE OF PRIMARY TREATMENT
Tracey Krupski, MD, MPH, Christopher Saigal, MD, MPH, Janet Hanley, MS and Mark Litwin, MD, MPH (Presented By: Tracey Krupski, MD, MPH)

Purpose: We sought to determine trends in patterns of care following failure of primary prostate cancer treatment and to determine whether nonclinical factors influenced the receipt of secondary treatment.

Methods: We identified 65,885 patients treated for nonmetastatic prostate cancer in the years 1991-1999 from the linked databases of Surveillance, Epidemiology, and End Results and Medicare. The outcome of interest was receipt of secondary therapy. We performed logistic regression analysis to investigate a link between the likelihood of receiving secondary treatment after either surgery or radiation and demographic information.

Results: Of 65,716 patients who met our inclusion criteria, 10,200 (15%) received some form of secondary therapy. For patients undergoing initial surgical therapy, tumor grade and geographic region were the only factors associated with secondary therapy. For patients undergoing initial radiation therapy, not only were tumor grade and geographic region significant; but also age, year of diagnosis, marital status, and ethnicity were associated with receipt of secondary therapy.

Conclusion: Patterns of care following primary prostate cancer radiotherapy vary to a great degree. Despite dissemination of standardized definitions variation by geographic and sociodemographic variables persist for all prostate cancer patients suggesting a need for large scale trials in order to promote evidence-based, high quality care.

Poster #5

PROGRESSION IN PATIENTS WITH UROTHELIAL CARCINOMA OF THE BLADDER WITH HISTORIC LIMITED PELVIC LYMPH NODE DISSECTION
Nivedita Dhar MD, Steven C. Campbell, MD, PhD, Alwyn M. Reuther, MPH, Amr Fergany MD, PhD, and Eric A. Klein, MD
The Cleveland Clinic Foundation, Cleveland, Ohio

Objectives: To evaluate the rates of local and systemic progression (LP and SP) of patients with urothelial carcinoma of the bladder (UCB) with limited PLND in the era of 1990-2000.

Patients and Methods: A consecutive series of 277 patients undergoing an historical limited pelvic lymphadenectomy and radical cystectomy between 1990 and 2000 was analyzed. All patients were staged N0, M0 preoperatively, and no patient received neoadjuvant radio/chemotherapy. Boundaries of the historic limited bilateral PLND is defined as: genitofemoral nerve to obturator nerve and bifurcation of iliac vessels to pelvic sidewall. A rigorous analysis of LP was performed. In each case LP was defined as a radiographic soft tissue density of > 2cm below the bifurcation of the aorta. Pathologic characteristics based on the 1997 tumor-node-metastasis system and metastatic patterns were determined.

Results: A median of 11 nodes per patient (range 0-32 nodes) were reported and surgical margins were negative in all cases. Follow up ranged from 1.1 months to 12.1 years (median of 45.2 months). Of the 277 patients, 77 (27.8%) had evidence of LP alone and 54 (19.5%) had evidence of SP. The table demonstrates the results in terms of stage, LP, SP, median number of nodes reported and median time to LP and SP.

Conclusion: Compared to published reports of a similar cohort of patients having undergone cystectomy with extended PLND, limited PLND is associated with increased rates of LP.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Total #</th>
<th>LP #</th>
<th>LP %</th>
<th>SP #</th>
<th>SP %</th>
<th>Median # of Nodes Reported</th>
<th>For LP+, Median Time-to-Event (months)</th>
<th>For SP+, Median Time-to-Event (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1N0</td>
<td>47</td>
<td>1</td>
<td>2.1</td>
<td>5</td>
<td>10.6</td>
<td>12</td>
<td>8.4</td>
<td>25.6</td>
</tr>
<tr>
<td>T2aN0</td>
<td>78</td>
<td>1</td>
<td>1.3</td>
<td>12</td>
<td>15.4</td>
<td>12</td>
<td>17.8</td>
<td>28.5</td>
</tr>
<tr>
<td>T2bN0</td>
<td>43</td>
<td>13</td>
<td>30.2</td>
<td>10</td>
<td>23.3</td>
<td>10</td>
<td>18.9</td>
<td>10.5</td>
</tr>
<tr>
<td>T3aN0</td>
<td>30</td>
<td>13</td>
<td>43.3</td>
<td>10</td>
<td>33.3</td>
<td>12.5</td>
<td>8.1</td>
<td>10.7</td>
</tr>
<tr>
<td>T3bN0</td>
<td>26</td>
<td>19</td>
<td>73.1</td>
<td>5</td>
<td>19.2</td>
<td>11</td>
<td>4.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Tany N+</td>
<td>34</td>
<td>22</td>
<td>64.7</td>
<td>8</td>
<td>23.5</td>
<td>12.5</td>
<td>6.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Tany Nx</td>
<td>19</td>
<td>8</td>
<td>42.1</td>
<td>4</td>
<td>21.1</td>
<td>NA</td>
<td>7.6</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Continues on next page
**Poster #6**

**EFFICACY OF ABLATIVE HIGH DOSE PER FRACTION RADIATION FOR IMPLANTED HUMAN RENAL CELL CANCER IN A NUDE MOUSE MODEL**

Lance Walsh¹, L. Chinsoo Cho², Cheng-hui Chang², Kenneth Forster², Wareef Kabbani³, Jeffrey A. Cadeddu¹, Jer-Tsong Hsieh¹, Hak Choy², Robert Timmerman², Yair Lotan¹
Departments of Urology¹, Radiation Oncology², and Pathology³, The University of Texas Southwestern Medical Center, Dallas, Texas

Stereotactic body radiation therapy (SBRT) is a new therapeutic paradigm using very large dose per fraction treatments (ablative hypofractionation). While SBRT has shown efficacy in treating patients with lung, liver, and spine tumors, there have been no pre-clinical studies evaluating efficacy of this treatment in renal cell carcinoma. We investigate the use of ablative hypofractionation in treating human renal cell carcinoma using a nude mouse model.

Nude mice were injected subcutaneously into the right flank with A498 human renal carcinoma cells grown in culture. Tumor-bearing animals were radiated with 3 fractions (one per week) for a total dose of 48 Gy (n=12), while untreated animals served as controls (n=7). The mice were weighed and tumor volumes were measured at baseline and weekly until 7 weeks post-treatment.

Control animals demonstrated progressive tumor growth and were sacrificed due to either tumor size or ulceration (Figure 1). Tumors in the treatment group grew to 3 times their initial size over the 3 weeks of treatment but subsequently progressively decreased to less than 30% of their initial volume. All treated tumors exhibited marked cytologic changes including nucleomegaly, cytoplasmic vacuolization, smudgy chromatin appearance and nuclear pseudo-inclusions. Tumors from mice sacrificed 4 weeks post-treatment (n=4) demonstrated no mitoses.

![Figure 1. Tumor volume normalized to initial volume. Treatment (T), Post-treatment (PT)](image)

Treatment with high-dose-per-fraction radiation to 48 Gy resulted in a sustained decrease in tumor volume and marked cytological changes. These results are promising and encourage further research into this application of ablative hypofractionated radiation for kidney cancer.

**Poster #7**

**EPIDEMIC INACTIVATION OF THE CANDIDATE TUMOR SUPPRESSOR GENE HOXB13 IN HUMAN RENAL CELL CARCINOMA**

Heiwa Okuda, Mutsuo Furihata, Waka Ishida, Fumiji Saito, Tatsuo Iiyama, Ichiro Yamasaki, Taro Shuin; Kochi Medical School, Nankoku, Japan

**Background:** Epigenetic alterations like DNA methylation and the resulting inactivation of cancer-related genes often contribute to the development of various cancers. However, comprehensive genomic screening of human renal cell carcinoma (RCC) to identify aberrantly methylated genes has not been performed. We applied methylated CpG island amplification/representational difference analysis (MCA/RDA)
to isolate the differentially methylated CpG islands in RCC lines for the first time. Subsequent methylation analysis of isolated CpG islands in primary RCC cases revealed that the \textit{HOXB13} gene was methylated at high frequency in a tumor specific manner.

**Methods:** Methylation of \textit{HOXB13} in primary cancer and RCC lines were analyzed by combined bisulfite restriction analysis (COBRA) and bisulfite sequencing. Expression of \textit{HOXB13} was assessed by RT-PCR and immunohistochemical analysis. The \textit{HOXB13} induced apoptosis was analyzed by flow cytometry and immunofluorescence microscopy.

**Results:** The methylation frequencies of \textit{HOXB13} in 56 primary RCC samples and 15 lines were 30\% and 73\%, respectively. The methylation status of \textit{HOXB13} correlated with the loss of its expression both in RCC lines and primary tumors, and methyltransferase inhibitor treatment induced the recovery of its expression. Exogenous expression of \textit{HOXB13} in RCC cells that lacked endogenous \textit{HOXB13} expression suppressed colony formation and induced apoptotic features. Furthermore, \textit{HOXB13} methylation correlated positively with tumor grade and microvessel invasion.

**Conclusions:** The study suggests that \textit{HOXB13} is a novel candidate tumor suppressor gene in RCC and that its inactivation may play an important role in both RCC tumorigenesis and progression. As \textit{HOXB13} is methylated specifically in RCC with a high frequency but not methylated in normal kidney tissues, the methylation of \textit{HOXB13} in clinical samples may serve as a valuable novel diagnostic biomarker for the early detection of RCC.

**Poster #8**

**THE INFLUENCE OF CLINICAL AND PATHOLOGIC STAGE DISCREPANCY ON CANCER-SPECIFIC SURVIVAL AMONG PATIENTS TREATED FOR RENAL CELL CARCINOMA**

Robert Svatek, MD, Michael Hermann, MD, Yair Lotan, MD, David Duchene, MD, Arthur Sagalowsky, MD and Jeffrey Cadeddu, MD

(Presented By: Robert Svatek, MD)

**Purpose:** To compare clinical and pathologic staging in a contemporary, consecutive series of patients who were treated with partial or radical nephrectomy for renal cell carcinoma (RCC) and to determine the effect of clinical and pathologic stage discrepancy on outcomes.

**Methods:** We collected retrospective clinical, pathologic, and survival data from 264 consecutive patients with clinical T1-3 RCC who were treated with laparoscopic or open partial or radical nephrectomy from a single institution from 1994 to 2003.

**Results:** Pathological upstaging occurred in 45 of 264 (17\%) patients. 25 of 135 (18.5\%) clinical T1 tumors were pathologically upstaged. 18 of 85 (21.2\%) clinical T2 tumors were pathologically upstaged. Patients with clinical T1-2 tumors were stratified into two groups: same clinical and pathologic stage or pathologically up-staged. 5-yr recurrence-free survival for same stage versus pathologically upstaged clinical T1 (84.3 +/- 4.4 v. 47.4 +/- 11.5) and clinical T2 tumors (80 +/- 6.8 v. 40.7 +/- 13.4) were significantly different (p<0.0002). 5-year cancer-specific survival for same stage versus pathologically upstaged clinical T1 (98.5 +/- 1.5 v. 69.7 +/- 11.3) were significantly different (p=0.0005) and clinical T2 (90.9 +/- 5.0 v. 72.7 +/- 13.4) tumors approached clinical significance (p=0.0501).

**Conclusion:** Stage discrepancy is common among surgically treated patients diagnosed with renal masses and has a significant impact on clinical outcome. Implications of such clinical and pathologic stage discrepancy should be considered when counseling patients and determining therapeutic approaches.

**Poster #9**

**HORMONE REGULATION OF TRANSITIONAL CELL CARCINOMA OF THE BLADDER**

Stephen Boorjian, Hideki Kawamoto, Steve Dong, Daniel Ari Barocas, Eric Smith, Xueke You, W. Reid Pitts, Jr., Satish K. Tickoo, Mohammed Akhtar, and Douglas S. Scherr

Departments of Urology and Pathology, New York Presbyterian Hospital-Weill-Cornell Medical Center, New York, NY

**Introduction and Objectives:** Transitional cell carcinoma (TCC) of the bladder is approximately three times more common in men than women. The etiology for this difference in incidence by gender is unknown, although a role for sex steroids in the biology of bladder cancer has been suggested. We previously demonstrated loss of androgen receptor expression in advanced stage bladder cancer. Here, we evaluated expression of the estrogen receptor β (ERβ), as well as the enzymes aromatase and 5 alpha-reductase (5αR), in patients with TCC of the bladder, and correlated expression with clinical outcome.

*Continues on next page*
Methods: We evaluated tumor specimens from patients treated for TCC of the bladder at our institution between June 2002 and April 2005. Immunohistochemistry for ERβ expression was performed in 41 patients (mean age 61 years, range 44-77), including 25 men and 16 women, using a polyclonal rabbit anti-ERβ antibody (Santa Cruz Biotechnology, Inc, Santa Cruz, CA). Mean follow-up for the patients evaluated for ERβ was 11.5 months (range 2-41). Aromatase expression was analyzed via immunohistochemistry with a monoclonal mouse anti-aromatase antibody (Serotec, Oxford, UK) in 37 patients (mean age 65.4 years, range 44-80), including 25 men and 12 women, with a mean follow-up of 8.1 months (range 1-18). For ERβ and aromatase, the presence or absence of staining was recorded and was correlated with pathologic tumor stage and grade. 5αR expression was assessed using immunohistochemistry with a polyclonal rabbit anti-5αR antibody (courtesy of Dr. Russell, University of Texas Southwestern, Dallas, TX) in 36 patients (mean age 65 years, range 43-88), including 23 men and 13 women, with a mean follow-up of 13.0 months (range 1-27). A semi-quantitative staining score (SS) was calculated for 5αR expression in each tumor from the percentage of cells staining positive and the intensity of staining. 5αR SS was then correlated with pathologic tumor stage and grade. Disease-free survival (DFS) was calculated using the Kaplan-Meier method, and the impact of ERβ, aromatase, and 5αR expression on survival was assessed by the log rank test. Lastly, gene expression in matched tumor and adjacent, non-tumor bladder specimens from 7 patients (mean age 72.1 years, range 50-80) was compared using DNA microarray technology.

Results: ERβ expression correlated with aggressive tumor pathology, as ERβ was expressed in 21/31 (67.7%) high grade lesions, compared to 2/10 (20%) low grade tumors (p=0.045). In addition, ERβ was expressed in 18/25 (72%) muscle invasive tumors versus 5/16 (31.2%) superficial lesions (p=0.01). However, the presence of ERβ expression did not predict DFS (p=0.52). Aromatase was similarly expressed in 17/23 (73.9%) muscle invasive tumors compared to 4/14 (28.6%) superficial lesions (p=0.0023). Aromatase expression also tended to occur in high grade tumors (17/27 (63%)) versus low grade lesions (4/10 (40%)), although this difference did not reach statistical significance (p=0.27). Aromatase expression did, on the other hand, correlate with decreased DFS in patients (p=0.0063). Meanwhile, 5αR expression correlated inversely with tumor pathology and clinical outcome, as a low SS (reflecting low expression) for 5αR was associated with high grade lesions (p=0.035) and stage pT3/pT4 tumors (p=0.0027). In addition, patients with a 5αR SS below the median had a significantly decreased DFS (p=0.03). Hierarchical clustering analysis from the DNA microarray demonstrated distinct gene expression patterns in tumor versus non-tumor specimens, including a 4-fold upregulation of ERβ expression in tumors (p<0.05).

Conclusions: We present evidence of a role for hormones in the biology of TCC of the bladder. Future studies are needed to further define the nature of hormone regulation in bladder cancer development and progression.

Poster #10

APHASE I/II RANDOMIZED TRIAL OF WT1-PEPTIDE BASED IMMUNOTHERAPY IN HLA-A*2402 PATIENTS INCLUDING UROLOGICAL CANCERS

Tatsuo Iiyama1, Keiko Udaka2, Tamotsu Takeuchi3, Yuji Ohtsuki3, Hiroko Nakajima4, Yoshiiro Oka2, Akihiro Tsuboi2, Yusuke Oji4, Haruo Sugiyama5, and Taro Shuin1

Departments of 1Urology, 2Molecular Immunology and 3Tumor Pathology, Kochi Medical School, Oko-cho, Nankoku City, Kochi, 783-8505, Japan. Departments of 4Functional Diagnostic Science and 5Cancer Immunotherapy, Osaka University Graduate School of Medicine, Suita City, Osaka 565-0871, Japan.

Background: Specific cytotoxic T cell immunotherapy against cancer-associated antigens offers the potential for less toxic and effective outcomes. The Wilms’ tumor gene WT1 is overexpressed in various types of solid tumors. The WT1 protein was demonstrated to be an attractive target for immunotherapy. We report the outcome of a phase I/II clinical study of WT1 peptide-based immunotherapy for patients with malignant tumors including urological cancers.

Methods: Patients were intradermally injected with an HLA-A*2402-restricted, modified 9-mer WT1 peptide emulsified with Montanide ISA51 adjuvant at 3.0 mg per body at 1 week intervals 12 times. Immune responses were monitored by T cell tetramer-assays at 1-month intervals. Tumor status was evaluated by radiological examinations based on the RECIST guideline.

Results: Seventy-seven patients, including renal cell carcinoma(RCC) in 13, bladder cancer in 1 and prostate cancer in 8, hoped for participation in this trial. Among patients who showed HLA-A*2402 and had WT1 positive tumor by immunohistochemistry, 17 patients started our treatment. Tumor progression were stopped in 3 cases, including 1 RCC case, that completed our protocol. Cytotoxic killing assay showed a relative high tumor killing activity of WT1- specific cytotoxic T lymphocytes after WT1 vaccination. Toxicity consisted only of local erythema at the vaccine injection.

Conclusions: Vaccination of HLA-A*2402 patients with WT1 peptide is well tolerated and induces WT1 specific T cell immunity. Induction of specific T cell immunity to WT1 peptide in patients may correlates with less disease progression.
Poster Session

Poster #11

A PHASE I/II PROSPECTIVE DOSE ESCALATING TRIAL OF LYCOPENE IN PATIENTS WITH BIOCHEMICAL RELAPSE OF PROSTATE CANCER FOLLOWING DEFINITIVE LOCAL THERAPY

Departments of *Urology, †Hematology and Oncology, and Cancer Biology, and the Comprehensive Cancer Center of Wake Forest University Health Sciences, Winston-Salem, NC.

¥: These authors contributed equally to this manuscript.

PURPOSE: We report a prospective trial of lycopene supplementation in biochemically relapsed prostate cancer.

MATERIALS AND METHODS: 36 men with biochemically relapsed prostate cancer were enrolled in a dose escalating, phase I/II trial of lycopene supplementation. Six consecutive cohorts of six patients each received daily supplementation with 15, 30, 45, 60, 90, and 120 mg/day for one year. Serum levels of prostate specific antigen (PSA) and plasma levels of lycopene were measured at baseline and every three months. Primary endpoints were PSA response (defined as a 50% decrease in serum PSA from baseline), pharmacokinetics, and the toxicity/tolerability of this regimen.

RESULTS: 36 patients were enrolled. The median age was 74 (range 56–83) years with a median serum PSA at entry of 4.4 (range 0.8-24.9) ng/ml. There were no observed serum PSA responses. 37% of patients had PSA progression. The median time to progression was not reached. Toxicity was mild with one patient discontinuing therapy due to toxicity (diarrhea). Significant elevations of plasma lycopene were noted at three months and then appeared to plateau for all six dose levels. The plasma levels for doses between 15-90 mg/day were similar with further elevation only at 120 mg/day.

CONCLUSIONS: Lycopene supplementation in men with biochemically relapsed prostate cancer is safe and well tolerated. Plasma levels of lycopene are similar over a wide dose range (15-90 mg/day) and plateau by three months. Lycopene supplementation at the doses utilized in this study did not result in any discernible response in serum PSA.

Funding: Supported in part by NIH grant #: P30-CA12197-2751

Poster #12

PHASE II TRIAL OF INTRANODALLY INJECTED AUTOLOGOUS DENDRITIC CELLS PULSED WITH AUTOLOGOUS TUMOR IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA—PROMISING EARLY RESULTS

Thomas Schwaab MD PhD, Christopher Tretter MD, Todd Crocenzi MD, John S. Seigne MB, Jan Fisher MS, Diane Mellinger, Jill Uhlenhake MS, Nancy Crosby ARNP AOCP, Denise Machado-Rogers, John A. Heaney MB FRCISI and Marc S. Ernstoff MD
From the Uro-Oncology Group, Norris Cotton Cancer Center, Dartmouth Hitchcock Medical Center

INTRODUCTION: Immunotherapeutic trials using Dendritic Cells (DC) in urologic malignancies have produced disappointing clinical results at large. Yet, their immunologic potential as the most powerful antigen-presenting cells is intriguing. Evidence suggests that immune inhibitory pathways limit the effectiveness of immunotherapy. Data from our laboratory suggests that injection of activated DC into inguinal lymph nodes enhances an antitumoral immune response. We hypothesized that intranodal DC vaccine and IL-2/IFN-α therapy would decrease immune inhibition and increase tumor-specific immune activation in renal cell carcinoma (RCC) patients. We here report promising early clinical results from a Phase II trial using a novel technique of intranodal DC vaccine administration.

METHODS: DC are isolated from peripheral blood mononuclear cells obtained via leukapheresis from consented patients with metastatic RCC. DC are grown in our cell-processing laboratory using IL-4 and GM-CSF. DC are pulsed with autologous tumor lysate and matured with TNF-α. A treatment cycle consists of pulsed and matured DC injected into inguinal lymphnodes under sonographic guidance at 1x10⁷/ml, followed the next day by intravenous IL-2 (18MiU/m²) for 5 days and 3 subcutaneous injections of IFN-α (6MiU) every other day for a total of 5 cycles. Clinical and biological responses are determined over the course of treatment.
RESULTS: Between 01/2004 and 04/2005, 10 patients with metastatic RCC were enrolled into this phase II trial. The pulsed DC expressed a mature phenotype. The monocyte marker CD14 was appropriately down-regulated and the activation markers CD83, HLA-DR, CD86, CD80 were up-regulated. All patients were injected with 1x10^7 pulsed DC. Patients received between 2 and 5 vaccine injections. Inguinal lymph node injection was very well tolerated with only minor local swelling and discomfort. All patients experienced significant grade III toxicities related to IL-2/IFN-α therapy. At this point, 1 patient (10%) exhibits a complete response, 4 patients (40%) exhibit a partial response, 3 patients (30%) had stable disease and 2 patients (20%) have progressed. This results in an overall response rate of 50%. Clinical responses were persistent up to 15 months.

CONCLUSION: We demonstrate that the injection of tumor-lysate-pulsed DC directly into the lymph node is safe and feasible. In addition, we show that it is possible to generate “high-quality”, mature, tumor-pulsed DC in a dedicated cell-processing facility. Finally, initial clinical results are promising. It is worth noting the uncharacteristically long duration of clinical responses.

Poster #13

POST-CHEMOTHERAPY LAPAROSCOPIC RETROPERITONEAL LYMPH NODE DISSECTION FOR NON-SEMINOMATOUS GERM CELL TUMORS IN WELL-SELECTED PATIENTS

Maximiliano Sorbellini, Christine Theodore, Mario Di Palma, Michel Carmel, Gerard Benoit, Stephane Droupy
1- University of Sherbrooke, Urology Department, Quebec, Canada
2- CHU-Bicetre, Urology Department, Bicetre, France
3- Gustave Roussy Institute Cancer Center, Medical Oncology Department, Villejuif, France

Purpose: Approximately 10-30% of patients undergoing surgical resection of a residual retroperitoneal mass after primary chemotherapy for CS (clinical stage) II NSGCT present with active malignant tumor. Alternative surgical approaches to the gold standard bilateral RPLND have been proposed in the recent years. We evaluate the feasibility and outcome of post-chemotherapy laparoscopic RPLND in a well-selected group of patients.

Materials and Methods: From 1997 to 2004, 26 consecutive patients with CS II and CS III NSGCT underwent RPLND for residual masses after primary platinum-based chemotherapy. Criteria for a laparoscopic approach included: unilateral adenopathy(ies) prior to primary chemotherapy, significant volume reduction of lesions post chemotherapy, negative tumor markers prior to surgery, no lymphatic invasion of the spermatic cord at orchiectomy and no “a priori” need for vascular repair nor for nephrectomy during surgery based on pre-operative CT images of the abdomen.

Results: 15 patients underwent laparoscopy and 11 patients open surgery. Only one conversion to open surgery was performed due to adherences to the left renal vein. Major intra-operative complications only involved vascular injuries in both groups: Two patients suffered major blood loss due to vascular injuries in the open group (2800cc and 1500cc) and 1 in the laparoscopic group (400 cc). Mean operative times were 175 min for the laparoscopic group and 310 min for the open group. In the laparoscopy group, necrosis represented 33% (5) of cases, mature teratoma 47% (7), active tumor 7% (1) and inflammatory nodes 13% (2). In the open group, necrosis was found in 9% (1) of cases, mature teratoma in 18% (2), active tumor in 64% (7), and inflammatory nodes in 9% (1). In the open group, one patient died of metastatic progression and two had retroperitoneal recurrences. No recurrences to date have been detected in the laparoscopy group. Mean follow up was 37 months for the open surgery group and 33 months for the laparoscopic group.

Conclusions: Post-Chemotherapy laparoscopic RPLND is feasible and appears oncologically adequate for well-selected patients with NSGCT residual masses.

Key Words: Laparoscopy, Testis cancer, NSGTC, residual masses.
**Poster #14**

**MANAGEMENT OF URETHRAL AND URETEROINTESTINAL ANASTOMOTIC RECURRENCES IN ORTHOTOPIC DIVERSIONS**

Philippe E. Spiess, MD, MS, Gordon Brown, MD, Wassim Kassouf, MD, Ping Liu, MS, Ashish M. Kamat, MD, Bogdan Czerniak, MD, PhD, Colin P.N. Dinney, MD, H. Barton Grossman, MD

Departments of Urology, Biostatistics and Applied Mathematics, and Pathology,
The University of Texas M. D. Anderson Cancer Center, Houston, Texas

**Introduction and Objective:** Evaluate our experience with urethral and ureterointestinal anastomotic recurrences in patients undergoing cystectomy and orthotopic urinary reconstruction for transitional cell carcinoma (TCC) of the bladder.

**Methods:** We retrospectively reviewed the records of patients treated with radical cystectomy and orthotopic urinary diversion (N=272) for bladder TCC from January 1980 to July 2004. There were 270 Studer and 2 Hautmann urinary diversions followed a median of 4.3 years (0.3-13.4 years). The pathologic stage of bladder cancer in these cases was pT0 (N=30, 11%), pTis (N=24, 8.8%), pTa (N=16, 5.9%), pT1 (N=35, 12.8%), pT2 (N=89, 32.7%), pT3 (N=47, 17.3%), and pT4 (N=31, 11%).

**Results obtained:** Two patients were treated for urethral recurrences following Studer diversions with the pathologic stage of bladder cancer in both cases being pT2. One of the urethral recurrences (0.4%) had a cystectomy at our center. This recurrence was treated by total urethrectomy and local cuff excision with no subsequent local or distant recurrences. He remains alive with no evidence of disease 1.1 years following urethrectomy. The other urethral recurrence was treated with systemic chemotherapy; however, he developed a pelvic recurrence and remains alive with disease 3 years following detection of the urethral recurrence. Two patients have been treated for ureterointestinal anastomotic recurrences at our center subsequent to the cystectomy and orthotopic urinary diversion with the pathologic stage of bladder cancer being pTis and pT2. Both patients received neoadjuvant chemotherapy followed by neobladder cuff excision and either distal ureterectomy or nephroureterectomy. These patients remain alive with no evidence of disease and a functioning neobladder at 8.1 months and 2.6 years following detection of these recurrences.

**Conclusions:** In our experience, local recurrences involving the urethra and ureterointestinal anastomosis are infrequent. Surgical therapy provides good outcome with short-term follow-up.

There are no sources of Financial Funding to Disclose

**Poster #15**

**QUANTIFYING THE PUBLIC HEALTH IMPACT OF LOW HOSPITAL VOLUME ON OUTCOMES FOLLOWING CANCER SURGERY**

Brent K. Hollenbeck, David C. Miller, David A. Taub, Rodney L. Dunn, and John T. Wei

University of Michigan, Ann Arbor, MI

**Context:** Mounting evidence suggests the importance of hospital volume on outcomes following complex surgical procedures.

**Objective:** To estimate the potential benefit of regionalizing surgical services to top performing hospitals from low and very low volume centers treating 1 of 9 malignancies.

**Design, Setting, and Participants:** We estimated the likelihood of an in-hospital death or a prolonged length of stay following cancer surgery using a nationally representative sample of discharge abstracts collected within the framework of the Nationwide Inpatient Sample between the years 1988 and 2002. The 9 surgical procedures abstracted included: prostatectomy, adrenalectomy, cystectomy, nephrectomy, esophagectomy, pancreatectomy, lobectomy/pneumonectomy, liver resection, and rectal resection. The likelihood of an adverse event within hospital volume categories were used to estimate the percent attributable risk of very low and low volume hospitals on in-hospital mortality and prolonged length of stay (LOS) outcomes compared to top performing hospitals.

**Main Outcome Measures:** The percent attributable risk of very low and low hospital volume on in-hospital mortality and prolonged LOS, and the number of lives saved/earlier discharges.

*Continues on next page*
**Results:** Relative to top performing hospitals, very low and low hospital volume was significantly associated with prolonged LOS and in-hospital mortality for 8 and 7 cancer procedures, respectively, after adjusting for case mix and demographics. The magnitude of effect was greatest for patients undergoing prostatectomy for prostate cancer at very low volume hospitals—prolonged LOS: OR 4.2 (95% CI 4.0-4.4); in-hospital mortality: OR 5.3 (95% CI 3.7-7.5)—corresponding to 44,927 earlier discharges and 1,037 lives-saved if the procedure were to be regionalized to top performing hospitals. The greatest impact of volume on in-hospital mortality was noted for lobectomy/pneumonectomy for lung cancer in which up to 4,191 deaths (279 annually) could be attributed to the low volume. Despite a strong volume-outcome effect, regionalization of uncommon surgical procedures such as esophagectomy and liver resection would have relatively small impact on avoidable in-hospital deaths in the U.S. (59 and 38 lives-saved per year, respectively). **Conclusions:** The public health impact of regionalizing patients undergoing cancer surgery to top performing centers is likely to be modest at best given the number of patients saved. Conversely, other clinical endpoints, such as prolonged LOS, may be more responsive to hospital volume and have broader implications to the U.S. public for volume-based initiatives.

*Source of funding:* Institutional

**Poster #16**

**CRYOABLATION VS EXTERNAL BEAM RADIOTHERAPY: A PROSPECTIVE RANDOMIZED TRIAL FOR LOCALLY ADVANCED PROSTATE CANCER**


Urology and Oncology Departments, London Health Sciences Centers, University of Western Ontario, London, Ontario, Canada

**Introduction:** To evaluate the clinical utility of cryoablation (CRYO) for locally advanced prostate cancer (CaP) by conducting a prospective randomized trial of CRYO against external beam radiotherapy (EBRT).

**Materials and Methods:** Commencing in 1995, patients with T2C and T3 CaP were randomized to either EBRT or CRYO. All patients (pts) received 6 months of maximum androgen blockade starting 3 months before the assigned therapy. Pts had either a negative staging lymphadenectomy or negative CT with risk of nodal involvement <15% according to Partin’s Tables. For the EBRT pts, the median dose of radiation was 70 Gy delivered in 35 fractions. For the CRYO pts, the Cryocare system with 3-D TRUS guidance (5 or 6 cryo-probes and 2 freeze-thaw cycles) was used. Biochemical failure was used as an endpoint for analysis according to ASTRO definition (3 consecutive rises in serum PSA after reaching nadir).

**Results:** The study was closed with an accrual of only 64 out of the planned 150 pts (33 CRYO, 31 EBRT), largely due to a shift in practice to longer-term hormonal therapy (as per Bolla et al) and higher doses of radiation for this cohort. Among those randomized, median PSA, Gleason score and T stage distribution for the 2 groups were not significantly different. With mean follow-up of 37 months, 35 pts have exhibited biochemical failure, 21/33 (64%) among the CRYO and 14/31 (45%) among the EBRT pts (p = 0.028). The positive biopsy rate was not significantly different (EBRT 12% vs. 20% for the CRYO pts). Mean actuarial biochemical disease-free survival (bDFS) was 28 months for CRYO pts and 41 months for the EBRT (p = 0.028). The 4-year bDFS was 13% and 47% for the CRYO and EBRT groups respectively. Clinical disease-free survival (95% vs. 97%) and overall survival (87% vs. 87%) were not significantly different. Gastrointestinal complications were more frequent in the EBRT group (100% vs. 45%, p < 0.001). Urinary complications were similar in both groups.

**Conclusion:** Both EBRT and CRYO for locally advanced CaP are well tolerated. Although the trial was abbreviated, our results on the actuarial bDFS showed a trend for more favorable bDFS with the EBRT group. Six months of hormone therapy combined with either EBRT or CRYO appear to be suboptimal therapy for locally advanced CaP, especially for the CRYO pts. We currently reserve CRYO for salvage therapy after radiation failure.

This project was funded by a research grant from AstraZeneca.
**Poster #17**

**DEVELOPMENT AND INTERNAL VALIDATION OF NOMOGRAMS FOR 1, 5, 10, 15, 20 AND 25 YEAR PREDICTIONS OF BIOCHEMICAL (BCR), LOCAL AND DISTANT RECURRENCE AFTER RADICAL PROSTATECTOMY FOR CLINICALLY LOCALIZED PROSTATE CANCER**

Christopher Porter, Koichi Kodama, Robert Gibbons and RJ Correa  
Virginia Mason Medical Center, Seattle, Washington.  
Paul Perrotte and Pierre Karakiewicz  
Cancer Prognostics and Health Outcomes Unit, University of Montreal, Montreal, Canada.

**Introduction:** We examined the long-term rate of biochemical recurrence (BCR), local recurrence (LR) and distant recurrence (DR) after radical prostatectomy (RP), and generated recurrence free probability prognostic models for each type of recurrence.

**Methods:** 798 consecutive men were treated in a single center between 12/1954-5/1994, by RP for localized PCA: 4 received neoadjuvant hormonal ablation and 11 were lost to follow-up. Therefore, a cohort of 779 men aged 43-78 years (median 64) was used in this analysis. The pathologic stages were T2a: 177 (22.8%); T2b: 234 (30.1%); T3a: 244 (31.4%); T3b: 97 (12.5%); T3c: 16 (2.1%), and N1: 10 (1.3%). Pathologic Gleason sums were 2:3 (0.4%); 3:20(2.6%); 4:51(6.6%); 5:150(19.3%); 6:304(39.1%); 7:180(23.1%); 8: 42(5.4%); 9:25(3.2%) and 10:3(0.4%). Kaplan-Meier and multivariate Cox regression were used to test the association between age at surgery, pathologic stage, and pathologic grade for three separate outcomes: BCR, LR, and DR. Cox regression coefficients were used for nomogram development. These were internally validated with 200 bootstrap resamples, to reduce over fit bias.

**Results:** BCRs were recorded in 209 men (26.9%). LRs were recorded in 67 men (8.6%). DRs were recorded in 91 men (11.7%). Actuarial BCR-free probabilities (%) at 12, 60, 120, 180, 240 and 300 months were 98.3 (97.2-99.0); 86.6 (83.9-88.9); 74.4 (70.9-77.7); 65.6 (61.3-69.6); 63.5 (58.8-67.8) and 60.4 (53.9-66.3). Actuarial LR-free probabilities at 12, 60, 120, 180, 240 and 300 months were 99.7 (98.9-99.9); 95.2 (93.4-96.6); 91.2 (88.7-93.1); 89.1 (86.3-91.5); 87.4 (83.7-90.3) and 87.4 (83.7-90.3). Actuarial DR-free probabilities at 12, 60, 120, 180, 240 and 300 months were 99.2 (98.3-99.6); 95.6 (93.8-96.9); 90.1 (87.5-92.2); 84.0 (80.3-87.1); 79.9 (75.0-84.0) and 78.8 (71.0-83.1). The bootstrap-corrected predictive accuracy values of the nomograms were BCR 0.709, LR 0.694 and DR 0.726.

**Conclusion:** After RP, men remain at risk of BCR, LR, and DR for as long as 20-25 years. These events may be accurately predicted (69.4-72.6%), and used for follow-up, treatment and counseling purposes.
**Poster #18**

**IMPACT OF RACE ON TIME TO ANDROGEN INDEPENDENCE AND SUBSEQUENT BIOCHEMICAL PROGRESSION IN MEN WITH ADVANCED PROSTATE CANCER**

James Thomasch, Erik Kouba, Adam Hickerson, Eric Wallen, Culley C. Carson, Raj S. Pruthi, Division of Urology, Chapel Hill, North Carolina.

**Objective:** Mortality from prostate cancer is 2-3 times greater among African-American men (AA) between the ages of 40 and 70 years than among similarly aged Caucasian American men (CA). This study sought to evaluate whether AA men who undergo androgen deprivation therapy (ADT) for prostate cancer have differences (vs. CA) with regard to time to androgen independence and subsequent PSA doubling time of hormone-refractory disease.

**Methods:** 158 men were started on ADT at our institution between 1/95 and 10/02. From this cohort, 90 patients had evidence of subsequent hormone-refractory disease and had complete biochemical and clinical follow-up. Patients with advanced prostate cancer were defined as pathological or radiological evidence of metastatic disease (N+, M+), or PSA > 40 with a PSADT < 6 months. Patients with PSA progression include those who underwent ADT for PSA progression after definitive surgery or radiation therapy. Time to androgen independence (TTP) and the subsequent PSADT (when hormone-refractory) were calculated for all patients.

**Results:** Table I demonstrates the outcomes of those started on ADT for advanced prostate cancer. There were no significant differences with regard to age, starting PSA, or TTP between AA and CA men: shorter PSADT observed in AA men approached (but did not reach) statistical significance (p=0.072).

No differences were observed in the disease-specific mortality rate between AA vs. CA during the study period (19% vs. 21%).

**Conclusions:** AA men do not appear to have a difference in their response to ADT with regard to time to hormone-refractory disease. Furthermore, subsequent PSA progression (i.e. PSADT when hormone-refractory) or cause-specific survival was not different in either the advanced cohort or the PSA progression subgroup. These findings would support the contention that biologic differences do not appear to account for differences in progression and mortality in patients receiving ADT for advanced disease.

**Poster #19**

**ADJUVANT ANDROGEN DEPRIVATION THERAPY IMPROVES SURVIVAL IN PATIENTS WITH PROSTATE CANCER INVADING THE SEMINAL VESICLES**

Brant Inman, Eugene Kwon, Robert Myers, Bradley Leibovich, Michael Blute, and Horst Zincke
Mayo Clinic College of Medicine, Rochester, MN

**Introduction:** Adjuvant androgen deprivation therapy (ADT) following radical retropubic prostatectomy (RRP) should ideally be reserved for patients who have a high likelihood of benefiting from its use. Controversy exists, however, as to which clinicopathologic prognostic features...
clearly identify patients that are likely to profit from ADT. We review our experience with surgically-treated prostate cancer that had invaded the seminal vesicles and provide evidence to support the use of adjuvant ADT in this setting.

**Methods:** The study cohort was comprised of patients with adenocarcinomas of the prostate that had undergone RRP with bilateral pelvic lymphadenectomy at the Mayo Clinic (Rochester) between January 1, 1987 and December 31, 2000. All cases had pathologically-confirmed seminal vesicle invasion and negative pelvic lymph nodes. Patients that had received any form of preoperative treatment for prostate cancer were excluded as were those that received immediate adjuvant radiation therapy. A total of 800 patients meeting the above criteria were included this study and, of these, 211 (26.4%) received adjuvant ADT within 90 days of RRP and 589 (73.6%) did not. Kaplan-Meier survival estimates were calculated after stratification of the cohort into two groups by ADT status (ADT+ and ADT-). Survival curves were compared with the log-rank test. The survival endpoints assessed included: biochemical recurrence-free survival (BRFS), clinical recurrence-free survival and cancer-specific survival (CSS). Biochemical failure was defined as a single serum PSA e” 0.4 ng/mL occurring later than 3 months postoperatively and clinical failure was defined as the development of a local recurrence or distant metastasis. A Cox proportional hazards model was created to assess whether ADT status was a predictor of survival that was independent of other covariables. The survival endpoints assessed included: biochemical recurrence-free survival (BRFS), clinical recurrence-free survival and cancer-specific survival (CSS). Biochemical failure was defined as a single serum PSA e” 0.4 ng/mL occurring later than 3 months postoperatively and clinical failure was defined as the development of a local recurrence or distant metastasis. A Cox proportional hazards model was created to assess whether ADT status was a predictor of survival that was independent of other covariables. The median follow-up for patients in this study was 8.4 years.

**Results:** The mean age at surgery was 66 years in both groups (ADT+ and ADT-). Patients that had received immediate adjuvant ADT had higher preoperative PSA values (13.9 ng/mL vs. 10.6 ng/mL, P=0.0009), higher clinical stages (P=0.044), higher pathologic Gleason scores (P=0.006), more positive surgical margins (76% vs. 44%, P<0.0001), and more aneuploid tumors (51% vs. 39%, P=0.0047). Remarkably, despite the presence of these multiple predictors of poor prognosis, patients that had received immediate adjuvant ADT actually had better oncologic outcomes than patients that had not received this treatment. Univariate analysis showed that the presence of ADT was associated with better 10-year BRFS (60% vs. 23%, P<0.0001) and CSS (97% vs. 90%, P=0.036). After adjusting for pathologic Gleason score, preoperative serum PSA, surgical margin status, and DNA ploidy, the multivariate Cox model showed an even more pronounced protective effect of ADT for BRFS (HR= 0.24, 95%CI: 0.18-0.31, P<0.0001), clinical recurrence-free survival (HR=0.38, 95%CI: 0.20-0.71, P=0.002) and CSS (HR=0.36, 95%CI: 0.14-0.94, P=0.036).

**Conclusions:** In the current study, patients treated with RRP for prostate cancer invading the seminal vesicles and who received immediate ADT had considerably better oncologic outcomes than those patients who did not receive such treatment. This survival advantage occurred despite the presence of significantly more aggressive prostate cancer in the group of patients immediately treated with adjuvant ADT. These results suggest that immediate adjuvant ADT should be strongly considered in patients with prostate cancer invading the seminal vesicles treated by surgery.

**Poster #20**

**DELAY IN RECEIVING RADICAL PROSTATECTOMY AND RISK OF BIOCHEMICAL PROGRESSION AMONG MEN WITH LOW-RISK PROSTATE CANCER**

Stephen J. Freedland, Christopher J. Kane, Christopher L. Amling, William J. Aronson, Joseph C. Presti Jr., and Martha K. Terris

Johns Hopkins School of Medicine, Baltimore, MD, Veterans Administration Medical Center San Francisco, CA, UCSF School of Medicine, San Francisco, CA, San Diego Naval Hospital, San Diego, CA, Veterans Administration Greater Los Angeles Healthcare System, Los Angeles, CA, UCLA School of Medicine, Los Angeles, CA, Stanford University School of Medicine, Palo Alto, CA, Veterans Administration Medical Center Palo Alto, CA, Veterans Administration Medical Center Augusta, Georgia, Medical College of Georgia, Augusta, GA

**Supported by:** Department of Veterans Affairs, NIH, Georgia Cancer Coalition, Center for Prostate Disease Research grant from the United States Army Medical Research and Materiel Command, the Department of Defense, and the American Foundation for Urological Disease/ American Urological Association Education and Research Scholarship Award

**Background:** Men newly diagnosed with prostate cancer are faced with multiple treatment options. Understanding these options, their associated side effects, and making a decision often takes time, resulting in a delay prior to receiving treatment. This is particularly pertinent among men with low-risk disease who may be considering watchful waiting and thus may not feel a strong pressure to undergo treatment promptly. Whether delays and especially prolonged delays (e.g. >180 days) prior to radical prostatectomy (RP) negatively impact on disease outcome is unclear.
Methods: We examined the association between time from diagnosis to surgery and pathological features of the RP specimen and risk of biochemical progression among 895 men with low-risk prostate cancer (PSA<10 ng/ml and biopsy Gleason sum <6) treated with RP between 1988 and 2004 within the SEARCH Database using logistic regression and Cox proportional hazards, respectively.

Results: Time from biopsy to surgery was not significantly related to high-grade disease in the RP specimen, positive surgical margins, or extraprostatic extension (all p-trend>0.05). After adjustment for multiple clinical covariates, a longer time from biopsy to surgery was significantly associated with an increased risk of biochemical progression (p-trend=0.002). However, this increased risk of progression was only apparent among men with delays >180 days (median delay = 263 days; RR 2.73, 95%CI 1.51 – 4.94 relative to men with delays <90 days).

Conclusions: Our data suggests that patients with low-risk prostate cancer can be reassured that immediate treatment is not necessary. Whether long delays (>180 days) reduce the likelihood of curability in some patients requires further study.

Poster #21

BILATERAL POST-CHEMOTHERAPY RETROPERITONEAL LYMPH NODE DISSECTION (PC-RPLND) IS THE TREATMENT OF CHOICE FOR MEN WITH METASTATIC NON-SEMINOMATOUS GERM CELL TUMORS (NSGCT)

Brett S Carver, Bobby Shayegan, Robert J Motzer, Jason Stasi, Dean Bajorin, George J Bosl, and Joel Sheinfeld
From the Departments of Urology and Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, New York

Introduction: The multidisciplinary approach to the management of NSGCT has resulted in survival rates greater than 90% overall. In an effort to minimize the morbidity of a PC-RPLND, several modified templates have been reported. We evaluated our experience with PC-RPLND to determine the incidence and clinical outcome of men with disease extending outside the boundaries of a modified PC-RPLND.

Materials and Methods: From 1989 through 2003, a total of 532 men underwent PC-RPLND for metastatic NSGCT. Of these, 269 (51%) had either viable GCT or teratoma present in the RPLND specimen. Clinical and pathologic data was obtained from our prospective surgical database. Disease outside the template was defined as the presence of viable GCT or teratoma outside the modified template reported by Weissbach. A logistic regression model was constructed to determine predictors for disease outside the modified template. Freedom from disease recurrence was analyzed using the Kaplan Meier Method.

Results: Of the 269 patients with viable GCT or teratoma, 86 (32%) had evidence of disease outside the modified template. Viable GCT and teratoma were identified outside the modified template dissection in 67 (25%) and 19 (7%) patients respectively. For left- and right-sided primary tumors disease outside the template occurred in 27% and 38% respectively. Post-chemotherapy CT Scan revealed a residual mass outside the primary landing sites in 24 (28%) patients with disease identified outside the modified template at PC-RPLND. On multivariable analysis, RP nodal size pre- and post-chemotherapy (p=0.002, p<0.001), imaging positive outside the template (p<0.001), and the presence of metastases outside the retroperitoneum (p=0.027) were independent predictors for the presence of disease outside a modified template. At a median follow-up of 55 months, 59 (69%) remained free of recurrence, 6 (7%) had progressive disease, and 20 (24%) suffered a recurrence. The 5-year probability of disease free survival was 70% for men with disease outside a modified template and 82% for men with disease confined to the primary landing zones (p=0.31).

Conclusion: A significant percentage of men with metastatic NSGCT will have viable GCT or teratoma outside the boundaries of a modified dissection. The presence of disease outside a modified template is associated with a decreased disease free survival. Bilateral infra-hilar RPLND is the treatment of choice for men undergoing PC-RPLND, and a nerve-sparring procedure should be performed when feasible.

Poster #22

POLLUTION SOURCE PREDICTORS OF BLADDER CANCER INCIDENCE
Rabii Madi, MD; Bunyan Bryant, PHD; Elaine Hockman, PHD; and Cheryl Lee, MD

Introduction: The etiology of existing disparities in bladder cancer incidence and mortality are unknown, but may relate to disparate exposure to environmental chemicals. Chemical exposures are known to increase bladder cancer risk, but the impact of pollution is less clear. This ecological study examines the effect of environmental pollutants on bladder cancer incidence in various age groups in regions of the state of Michigan.
**Methods:** Records of new cancer diagnoses were obtained from the Michigan Department of Community Health for the years 1987, 1990, 1993, 1995, and 2000. Records were aggregated by age group (<15, 15-29, 30-44, 45-64, 65-74, 75+) and zip code of patients’ residence. Aggregated records were merged with institutional datasets from the University of Michigan School of Natural Resources and the Environmental Justice Initiative. Total numbers of cancer cases were converted to rates per thousand for each age group in each of 455 zip codes. Zip codes were classified by presence or absence of bladder/urinary cancers. Six categories of pollution source were examined in a logistic regression to predict bladder cancer incidence.

**Results:** Of 177,742 cancer records reviewed, bladder/urinary cancers were consistently 4.9% of new cancer cases across the five study years. Of several pollution sources, LUSTs (Leaking Underground Storage Tanks; p=.01; OR 1.5) was the most significant predictor of bladder/urinary cancer incidence. Zip codes with the highest rate of overall pollution density (number of identified pollution problems per square mile) were also associated with increased bladder/urinary cancer incidence (p<.001). Increasing incidence directly correlated with increasing pollution density across the five age categories over 15 years (each, p < .001).

**Conclusions:** Specific pollution sources and aggregate pollution density can increase the risk of bladder cancer incidence, particularly in older individuals. Regions with large numbers of LUSTs, as well as high pollution density, should be studied to determine whether disproportionate minority or low income populations reside in these communities and whether more aggressive tumors develop under prolonged pollutant exposure.

**Poster #23**

**CANCER-SPECIFIC MORTALITY IS INCREASED BY ERYTHROCYTE TRANSFUSION IN PATIENTS UNDERGOING SURGERY FOR CLEAR CELL RENAL CELL CARCINOMA**

Jonathan C. Routh¹, Christine M. Lohse², John C. Cheville³, Igor Frank¹, Michael L. Blute¹, Eugene D. Kwon¹⁴, and Bradley C. Leibovich¹,
Departments of ¹Urology, ²Biostatistics, ³Pathology, and ⁴Immunology, Mayo Clinic, Rochester, MN

**Introduction and Objectives:** Blood loss during the course of surgery for renal cell carcinoma (RCC) is occasionally severe enough to merit blood transfusion. In studies examining outcomes in multiple human malignancies, perioperative transfusion has been associated with increased mortality. This is likely due to immunomodulation induced by the transfusions, the mechanism of which is as yet unclear. Little data exist exploring this phenomenon in urologic malignancies, particularly in RCC. We therefore sought to review our own institutional experience to determine if this is a relevant concern in patients undergoing radical nephrectomy or nephron-sparing surgery for clear cell RCC.

**Methods:** We identified 2,442 patients who underwent radical nephrectomy or nephron-sparing surgery for unilateral, sporadic clear cell RCC at our institution between 1970 and 2002. The associations of perioperative transfusions with death from RCC were assessed using Cox proportional hazards regression models univariately and after adjusting for TNM stage, tumor size, nuclear grade, and coagulative tumor necrosis.

**Results:** Of the 2,442 patients studied, 1,504 died, including 814 patients who died from RCC at a median of 1.8 years following surgery (range 0-26). Among the 938 patients who were still alive at last follow-up the median duration of follow-up was 7.1 years (range 0-34). A total of 886 (36%) patients received perioperative transfusions. Patients transfused were three times more likely to die from RCC compared with those who were not transfused (risk ratio 3.39, p<0.001). This difference persisted even after adjusting for TNM stage, tumor size, nuclear grade, and histologic tumor necrosis (risk ratio 1.48, p<0.001). The cancer-specific survival rates at 5 years following surgery were 83.1% for patients who were not transfused compared with 51.7% for patients who were transfused.

**Conclusions:** Patients with clear cell RCC who receive perioperative transfusions have a decreased cancer-specific survival compared with patients who do not receive perioperative transfusions, even after adjusting for traditional prognostic pathologic features. It is possible that transfusion-associated immunomodulation is responsible for this decreased survival, and as such conservative transfusion criteria are indicated when treating patients with RCC.
**Poster #24**

**ASSOCIATION OF PREOPERATIVE ELEVATED ERYTHROCYTE SEDIMENTATION RATE AND ANEMIA WITH SURVIVAL FOLLOWING RADICAL NEPHRECTOMY FOR CHROMOPHobe, PAPILLARY, AND CLEAR CELL RENAL CELL CARCINOMA**

James S. Magera, Bradley C. Leibovich, Christine M. Lohse, Shomik Sengupta, John C. Cheville, Horst Zincke, Eugene D. Kwon, Michael L. Blute, Mayo Clinic, Rochester, Minnesota

**Introduction and Objectives:** Our objective was to evaluate the association of elevated erythrocyte sedimentation rate (ESR) defined as greater than 22mm per hour for women and 29mm per hour for men and anemia defined as less than 12.0 g/dL for women and 13.5 g/dL for men with survival following radical nephrectomy for chromophobe, papillary, and clear cell renal cell carcinoma (RCC).

**Methods:** We identified 2,537 patients with sporadic, unilateral RCC treated with radical nephrectomy between 1970 and 2002. The associations of elevated ESR and anemia with death from RCC were evaluated using Cox proportional hazards regression.

**Results Obtained:** There were 117 (4.6%) patients with chromophobe RCC, 19 of whom died of their disease. ESR was recorded in 46 patients, 19 (41.3%) of whom had an elevated rate. An elevated ESR was univariately associated with death from chromophobe RCC (RR 10.59; 95% CI 1.22 - 91.69; p=0.032). Preoperative hemoglobin was measured in 116 patients, 37 (31.9%) of whom had anemia. Anemia was also univariately associated with death from chromophobe RCC (RR 3.55; 95% CI 1.43 - 8.78; p=0.006).

There were 280 (11.0%) patients with papillary RCC, 43 of whom died of their disease. ESR was recorded in 98 patients; 30 (30.6%) of these patients had an elevated ESR. An elevated ESR was univariately associated with death from papillary RCC (RR 4.19, 95% CI 1.51 - 11.64; p=0.006). Anemia was observed in 77 (27.7%) of the 278 patients with a preoperative hemoglobin, and this was univariately associated with death from papillary RCC (RR 2.81, 95% CI 1.52 - 5.20; p=0.001).

There were 2,140 (83.4%) patients with clear cell RCC, 792 of whom died from their disease. Of the 839 patients with a preoperative ESR recorded, 422 (50.3%) had an elevated rate. Elevated ESR was significantly associated with death univariately and after controlling for the known prognostic features of TNM stage, tumor size, nuclear grade, and coagulative tumor necrosis (RR 1.47; 95% CI 1.4 - 1.91; p=0.004). Anemia was observed in 834 (39.2%) of the 2,127 patients with a preoperative hemoglobin, and this was also significantly associated with death from clear cell RCC both univariately and after multivariate adjustment (RR 1.27; 95% CI 1.09 - 1.48; p=0.002).

**Conclusions:** Although the rates of elevated ESR and anemia differed among patients with chromophobe, papillary, and clear cell RCC, both preoperative assessments were significantly associated with death for all three subtypes. To our knowledge, this is the first study to demonstrate this association for the chromophobe and papillary RCC subtypes.

**Poster #25**

**CYTOREDUCTIVE NEPHRECTOMY FOR METASTATIC RENAL CELL CARCINOMA: COMPARING SURGICAL OUTCOMES OF LAPAROSCOPIC vs. OPEN PROCEDURES: EXPERIENCE FROM A SINGLE CANADIAN CENTER**

Cox AR, Luke PP, Izawa JI, Pautler SE

Divisions of Urology and Surgical Oncology, Department of Surgery, University of Western Ontario, London, Ontario

**INTRODUCTION:** Cytoreductive nephrectomy in renal cell carcinoma (RCC) has been suggested to delay tumour progression and enhance survival when performed prior to systemic immunotherapy with interferon (IFN) or interleukin-2 (IL-2). Laparoscopic nephrectomy has been shown to decrease post-operative morbidity while providing equivalent long-term disease control, when compared to open nephrectomy in patients with non-metastatic RCC. Open cytoreduction may result in significant morbidity, prolonging or preventing immunotherapy. Minimally invasive cytoreduction may decrease post-operative morbidity and improve ability to receive and tolerate immunotherapy.

**OBJECTIVES:** To provide preliminary data on the surgical outcomes of cytoreductive open and laparoscopic nephrectomy performed in patients with metastatic RCC prior to IFN or IL-2 systemic therapy.

**METHODS:** A retrospective chart review was conducted on patients diagnosed with metastatic RCC who went on to have a cytoreductive nephrectomy. Eighteen charts were reviewed from our institution. Between 2001 and 2005, open cytoreductive(OCN) nephrectomy was performed in 8 patients (median age 63, range 48-71), while 10 patients (median 55.5, range 46-74) underwent laparoscopic procedures (LCN).

**CONCLUSIONS:**
RESULTS OBTAINED: Median tumour size was 9.5 cm (range 8.2-12) and 8.2 cm (range 3.5-15) in the OCN and LCN groups, respectively. Median follow-up was 11 mos (1-36 mos). The median operative time and the median estimated blood loss were 263.5 min (range 155-515) vs. 244 min (range 165-355) and 1500 ml (range 100-7000) vs. 200 ml (range 100-3000), OCN vs LCN respectively. 62.5 % of OCN required intraoperative transfusions opposed to only 20% of the LCN. Mean stay in hospital was 7.6 days in OCN and 4.5 days in LCN. 75% of OCN went on to receive systemic therapy compared to 40% of LCN; however another 20% were pending treatment at the time of review. The median time interval to receiving immunotherapy was 4 mos for OCN (range 1-22) and 3.5 mos for LCN (range 1-15). One patient did receive systemic immunotherapy prior to surgery. Disease recurred in 66.7% and 75% of OCN and LCN patients, on average 10.5 mos and 2 mos following initiation of systemic therapy. The mean survival of patients receiving immunotherapy was 11.8 mos OCN and 12.5 mos LCN. Overall mean survival was 10.1 mos and 12.7 mos in the OCN and LCN groups, respectively.

CONCLUSION: Preliminary data suggests laparoscopic cytoreductive nephrectomy decreases the morbidity associated with open procedures. The interval to receiving immunotherapy may be shortened with minimally invasive procedures but there is no set protocol for administration of immunotherapy in Canada, which creates inconsistent data. Further study of surgical approaches for cytoreductive nephrectomy is required.

Poster #26

TECHNIQUES, SAFETY AND ACCURACY OF NEEDLE BIOPSY OF RENAL TUMOURS: REVIEW OF THE TORONTO UHN EXPERIENCE

Alessandro Volpe¹, John Kachura², Andrew Evans³, William Geddie³, Arash Gharajeh¹, Arthy Saravanan¹ and Michael A.S. Jewett¹

Division of Urology, Departments of Surgical Oncology¹, Medical Imaging² and Pathology³, Princess Margaret Hospital and the University Health Network, University of Toronto, Ontario, Canada

Introduction and Objectives: The incidence of renal cell carcinoma (RCC) is increasing worldwide. The majority of RCC’s are now incidentally detected as small renal masses on imaging. The current standard of treatment for localized renal tumours is partial or radical nephrectomy. However many small masses are benign tumours or low grade RCC’s that are likely to have an indolent behaviour. There is increasing evidence that in selected patients small renal tumours can be safely managed with an initial period of active surveillance and delayed intervention for those that progress with a rapid growth rate. In the completely different clinical scenario of metastatic RCC, patients with clear cell type histology are more likely to benefit from adjuvant therapy with biological modifiers following cytoreductive nephrectomy. Percutaneous biopsy of renal tumours for pathological diagnosis and to aid treatment decision making has not been widely used in North America because of concerns about tumor implantation and sampling errors. The presence of intratumoral heterogeneity has been considered a significant issue, since it may preclude an accurate histological diagnosis. We reviewed the UHN clinical experience with percutaneous needle core biopsy of renal masses to assess safety and diagnostic accuracy.

Methods: 49 needle core biopsies of renal masses were identified in the UHN Department of Pathology database from January 2001 to May 2005. In 25/49 cases fine-needle aspiration (FNA) was performed in the same setting. The biopsies were performed under ultrasound and/or CT guidance. An 18-gauge side-cutting needle was used to obtain cores and a 22-gauge fine needle was used for aspiration of cytological specimens. A retrospective chart review was performed to document the complication rate and the ability to obtain sufficient tissue for diagnosis. To assess intratumoral heterogeneity in small renal tumors we reviewed the slides of 27 <3 cm. RCC’s that were surgically removed from 2001 to 2004. Each case was examined by a single pathologist. Significant heterogeneity was defined as a two-point difference in Fuhrman score in different areas of the same tumor (i.e., grade 1 to 3 or 2 to 4).

Results: Three of 49 biopsies (6.8%) produced minor bleeding that was easily controlled with the placement of gelfoam pledges through the biopsy coaxial sheath. No other significant complications and no cases of tumor seeding were reported. 45 of 49 biopsies (91.8%) were diagnostic. 14 patients underwent a radical or partial nephrectomy after a diagnostic needle biopsy. In all these cases pathology on the biopsy and on the surgical specimen were concordant. 2 masses were removed after a non diagnostic biopsy and were found to be RCC (1 papillary and 1 chromophobe). As far as tumor heterogeneity is concerned, only 1 of the 27 small tumors that were reviewed (4%) displayed significant heterogeneity.

Conclusion: In our experience percutaneous needle core biopsy of renal masses is a safe and accurate diagnostic procedure. Intratumoral heterogeneity seems to be a rare entity. Needle biopsies are therefore likely to provide tissue samples that are representative of the entire tumour in the vast majority of the cases. In our opinion, percutaneous biopsy should have an increasing role in the diagnostic management of renal masses and can have a significant impact in treatment decision making. This is particularly true in elderly or unfit patients diagnosed with small incidental masses or in patients with metastatic disease being considered for cytoreductive surgery and/or therapy with biological modifiers.
**PREVENTION OF BLADDER CANCER IN THE FHIT KNOCK-OUT MOUSE MODEL WITH ROFECOXIB, A COX-2 INHIBITOR**

James LeNoir, Domenico D’Arca, Fedra Gottardo, Emma Bragantini, Bernadette Wildemore, Dolores Shupp-Byrne, Nicola Zanesi, Carlo M. Croce, Leonard G. Gomella, Raffaele Baffa. Department of Urology, Thomas Jefferson University, Kimmel Cancer Center, Philadelphia, PA; Comprehensive Cancer Center, Ohio State University, Columbus OH. *This work was supported by a Merck and Co., Inc- Medical School Grant

**INTRODUCTION:** Epidemiological studies have indicated that non-steroidal, anti-inflammatory drugs (NSAIDS) may have a role in the prevention of human cancers. A number of pre-clinical studies have suggested that inhibition of cyclo-oxygenase (COX) with NSAIDS has an anti-cancer effect in animal models of colon, urinary bladder, skin, and breast. Molecular based targeting of the COX-2 isoform has lead to the development of COX-2 selective inhibitors such as rofecoxib, which potentially inhibit COX-2 dependent inflammation while avoiding typical NSAID associated side effects. Although the initial premise for developing these drugs was their potential for inhibiting the inflammation and pain of some forms of arthritis, these agents may present a promising strategy for various epithelial cancers. Previous studies have shown that administration of COX-2 inhibitors, while decreasing overall morbidity do not decrease the incidence of pre-neoplastic lesions in the murine model. Our hypothesis is that rofecoxib will inhibit or slow the development of BBN- induced urinary bladder cancers in mice lacking the FHIT tumor suppressor gene.

**OBJECTIVES:** Our laboratory has demonstrated that mice lacking the FHIT tumor suppressor gene are more susceptible than controls to the carcinogenic effect of N-Butyl-N-(-4-hydroxybutyl)-nitrosamine (BBN). Treatment of mice with BBN results in the development of transitional cell carcinomas of the urinary bladder that bear significant histopathological similarities to the human disease. Therefore, we chose the Fhit knock-out mouse to study the effectiveness of rofecoxib, a COX-2 inhibitor, in bladder cancer prevention.

**METHODS:** 208 mice consisting of 50 Fhit +/+, 63 Fhit +/-, and 95 Fhit -/-, were divided into five treatment groups: 1) 0.1% BBN and rofecoxib; 2) 0.01 % BBN and rofecoxib (only Fhit -/- mice); 3) rofecoxib alone; 4) 0.1% BBN alone; and 5) 0.01% BBN alone (only Fhit -/- mice). Each of the three genotypes were taken through a 13 week dietary cycle of rofecoxib at the concentration of 150 ppm administered in mouse chow. BBN was dissolved in water. After the 13th week, BBN was no longer administered to the mice. At the end of the 15th week the mice were sacrificed and their bladders collected for histological analysis. The mice fed 150 ppm rofecoxib had blood samples taken twice during the 13 weeks to verify the blood serum concentration of rofecoxib.

**RESULTS:** The mean concentration of rofecoxib in the blood serum was 0.37-μg/mL (± 0.15). The mice that received only rofecoxib and no BBN presented normal bladders, regardless of the genotype. The association between Fhit genotype, rofecoxib treatment, presence of pre-neoplastic lesions and bladder tumors, was evaluated via the two sided Fisher’s exact test (α of 0.05). Comparing the means of each group the pair wise Ps were as follows: Group 1 vs. Group 4 p=1 for Fhit +/+; p=0.687 for Fhit +/-; p=0.107 for Fhit -/-; p=0.114. Comparing Group 2 vs. Group 5 p= 0.114. The difference between the groups was not statistically significant. There was a significant increase in neoplastic lesions in the Fhit +/- and Fhit -/- vs. Fhit +/- mice after BBN treatment.

**CONCLUSIONS:** Our results confirmed that Fhit knock-out mice, both Fhit +/- and Fhit -/-, are exquisitely sensitive to the carcinogenic effect of BBN and that the Fhit knock-out mouse is an extremely valid model to study in vivo bladder cancer tumorigenesis. Our preliminary results suggest also that rofecoxib does not provide a therapeutic defense in our chemically induced mouse bladder cancer model.

---

**LAPAROSCOPIC CYTOREDUCTIVE NEPHRECTOMY: THE MD ANDERSON CANCER CENTER EXPERIENCE**

Surena F. Matin, Lydia Madsen, and Christopher G. Wood, University of Texas M.D. Anderson Cancer Center, Houston, TX

**Introduction:** Cytoreductive nephrectomy (CN) is increasingly accepted as an integral component in the management of select patients with metastatic renal cell carcinoma. Critics of CN have argued that perioperative morbidity or postoperative disease progression may preclude some patients from receiving systemic therapy. Laparoscopic cytoreductive nephrectomy (LCN) may allow a significant reduction in morbidity and provide a greater likelihood of patients receiving timely postoperative systemic therapy.

**Methods:** From April 2001 to March 2005, 38 patients underwent LCN at our institution. From their records, were evaluated perioperative parameters such as demographics, blood loss, operative time, complications, time to follow-up, time to adjuvant therapy, and survival.
Results: The median patient was 62 years old (range 41-82 years). Most patients had a performance status of 1 or lower. The median operative time was 188 min, and the median amount of blood loss was 175 ml. All specimens were removed intact. The median tumor size was 8 cm (range 3.5-14 cm). Median duration of hospitalization was 3 days. There were 2 major (5.7%) and 4 minor (11.4%) complications and no perioperative mortality. Postoperatively, 97.4% of patients were eligible for or received systemic therapy at a median of 41 days. Overall median survival duration was 18.1 months.

Conclusions: LCN is a safe and effective surgical approach for select patients with metastatic renal cell carcinoma. Our initial results indicate that with proper patient selection, LCN is feasible, postoperative morbidity is minimized, and systemic therapy may be delivered in a timely fashion in nearly all patients.

Poster #29
PRESENCE AND LOCATION OF PROSTATE CANCER IN PATIENTS UNDERGOING RADICAL CYSTOPROSTATECTOMY: FEASIBILITY OF PROSTATE CAPSULE SPARING CYSTECTOMY
Alon Z. Weizer, Rajal B. Shah, Scott Gilbert, Stephanie Faruzzi, Cheryl T. Lee, James E. Montie, and David P. Wood, Jr. from the Department of Urology and Pathology, University of Michigan, Ann Arbor, MI

Introduction and Objectives: Surgical removal of the bladder with preservation of the entire or part of the prostate with orthotopic diversion has been performed to preserve sexual function and improve urinary control. Concern remains over the risk of leaving prostate cancer behind with less radical surgery. We evaluated the risk of prostate cancer in a cohort of patients undergoing radical cystoprostatectomy (RCP)

Methods: Thirty-five men who underwent RCP had pathologic submission of the prostate capsule separately from the prostate adenoma and bladder at the time of surgery. The pathologist evaluated these specimens for bladder and prostate cancer grade and stage. In addition when present, the greatest diameter of the largest prostate cancer was measured. Demographic and peri-operative information was obtained from our institutional bladder cancer database. These variables were compared between the prostate cancer and no prostate cancer group.

Results: Only one patient had invasive urothelial carcinoma into the prostate adenoma with no cases of carcinoma in situ present in the prostatic urethra. Of 35 patients, 16 (46.5%) had prostate cancer with 15/16 present in both the capsule and the adenoma and 1/16 in the prostate adenoma only. Four patients (11%) had clinically significant prostate cancer in the prostate capsule using the definition of Gleason grade (GG) >6 and tumor volume > 0.5 cm³. Body mass index, pre-operative prostate specific antigen (PSA) (n=21), abnormal digital rectal exam, prostate volume, family history and pre-operative bladder tumor pathology did not distinguish between the prostate cancer and no cancer groups. Patients with clinically significant prostate cancer (mean age= 72 yo) and all prostate cancers (67.6 yo) were older than patients without prostate cancer (61.9 yo).

Conclusion: Only age appeared to distinguish between bladder cancer patients with clinically significant capsular prostate cancer, capsular prostate cancer overall, and no prostate cancer. Appropriately selected younger patients may benefit from cystectomy with partial prostate preservation. Prospective clinical trials are needed to evaluate quality of life and oncologic control of these procedures.

Poster #30
ANDROGEN RECEPTOR MUTATION (T877A) PROMOTES PROSTATE CANCER CELL GROWTH/CELL SURVIVAL AND ABROGRATES P53 MEDIATED APOPTOSIS
Chen Sun, Yinghui Shi, Linda L. Xu, Chilukuri Nageswararao, Leland D. Davis, Takehiko Segawa, Albert Dobi, David G Mcleod, and Shiv Srivastava

1Center for Prostate Disease Research (CPDR), Department of Surgery, Uniformed Services University, Rockville, Maryland; and 2Urology Service, Walter Reed Army Medical Center, Washington, DC

Alteration of the AR functions due to amplification, overexpression and somatic mutation of the AR itself or altered interaction of AR with other cell growth regulatory proteins, may contribute to a significant subset of advanced prostate cancer (CaP). Here we provide direct evidence showing cell growth/cell survival promoting effects of a widely studied CaP associated AR mutation (T877A). Ad-mtAR (T877A) infected
LNCaP or LAPC4 cells continued to grow in the androgen-deprived medium and exhibited an androgen independent AR-transcription factor activity, in contrast to the Ad-wtAR or Ad-control infected cells. Ad-mtAR (T877A) infected LNCaP or LAPC4 cells exhibited enhanced cell growth in the presence of lower concentrations of the synthetic androgen, R1881. Ad-mtAR (T877A) infected LNCaP cells showed striking resistance to cell growth inhibition/apoptosis mediated by the wt p53. Taken together, these findings provide novel biologic insights into the AR dysfunctions resulting from the T877A mutation and potentially similar AR alterations that may provide selective cell growth/survival advantage for CaP progression. These observations have important implications for developing biology based prognostic biomarkers and therapeutic strategies for CaP showing such Arand p53 dysfunctions.

**Poster #31**

**RESPONSE TO INTRAVESICAL IMMUNOTHERAPY IN BCG NAIÊVE AND BCG TREATED PATIENTS WITH DIFFERENT FAILURE PATTERNS**

Fadi N. Joudi, Brian L. Gallagher, Michael A. O’Donnell, University of Iowa, Iowa City, IA

**Objective:** The objective of our study was to determine response rates of BCG naïve and BCG treated superficial bladder cancer patients with different failure patterns.

**Methods:** Data from a national phase II multicenter trial for BCG+interferon (IFN)-α intravesical therapy were analyzed and response rates for BCG naïve patients (n=536) and BCG treated patients with recurrent disease (n=467) with different patterns of failure were obtained (refractory, <6 mos., 6-12 mos., 12-24 mos., and >24 mos., median follow-up 24 mos.). Intravesical immunotherapy regimens given have been previously reported (O’Donnell et. al. JU Sept 2004). Kaplan Meier survival curves were obtained. We also performed a multivariate analysis comparing response rates between the different groups.

**Results:** Of the BCG naïve patients, 59% were cancer-free at 24 months median follow up. BCG treated patients who were BCG refractory, those who recurred within 6 months, 6-12 months, 12-24 months, and >24 months had response rates of 34%, 41%, 43%, 53%, and 66% respectively (p = 0.0005 for trend). When we compared patients that failed >24 months vs those that failed <24 months, and those that failed >12 months vs <12 months the differences in response rates were significant (66% vs 44%, p=0.0134 and 58% vs 42%, p=0.0049). When we compared patients that failed >6 months vs <6 months the difference was not significant (p=0.075). There was no difference between patients that failed after 12 months as compared to those that failed after 24 months (p=0.79). We then compared response rates of BCG naïve patients to patients that failed after 12 and 24 months, there was no statistically significant difference (p=0.335 and 0.97, respectively). The cut off point seems to be at 12 months. Using a multivariate analysis, BCG naïve patients had different response from BCG treated patients that failed within 12 months but similar response to those that failed after 12 months.

**Conclusion:** Patients with recurrent superficial bladder cancer after 12 months of remission have similar response rates as BCG naïve patients.

The phase II BCG IFN-alpha study was supported by Schering-Plough. The investigators retained full independence in the conduct of this research.

**Poster #32**

**QUANTITATIVE GENE EXPRESSION ANALYSIS OF ANDROGEN RECEPTOR IN BENIGN AND NEOPLASTIC PROSTATE EPITHELIAL CELLS MAY PREDICT PSA RECURRENCE**

Inger L Rosner³, Lakshmi Ravindranath¹, Bungo Furusato³, Yongmei Chen³, Jennifer Cullen¹, Isabell A. Sesterhenn³, David G. Mcleod², Shiv Srivastava¹, Gyorgy Petrovics¹

¹Center for Prostate Disease Research (CPDR), Department of Surgery and US Military Cancer Institute, Uniformed Services University, Rockville, MD 20852; ²Urology Service, Walter Reed Army Medical Center, Washington, DC 20307; ³Department of Genitourinary Pathology, Armed Forces Institute of Pathology, Washington, DC 20306;

**Introduction:** Alterations of androgen receptor (AR) functions due to overexpression, amplification, or mutation have been described in a significant subset of advanced prostate cancer (CaP). Quantitative determination of AR expression levels in the prostate tumor cells may have
potential to predict aggressive clinical behavior in newly diagnosed patients. In this study laser capture microdissected (LCM) benign and neoplastic epithelial cells from prostatectomy specimens were analyzed for correlation of \(AR\) expression with disease progression.

**Methods:** 105 hormone-naïve patients post radical prostatectomy were studied. Benign and neoplastic prostate epithelial cells were collected with LCM from frozen tissue slides. Expression of \(AR\) and \(GAPDH\) genes were measured by duplex quantitative real-time RT-PCR in 210 specimens. The expression of \(AR\), normalized to \(GAPDH\) expression in the same specimens, was compared in tumor and benign epithelial cells, and a correlation with clinico-pathological features was evaluated.

**Results:** Paired t-test was used to compare \(AR\) expression between tumor and benign prostate cells of each patient. Overall a 50% lower \(AR\) expression was detected in tumor tissue than in benign tissue (\(p=0.0037\)). However, patients with the highest \(AR\) expression in their tumor cells, compared to matched benign cells, were more likely to have biochemical disease recurrence (\(p=0.0183\)). Stepwise logistic regression analysis with age, race, PSA at diagnosis, pathologic stage, Gleason sum, follow up time and \(AR\) expression suggested that increased tumor versus benign \(AR\) expression ratio is an independent factor predicting PSA recurrence (\(p=0.0381\)). With each 2-fold increase in \(AR\) expression ratio the odds of PSA recurrence increased by 36.4%.

**Conclusions:** \(AR\) expression, as determined in LCM-derived malignant and benign prostate cells, was lower overall in tumor cells, however patients with increased expression of \(AR\) in their tumor versus benign cells have an increased risk of PSA recurrence. Therefore, quantitative determination of \(AR\) gene expression levels in prostate epithelial cells may be useful for predicting PSA recurrence. This study supports the accumulating data suggesting that gain of elevated \(AR\) functions may contribute to CaP progression.

---

**Poster #33**

**DEMOGRAPHIC TRENDS IN RENAL TUMORS OVER THE LAST 15 YEARS**

Joseph A. Pettus\(^1\), Scott Eggner\(^1\), Mark E. Snyder\(^1\), Robert Motzer\(^2\), Victor E. Reuter\(^3\), Paul Russo\(^4\)

\(^1\)Department of Urology, \(^2\)Department of Genitourinary Oncology, and \(^3\)Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA

**Introduction and Objectives:** Renal cell carcinoma has undergone significant stage migration in the United States and Europe over the last fifteen years. The purpose of this study was to examine the effects of stage migration on tumor characteristics, practice patterns, and survival of patients with renal cortical tumors over the last fifteen years.

**Methods:** We reviewed the Memorial Sloan Kettering renal tumor database and identified patients who underwent surgery for renal neoplasms between January 1989 and July 2005. Patients with non-renal primary tumors or who were treated for renal cell carcinoma recurrence were excluded. Time-dependent trends in age, presentation, stage, histology, tumor size, type of surgery, blood loss, and hospital stay were assessed. Continuous variables were analyzed using ANOVA, categorical variables by chi square method, and survival using Kaplan-Meier curves with the log-rank test.

**Results:** We identified 2,074 patients undergoing surgery for renal cortical tumors with a mean follow up of 43.8 months. Mean age was 61.3 years and did not significantly change over the study period. We observed a downward stage migration as the mean tumor size decreased from 7.5 to 4.0 cm over the study period (\(p<0.001\)). The percentage of incidentally detected tumors increased from 54% to 75% (\(p<0.001\)) and the proportion of nephron-sparing procedures increased from 8% to 60% over the study period (\(p<0.001\)). Mean hospital stay (9.9 to 4.1 days) and mean blood loss (1665 to 409cc) decreased over the same period. A symptomatic presentation, higher pathologic stage, and clear cell histology each had a negative impact on survival.

**Conclusions:** A significant stage migration has occurred in renal cortical tumors over the last fifteen years, leading to more nephron-sparing procedures, lower blood loss, and shorter hospital stays. Advanced disease continues to portend a poor prognosis.

**Funding:** None

---

*Continues on next page*
**Poster Session**

Continued from previous page

**Poster #34**

**IS RENAL SINUS FAT INVASION THE SAME AS PERINEPHRIC FAT INVASION FOR pT3a RENAL CELLCARCINOMA?**

R. Houston Thompson, Bradley C. Leibovich, John C. Cheville, M.D., W. Scott Webster, Christine M. Lohse, Eugene D. Kwon, Igor Frank, Horst Zincke, and Michael L. Blute, Mayo Clinic, Rochester, Minnesota

**Introduction:** Both perinephric and renal sinus fat invasion are classified as pT3a renal cell carcinoma (RCC) according to the 2002 American Joint Committee on Cancer. We investigated the prognostic significance of each of these pathologic features using a cohort of pT3a patients.

**Materials and Methods:** Between 1970 and 2002, 205 patients without direct adrenal invasion underwent nephrectomy for pT3a clear cell RCC at our institution. Survival was estimated using the Kaplan-Meier method and the associations of fat invasion with death from RCC were evaluated using Cox proportional hazards regression models.

**Results:** Among the 205 patients, 162 (59%) had perinephric fat invasion and 43 (72%) had renal sinus fat invasion. At last follow-up, 126 patients died from RCC. Median follow-up for patients still alive was 6.0 years. Patients with renal sinus fat invasion were significantly more likely to have positive lymph nodes (p=0.041), higher nuclear grade (p=0.014), and sarcomatoid differentiation (p=0.006) compared to those with perinephric fat invasion. In addition, patients with renal sinus fat invasion were 63% more likely to die from RCC compared to those with perinephric fat invasion (risk ratio 1.63; 95% confidence interval 1.09 - 2.46; p=0.018). The risk of death persisted in multivariate analysis after adjusting for regional lymph nodes and distant metastasis (risk ratio 1.91; 95% confidence interval 1.26 - 2.89; p=0.002) and after adjusting for the Mayo Clinic SIGN (Stage, Size, Grade, and Necrosis) score (risk ratio 1.90; 95% confidence interval 1.25 - 2.88; p=0.003).

**Conclusion:** RCC tumors invading the renal sinus fat are associated with aggressive pathologic features, including positive lymph nodes, compared with tumors invading the perinephric fat. We believe both of these features should be individually assessed during routine pathologic examination. Patients with renal sinus fat invasion are at significant risk of death compared with patients with perinephric fat invasion even after multivariate adjustment.

**Poster #35**

**THE IMPACT OF RENAL IMPAIRMENT ON ELIGIBILITY FOR ADJUVANT CISPLATIN-BASED CHEMOTHERAPY IN PATIENTS WITH BLADDER TRANSITIONAL CELL CARCINOMA**

Atreya Dash, Matthew D. Galsky, Andrew J. Vickers, Angel M. Serio, Theresa M. Koppie, Guido Dalbagni, Bernard H. Bochner, Memorial Sloan-Kettering Cancer Center, New York, NY

**Introduction:** Perioperative cisplatin-based chemotherapy is effective in patients with locally advanced urothelial bladder cancer, but it is not widely used. Renal impairment may be a major factor limiting its use. We therefore sought to determine the proportion of patients ineligible for adjuvant cisplatin-based chemotherapy based on inadequate renal function alone.

**Methods:** We identified patients who underwent radical cystectomy for urothelial cancer of the bladder with evidence of extravesical disease (e”pT3 or any N+). Patients who received neoadjuvant chemotherapy were excluded. Serum creatinine immediately before and nadir serum creatinine after cystectomy were used to calculate creatinine clearance (CrCl) or glomerular filtration rate (GFR) using the Cockcroft-Gault (CG), Jelliffe, and Modification of Diet in Renal Disease (MDRD) Study formulas. A cutoff of CrCl <60 mL/min or GFR <60 mL/min/1.73 m2 was used to determine eligibility for cisplatin-based chemotherapy. The proportion of patients ineligible by each formula was compared by univariate logistic regression. Univariate linear regression was performed to determine the effect of age and on CrCl or GFR.

**Results:** Most patients were pT3 or greater; 39% were lymph node positive. The overall proportions of patients ineligible for cisplatin-based chemotherapy was 28% by the CG formula, 52% by Jelliffe, and 24% by MDRD. Concordance between formulas was low: only 64% of patient received the same eligibility recommendation using all three formulas. With all formulas the probability of ineligibility increased with age; by the CG equation, ~45% of patients >70 years old were ineligible.

**Conclusions:** A large proportion of high-risk bladder cancer patients are ineligible for cisplatin-based perioperative chemotherapy due to impaired renal function. This finding is most striking in the elderly. Better selection of patients who may safely receive cisplatin and more effective regimens devoid of cisplatin are required for improving outcomes in this subset of patients.
Poster #36

NATURAL HISTORY OF BLADDER CANCER IN PATIENTS WHO ARE pT0 AT RADICAL CYSTECTOMY
University of Texas M. D. Anderson Cancer Center, Houston, Texas

Introduction: A pT0 surgical specimen is not uncommon in patients treated for bladder cancer. We evaluated its prognostic relevance in a contemporary series of patients treated with radical cystectomy.

Materials and Methods: From 1993-2003, 857 patients with bladder cancer underwent radical cystectomy at our institution. Of these, 95 (11%) were found to have pT0N0M0 in the surgical specimen and form the basis of this report. Overall survival (OS), disease-specific survival (DSS), and recurrence-free survival (RFS) data were analyzed by the method of Kaplan and Meier, with log rank tests to evaluate associations between survival and variables studied.

Results: The median age of patients was 63 years (range 34 to 83 years) with a mean follow-up of 48 months (range 1 to 177 months). Clinical stages were cT1: 12, cT2: 48, cT3b: 25, cT4a: 8, and cT4b: 2. Sixty-nine patients received preoperative chemotherapy; the majority (90%) were platinum-based regimens. The 5-year OS, DSS, and RFS rates were 86%, 91%, and 86% respectively. Eight patients developed recurrences (cT1:2, cT2:1, cT3b:3, and cT4:2), 7 of whom died of disease. Median time to recurrence of these patients was 7.7 months (range 3 to 64 months). Patients that received neoadjuvant chemotherapy had similar 5-year RFS compared with those who did not (83% vs 92%, p = 0.32). Presence of lymphovascular invasion on TURBT specimen (p=0.02) was significantly associated with shorter OS on multivariate analysis. Clinical stage, presence of carcinoma in situ, hydronephrosis, presence of variant histology, and number of nodes excised were not significantly associated with OS on multivariate analysis.

Conclusion: Although patients with pT0 in the cystectomy specimen have a good prognosis, not all can be considered cured of their disease. Although the majority of recurrences develop within the first year, delayed recurrences can occur even beyond 5 years. Thus even patients who are pT0N0M0 need life-long surveillance.

Source of funding: NIH-Bladder SPORE CA91846 and T32 training grant

Poster #37

THE VEGF405 CC POLYMORPHISM IS ASSOCIATED WITH PROSTATE CANCERS OF POOR PROGNOSIS
Edith Canby-Hagino, MD, Dawn Garcia, MS, Ian Thompson, MD, Dean Troyer, MD, Jacques Baillargeon, PhD, Timothy Brand, MD, Robin Leach, PhD, Susan Naylor, PhD, (Presented By: Edith Canby-Hagino, MD)

Introduction and Objectives: Vascular endothelial growth factor (VEGF) is requisite for supporting growth and metastasis of malignant neoplasms, including prostate cancer. A single nucleotide polymorphism (snp) of the VEGF gene positioned at +405 is associated with increased production of VEGF and neovascularity in non-malignant conditions. We examined this polymorphism in a case-control study to determine prostate cancer risk and prognosis associated with this variant.

Materials and Methods: A total of 643 cases and 1071 controls were genotyped. Controls were limited to male participants in the San Antonio Center of Biomarkers of Risk for Prostate Cancer (SABOR) prospective cohort study who were older than 40 years with a normal prostate examination and a prostate specific antigen of <2.5 ng/ml, and no diagnosis of prostate cancer. Cases included individuals with incident prostate cancer diagnosed through the SABOR program as well as individuals with a history of prostate cancer accrued from the greater San Antonio area.

Results: In the total study population, a diagnosis of prostate cancer was not significantly associated with increases odds for any VEGF+405 polymorphism, but the CC genotype at this locus was associated with cancers of poor prognosis, as determined by Gleason score and stage. The CC genotype was associated with an increased risk for prostate cancer with a Gleason grade of 7 or higher for all ethnicities, with an odds ratio (OR) of 1.97 (95% CI 1.120-3.479). The CC genotype was most strongly associated with this higher Gleason score in Hispanics, with an OR of 3.31 (95% CI 1.022-10.701). In addition, for the entire population, the CC genotype was associated with prostate cancers of bad outcome, as determined by Gleason score of 8 or higher or stage T3b or higher, with an OR of 2.37 (95% CI 1.250-4.506). This associated was also significant for the subgroup of non-Hispanic Caucasians (OR 2.25, 95% CI 1.043-4.876).

Conclusions: The CC genotype at VEG+405 is associated with prostate cancer of worse prognosis, as determined by Gleason score and stage.

Continues on next page
**Poster Session**

**Poster #38**

**PROTEASE ACTIVATED RECEPTOR-1 (PAR-1) EXPRESSION PREDICTS BIOCHEMICAL RECURRENCE IN PATIENTS WITH PROSTATE CANCER**

Peter C. Black¹, Gregory J. Mize¹, Daniel L. Greenberg², Robert L. Vessella¹, Ruth Etzioni³, Lawrence D. True⁴, Thomas Takayama¹

Departments of ¹Urology, ²Medicine and ⁴Pathology, University of Washington, and ³Fred Hutchinson Cancer Research Center, Seattle, WA.

**Introduction:** The protease activated receptors (PAR) are G-protein coupled receptors implicated in the progression of a variety of cancers.

**Methods:** Forty formalin-fixed and paraffin-embedded radical prostatectomy specimens from the GU Cancer Tissue Bank were analyzed by immunohistochemistry (IHC) using an antigen retrieval protocol and a standard IHC kit with Avidin/Biotin amplification. Monoclonal antibodies to PAR-1, PAR-2 and PAR-4 were employed. Staining was categorized as present or absent, and the degree of staining was quantified as 1+ to 3+. Biochemical recurrence free survival related to staining for each PAR was analyzed by Kaplan-Meier plot and multivariate analysis was performed.

**Results:** Increased expression of PAR-1, PAR-2 and PAR-4 in the cancerous epithelial cells when compared to normal glands was seen in 45%, 42% and 68% of specimens. PAR-1 staining was remarkable for increased staining in the stromal cells immediately adjacent (“subepithelial”) to the cancerous cells in 60% of patients. By Kaplan-Meier plots, this subepithelial staining for PAR-1 but not the epithelial staining for PAR-1, -2 or -4 was a significant predictor of biochemical recurrence (Figure 1).

**Conclusions:** Subepithelial staining for PAR-1 predicts biochemical recurrence of prostate cancer. This is preliminary evidence indicating that this pattern of staining may be useful as prognostic marker. Moreover, the PAR-1 subepithelial staining pattern suggests that this receptor may be involved in paracrine stimulation of the adjacent stroma by serine proteases produced by prostate carcinoma.

**Figure 1.**

---

**Poster #39**

**RADICAL CYSTECTOMY FOR TRANSITIONAL CELL CARCINOMA OF THE BLADDER: WHAT PERCENTAGE OF PATIENTS QUALIFY FOR BLADDER PRESERVATION PROTOCOLS?**

Vitaly Margulis, Joshua Stern, Yair Lotan and Arthur I. Sagalowsky. University of Texas Southwestern Medical Center, Dallas, Texas

**Introduction:** The purpose of this study was to determine what percentage of patients who underwent radical cystectomy for transitional cell carcinoma (TCC) of the urinary bladder would also qualify for bladder preservation protocols with a tri-modality approach.

**Methods:** A chart review was performed for consecutive patients (n=58) who were both diagnosed with TCC and underwent radical cystectomy at the University of Texas Southwestern Medical Center. Pre-cystectomy parameters reviewed included tumor depth, focality and resectability during transurethral resection (TUR), as well as radiologic evidence of extravesical disease, hydroureronephrosis and lymphadenopathy. Final cystectomy pathologic stage was available for all patients.
**Results:** Baseline demographics included: median age 64 years (range 43-88), 41 (70.7%) male. Clinical stage: 6 (10.3%) TIS, 6 (10.3%) Ta, 23 (39.7%) T1, 20 (34.5%) T2, and 3 (5.2%) T4. Based on clinical staging criteria 19 (32.2%) of patients were deemed appropriate candidates for chemo-radiation bladder preservation protocol, while 39 (67.8%) met one or more of the following exclusion criteria: 18 (46.2%) incomplete transurethral resection, 27 (69.2%) multifocal disease, 17 (43.6%) carcinoma in situ on random bladder biopsies, 1 (2.6%) gross extravesical disease, and 9 (23.1%) presence of hydroureteronephrosis. 4 (21%) of 19 candidates for bladder preservation were found to have gross extravesical disease and/or metastatic lymph node deposits on final pathologic staging.

**Conclusions:** While bladder preservation is feasible for a number of selected patients with muscle-invasive bladder cancer, only a minority of patients that were treated with radical cystectomy qualified for a bladder sparing approach.

---

**Poster #40**

**THE LAPAROSCOPIC ONCOLOGIST'S DILEMMA: PURE LAPAROSCOPIC RADICAL PROSTATECTOMY VERSUS ROBOTIC ASSISTED RADICAL PROSTATECTOMY, AN ANALYSIS OF SHORT TERM OUTCOMES FROM A SINGLE INSTITUTION**

John W. Davis, MD, Scott Hubosky, MD, Robert Given, MD, Donald Lynch, MD, and Michael Fabrizio, MD. The Department of Urology of Eastern Virginia Medical School, Devine-Tidewater Urology, and Sentara Norfolk General Hospital, Norfolk Virginia.

**Introduction and Objectives:** Since 2001, our department has offered patients with localized prostate cancer the option of laparoscopic radical prostatectomy (LRP). In the past year, we have transitioned to the robotic assisted laparoscopic radical prostatectomy with the daVinci system (dVP). We sought to determine if there are differences in short-term outcomes of these techniques.

**Methods:** From 2001-2004, 168 LRP procedures were performed by two surgeons with fellowship training in endourology/laparoscopy (MDF) or urologic oncology (JWD). Both surgeons were mentored for 6 months by an experienced LRP surgeon with >200 case experience. LRP was performed by the Montsouris technique. From July 2004-July 2005, 153 dVP procedures were performed by the two LRP surgeons and an open surgeon with a urologic oncology fellowship (RWG). All three surgeons were proctored for their first three cases. Technical difference of LRP vs. dVP include 1) initial posterior dissection versus anterior dissection, 2) pedicle division with harmonic scalpel versus clips/cold scissors, and interrupted versus running anastomosis. Data was prospectively gathered under an IRB approved protocol, and all learning curve cases were included.

**Results:** Short-term results are displayed in the table with T-test p values. Anastomotic leaks were defined as any known urine leak (e.g. elevated drain creatinine) or catheter time > 21 days. Procedure times exclude setup/take-down time. All LRP rectal injuries were during non-nerve sparing dissection, and were spread throughout the case series.

<table>
<thead>
<tr>
<th></th>
<th>LRP (n=168)</th>
<th>dVP (n=153)</th>
<th>P =</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure time, min. - plnd</td>
<td>276</td>
<td>245</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Procedure time, min., +plnd</td>
<td>320</td>
<td>258</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hospital stay, median days</td>
<td>3</td>
<td>2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Catheter days, median</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Blood loss, ml, median</td>
<td>250</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td># patients transfused</td>
<td>3</td>
<td>0</td>
<td>0.09</td>
</tr>
<tr>
<td>Rectal injury</td>
<td>7 (4%)</td>
<td>0</td>
<td>0.01</td>
</tr>
<tr>
<td>Ureteral obstruction</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bladder neck contracture</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>13 (7.7%)</td>
<td>9 (5.8%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Ileus</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Neuralgia</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Open conversion</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>PT2 positive margins</td>
<td>13/129 (10%)</td>
<td>15/117 (12.8%)</td>
<td>0.50</td>
</tr>
</tbody>
</table>

**Conclusions:** Transitioning an established LRP program to dVP at a single institution resulted in shorter OR times, shorter length of stay, and elimination of rectal injuries. The shorter procedure times and ergonomics of dVP enabled the routine performance of two procedures per day. Long-term quality of life data collection is ongoing.

**Funding Source:** Departmental.

*Continues on next page*
Poster Session

**Poster #41**

**INHIBITION OF THE C-TERMINAL PORTION OF HEAT SHOCK PROTEIN 90 RESULTS IN DOWNREGULATION OF ONCOGENIC PROTEINS IN PROSTATE CANCER CELLS**

Jeffrey M. Holzbeierlein, MD1, Benjamin Cronk1, Len Necker, PhD2, Brian SJ Blagg, PhD3 1Department of Urological Surgery, University of Kansas Medical Center, Kansas City, KS 2 Cell and Cancer Biology Branch, National Cancer Institute, NIH, Rockville, MD 3 Department of Medicinal Chemistry and The Center for Protein Structure and Function, The University of Kansas, Lawrence KS

**Introduction:** Heat shock protein 90 has been demonstrated to be critical in the folding of a number of proteins important for the development and maintenance of prostate cancer. Inhibitors of Hsp 90 lead to ubiquitination and proteasomal degradation of many of these oncoproteins. Inhibitors of the N-terminal portion of Hsp 90 are currently in clinical trials for the treatment of prostate cancer. However, their use has been hampered by their significant toxicity and poor pharmacologic properties. We report the in vitro activity of a novel compound that inhibits the C-terminal portion of Hsp 90.

**Methods:** We applied the novel C-terminal Hsp 90 inhibitor KU-1 to LNCaP and LAPC-4 cells at various concentrations. Western blots were performed for the following proteins in cells: Akt, androgen receptor, HER2, HIF1alpha, and Hsp90 and actin as controls.

**Results:** The application of KU-1 resulted in inhibition of critical prostate cancer oncogenic proteins Akt, androgen receptor, HER2, and HIF1alpha at concentrations of 1μM-100μM in LNCaP cells. Inhibition of the AR occurred at 100nM of KU-1 in LAPC-4 cells. No difference was observed in actin and an accumulation of Hsp90 similar to the findings of the N-terminal inhibitors was observed.

**Conclusions:** KU-1, an inhibitor of the C-terminal portion of Hsp90 is able to inhibit a number of proteins thought to be critical in prostate cancer at low concentrations. This may represent an exciting, novel agent for prostate cancer treatment.

---

**Poster #42**

**PATIENTS UNDERGOING RADICAL NEPHRECTOMY FOR SMALL RENAL CORTICAL TUMORS MAY BE AT SIGNIFICANT RISK FOR DEVELOPING CHRONIC RENAL INSUFFICIENCY**

William C Huang,* Mark Snyder, Angel Serio, Ganesh V Raj, Andrew Vickers, Paul Russo, Memorial Sloan Kettering Cancer Center, New York, NY.

**Introduction and Objective:** In 2003, the National Kidney Foundation (NKF) released practice guidelines to identify and stratify patients with chronic renal insufficiency (CRI). Subsequently, CRI has been identified as a graded and independent risk factor for significant co-morbidities such as cardiovascular disease and even death. Based on these findings, we examined the effects of radical nephrectomy (RN) and partial (PN) nephrectomy on the renal function of patients with small renal cortical tumors.

**Methods:** Among 2,200 nephrectomies performed at our institution between 1989-2005, we identified 699 patients with a normal serum creatinine (<1.4 mg/dL) and a normal contra-lateral kidney who underwent surgery for a single renal cortical tumor <4 cm. Based on NKF practice guidelines, renal function was assessed by estimating glomerular filtration rate (GFR) in ml/min/1.73m² using the Modification in Diet and Renal Disease (MDRD) formula. We defined CRI as a GFR of <60 and severe CRI as a GFR of <45. Statistical analysis was performed using Kaplan-Meier and Cox proportional hazards analyses.

**Results:** Pre-operative variables including age, race, hypertension, and Charlson-Romano Index were similar in both surgical groups. Median pre-operative GFRs in the RN and PN groups were 69.4 and 69.3, respectively. Despite a normal pre-operative creatinine and contra-lateral kidney, 27% of the patients in the PN group and 24% of patients in the RN group had a GFR <60 prior to surgery. Based on univariate analysis, the 3-yr and 5-yr probabilities of freedom from developing CRI and severe CRI were significantly lower in the RN group (log rank - p <0.001). The median time to CRI in the RN group was 7.1 months vs. 74.5 months in the PN group. The median time to severe CRI in the RN group was 77 months (not reached in PN group) (Figure 1). On multivariate analysis, RN remained an independent risk factor for developing CRI (HR 2.9) and severe CRI (HR 11.32) (p <0.005) (Table 1). **Conclusions:** Using NKF practice guidelines, the pre-operative renal function of patients in our series was considerably worse than previously recognized. Our study suggests that patients undergoing RN for small renal cortical tumors are at significant risk for developing CRI and severe CRI.

---

**Table 1.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>GFR &lt; 60</th>
<th>GFR &lt; 45</th>
</tr>
</thead>
<tbody>
<tr>
<td>surgery (RN)</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Age</td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Charlson</td>
<td>1.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>

**Figure 1.** Kaplan-Meier probabilities of patients from severe CRI.

<table>
<thead>
<tr>
<th>Surgery (RN) vs. PN</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.0</td>
<td>0.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Charlson</td>
<td>1.0</td>
<td>0.9</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Figure 2.** Kaplan-Meier probabilities of patients from severe CRI.
**Poster #43**

**PRIMARY CRYOSURGICAL ABLATION FOR CLINICALLY LOCALIZED PROSTATE CANCER USING 17G CRYONEEDLES: THE INITIAL DUKE EXPERIENCE**

V. Mouraviev MD PhD, I. Nosnik MD, and T.J. Polascik MD
Duke Prostate Center and Division of Urologic Surgery, Duke University Medical Center, Durham, NC

**Introduction:** Percutaneous perineal cryoablation of the prostate is becoming a feasible treatment modality for clinically localized prostate carcinoma. We report our initial outcomes using a TRUS-guided, argon/helium cryotherapy system.

**Materials and methods:** Between January 2002 and July 2005 54 men with biopsy-proven prostate cancer underwent primary cryosurgery for clinically localized prostate carcinoma. Patients who had previously undergone surgery, radiation therapy or prior cryoablation for prostate carcinoma were excluded from the study. All patients underwent a dual freeze-thaw cycle using third generation cryotechnology with ultrathin 17G cryoneedles (Oncura Inc., Plymouth Meeting, PA). Patients were followed with physical examination and PSA surveillance every 3 months and with radiologic imaging (MRI, CT or ProstaScint scan) when indicated.

**Results:** The median patient age was 68 years (range: 50-83) and the median follow-up was 18 months (range: 1- 41). The clinical stage was T1C-46, T2A-6 and T2B-2 and the median pretreatment PSA was 12.0 (range: 2.0- 37 ng/ml). Biopsy Gleason score was 5 in 4% of cases, 6 in 50%, 7 in 33%, 8 in 11%, and 9 in 2% of patients. Preoperative median TRUS volume was 25cc (range: 10-58). 11 patients with pretherap y prostate volumes exceeding 40 cc were treated with neoadjuvant hormone therapy for 3-6 months for volume reduction.

Eighty five percent of patients were impotent prior to treatment, and of the 8 preoperatively potent patients, 53% responded to 5-phosphodiesterase inhibitors after surgery. 51 patients remained completely continent while 3 patients reported mild incontinence (1 was incontinent before cryosurgery) requiring 1-2 pads per day after therapy. Only 1 patient had experienced urethral slough without clinical sequelae and another had transient penoscrotal edema. The median postoperative PSA nadir was 0.18 (range: 0.00- 7.9). The distribution of the latest PSA for all patients at the time of last followup was as follows: <0.2 ng/ml (71%), <0.4 (82%) and <1.0 (91%). Four patients had PSA progression: 1 patient had a Gleason 8 biopsied from the seminal vesicles; 1 patient began hormonal and external beam therapy for a rising PSA with a negative metastatic evaluation; 1 patient began hormonal therapy for a rising PSA despite a negative prostate biopsy and metastatic evaluation; and 1 patient with a negative prostate biopsy and metastatic evaluation is on expectant management. Overall survival rate was 100%.

**Conclusions:** Cryoablation of the prostate is a feasible and safe treatment option in patients with organ-confined prostate cancer. Further studies with longer follow-up will be necessary to determine the sustained efficacy of this procedure.

---

**Poster #44**

**EFFECT OF POSITIVE SURGICAL MARGINS ON BIOCHEMICAL RECURRENCE IN LOW STAGE PROSTATE CANCER**

Nicholas J. Fitzsimons, Leon L. Sun, Cary N. Robertson, Thomas J. Polascik, Craig F. Donatucci, Judd W. Moul
Division of Urology, Department of Surgery, Duke Prostate Center, Duke University Medical Center, Durham NC

**PURPOSE:** Positive surgical margin status (SM) has been shown to increase the risk of biochemical recurrence (BCR) in prostate cancer, even in patients without extracapsular extension. However, no consensus exists on whether patients with positive surgical margins should undergo adjuvant therapy versus expectant management. We sought to identify a subgroup of post-prostatectomy patients in which margin status negatively impacted BCR.

**METHODS:** We analyzed data on 968 men from the Duke Prostate Center database who underwent radical prostatectomy for CaP diagnosed between March 1991 and August 2004. BCR was defined as any post-operative PSA >0.2. Patients were grouped according to pTNM stage and BCR was compared between those with positive SM and negative SM.

**RESULTS:** Patients with pT2A (n=138) and pT2B (n=502) disease were well-matched for age, follow-up time, pre-biopsy PSA, and biopsy Gleason Score. Recurrence rates for pT2A disease were 15.9% and 16.7% in patients with negative and positive SM, respectively. In pT2B patients, however, BCR rates increased from 12.9% with negative SM to 31.5% (p<0.001) with positive SM. BCR did not differ significantly with regards to margin status in pT3 and pT4 disease. pT2B patients were further stratified into low (Gleason Score 2-6 and PSA <10), intermediate (Gleason 7 or PSA 10.1-20), and high risk (Gleason >8 or PSA >20) groups. In the intermediate risk group, BCR rates increased from 19% to 39% (p <0.001) in negative and positive SM patients, respectively. The low risk and high risk groups both showed a trend towards increased BCR rates with positive SM, but these findings were not statistically significant.

Continues on next page
CONCLUSIONS: Patients with pT2A disease and positive surgical margins have no increased risk of biochemical recurrence and can therefore be managed expectantly. However in pT2B patients, especially those who fall into the medium risk category, there is a significantly increased risk of recurrence with positive surgical margins. If confirmed at other institutions, consideration should be given to adjuvant radiation or hormonal therapy in these patients.

Poster #45

PROSTATE CANCER: DUKE’S EXPERIENCE IN THE PAST THREE DECADES
L Sun, JW Moul, C Donatucci, P Dahm, M Anscher, C Robertson, T Polascik, D George, NJ Fitzsimons
Division of Urologic Surgery, Department of Surgery and Duke Prostate Center (DPC)
Duke University Medical Center, Durham, NC

OBJECTIVE: This study is aimed to examine the epidemiology of prostate cancer patients at Duke over the past 35 years.

METHODS: The data was retrieved from the Duke Prostate Center (DPC) database that integrates the data sets from daily clinics, the departments of Business Information Systems, Information Technology, Surgery, Tumor Registry, Health Information Services, and the Division of Urology. About 2 million clinical records were included (40,978 patients). Endpoints examined included diagnosis rates between races and age groups, survival between races, and comorbid conditions

RESULTS: 12,018 patients were identified with a diagnosis of prostate cancer since 1970, with 7655 (63.6%) having been diagnosed since 1988. A peak of diagnosis was seen from 1990 (n = 215) to 1992 (n=605). Diagnosis rate have increased steadily increased in all age groups since 1992, except men >70. Among all death cases, overall 2 year, 2-5 year, 5-10 year, and >10 year survival for Caucasian men after CaP diagnosis was 64%, 71%, 79%, and 86% respectively. For African-Americans, the rates were 36%, 29%, 21% and 14%, respectively. In these death cases, cancer-specific survival for Caucasians was 58%, 71%, 78%, and 82%, respectively, and 42%, 29%, 22%, and 18%, respectively, for African-Americans. The most common comorbidities in all men with prostate cancer were hypertension (4.7%), erectile dysfunction (2.4%), coronary artery disease (1.7%), and diabetes (1.5%).

CONCLUSIONS: Examination of the newly created Duke Prostate Center database demonstrates a peak of CaP diagnoses in 1992 with a gradual decline since then. Caucasian men with CaP experience higher survival rates as time from diagnosis increases, while African-American men suffer from much lower survival rates, consistent with data from other institutions.

Poster #46

AFRICAN-AMERICAN RACE DOES NOT INDEPENDENTLY PREDICT ADVERSE OUTCOME FOLLOWING RADICAL RETROPUBIC PROSTATECTOMY AT A TERTIARY REFERRAL CENTER
Matthew E. Nielsen1, Misop Han2, Leslie Mangold1, Elizabeth Humphreys1, Patrick C. Walsh,1 Alan W. Partin1, and Stephen J. Freedland1
1Department of Urology, The Johns Hopkins School of Medicine, Baltimore, MD, Department of Urology, 2Northwestern University Feinberg School of Medicine, Chicago, IL

Supported by the National Institutes of Health / National Cancer Institute - SPORE Grant #P50CA58326, The Prostate Cancer Foundation, the Department of Defense Prostate Cancer Research Program PC030666, and the American Foundation for Urological Disease / American Urological Association Education and Research Scholarship Award. Views and opinions of, and endorsements by the author(s) do not reflect those of the US Army or the Department of Defense

Introduction and Objectives: There is controversy in the literature as to whether African-American race is associated with poorer oncological outcomes among men undergoing radical prostatectomy for clinically localized prostate cancer. To address this, we examined the outcomes of a cohort of African-American and Caucasian men treated by multiple surgeons at our institution.

Methods: The study population consisted of 4,962 Caucasian and 326 African-American men treated by anatomic radical retropubic prostatectomy between 1988 and 2004 by 10 different surgeons at the Johns Hopkins Hospital, a tertiary care referral center. We evaluated the association between race and adverse pathological features and biochemical progression.
Results: African-American men had significantly higher preoperative serum PSA (mean: 7.2 vs. 6.0 ng/mL, p<0.001), body mass index (median: 27.4 vs. 26.3 kg/m², p<0.001) and incidence of higher grade disease (Gleason sum ≥4+3) on prostate biopsy (17% vs. 14%, p=0.011). After adjustment for multiple clinical variables, there was no statistically significant association between race and the adverse pathological characteristics of high grade disease, positive surgical margins, extraprostatic extension, or seminal vesicle invasion. African-American race was associated with a significantly increased risk of biochemical progression on univariate analysis (HR 1.52, 95% CI, 1.16-2.00, p=0.002). However, after adjusting for clinical and pathological characteristics, African-American race was not an independent predictor of biochemical progression (HR 1.09, 95% CI, 0.81-1.45, p=0.578).

Conclusions: African-American men were more likely to be obese and present with adverse preoperative clinical features at a younger age and have a higher rate of biochemical progression; however on multivariable analysis African-American race was not an independent predictor of adverse pathologic outcome or biochemical recurrence. Further efforts are needed to detect prostate cancer earlier among African-American men.

Poster #47

PATHOLOGIC ANALYSIS OF LAPAROSCOPIC VERSUS OPEN RADICAL PROSTATECTOMY: 1000 CONSECUTIVE CASES
Douglas M. Dahl, MD*, Wen-Lei He, MD^, and Chin-Lee Wu, MD, PhD^
Departments of Urology* and Pathology^, Massachusetts General Hospital, Boston, MA

Introduction: Minimally invasive therapy is gaining popularity, yet little rigorous analysis has been completed of pathologic outcomes of contemporary patients undergoing radical retropubic prostatectomy and laparoscopic prostatectomy. We evaluated 1000 consecutive pathologic specimens obtained by radical prostatectomy by experienced open and laparoscopic surgeons and correlated outcomes with surgical technique.

Materials and Methods: All patients studied were enrolled in a tumor bank specimen collection protocol. 1000 consecutive specimens from October 2001 to May 2005 were included in this analysis. 286 were obtained by a laparoscopic technique (LRP) performed by a single experienced laparoscopic surgeon, and 714 were obtained by open radical retropubic technique (RRP) by four experienced surgeons. All specimens were processed by the same technique and analyzed by our staff of dedicated genito-urinary pathologists.

Results: Preoperative clinical staging and pathological data were compared between the LRP and RRP group. There was no statistical difference between the two groups in clinical stage, average PSA, or Gleason score. 89% of patients were clinical stage T1c; 11% clinical stage T2. 90% of patients had a preoperative PSA <10. Pathologic analysis was compared between the two groups. The Wilcoxon test was used to evaluate for differences. There was no statistical difference between the two groups in pathologic T stage or Gleason score. Positive margin rate for LRP was 15% and for RRP was 17.4%. This was not statistically different. Detailed subset analysis was performed. There was no difference between open or laparoscopic surgical technique in location of positive margins. Positive surgical margins were seen in approximately 30% of patients with pathologic T3 or Gleason score 8-10 cancer in both groups.

Conclusion: Experienced surgeons performing open radical prostatectomy and laparoscopy radical prostatectomy have comparable pathologic outcomes. There is no indication that the minimally invasive technique compromises oncologic results.

Departmental Funding supported this research.

Poster #48

ATORVASTATIN CALCIUM INHIBITS LNCaP GROWTH AND DOWNREGULATES EGF WITHOUT AFFECTING PSA PRODUCTION
Daniel J. Cunningham, Thomas Tarter, and R. Jeffrey Karnes

Atorvastatin calcium is a member of the statin family of drugs used to treat cholesterol related circulatory diseases. Atorvastatin calcium prevents mevalonate pathway derived cholesterol synthesis by inhibiting the conversion of acetyl coenzyme A (acetyl CoA) to 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) by competitively binding HMG CoA reductase. Cholesterol has been reported to accumulate in several tumor types including prostate tumors and is a precursor compound in the biosynthetic pathway of testosterone. Testosterone is converted to dihydrotestosterone by the enzyme 5-alpha reductase which is involved in androgen mediated gene expression. Loss of 5-alpha reductase
activity by inhibition in LNCaP cells results in decreased proliferation and downregulation of proliferation genes. Although statins are known to lower serum levels of cholesterol, it is unknown if atorvastatin calcium reduces prostatic levels of cholesterol or what effect it has on cell proliferation or protein synthesis. Therefore we investigated the effect of atorvastatin calcium on prostate cancer proliferation and androgen mediated synthesis of epidermal growth factor (EGF) and prostate specific antigen (PSA). Cell proliferation assays indicated that atorvastatin calcium inhibits the growth of androgen dependent LNCaP cells but not androgen independent PC-3 cells. Cell mortality and cytotoxic effects of atorvastatin calcium on LNCaP cells showed a ~50 % decrease in cell viability after 5 days in LNCaP cells. Atorvastatin calcium treatment inhibited production of EGF in LNCaP cells but not PSA.

**Poster #49**

**C-KIT PROTEIN EXPRESSION IN GRADE 4 RENAL CELL CARCINOMA WITH OR WITHOUT SARCOMATOID DIFFERENTIATION**

Shomik Sengupta*, Bradley C. Leibovich, Christopher L Corless, John C. Cheville, Christine M. Lohse, Michael C Heinrich, Horst Zincke, Eugene D. Kwon and Michael L. Blute

Mayo Clinic, Rochester, Minnesota and OHSU, Portland, Oregon

**PURPOSE:** Renal cell carcinomas (RCC) with sarcomatoid differentiation have been reported to frequently express KIT protein, suggesting that imatinib mesylate (STI-571 or Gleevec™) may be an effective treatment for these aggressive tumors. The aim of this study was to determine the frequency of KIT expression and mutation in a large series of high-grade RCCs.

**PATIENTS AND METHODS:** We identified 194 patients who underwent nephrectomy for unilateral, sporadic nuclear grade 4 RCC between 1970 and 2002, including 123 with sarcomatoid differentiation. Sections from representative paraffin-embedded tissue blocks were immunostained in a BioTek autostainer, using EDTA antigen-retrieval, a polyclonal KIT antibody and the avidin-biotin peroxidase complex method. Mutational analysis was performed on all immuno-positive and selected negative cases by polymerase chain reaction amplification of KIT exons 9, 11, 13, and 17.

**RESULTS:** Only 7 (3.6%) tumors showed KIT expression, including 5 (4.1%) among the 123 with sarcomatoid differentiation. Four of the 7 showed focal staining only. No mutations were identified among the 7 positive cases or among 8 randomly selected negative samples. Death from RCC occurred in all 7 patients with KIT-positive tumors at a median of 0.6 years (range 0.3 - 2.3), and in 139 of 187 patients with KIT-negative tumors at a median of 0.8 years (range 0 – 10.2).

**CONCLUSIONS:** KIT expression was identified in less than 5% of high-grade RCCs, with or without sarcomatoid differentiation, but none of the tumors exhibited KIT mutations. These findings indicate that imatinib therapy is unlikely to be effective in patients with high-grade RCC.

**Poster #50**

**RENAZ CELL CARCINOMA SUB-TYPING BY HISTOPATHOLOGY AND FLUORESCENCE IN-SITU HYBRIDIZATION ON A NEEDLE BIOPSY SPECIMEN**

D. Barocas, S. Mathew, J. DelPizzo, E. D. Vaughan, R. Gurevich, M. Akhtar, D. S. Scherr

Departments of Urology and Pathology of New York Presbyterian Hospital – Weill Cornell Medical Center, New York, NY

**Objectives:** We set out to determine the sub-type of renal cell carcinoma (RCC) on needle core biopsies of renal masses using histopathology and fluorescence in-situ hybridization (FISH). Stage migration, decrease in the proportion of aggressive tumors, and the expanding options for treating and observing renal masses are likely to increase the role of preoperative diagnostics. Biopsy alone has a fairly high accuracy rate historically (80-90% in most series). Since each of the different histologic sub-types of RCC has distinct cytogenetic abnormalities (loss of 3p in clear cell, trisomy 7 or 17 in papillary and widespread chromosomal losses in chromophobe), we hypothesized that the addition of FISH to histology would improve the accuracy of needle core biopsies.

**Methods:** Forty patients with renal masses of undetermined histology underwent partial or radical nephrectomy, yielding a total of 42 tumors. Needle core biopsies were taken of the mass immediately following surgery. One core was mechanically disaggregated to form a single cell suspension, dropped onto slides and fixed. Next, FISH was performed for the centromeres of chromosomes 3, 7, 10, 17, for standard enumeration loci on chromosomes 13 and 21 and for the locus 3p25-26. A cytogenetic interpretation was rendered based on the percentage of cells containing one, two, three, four, or more than four copies of each locus probed. Histopathology was performed on a second core. Results of FISH and the histopathology were compared with final pathology.
Results: Adequate material was obtained for histopathology in 37 of 42 cases (88.1%). Of these 37 cases, 32 were RCC or oncocytoma. Histopathology of the needle core correctly identified the tumor sub-type in 26 of 32 cases (81.3%). FISH was informative in 30/32 cases (93.8%). Loss of 3p25-26 was demonstrated in 11 specimens overall and 8 of 15 (53.3%) specimens that were clear cell on final pathology. Trisomy 7 or 17 was present in 9 cases overall and 6 of 7 (85.7%) specimens that were papillary on final pathology. Two of 3 chromophobes had losses of at least two of the chromosomes probed. Two of the 5 oncocytomas had no cytogenetic abnormalities, while 3 had isolated losses. FISH findings were in accord with final pathology in 18 of 32 cases.

Table: Cases improperly sub-typed on histopathology of biopsy

<table>
<thead>
<tr>
<th>Case</th>
<th>Problem with Histopathology</th>
<th>FISH Result</th>
<th>Final Pathologic Sub-type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No tissue available</td>
<td>Loss of 3p</td>
<td>Clear cell</td>
</tr>
<tr>
<td>3</td>
<td>Mistaken for oncocytoma</td>
<td>Normal</td>
<td>Chromophobe</td>
</tr>
<tr>
<td>15</td>
<td>No tissue available</td>
<td>Trisomy 7 and 17</td>
<td>Clear cell w/ papillary features</td>
</tr>
<tr>
<td>21</td>
<td>Equivocal reading</td>
<td>Loss of 3p</td>
<td>Clear cell</td>
</tr>
<tr>
<td>22</td>
<td>Equivocal reading</td>
<td>Loss of 3p</td>
<td>Clear cell</td>
</tr>
<tr>
<td>27</td>
<td>Mistaken for chromophobe</td>
<td>Trisomy 7 and 17</td>
<td>Papillary</td>
</tr>
</tbody>
</table>

Conclusion: Needle core biopsy of renal tumors provides adequate material for evaluation of histologic sub-type, providing important prognostic information. Adding the FISH could improve the accuracy of needle core biopsies by clarifying some cases. This method of determining the histologic sub-type of RCC may have applications for preoperative diagnosis, guiding therapeutic options.

Poster #51

SURVIVAL FOLLOWING HORMONAL THERAPY: MEN WHO DEVELOP METASTASIS MORE THAN FIVE YEARS FOLLOWING RADICAL PROSTATECTOMY LIVE LONGER

Danil V. Makarov, Elizabeth B. Humphreys, Leslie A. Mangold, Mario Eisenberger, Alan W. Partin, Patrick C. Walsh
The James Buchanan Brady Urological Institute and the Departments of Urology and Oncology, The Johns Hopkins Medical Institutions, Baltimore, MD

Introduction and Objective: Previously our group has reported that Gleason score, PSA doubling time, and time to first PSA failure correlate with prostate cancer specific survival. In this study we evaluate the association between time from radical prostatectomy to metastasis and time to prostate cancer specific death.

Methods: From a total of 3,658 men with adenocarcinoma of the prostate who underwent radical prostatectomy by a single surgeon at Johns Hopkins Hospital from 4/82 until 6/05, we identified 216 men who developed metastasis. Excluded were 13 men with incomplete documentation of hormonal therapy, 37 men who initiated hormonal therapy prior to documentation of metastasis, and 6 patients had no further follow up after developing metastasis, leaving a total study population of 160 patients. We performed survival time analysis using univariable and multivariable Cox multiple hazards and Kaplan-Meier survival models.

Results: When examined as a continuous variable, time from radical prostatectomy to metastasis was inversely associated with risk of prostate cancer specific death (relative risk 0.91, 95% confidence interval 0.85-0.97, p=0.006). The association remained significant controlling for patient age and date of surgery (relative risk 0.88, 95% confidence interval 0.82-0.94, p<0.001). Examining time from radical prostatectomy to metastasis as a dichotomous, categorical variable with various cut points also yielded significant, inverse associations with risk of prostate cancer specific death. See table.

<table>
<thead>
<tr>
<th>Cut Point (Years After RRP)</th>
<th>Ratio of Patients Below:Above Cut Point</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>P value</th>
<th>Median Survival (Years after metastasis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>83:77</td>
<td>0.58</td>
<td>0.37-0.89</td>
<td>0.014</td>
<td>5 ≤ Cutpoint 8 &gt; Cut Point</td>
</tr>
<tr>
<td>6</td>
<td>96:62</td>
<td>0.59</td>
<td>0.37-0.94</td>
<td>0.025</td>
<td>5 ≤ Cutpoint 8 &gt; Cut Point</td>
</tr>
<tr>
<td>7</td>
<td>112:48</td>
<td>0.53</td>
<td>0.31-0.91</td>
<td>0.022</td>
<td>5 ≤ Cutpoint DNRMS 11</td>
</tr>
<tr>
<td>8</td>
<td>126:34</td>
<td>0.52</td>
<td>0.27-1.01</td>
<td>0.052</td>
<td>6 ≤ Cutpoint DNRMS 10</td>
</tr>
<tr>
<td>9</td>
<td>130:30</td>
<td>0.43</td>
<td>0.20-0.93</td>
<td>0.031</td>
<td>6 ≤ Cutpoint DNRMS 8</td>
</tr>
<tr>
<td>10</td>
<td>137:23</td>
<td>0.45</td>
<td>0.18-1.11</td>
<td>0.083</td>
<td>6 ≤ Cutpoint DNRMS 9</td>
</tr>
</tbody>
</table>

DNRMS: did not reach median survival at

Continues on next page
**Conclusions:** Patients who develop metastasis more than 5 years after radical prostatectomy have improved prostate cancer specific survival after initiation of hormone therapy than those who develop metastasis in 5 years or less. This finding should prove reassuring to those patients who develop metastasis late in their course and to their physicians, who might have previously believed that all patients with metastasis have poor outcomes.

**Poster #52**

**PROGNOSTIC POTENTIAL OF ERG1 EXPRESSION IN PROSTATE CANCER**

Gyorgy Petrovics¹, Govindan Vaidyanathan¹, Syed Shaheduzzaman¹, Bungo Furusato², Vasantha Srikantan¹, Isabell A Sesterhenn², David G McLeod¹,³, Shiv Srivastava¹

¹Center for Prostate Disease Research (CPDR), Department of Surgery and US Military Cancer Institute, Uniformed Services University, Rockville, MD 20852; ²Department of Genitourinary Pathology, Armed Forces Institute of Pathology, Washington, DC 20306; ³Urology Service, Walter Reed Army Medical Center, Washington, DC 20307

**Introduction:** Despite intensive search, alterations of oncogenes or tumor suppressor genes that are prevalent in primary prostate cancer (CaP) are not well defined. Our laboratory recently identified ERG1, a member of the ETS transcription factor family, as one of the most frequently overexpressed proto-oncogene in the transcriptome of malignant prostate epithelial cells (Petrovics et al., Oncogene 24, 3847-52, 2005). However, increased expression of ERG1 in prostate tumor cells relative to benign epithelial cells was associated with disease free survival after radical prostatectomy. Although ERG and other ETS family members are implicated in a variety of cancers, there is very little known about the functional role of these proto-oncogenes in the development and progression of CaP. The overall hypothesis of this project is that overexpression of ERG1 may play a critical role in prostate biology and in the development/progression of CaP.

**Methods:** Meta-analysis of ERG expression was performed using Oncomine database and software (oncomine.org). ERG1 (Acc.# AH001456) was sub-cloned into tetracycline regulated mammalian expression vectors (pTet-off). ERG1 expression was analyzed by Northern blot and real time QRT-PCR (TaqMan, ABI) using ERG1 isoform specific probes/primers, and by Western blot. HEK-293 cells (10⁶ cells, ATCC) were transfected by lipofectamin (Invitrogen) and assayed for colony formation under G418 selection (800 ug/ml, GIBCO) in duplicate with and without tetracycline.

**Results:** Meta-analysis of published CaP microarray or GeneChip studies (Oncomine database) revealed significant ERG overexpression in primary CaP in 2 of 7 studies (p=3.7x10⁻⁸ and p=0.004) (84 primary CaP versus 15 benign and 16 BPH). Higher ERG expression in primary CaP compared to other cancers was found in 1 of 2 studies (p=0.001) (26 primary CaP versus 148 other cancers). In addition, 1 of 3 studies showed significantly decreased ERG expression in metastatic CaP, especially in bone, compared to primary CaP (p=0.023) (59 primary CaP versus 20 metastatic CaP). These data support and further extend our original findings regarding ERG expression in CaP.

As a comparison the expression of other known CaP marker genes was also analyzed in the Oncomine database. Interestingly, similarly to ERG1, both AMACR and Hepsin, two of the most consistently overexpressed genes in primary CaP, showed a downregulation in metastatic compared to primary CaP in 1 of 3 studies (p=0.005 and p=0.035, respectively). In addition, early growth response gene EGR1 was significantly downregulated in metastasis in all 3 studies. The biphasic temporary expression pattern of a significant portion of CaP associated genes, including ERG1, underline the biological change that prostate tumor cells undergo during transition from primary to metastatic state.

Tetracycline-regulated (Tet-off) ERG1 expression constructs were generated to define the influence of ERG1 on cell growth/survival in clonogenic assays. HEK-293 cells transfected with pTet-ERG1 exhibited a 5 to 6 fold increase in colony number compared to vector control transfectants.

**Conclusions:** ERG gene expression is consistently upregulated in primary CaP compared to benign prostate and BPH. However, it is significantly decreased in metastatic CaP, and decreased ERG expression in primary CaP is associated with biochemical recurrence. These findings, in support of our original report, underscore both diagnostic and prognostic features of ERG expression in CaP. In addition, this study provides rationale for future investigations of ERG1 functions in CaP biology.
**Poster #53**

**GENE EXPRESSION SIGNATURES IN BENIGN AND MALIGNANT EPITHELIAL CELLS FROM FORMALIN-FIXED PARAFFIN-EMBEDDED (FPPE) TISSUES OF PROSTATE CANCER PATIENTS**

Bungo Furusato 1,2, Gyorgy Petrovics 2, Vasantha Srikantan 2, Syed Shaheduzzaman 2, Lakshmi Ravindranath 2, Martin E. Nau 3, Maryanne Vahey 3, David G. McLeod 4, Shiv Srivastava 2 and Isabell A. Sesterhenn 1

1 Department of Genitourinary Pathology, Armed Forces Institute of Pathology; 2 Center for Prostate Disease Research, Department of Surgery, USUHS; 3 Affymetrix Gene Array Laboratory, Division of Retrovirology, WRAIR; 4 Urology Service, Walter Reed Army Medical Center.

**Introduction & Objectives:** We have focused on discovery of Prostate Cancer (CaP) gene specific expression biomarkers using OCT embedded frozen prostate tissue specimens, laser-capture micro-dissections (LCM) and GeneChips. The ability to use clinical specimens for GeneChip assays, such as formalin fixed paraffin embedded (FFPE) tissues, will enhance and integrate the discovery of clinically relevant diagnostic/prognostic markers for CaP. This is a feasibility study for evaluating CaP associated gene expression signatures in FFPE CaP tissues.

**Methods:** Matched benign and malignant epithelial cells were obtained from 7-micron sections of FFPE whole-mounted radical prostatectomy specimen, which included the site from which frozen tissue was retrieved for an earlier GeneChip study. LCM derived epithelial cells from benign and malignant glands were analyzed by Affymetrix HG U133a and Human X3P GeneChips and tumor cell specific gene expression signatures were evaluated using the GeneSpring software (Silicon Genetics). The results were compared to GeneChip data from corresponding frozen prostate tissue specimens embedded in OCT.

**Results:** Evaluation of the expression patterns in paired benign and malignant epithelial cells from FFPE was compared with GeneChip data from corresponding frozen tissue specimens. Analysis of gene expression patterns in LCM derived epithelial cells from FFPE tissues revealed similarity to a subset of genes exhibiting tumor cell specific differential expression in the study of LCM derived benign and malignant cells from frozen OCT-embedded prostate tissues. This subset of 224 genes included AMACR, ERG1, HOXC6, NPY, CLDN8, CCT6A, MYO6, FOLH1, TMSNB, SUMO2, and PAP. Among these genes, apoptosis regulators, growth/DNA synthesis promoters, antioxidant response modulators, cell-cell adhesion molecules and transcription factors showed similar expression patterns between FPPE and OCT embedded frozen tissues.

**Conclusions:** Our preliminary studies provide proof of principle that FFPE CaP tissue can be used for cell specific gene expression analysis. This will help us to validate the utility and limitation of FFPE CaP tissues. Utilization of FFPE tissue for GeneChip studies will enhance the pathologic correlations of CaP associated gene expression biomarkers; especially for cancer specimens linked to long term follow-ups, generally not available in frozen tissue banks.

**Poster #54**

**INCIDENCE OF UPPER TRACT RECURRENCE IN PATIENTS WITH AND WITHOUT URETERAL INVOLVEMENT AND CARCINOMA IN SITU ON PERMANENT SECTION AT THE TIME OF RADICAL CYSTECTOMY**

Lincoln Olsen, MD, Apostolos Evangelidis, MD, Michael Karellas, MD, Jeffrey Holzbeierlein, MD, J. Brantley Thrasher, MD.

University of Kansas Department of Urology, Kansas City, Kansas

**Introduction:** Upper tract recurrence following radical cystectomy for transitional cell carcinoma (TCC) of the bladder occurs in 2-4% of patients. Traditionally frozen section analysis of the ureter has been performed to ensure that there is no TCC involvement at the ureteroenteric anastomotic site. Controversy exists as to the usefulness of this practice with some series reporting an increased risk and others reporting no increased risk of upper tract recurrence with ureteral involvement at the time of radical cystectomy. This investigation was performed to determine the incidence of upper tract recurrence in patients with and without ureteral involvement at the time of cystectomy. In addition we have analyzed the risk of upper tract recurrence in patients with and without carcinoma in situ (CIS) of the bladder at the time of operation.

**Methods:** A database of 149 consecutive cystectomies performed for primary TCC of the bladder at the University of Kansas was compiled and analyzed. All pathology reports were reviewed for evidence of tumor in either ureter and the presence or absence of CIS on permanent section at the time of radical cystectomy. A thorough review of hospital charts, urology clinic notes, pathology reports, and cancer registry information was undertaken to identify those patients that progressed to upper tract recurrence. This study was funded by the University of Kansas Department of Urology.

*Continues on next page*
**Results:** Mean follow up for our series of cystectomy patients was 19.6 months. At the time of cystectomy 13 (8.7%) of these patients were found to have ureteral involvement and 79 (53%) had CIS present in the bladder. The mean time to recurrence was 9.6 months. Four (2.7%) patients had an upper tract recurrence. Of those with recurrence only one had ureteral involvement at the time of cystectomy and only one had CIS in the bladder at the time of cystectomy. The rate of upper tract recurrence in patients with and without ureteral involvement was not statistically significant (p=0.30) nor was the rate of recurrence in patients with and without CIS (p=0.34).

**Conclusions:** Our population of patients does not have an increased risk of upper tract recurrence when the ureters are affected with TCC or if CIS is present in the bladder at the time of radical cystectomy. These results argue against the necessity for frozen section analysis of the ureteral margin at the time of cystectomy as long as there is no gross pathologic involvement at the planned ureteroenteric anastomotic site.

**Poster #55**

BRANCHING PHENOTYPE OF RENAL CELL CARCINOMA IS ABROGATED BY NOX4 SILENCING
Jodi K Maranchie*, Ye Zhan, Worcester, MA.

**Introduction and Objective:** Inactivation of the von Hippel Lindau tumor suppressor (VHL) is an early event in 60-80% of sporadic clear cell renal cell carcinoma (RCC). VHL functions as a ubiquitin ligase for hypoxia-inducible transcription factors (HIF-alpha). We previously showed that generation of reactive oxygen species (ROS) by the kidney-specific NADPH oxidase, Nox4, is critical for expression and activity of HIF2-alpha. Knockdown results in dramatic reduction of HIF transcriptional activity even in the absence of VHL. VHL-deficient cells demonstrate a characteristic branching phenotype when exposed to hepatocyte growth factor-scatter factor (HGF-SF) that can be abrogated by re-expression of VHL. To determine the effect of Nox4 silencing on the branching phenotype of RCC, we examined VHL positive and negative cells after stable Nox4 knockdown.

**Methods:** Small inhibitory RNA able to knockdown Nox4 by at least 80% (siRNA) and a non-specific siRNA (scramble) were cloned into pSilencer™ 4.1-CMV puro (Ambion) as 54 nucleotide hairpin loops. The resulting vectors were used to transfect paired VHL-deficient human RCC cell lines expressing empty vector (786-0 pRC) or wild type VHL (786-0 WT). After selection with puromycin, single cell clones were screened for reduced production of ROS using a 2',7'-dichlorofluorescin diacetate fluorescent assay. Stable transfectants and parental 786-0 cells were suspended in matrigel and incubated with recombinant HGF-SF at 37°C, for 72 hours. Triplicate wells were evaluated by counting non-branching cells in 3 high power fields per well.

**Results:** Cells expressing VHL were rounded with minimal branching. No differences were seen between 786-0 WT cells expressing siRNA or scramble. VHL-deficient cells expressing pSilencer-scramble developed marked branching of the majority of cells, and were indistinguishable from parental 786-0 cells. However, after stable knockdown of Nox4 in 786-0-PRC, both the number of branching cells and the average number of branches per cell were decreased by greater than 50%.

**Conclusions:** ROS production by Nox4 is necessary for the full branching phenotype of VHL-deficient RCC cells. The branching phenotype, commonly seen following malignant transformation, correlates with increased mitogenesis, morphogenesis and motility in cancer cells. These results suggest that branching in response to HGF-SF occurs downstream of HIF activation, consistent with our earlier finding that constitutive expression of mutant HIF-alpha resulted in branching of VHL positive cells. Branching represents yet another established RCC phenotype down-regulated by inhibition of Nox4 activity, further supporting Nox4 as a candidate for molecularly targeted RCC therapy.

**Funding:** NIDDK064887.

**Poster #56**

GENE EXPRESSION SIGNATURES OF PROSTATE CANCER WITH POOR PROGNOSIS
Gao CL, Shaheduzzaman, S1, Petrovics, G1, Furusato, B2, Nau, M5, Ravindranath, L1, Chen, Y4, Srikanthan, V1, McLeod, DG3, Vahey, M5, Sesterhenn, IA2, Srivastava, S, 1

1CPDR, Department of Surgery, USU, Rockville, MD; 2Department of Genitourinary Pathology, AFIP, Washington, DC; 3Urology Service, WRAMC, Washington, DC 4Cancer Genetics Branch, NHGRI, NIH, Bethesda, MD; 5Division of Retrovirology, WRAIR, Rockville, MD.
**Introduction and objective:** Prostate Cancer (CaP) is the most common malignancy in American men and the second leading cause of cancer mortality. The serum prostate-specific antigen (PSA) test has revolutionized the early detection of CaP. However, it remains a challenge to determine the prognosis of a large portion of patients treated for the organ confined CaP. Identification of CaPs with poor prognosis will tremendously improve the management and treatment of CaP. The objective of this study is to discover and define gene expression signatures of CaP predictive of poor prognosis. In this study we have identified gene expression signature of 17 genes that differentiate between tumor and benign cells from patients with high risk (HR) and moderate risk (MR) of disease progression after radical prostatectomy (RP). Promising candidate genes, HIPPI (Estrogen-Related Receptor-Beta-Like 1; ESRRBL1; HIP1 Protein Interactor), KIF5C, ELK4 and GBP1 defined from this study were followed up for further validation.

**Materials and Methods:** Matched benign and malignant epithelial cells were obtained from RP specimens (tissues from both the HR and MR form of the disease) by laser capture micro-dissection (LCM). The HR was defined as those with cancer recurrence, Gleason score 8-9, poorly differentiated tumor cells, and the MR group included those patients with no cancer recurrence, Gleason score 6-7 and well to moderately differentiated tumor cells. RNA specimens from these cells were analyzed for global gene expression using Affymetrix U133a GeneChips and Microarray Data Analysis software (NHGRI, NIH). Quantitative expression analyses of HIPPI, KIF5C, ELK4, GBP1 and two other genes commonly over expressed in CaP cells (AMACR and DD3) was performed by real time/Taqman PCR.

**Results:** We evaluated prostate epithelial cell (PEC) transcriptome using LCM derived benign and tumor epithelial cells and HG U133A Affymetrix GeneChips analyzed by MDS (Multi Dimensional Scaling, NHGRI Microarray Analysis Software), which revealed that HIPPI (p-value of 0.003045), KIF5C (p-value of 0.000115), ELK4 (p-value of 0.004804) and GBP1 (p-value of 0.004804), was among the top four genes that were differentially expressed in HR and MR CaP. We have confirmed the expression level of HIPPI in tumor and benign epithelial cells (76 specimens from 19 HR and 19 MR form of CaP) by using QRT-PCR. HIPPI significantly discriminated HR form of CaP (upregulated) from MR (downregulated) form of the disease. This observation is being extended to an additional 84 samples. Further validation of the discriminatory potential of HIPPI between HR and MR form of CaP using immunohistochemistry is under progress.

Conclusions: Our study defines gene expression signatures that have potential in distinguishing CaP cells with HR and MR disease progression features. However, independent validation of gene expression signatures is critical. One of these genes exhibited similar patterns between GeneChip and QRT-PCR. HIPPI may play a role in the suppression of apoptosis in normal cells; therefore upregulation of HIPPI may favor the continued survival and evolution of cancer cells, which is the hallmark of highly malignant cancer cells. Further evaluations of HIPPI are warranted in CaP progression.

**Poster #57**

**TWO-YEAR OUTCOME OF UNILATERAL SURAL NERVE INTERPOSITION GRAFT AFTER RADICAL PROSTATECTOMY**

Hong Gee Sim, Michel Kliot, Paul H. Lange, William J. Ellis, Claire Yang. University of Washington, Seattle, WA

**Objectives:** We studied 40 men who underwent unilateral nerve sparing radical prostatectomy for prostate cancer with contralateral sural nerve grafting between January 2000 to September 2003.

**Materials and methods:** Patients were considered for sural nerve grafting if they were high risk before or during surgery for extracapsular extension, less than 70 years of age with good pre-operative erectile function, sexually active, with no previous history of peripheral vascular neuropathy, and psychiatric, vascular or neurological cause of impotence. Potency was assessed by patient-reported questionnaires including the IIEF erectile domain.

**Results:** The mean follow-up was 22.6 ± 6.3 months. At 12 months, 35% had full erections for intercourse with and without PDE5-I and 6% of patients had slightly diminished erections sufficient for intercourse. The remainder had either partial erections occasionally satisfactory (32%), or not satisfactory (15%) for intercourse, or no erections (6%). At 24 months, 60.0% had full erections for intercourse and 3% of patients had slightly diminished erections sufficient for intercourse. The remaining had either partial erections that were occasionally satisfactory (7%), or unsatisfactory (13%) for intercourse or no erections (7%). Retrospective comparison to a group of men who underwent unilateral nerve sparing prostatectomy during the same time period at our institution revealed 20% had rigid erections, and 6% with slightly diminished erections, at 24 months follow up. Patient pathological outcomes in these patients will be presented.

**Conclusion:** At 24 months follow up, contralateral sural nerve interposition graft seems to improve the rate of return of erectile function over unilateral nerve preservation alone. However, more experience and/or more controlled studies are necessary to be sure.

No financing funding was used for this study.
**Poster #58**

**RENAL CELL CARCINOMA IN AFRICAN AMERICAN PATIENTS: INCREASED INCIDENCE OF PAPILLARY HISTOLOGY**
Ricardo Sánchez-Ortiz, Estrella Carballido, Pheroze Tamboli, Lydia T. Madsen, David A. Swanson, Curtis A. Pettaway, and Christopher G. Wood.
The University of Texas M. D. Anderson Cancer Center, Houston, Texas

**OBJECTIVE:** To compare the clinical and pathologic characteristics of renal cell carcinoma (RCC) in African American patients to an age-matched cohort of Caucasian patients.

**METHODS:** We retrospectively reviewed the records of 72 consecutive African American (AA) and 161 age-matched Caucasian patients who underwent nephrectomy for RCC at our institution between 1992 and 2002. Clinical and pathologic characteristics, tumor recurrence, and disease-specific survival were compared between races.

**RESULTS:** Mean age for AA patients was 53.3 years (range 18 to 76) and 53.7 years for Caucasians. Median follow-up for the cohort was 27.8 months. Compared with Caucasians, AA patients exhibited a higher incidence of papillary histology (20.8% vs. 8.1%, P = 0.01) and were more likely to have a history of hypertension (52.8% vs. 32.9%, P = 0.01). No significant differences were identified between AA and Caucasian patients regarding tumor size (7.2 vs. 7.6 cm), Fuhrman grade (e+ 3 in 65.2% vs. 67.1), sarcomatoid histology (5.6% vs. 9.9%), pathologic stage (e+ T3a in 29.4% vs. 39.8%, P = 0.18), nodal involvement (13.9% vs. 15.6%), or metastatic disease (20.8% vs. 32.9%, P = 0.06), respectively. Similarly, there were no differences by race in initial presentation (incidental 22.2% vs. 28.1%), bilaterality (5.6% vs. 6.8%), sex (female 41.7% vs. 31.1%), family history of RCC (5.6% in both), history of smoking (52.1% vs. 57.1%), or body-mass index (30.6 vs. 28.8). While AA patients had a tendency for improved recurrence-free survival (in M0 patients, 77.8% vs. 72.3% at 5-years) and disease specific survival (71.8% vs. 55.7% at 5 years, P =0.21) compared with Caucasians, these differences were not significant on univariate or multivariate Cox regression analyses. There were no racial differences in outcome for the subset of patients with papillary RCC.

**CONCLUSION:** Compared with an age-matched cohort of Caucasians, AA patients with RCC exhibited an increased incidence of papillary tumor histology and were more likely to have a history of systemic hypertension. No statistically significant differences in tumor recurrence or survival were identified by race.

**FUNDING:** none

---

**Poster #59**

**LONGITUDINAL CORRELATION BETWEEN GRADE OF UPPER TRACT AND BLADDER TCC IN PATIENTS WITH CONCURRENT DISEASE**
Thomas Jefferson University, Philadelphia, PA

**Objective:** To examine the relationship between upper tract and bladder transitional cell carcinoma (TCC) in patients with concurrent disease. All patients underwent endoscopic surveillance consisting of ureretoscopy and cystoscopy with biopsy and treatment. Biopsy specimens from the upper tract were examined with both cytology and cell-block techniques. Bladder tumor specimens underwent routine histopathological analysis. Tumor grade was reported as Grade 1, 2, or 3 with CIS lesions being classified as grade 3.

**Methods:** A retrospective review of our upper tract TCC database identified 38 patients with concurrent bladder and upper tract disease. All patients underwent endoscopic surveillance consisting of ureteroscopy and cystoscopy with biopsy and treatment. Biopsy specimens from the upper tract were examined with both cytology and cell-block techniques. Bladder tumor specimens underwent routine histopathological analysis. Tumor grade was reported as Grade 1, 2, or 3 with CIS lesions being classified as grade 3.

**Results:** 38 patients (27 males, 11 females) with an average age of 71.5 years (range: 54.3-95.1) underwent surveillance over a mean interval of 29 months (range: 2-136). A total of 262 evaluations were performed with 174 upper tract recurrences and 117 bladder recurrences. 79 of the 263 evaluations (30%) revealed concurrent upper tract and bladder disease. Initial upper tract pathology revealed that 41% of lesions were grade 1, 41% grade 2, and 18% grade 3. Initial bladder pathology revealed that 42% of lesions were grade 1, 29% grade 2, and 29% grade 3. Upper and lower tract pathology was the same in 42% of cases. In the discordant cases 50% of the upper tract lesions were of higher grade, and 50% of the bladder lesions were of higher grade. Over the course of follow-up 34% of upper tract lesions remained the same, 17% progressed in grade, 20% decreased in grade, and 29% had fluctuating grade. In the bladder 31% of the lesions remained the same, 46% increased in grade, 14% decreased in grade, and 9% fluctuated.

**Conclusions:** Concurrent upper tract and bladder TCC show grade discordance in over 50% of cases. Over extended follow up, grade fluctuation was seen both in the bladder and upper tract TCC.
Poster #60

ASAP AND PIN AS PREDICTORS OF PROSTATE CANCER: EVALUATION IN AN AFRICAN-AMERICAN POPULATION
Charles R Powell, David Hepps, Tom Clements, Roohollah Sharifi, University of Illinois at Chicago, Chicago, IL

Introduction: Studies indicate that prostate intraepithelial neoplasia (PIN) and atypical small acinar proliferation (ASAP) are strongly associated with prostate cancer. We evaluated this correlation in an African-American population.

Materials and methods: We retrospectively studied African-American men undergoing prostate needle biopsy for PSA elevation or abnormal digital rectal exam (DRE). Those patients with PIN, ASAP, persistently rising PSA or suspicious DRE underwent repeat biopsy. The incidence of prostate cancer after an initial biopsy revealing PIN or ASAP was evaluated.

Results: A total of 721 African-American men underwent prostate needle biopsy. PIN was found in 56 patients and ASAP in 86 patients. These men underwent at least one re-biopsy revealing prostate cancer in 13 patients with PIN (22%) and 20 patients with ASAP (23%). Of those men who underwent repeat biopsy for reasons other then PIN or ASAP (rising PSA or abnormal DRE) 21% (30/142) were found to have prostate cancer. On repeat biopsy, there was no significant difference in the incidence of prostate cancer after an initial biopsy with PIN, ASAP, abnormal DRE or rising PSA (p>0.05).

Conclusions: In our African-American patient population PIN or ASAP does not appear to be a better predictor of prostate cancer on repeat biopsy then persistent PSA elevation or suspicious DRE.

Poster #61

LAPAROSCOPIC NEPHRON SPARING SURGERY FOR RENAL MASS WITH CONCOMITANT NEPHROLITHIASIS OR UPJ OBSTRUCTION
Angelo A. Baccala, Jr., MD, Una Lee, MD, Nicholas Hegarty, MD, Mihir Desai, MD, Jihad Kaouk, MD, Inderbir Gill, MD
Cleveland Clinic Foundation, Cleveland, OH

Background and Purpose: The concomitant existence of a renal mass with renal calculus or UPJO is rare, but when it occurs it poses a management dilemma. The success of the laparoscopic partial nephrectomy (LPN) depends greatly on the absence of postoperative ureteral obstruction. We present our experience with 15 patients that had a renal mass and concomitant calculus or UPJO.

Patients and Methods: Fifteen patients (13 males, 2 females) with a mean age of 55.6 years (range 42 to 71 years) underwent laparoscopic partial nephrectomy. Their concomitant condition was treated either prior to, during, or after treatment of their renal mass depending on the presence of obstruction.

Results: The mean LPN operative time was 233.3 minutes (range 120-360 minutes). The mean warm ischemia time was 34.8 minutes (range 22 to 53 minutes). The stone burden for the majority of patients (69%) was punctate or non-obstructing and therefore not treated prior to LPN. One patient had an obstructing 1.6 x 0.7 cm calculus. Percutaneous nephroscopy was performed at the time of LPN but the stone was not visualized. Another patient had a 3 x 5mm partially obstructing UPJ calculus and renal mass. An indwelling stent was placed prior to LPN and SWL was performed 6 weeks after LPN. One patient had a kidney mass located in a position where an intra-operative decision as to LPN vs. laparoscopic nephrectomy would have to be determined. A non-obstructing 6 mm calculus in the contralateral kidney was treated preoperatively with ureteroscopy and laser lithotripsy in order to secure unobstructed renal function. Two patients presented with concomitant UPJ obstruction. Both of these patients had simultaneous laparoscopic pyeloplasty and LPN.

Conclusion: Although rare, renal mass and stone or UPJO can exist concomitantly and outflow obstruction should be managed prior to partial nephrectomy in the same kidney. Ureteral patency with a double-J catheter is sufficient prior to LPN if obstruction from a calculus is present. Laparoscopic pyeloplasty should be performed at the time of LPN in the case of UPJO.
**Poster Session**

**Poster #62**

**GENDER DIFFERENCES IN RENAL CELL CANCER PRESENTATION AND SURVIVAL: AN ANALYSIS OF THE NATIONAL CANCER DATABASE, 1993-2003**
Jeffrey M. Woldrich, Christopher J. Kane, Jamie Ritchey, Andrew K. Stewart, Peter R. Carroll
UCSF, San Francisco, CA

**Introduction:** While it has long been accepted that there are gender specific differences in renal cell carcinoma (RCC) incidence, more specific studies in cancer presentation and long term outcome have not been completed. We sought to analyze patterns of disease presentation and outcome of RCC by gender using data from the National Cancer Database (NCDB) over a ten-year period.

**Methods:** The NCDB is a nationwide oncology dataset that currently captures approximately 75% of all diagnosed cancer cases from over 1,400 facility-based cancer registries. The NCDB was queried for adults with RCC diagnosed between 1993 and 2003. Cases were examined according to gender in relation to mean age, AJCC stage, histology, grade, tumor size, mortality, and race. SPSS™ was used for Student T-Test and Pearson’s Chi Square tests.

**Results:** A total of 213,051 patients with RCC between 1993 and 2003 were captured from NCDB. A total of 79,728 (37.4%) were female, and 133,266 (62.6%) male. Mean age was greater in females, 64.2±0.048, than in males, 62.9±0.034 (p<0.001). Women had a higher percentage of stage I tumors 45.9% v. 40.9% (p<0.001). Progressive stage migration was documented in both men and women with 41.4% of men stage I in 1993 v. 54% in 2003 and 45.4% of women stage I in 1993 v. 60.1% in 2003 (p<0.001). 15.0% of women had grade I tumors compared to 11.1% of men (p<0.001).

**Conclusion:** Women are more likely to have RCC stage I tumors than men. Both genders have demonstrated stage migration, although women more so than men. These differences may contribute to a small, yet significant survival advantage for women.

**Poster #63**

**TREATMENT FAILURE AFTER PRIMARY AND SALVAGE THERAPY FOR PROSTATE CANCER: LIKELIHOOD, PATTERNS OF CARE, AND OUTCOMES**
Piyush K. Agarwal†, Natalia Sadetsky‡, Janeen DuChane*, Martin I. Resnick†, Peter R. Carroll‡, and the CaPSURE™ Investigators
†Case Western Reserve University School of Medicine and University Hospitals of Cleveland, Cleveland, OH
‡University of California, San Francisco School of Medicine, San Francisco, CA
*TAP Pharmaceutical Products, Inc, Lake Forest, IL

**Introduction and Objectives:** Upon diagnosis, most men with prostate cancer are thought to have clinically localized disease amenable to cure with either radical prostatectomy (RP) or radiation therapy (RT). Herein we report on the likelihood of treatment failure and the patterns and outcomes of salvage therapy.

**Methods:** CaPSURE database query identified 12,005 patients with prostate cancer. Among them, 5,277 were treated with either RP (4,342) or RT (935) initially and had adequate follow-up to assess for biochemical recurrence (BCR) defined as two consecutive PSA values > 0.2 ng/dL in the RP group, three consecutive PSA increases from a nadir in the RT group, and any secondary treatment. Outcomes of patients with BCR and subsequent salvage therapy were assessed using chi-square and ANOVA analyses.

**Results:** BCR developed in 1,590 (30%) of the 5,277 patients including 1,003 (23%) of the RP patients and 587 (63%) of the RT patients. Patients with BCR had a median age of 66 years, a median PSA at diagnosis of 10.34 ng/dL, a median Gleason biopsy score of 5-6, and a median clinical T stage of T2. The mean time to BCR after primary treatment was 34 months (RP) and 38 months (RT) (p=0.003). Data after salvage therapy were available on 1,050 (620 RP and 430 RT) patients. The most common salvage treatment in both groups was androgen deprivation therapy (ADT) in 367 (59%) of the 620 RP patients and 402 (93%) of the 430 RT patients, followed by radiation therapy in 248 (40%) of the 620 RP patients and cryotherapy in 13 (3%) of the 430 RT patients. Overall, 420 (68%) of the 620 RP patients and 319 (74%) of the 430 RT patients failed salvage therapy by having a detectable PSA (PSA > 0.2 ng/dL). Mean detectable PSA values for these subgroups were 16.8 ng/dL (RP) and 42.7 ng/dL.
POSTER SESSION

(RT) \((p=0.0347)\) and occurred at a mean time of 43.6 and 43.8 months \((p=0.95)\) after the initiation of salvage therapy respectively. No survival benefit in prostate cancer related death \((p=0.91)\) was identified with a particular strategy of initial and salvage treatments.

Conclusions: Despite substantial stage migration with prostate cancer screening, a significant number of men fail primary therapy with surgery or radiation. The risk of failure can be predicted based on cancer grade, T stage, and serum PSA. ADT was the most common salvage therapy used after failure with either RP or RT. Salvage therapy response appeared to be similar between groups. CaPSURE database analysis demonstrated no survival benefit for a particular combination of primary and salvage therapy during the limited follow-up period.

Funding: CaPSURE™ is supported by TAP Pharmaceutical Products Inc. (Lake Forest, IL). This research was additionally funded by the NIH/NCI University of California-San Francisco SPORE grant P50 C89520.

Poster #64

SOLUBLE HEPARIN-BINDING EPIDERMAL GROWTH FACTOR AS A PREDICTOR FOR BLADDER TRANSITIONAL CARCINOMA
Bryan B. Voelzke, Mary Pat Fitzgerald, Susan O. McGuire, Marcus L. Quek, Thomas M.T. Turk, Matthew J. Hejna, Robert C. Flanigan. Loyola University Medical Center, Maywood, IL

Introduction and objectives: A member of the epidermal growth factor (EGF) family, HB-EGF exists as a cell membrane-anchored protein (proHB-EGF) that can be processed to a soluble form (sHB-EGF). sHB-EGF has been shown to promote tumor growth and angiogenesis via acceleration of cyclin D1, matrix metalloproteases, and vascular endothelial growth factor. While tissue expression of the membrane-bound form has previously been correlated with survival outcomes in bladder transitional cell carcinoma (TCC) patients, it is not known whether soluble HB-EGF can offer any further diagnostic or prognostic stratification. We evaluated urinary sHB-EGF in patients with and without bladder TCC to determine whether alteration in sHB-EGF concentrations is associated with bladder cancer.

Methods: A prospective cohort study involving 10 male bladder TCC patients and 9 age-matched controls was performed. sHB-EGF concentrations were determined using an enzyme linked immunoassay (ELISA) on voided urinary specimens from each patient. Only those with a normal urinalysis, no irritative voiding symptoms, and absence of medications for benign prostatic hyperplasia (alpha-blockers or 5-alpha reductase inhibitors) were included as controls.

Results obtained: Pathologic stage (based on either transurethral resection or radical cystectomy) for the TCC patients were as follows: pTis \((n=5)\), pT1 \((n=5)\), pT2a \((n=2)\), and pT3b \((n=1)\). Mean sHB-EGF level +/- SEM in the urine of the patients with TCC was 4.85 + 1.28 ng/ml, compared to 7.37 + 1.42 n/ml in the urine of the control patients. Although there was a trend toward lower sHB-EGF levels in the cancer patients, this did not reach statistical significance \((p=0.2)\).

Conclusions: Urinary sHB-EGF levels appear to be reduced in patients with bladder cancer when compared to age-matched controls. Our findings of decreased sHB-EGF in voided urine from TCC patients, as well as prior studies documenting a negative correlation between proHB-EGF levels in biopsy tissue and survival outcomes, suggest that aberrant cleavage of the proHB-EGF protein may contribute to the development and/or progression of urothelial carcinoma.

Financial Funding: None

Poster #65

TARGETED BIOPSY WITH COLOR DOPPLER AND ELASTOGRAPHY: A COMPARISON OF GLEASON SCORES
Eric D Nelson, Craig B Slotoroff, Leonard G Gomella, Ethan J Halpern, Thomas Jefferson University Hospital, Philadelphia, PA

Introduction and Objectives: Both color Doppler imaging and real time elastography may be useful to identify cancer within the prostate. We evaluated the distribution of Gleason scores found by systematic biopsy as well as targeted biopsy of the prostate with color Doppler and elastography.

Methods: One hundred and sixteen patients referred for prostate biopsy were evaluated with gray scale, color Doppler, and elastography using an end-fire transrectal probe (Hi-Vision 8500; Hitachi Medical Systems). Manual compression of the prostate with the probe was used to generate real time elastograms. Targeted core biopsy specimens were obtained from areas of increased color flow and decreased elasticity. Six

Continues on next page
laterally distributed systematic biopsy specimens were obtained from all subjects. Color Doppler and elastography were prospectively graded as normal/abnormal at each biopsy site. The presence of abnormality on Doppler or elastography was tabulated as a function of Gleason score; statistical analysis was performed with a Chi-square for linear trend.

**Results Obtained**: The diagnosis of prostate cancer was pathologically established in 52/116 (45%) of subjects, 80/386 (21%) of targeted cores and 95/696 (14%) of systematic cores. Among 175 positive biopsy sites, color Doppler was abnormal in 77 and elastography was abnormal in 68. A significant trend for increasing Gleason score was present with color Doppler ($\chi^2 = 19.65, p < 0.001$) and elastography ($\chi^2 = 24.68, p < 0.001$). Abnormal color flow was strongly associated with Gleason 8 (OR=3.45) and Gleason 9/10 (OR=10.65) lesions, but was minimally associated with Gleason 6 (OR=1.03) and Gleason 7 (OR=1.06) lesions. Elastography also demonstrated a stronger association with higher Gleason scores (Gleason 8 – OR=3.01 and Gleason 9/10 – OR=4.13), but was more strongly associated with Gleason 6/7 lesions as compared to color Doppler (Gleason 6 – OR=1.71 and Gleason 7 – OR=2.66).

**Conclusions**: A higher frequency of positive color Doppler and elastography findings are associated with higher Gleason scores. Positive color Doppler findings are strongly associated with high grade cancer, whereas positive elastography findings are associated with both moderate and high grade cancer.

**Poster #66**

**DELAYED MANAGEMENT OF HIGH GRADE RENAL TUMORS**
Rosalia Viterbo, Paul Crispen, Richard E Greenberg, David Y.T. Chen, Robert G Uzzo, Fox Chase Cancer Center, Philadelphia PA

**Objective**: The standard of care for solid localized renal tumors is excision, either radical nephrectomy or partial nephrectomy. Definitive therapy may often be delayed for various reasons. We assessed whether histologic Fuhrman grade was predictive of a worse outcome in patients who underwent delayed treatment of their renal tumors.

**Materials and Methods**: We searched our institutional tumor registry to identify enhancing renal masses in which treatment was initially withheld, delayed or refused. Of 147 solid enhancing renal masses in 124 patients in which management was postponed 50 patients with 55 tumors underwent delayed definitive treatment. We identified 11 patients who were found to have high grade RCC. Contrast enhanced serial sectional imaging was obtained and reviewed at 3-6 month intervals or until surgical management was completed. The interval between diagnosis and definitive treatment was calculated for each patient. Clinical, radiographic and pathological records were reviewed to determine local tumor growth rate, stage migration, and alterations in treatment plan due to delay.

**Results**: We identified 147 solid enhancing renal masses in 124 patients over a 13-year period in which management was postponed for a median time of 15 month (range 2-138). Of these, 50 patients (median age 70 (range 36-91)) with 55 tumors underwent delayed definitive treatment. The median tumor size at presentation was 2.6 cm (range 1.2-7.0). The median delay was 14 months (range 2-60) with 82% (9/11) delayed > 6 months from presentation. Definitive surgical intervention was pursued due to interval growth, improved PS, and/or patient choice. Treatments included laparoscopic cryoablation (n=1), open or laparoscopic nephron sparing surgery (NSS) (n=6), laparoscopic or open radical nephrectomy (n=4). Pathology confirmed clear cell RCC in 10 tumors, and papillary in 1. No patient progressed to metastatic disease due to delayed treatment even in high-grade lesions (Fuhrman 3 or 4). Comparing clinical T stage at presentation to pathological stage at treatment, no tumors were upstaged. Treatment options were not compromised due to delay, such that 64% underwent nephron sparing approaches.

**Conclusion**: The natural history of incidental localized renal masses is being defined. Management of high-grade lesions may be cautiously delayed without increase risk of disease progression, metastasis or limitations to treatment options. Delay in surgery is not associated with advanced pathological stage or decreased survival.

**Poster #67**

**CONTEMPORARY OPEN RADICAL CYSTECTOMY SERIES: ANALYSIS OF PERIOPERATIVE OUTCOMES FOR FUTURE COMPARISONS WITH MINIMALLY INVASIVE TECHNIQUES**
William T. Lowrance, Jon A. Rumohr, Michael S. Cookson, Sam S. Chang, and Joseph A. Smith, Jr., Vanderbilt University Medical Center, Nashville, TN

**Introduction and Objectives**: The feasibility of laparoscopic radical cystectomy with or without robotic assistance has been demonstrated in several small series. The implication of these efforts is that this approach will decrease patient morbidity, but the specific areas in which improvement is intended are uncertain. In order to establish a contemporary benchmark for open radical cystectomy, we reviewed our series and specifically evaluated perioperative patient outcome measures which conceivably could be affected by surgical approach.
Methods: The medical records of 554 consecutive open cystectomies from January 2000 through June of 2005 were reviewed. Perioperative data including, age, American Society of Anesthesiologists (ASA) classification, operative time, blood loss, transfusion rate, type of urinary diversion, hospital stay, complications, perioperative mortality, pathologic grade and stage, and surgical margin status were examined.

Results Obtained: All operations were completed by one of three experienced urologic surgeons. The median age was 69 (range 22-94) and average ASA classification was 2.8. The median operative time was 258 minutes (range 89-801). Mean operative time for ileal conduit diversion was 271 minutes versus 312 minutes for neobladder diversion. The median blood loss was 600 milliliters (ml) (range 200-4200). 218 patients (39%) received a blood transfusion either intraoperatively or within the first 30 days of their procedure. 342 patients (61.7%) underwent ileal conduit urinary diversion and 205 patients (37%) had an orthotopic neobladder. 7 patients (1.3%) underwent a continent cutaneous urinary diversion. Median length of hospital stay was 6 days (range 4-79). Minor and major complications occurred in 134 (24%) and 37 (6.7%) patients, respectively. Perioperative mortality was approximately 1%. Most tumors were high grade and muscle invasive. Positive surgical margins were found in 58 patients (10%).

Conclusions: These results demonstrate that radical cystectomy can be accomplished consistently with acceptable morbidity, minimal mortality, a median length of stay of less than one week, and blood loss of around 1 to 2 units even without selecting a more favorable patient group as may occur with laparoscopic series. Efforts to improve these statistics should continue, but whether laparoscopic approaches will offer any advantages for radical cystectomy remains highly uncertain.

Financial funding: None

Poster #69

USE OF SHORT HAIRPIN-RNA TO TARGET THE EPIDERMAL GROWTH FACTOR RECEPTOR IN 786.0 RENAL CELL CANCER LINE RESULTS IN EFFECTIVE ABROGATION OF TUMOR GROWTH IN A MURINE XENOGRAFT MODEL
S. Justin Lee, Gennady Bratslavsky, Julie Xanthopoulos, Adam Bullock, Ershad Elahi, James Vasselli, W. Marston Linehan

INTRODUCTION AND OBJECTIVE: The epidermal growth factor receptor (EGFR) is a tyrosine kinase transmembrane receptor belonging to the erbB family involved in many critical pathways of cellular biology including proliferation, invasion, mitogenesis, and apoptosis. Aberrant EGFR activity has been implicated in the induction and progression of renal cell carcinoma (RCC) as well as many other malignancies including breast, colorectal, and non-small cell lung cancer. The clear cell renal carcinoma, from which the cell line 786.0 has been derived, lacks a functional wild type von Hippel-Lindau protein and subsequently upregulates levels of tumor growth factor á (TGFá), a ligand for the EGFR. Some initial clinical trials of drugs targeting the EGFR have shown some promising results. The objective of this study is to determine the role of the EGFR pathway in clear cell renal carcinomas and characterize some of the phenotypes of knockdown in the EGFR pathway.

METHODS: For stable transfection of 786.0 renal cell lines, short-hairpin RNA (shRNA) technique was used to create cell lines with mRNA knockdown of EGFR and some of its downstream targets including Mitogen Activated Protein Kinase Kinase 1 (MEK1) and protein-serine/threonine kinase (AKT1). Two million cells of each constructed cell line were injected subcutaneously into each immunocompromised male SCID/beige mice. Mean tumor volumes for five mice per cell line were recorded. Additionally, branching morphogenesis assays of the various cell lines were performed in the presence of TGFá.

RESULTS: Tumor volumes of cell lines containing shRNA targeting the EGFR, MEK1, and AKT1 (designated AKT1D1, AKT1D2, EGFRD1 and MEK) showed dramatically decreased growth compared to cell lines containing a control non-targeting scramble sequence at 100 days. Branching morphogenetic assays revealed decreased branching in MEK1 targeted lines and to a lesser extent the EGFR and the AKT1 targeted lines.

CONCLUSIONS: Targeting the EGFR pathway results in effective abrogation of growth of the 786.0 renal cell line in a murine xenograft model of RCC. The EGFR pathway should be pursued in further studies to elucidate its role in the pathogenesis of clear cell renal carcinoma.

Sub-q Tumor Volume in 786-0 Murine Xenograft

Continues on next page
**Poster Session**

**Poster #70**

**DOES TYPE OF VHL MUTATION DETERMINE METASTATIC POTENTIAL OF RENAL CELL CARCINOMA? NCI EXPERIENCE OF 17 YEARS**

Gennady Bratslavsky, MD, S. Justin Lee, MD, Nicol Corbin, MD, Nadeem Dhanani, MD, Lynda Choyke, DPM, James Peterson, MS, Ramaprasad Srinivasan, MD, Peter Pinto, MD, Jonathan Coleman, MD and W. Marston Linehan, MD (Presented By: Gennady Bratslavsky, MD)

**Introduction and objectives:** The role of the von Hippel-Lindau (VHL) gene in hereditary and sporadic renal cell carcinoma (RCC) is well established. It has been shown that the type of genotypic mutation determines distinct phenotypic manifestations. Although nuclear grade and pathologic stage are the best known predictors of metastasis, the effect of specific VHL gene alterations on metastatic potential is not known. Our study evaluates whether the type of mutation of the VHL gene affects the metastatic behavior of renal lesions.

**Methods:** We retrospectively reviewed charts of 891 patients enrolled in a VHL protocol at the National Cancer Institute from October 1988 to October 2005. We also queried the NCI general and thoracic surgical pathology databases for any patients diagnosed with VHL requiring surgical intervention. Any patient with evidence of metastatic disease documented either radiographically or pathologically was included in the analysis. The size of the largest solid renal tumor was determined by radiographic or pathologic reports. The highest Fuhrman grade of the specimen was also recorded when available. The specific types of VHL mutations were analyzed for their association with metastatic disease and compared with overall prevalence of mutations in the entire VHL cohort with renal lesions.

**Results:** We identified 418 patients with renal lesions. Twenty-five out of 418 (6%) VHL patients had metastatic disease. There were 16 males and 9 females. Average age at the time of metastasis was 44 years (range 25-65). The most common sites of metastases were lung (64%), bone (24%), lymph nodes (20%), liver (16%), and brain (12%). Sixty-eight percent of all metastatic sites were proven by pathological examination. The mean size of the largest renal tumor was 7.1 cm (2.8-11.5) and Fuhrman Grade 2 was most common (1-4). Mutation analyses were available for 24 out of 25 patients (96%). The most common mutation type was missense (44%), followed by truncating mutations (40%), deletions (8%), and splice donors (4%). The frequency of mutation types in metastatic patients was not statistically different from overall prevalence of mutation types in the entire VHL cohort with renal lesions.

**Discussion:** We found that no specific VHL mutation was associated with development of metastatic RCC. It appears that any alteration of a VHL protein, whether aberrant full length, truncated, or completely absent carries a risk of developing metastatic disease that parallels the prevalence of mutations in the entire VHL cohort with renal lesions.

**Poster #71**

**DOES THE PROSTATE SIZE REALLY AFFECT THE BIOPSY GLEASON SCORE?**

Ashraf Abusamra, MD, FRCSC, Mazen Abdelhady, MD, MSc, Naji Touma, MD, Alp Sener, MD, Anthony Bella, MD, FRCSC, Jonathan Izawa, MD, FRCSC, Donal Downey, MD, FRCPC, Madeleine Moussa, MD, FRCPC and Joseph Chin, MD, FRCSC (Presented By: Ashraf Abusamra, MD, FRCSC)

**Introduction:** Recent reports have suggested that larger prostate size may mask the higher Gleason scores on biopsy. We analyzed our prostate cancer database to investigate the relationship between prostate size, biopsy Gleason score (bGS), and radical prostatectomy Gleason score (rpGS).

**Methods:** The radical prostatectomy (RP) database from 2000-3 was studied. All transrectal ultrasound (TRUS) and biopsies in this period were done by a single radiologist. The variables assessed included: prostate size on TRUS, bGS, and rpGS. We subdivided the data according to prostate sizes (< or ≥ 30g, < or ≥ 35g, and < or ≥ 40g), and bGS in three separate analyses using Chi square test.

**Results:** Complete patient (pt) data was available for 291 of 376 pts. 154 pts had bGS < 6, of these 82 (53%) were upgraded to rpGS ≥ 7. 137 pts had bGS ≥ 7, of these 26 (23%) were downgraded to bGS < 6.

<table>
<thead>
<tr>
<th>Prostate size</th>
<th>Number of patients (n= 291)</th>
<th>Upgrading on rpGS %</th>
<th>Downgrading on rpGS %</th>
<th>Same grade on rpGS %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30g</td>
<td>92</td>
<td>33</td>
<td>18</td>
<td>49</td>
</tr>
<tr>
<td>≥ 30g</td>
<td>199</td>
<td>NS</td>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>&lt; 35g</td>
<td>145</td>
<td>35</td>
<td>19</td>
<td>46</td>
</tr>
<tr>
<td>≥ 35g</td>
<td>151</td>
<td>44</td>
<td>11</td>
<td>45</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>&lt; 40g</td>
<td>178</td>
<td>34</td>
<td>19</td>
<td>47</td>
</tr>
<tr>
<td>≥ 40g</td>
<td>113</td>
<td>44</td>
<td>10</td>
<td>46</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>NS</td>
<td>p = 0.03</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prostate size</th>
<th>bGS ≤ 6 upgraded to rpGS ≥ 7</th>
<th>n = 82 (%)</th>
<th>bGS ≥ 7 downgraded to rpGS ≤ 6, n = 26 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30g</td>
<td>23 (28)</td>
<td>12 (46)</td>
<td>14 (54)</td>
</tr>
<tr>
<td>≥ 30g</td>
<td>59 (72)</td>
<td>18 (69)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>&lt; 35g</td>
<td>38 (46)</td>
<td>18 (69)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>≥ 35g</td>
<td>44 (54)</td>
<td>8 (31)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>&lt; 40g</td>
<td>43 (52)</td>
<td>20 (77)</td>
<td>6 (23)</td>
</tr>
<tr>
<td>≥ 40g</td>
<td>38 (46)</td>
<td>6 (23)</td>
<td>6 (23)</td>
</tr>
</tbody>
</table>
Conclusions: Our analysis of the relationship between Gleason score differences on biopsy and radical prostatectomy did not reveal a significant effect of prostate size on upgrading. This finding contradicts recent reports which have implicated larger prostate size in masking a higher Gleason score on biopsy i.e. bGS is as accurate in smaller prostates as in larger ones.

Poster #72

NOVEL DIETARY FLAVONOIDS MODULATE MULTIPLE KEY CELLULAR PATHWAYS IN PROSTATE CARCINOGENESIS
A.Haddad¹, V.Venkateswaran¹, B.Saour¹, A.Haegert², N.Tomlinson², C.Nelson², N.Fleshner³, L.Klotz¹
¹ Sunnybrook & Women’s College Health Sciences Centre, Toronto, ON, Canada
² Jack Bell Research Centre, Vancouver, BC, Canada
³ Princess Margaret Hospital, Toronto, ON, Canada

Introduction and Objective: Diets rich in flavonoids are associated with reduced risk of prostate cancer (PCa). Despite the large number of different flavonoids (over 4000) only a few have been studied in PCa to date. Based on a previous screening of 30 flavonoids in our lab, we identified two novel flavonoids- 2,2’-dihydroxychalcone (2,2’-DHC) and fisetin- with potent anti-proliferative properties in PCa cell lines. Our objective in this study was to determine molecular mechanisms of action of 2,2’-DHC and fisetin by examining global gene expression effects in human PCa cell lines using cDNA microarray.

Methods: LNCaP and PC3 human prostate cancer cells were exposed to 15µM 2,2’-DHC, 25µM fisetin, or vehicle control (0.1% DMSO) for 6, 12 and 24h. cDNA from each sample (including DMSO control) was labeled using cyanine5 (cy5) and hybridized onto a custom made 2-color microarray slide spotted with 22,000 genes. cDNA obtained from universal human RNA was labeled with cyanine 3 (cy3) and hybridized onto all slides. The gene expression level of all samples from the scanned slides was normalized using the LOWESS method. 2-fold changed genes were identified and ANOVA was used to determine statistically significant gene expression alterations between groups. K-means cluster analysis and biological data mining using the GO database was performed. Quantitative RT-PCR and Western blotting for 10 genes was performed to validate the results of the microarray.

Results: A total of 736 significantly altered genes were identified in the analysis. Classification of the genes by gene ontology (GO) showed that key genes involved in cell cycle and mitosis were down-regulated by both flavonoids at all time points. Among this group were the G2 checkpoint proteins cyclin B1, cdc2 and cdc25A, while the cyclin dependent kinase inhibitor p21 was consistently up-regulated. Furthermore, a number of spindle checkpoint genes showed reduced expression, including bub1 and plk1. Changes in known mitogenic pathways included reduction in levels of hepatocyte growth factor and its receptor, and reduction of IGF1 receptor. Finally, a number of novel genes such as TWIST1 and sestrin were highly differentially regulated. K-means clustering by expression pattern demonstrated that the majority of cell cycle genes being modulated by flavonoids in a similar fashion, as the majority of these genes clustered together. The results of quantitative RT-PCR and Western blotting performed for 10 genes were in direct agreement with the microarray data.

Conclusions: Flavonoid treatment results in alterations in multiple cellular pathways that are important in prostate carcinogenesis. Modulation of such pathways may explain many of the beneficial anti-cancer properties associated with flavonoids.

Funding: Canadian Prostate Cancer Initiative, CPC-Bionet.

Poster #73

IMPACT OF SUPER-RADICAL PROSTATECTOMY ON MARGIN STATUS AND 5-YEAR PROGRESSION FREE SURVIVAL IN CLINICALLY LOCALIZED PROSTATE CANCER
Gregg E. Zimmerman, Satish Sharma, Hyung L. Kim, James L. Mohler, Roswell Park Cancer Institute, Buffalo, New York

Introduction and Objective: Radical prostatectomy is the gold standard for surgical treatment of clinically localized prostate cancer. Wide excision of the neurovascular bundles (super-radical prostatectomy) may decrease the positive margin rate and improve disease-free survival.

Methods: 516 patients who underwent radical prostatectomy by a single surgeon were selected for bilateral nerve-sparing, unilateral nerve-sparing with contralateral super-radical, or bilateral super-radical prostatectomy by pre-operative clinical characteristics. Super-radical prostatectomy was performed for palpable disease, Gleason sum 7 or greater cancer in the apical biopsy, or impotence. Survival data was calculated using men with 5 years of follow-up.
Results:

<table>
<thead>
<tr>
<th></th>
<th>Bilateral Nerve-Sparing</th>
<th>Unilateral Nerve-Sparing/Unilateral Super-Radical</th>
<th>Bilateral Super-Radical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>369</td>
<td>74</td>
<td>73</td>
</tr>
<tr>
<td>Age</td>
<td>61 +/- .4</td>
<td>61 +/- 1</td>
<td>62 +/- 1</td>
</tr>
<tr>
<td>PSA</td>
<td>8.8 +/- 0.5</td>
<td>9.6 +/- 1.0</td>
<td>15.4 +/- 4.6</td>
</tr>
<tr>
<td>Clinical Stage T1</td>
<td>194</td>
<td>26</td>
<td>37</td>
</tr>
<tr>
<td>Clinical Gleason Sum</td>
<td>6.1 +/- 0.1</td>
<td>6.5 +/- 0.2</td>
<td>6.2 +/- 0.2</td>
</tr>
<tr>
<td>pT3 Patients</td>
<td>112</td>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>Positive Margins</td>
<td>16 (14%)</td>
<td>1 (4%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>pT2 Patients</td>
<td>257</td>
<td>46</td>
<td>46</td>
</tr>
<tr>
<td>Number of Positive Margins</td>
<td>34 (13%)</td>
<td>8 (17%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>5-Year Progression Free Survival (All Patients)</td>
<td>94%</td>
<td>100%</td>
<td>91%</td>
</tr>
<tr>
<td>5-Year Progression Free Survival (pT3)</td>
<td>95%</td>
<td>100%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Log rank analysis of Kaplan-Meier progression free survival showed the 3 groups were similar. When progression free survival was corrected for PSA as a surrogate for tumor volume, men undergoing super-radical prostatectomy actually had better outcome (Hazard Ratio 0.66 for all patients, 2.4 for pT3 patients).

Conclusion: Appropriate selection of men for super-radical dissection may allow high rates of progression free survival in patients with aggressive prostate cancer.

Poster #74

CORRELATION OF COLOR DOPPLER ULTRASONOGRAPHY WITH HISTOLOGY OF RENAL LESIONS
Ganesh V Raj*, Ariadne Bach, Alexia Iasonos, Jeffrey Blitstein, Lucy Hann, Paul Russo, Memorial Sloan-Kettering Cancer Center, New York, NY

Introduction and Objective: Standard abdominal imaging used to diagnose renal lesions cannot reliably differentiate between indolent and malignant neoplasms. Since most clear cell carcinomas are highly vascular, we evaluated renal lesions using pre-operative color doppler ultrasonography (DUS) to examine the association between vascular flow and surgical pathology.

Methods: All nephrectomies performed at our institution between 1/2001 and 1/2005 were retrospectively evaluated. Any evidence of vascular flow detected by DUS within renal lesions was defined as positive flow. To overcome limitations of retrospective analyses, a prospective study was then performed for validation from 1/2005 - 9/2005. Statistical analyses were performed using SAS software.

Results: Of 299 renal lesions with evaluable preoperative DUS in the retrospective cohort, 210 (70%) had evidence of vascular flow. Vascular flow was associated with 146 of 159 (92%) renal lesions with clear cell histology (p<0.0001, chi square analyses), resulting in 92% sensitivity and 54% specificity. Vascular flow was also noted in 8/41 (20%) papillary, 18/37 (49%) chromophobe, 25/49 (51%) benign and 13/13 (100%) metastatic renal lesions respectively. Using logistic regression analyses, vascular flow on DUS was predictive of clear cell histology (Odds ratio 18.6, 95% CI 8.7-39.8, p<0.0001).

These findings were validated in a prospective cohort of 97 patients, of whom 64 (66%) had vascular flow within the renal mass, including 51 of 61 (84%) renal lesions with clear cell histology (p<0.0001), resulting in 84% sensitivity and 64% specificity. Vascular flow was also seen in 1/12 (8%) papillary, 4/9 (44%) chromophobe and 8/15 (53%) benign renal lesions (Table). Again, renal lesions with vascular flow were likely to be clear cell (Odds ratio 9.0, 95% CI 3.5-23.6, p<0.0001).

Conclusions: We have validated the association between vascular flow within a renal lesion detected by a non-invasive technique (DUS) and clear cell histology. However the lack of specificity limits the ability of DUS alone to reliably predict histology. In conjunction with clinical parameters such as tumor size, type, location and multifocality, DUS may help accurately characterize renal lesions. Multivariable predictive models are required to test this hypothesis.
ORTHOTOPIC NEOBLADDER RECONSTRUCTION FOLLOWING CYSTECTOMY FOR BLADDER CANCER: IS ADJUVANT CHEMOTHERAPY SAFE?

Brian Cohen, Murugesan Manoharan, Martha Reyes, Alan Nieder and Mark Soloway
Dept Of Urology, Miller School of Medicine, University of Miami, Miami, FL, USA

Objective: Bladder cancer patients undergoing radical cystectomy (RC) and urinary diversion, who are at high risk for recurrent disease such as clinical stage > T2, positive lymph nodes may be treated with adjuvant chemotherapy (AC). These high-risk patients are more frequently offered orthotopic neobladder (NB) as an option for urinary diversion. However, there are concerns about the safety and complications associated with AC in these patients. There is a paucity of data in the current literature regarding AC in patients with NB. We examined our database of patients undergoing RC with orthotopic NB to determine whether adjuvant chemotherapy in this group is safe.

Methods: We performed a retrospective analysis of patients who underwent radical cystectomy and urinary diversion between 1992 and December 2004. Relevant clinical and therapeutic data were entered into a database. Patients with high risk bladder cancer who underwent NB were identified. They were stratified into 2 groups, those who received adjuvant chemotherapy and those who did not. The incidence of complications between these 2 were analyzed and compared.

Results: Over the 12 year period, 136 patients underwent RC and NB construction for bladder cancer. Of this, 83 patients were at high risk for recurrence. Of these, 14 patients received adjuvant chemotherapy. The patient characteristics between the 2 groups were similar. The details of chemotherapy regimen are given in Table 1. Complication rate in the adjuvant chemotherapy group was 71% and 20% in the NB group alone. Most of these complications were < grade 3 severity and only 2 patients with grade 4 toxicity in the adjuvant chemotherapy group. Though there were significant differences in the incidence of complications, none were life-threatening requiring only conservative treatment with no lasting disability (Table 3).

Conclusions: Adjuvant chemotherapy is a safe treatment for patients undergoing RC and NB substitution. No increased incidence of wound infections or urinary tract infections was found in both groups of patients. Hence the option of orthotopic NB should not be denied in selected bladder cancer patients with high risk for recurrent disease who may require adjuvant chemotherapy..

Table 1. Chemotherapy regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVAC</td>
<td>8</td>
</tr>
<tr>
<td>Gemcitabine &amp; cisplatin</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
</tr>
</tbody>
</table>

Table 2. Severity of toxicity

<table>
<thead>
<tr>
<th>Toxicity type</th>
<th>Group 1 (n=14) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>27</td>
</tr>
<tr>
<td>Grade 2</td>
<td>7</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>20</td>
</tr>
<tr>
<td>Grade 2</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>20</td>
</tr>
<tr>
<td>Grade 4</td>
<td>13</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>13</td>
</tr>
<tr>
<td>Grade 2</td>
<td>7</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3. Complications

<table>
<thead>
<tr>
<th>Urinary Tract Infection</th>
<th>NB with adjuvant (%)</th>
<th>NB alone (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>14%</td>
<td>7%</td>
<td>0.39</td>
</tr>
<tr>
<td>Hematologic</td>
<td>38%</td>
<td>3%</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Wound infection</td>
<td>0%</td>
<td>3%</td>
<td>0.51</td>
</tr>
<tr>
<td>Others</td>
<td>21%</td>
<td>9%</td>
<td>0.52</td>
</tr>
<tr>
<td>Total</td>
<td>71%</td>
<td>20%</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>
AN IMAGE-GUIDED SURGICAL NAVIGATION SYSTEM FOR UROLOGY


Division of Urology, Department of Surgical Oncology, Departments of Medical Imaging and Department of Pathology
University Health Network, University of Toronto.
Department of Radiation Oncology, Princess Margaret Hospital, Toronto.

OBJECTIVES: To adapt a computer-assisted real-time infrared camera based three-dimensional (3D) navigation system for urology procedures to evaluate its accuracy and ability to increase anatomic precision.

INTRODUCTION: Surgical navigation (SN) is simultaneous real time 3-D visualization of instruments and anatomy during surgery. Image-guided surgical navigation (IGSN) has the potential to improve the accuracy and safety of critical aspects of surgery and to create new, less morbid procedures that are primarily based on image guidance. It has been improved during the last two decades and the most common system is infrared (IR) camera based in which the camera uses reflected IR waves to calculates real time instrument position. We are developing a system for urology by studying the pattern of lymph node metastases in bladder cancer which will enable the surgeon to identify an area of interest within the pelvis and retroperitoneum, and then to simultaneously (and in real-time) display the corresponding area on previously acquired MR images.

METHODS: MR imaging using ferumoxtran-10 (Combidex®, Advanced Magnetics Inc., Cambridge, MA), an ultra-small iron oxide nanoparticle (USPIO), was used to localize nodes in patients who were undergoing radical cystectomy for bladder cancer. Correspondence between the tracking system’s coordinates and the MR image coordinates was established through MR-visible fiducial markers (external registration) and bony/vessel landmarks (internal registration) using custom software developed in-house. A set of IR-reflective spheres on a pointing hand piece tracked in real time by an IR camera, which was used to provide real-time annotation of the hand piece position and orientation overlaid on the MR images to identify/localize lymph nodes of interest. System accuracy was assessed by correlating the location of the (i) pre operative skin fiducial markers (surface measurement), and, (ii) the intrapelvic and retroperitoneal structures during surgery (actual measurement) with their position in the previously acquired MR image accuracy.

RESULTS: Six patients were studied, all of them males, median age 62.5 (range 45-77). Four had invasive urothelial carcinoma (TCC-stages T2-T4), and two had superficial disease, one carcinoma-in-situ. We observed a small surface measurement error (mean 1.95mm, range 0.66-2.48) but the mean measured actual error was 17mm (range 5.97-30.67). Intraoperatively the anterior abdominal retractors created movement of the external iliac vessels created this error by exacerbating misregistration between these vessels and associated lymph nodes and the pre-operative MRI. Ferumoxtran-10 aided in visualization of small lymph nodes (< 5mm in size) in all cases.

CONCLUSIONS: Fiducial registration for pelvic node mapping with ferumoxtran-10 enhanced MRI is promising but displacement related to tissue deformation from retractors and variations in patient positioning preclude a high level of accuracy in nodal localization. Ferumoxtran-10 improves visualization of small nodes for surgical navigation. In the future, it is anticipated that the use of intra-operative registration using fixed internal bony/vessel anatomical landmarks. As well, using intraoperative imaging, or image fusion techniques (cross-correlation between other imaging) will improve accuracy.

Funding: none

LAPAROSCOPIC PELVIC LYMPH NODE DISSECTION FOR PROSTATE CANCER: EXTENDED VS. LIMITED DISSECTION AND VALUE OF PARTIN TABLES IN SELECTING PATIENTS FOR LYMPHADENECTOMY

Karim Touijer, Farhang Rabbani, Javier Romero, Bertrand Guillonneau

Objectives: To evaluate the value of the Partin tables’ prediction of lymph node invasion in selecting patients for pelvic lymphadenectomy during radical prostatectomy.

To compare the results of an extended vs. limited pelvic lymphadenectomy (PLND) during radical prostatectomy.
Material and Methods: A total of 485 patients with clinically localized prostate cancer underwent a laparoscopic radical prostatectomy. In the first 362 patients, a cutoff of 1% on the Partin tables’ predicted probability of lymph node invasion (PPLNI) was used to select patients for a limited PLND (external iliac nodes only). In the following 123 patients, all patients underwent an extended PLND (external iliac, obturator and hypogastric nodes).

Patients were classified into 4 groups: Group I, 185 patients with a PPLNI < 1% who underwent LRP without node dissection, Group II, 64 patients with PPLNI < 1%, who underwent LRP with extended node dissection, Group III, 177 patients with PPLNI > 1% underwent LRP with limited node dissection and Group IV, 59 patients with PPLNI > 1% who underwent LRP with extended node dissection.

We compared Group I and II to assess the value of the Partin tables in selecting low risk patients for nodal metastasis. Logistic regression analysis was performed to compare the node positivity rate between groups III and IV, controlling for preoperative and pathological parameters.

Results: None of the patients in group II had a positive lymph node after an extended PLND. On multivariate logistic regression analysis, controlling for preoperative PSA, biopsy Gleason sum, clinical stage, pathological Gleason sum, pathologic stage, and seminal vesicle invasion, the extended PLND independently impacted the rate of positive lymph nodes retrieved with a relative risk (RR) of 21.2 (95% CI 3.4 – 133, p=0.001) vs a limited PLND. Other independent predictors of node positivity were seminal vesicle invasion (RR: 42.6, 95% CI: 3.9 - 462, p=0.002) and clinical stage T3 vs T1c (RR 14.7, 95% CI 1.99 – 109, p=0.008). The median (mean) number of lymph nodes retrieved was 9 (10) and 14 (15) after limited and extended PLND respectively (p=0.001, 95% CI: 2.8-6.4).

Conclusions: A lymph node dissection including the external iliac, obturator and hypogastric lymph node groups yields positive nodes more frequently and detects significantly more positive lymph nodes, retrieving a higher total nodal count than the often-performed lymphadenectomy limited to the external iliac nodes.

Forgoing a lymph node dissection in low risk patient may be safe; however, this selective omission of lymphadenectomy in low-risk patients needs to be validated by long-term biochemical recurrence data.

Poster #78

GENOME-WIDE ASSOCIATION STUDY FOR PROSTATE CANCER USING THE AFFYMETRIX 10K GENECHIP AND EVALUATION OF SUSCEPTIBILITY GENES FOR PROSTATE CANCER IN A CLINICAL SETTING
Robert K Nam*, William Zhang, Laurence H. Klotz, John Trachtenberg, Michael A.S. Jewett, Steven A. Narod, Toronto, ON, Canada

Introduction and Objective: New susceptibility genes are needed for prostate cancer to improve methods for prostate cancer detection. High throughput DNA microarray methods that examine for single nucleotide polymorphisms (SNPs) across the whole-genome have been used to identify new genes for many diseases. We conducted a genome-wide association study for new gene discovery for prostate cancer among 40 cases and 40 controls and then genotyped positive SNPs from this analysis among 2169 men who underwent a prostate biopsy.

Methods: We conducted a case-control study and used the 10,000 (10K) Affymetrix GeneChip to examine for SNPs across the genome. Cases were 40 patients diagnosed with high grade cancer (Gleason score 8 or more), PSA <10 ng/mL, cT1c, and of Caucasian background. Controls were 40 patients with no evidence of prostate cancer by biopsy, matched by PSA, DRE and ethnicity. We then genotyped positive SNPs found by the 10K GeneChip among 2169 men who underwent a prostate biopsy for prostate cancer.

Results: Among the 40 cases and 40 controls, we found 237 SNPs across the genome to be positively associated with prostate cancer using the Affymetrix GeneChip. The p-values for these SNPs associated with prostate cancer ranged from p=0.05 to p=0.00001. Using the NCBI builds to correlate these SNPs to the described genome, we selected 16 SNPs to genotype 2169 men who underwent a prostate biopsy. Among the 2169 men who underwent one or prostate biopsies, 1073 (49.5%) were diagnosed with cancer. We then genotyped positive SNPs found by the 10K GeneChip among 2169 men who underwent a prostate biopsy for an abnormal PSA to determine the odds ratio for prostate cancer.

Conclusion: Among the 40 cases and 40 controls, we found 237 SNPs across the genome to be positively associated with prostate cancer using the Affymetrix GeneChip. The p-values for these SNPs associated with prostate cancer ranged from p=0.05 to p=0.00001. Using the NCBI builds to correlate these SNPs to the described genome, we selected 16 SNPs to genotype 2169 men who underwent a prostate biopsy. Among the 2169 men who underwent one or prostate biopsies, 1073 (49.5%) were diagnosed with cancer. Among the 16 SNPs, we found one SNP, rs552895, to be strongly associated with increased prostate cancer risk. This SNP is a Cytosine for Guanine polymorphism and we found that 56.4% of cases had the variant homozygous genotype compared to 44.5% in the controls (p=0.0003, chi-square=15.9). The adjusted odds ratio for prostate cancer for patients with the CC genotype and the CG genotype compared to the GG genotype was 1.67 (95% CI: 1.3 - 2.1, p<0.0001) and 1.31 (95% CI: 1.1 - 1.6, p=0.006), respectively. This SNP maps to chromosome 9p22.3 (Build 88, NCBI).

Conclusions: Genome-wide association studies for prostate cancer are feasible using high throughput DNA microarray chips. These SNPs found to be associated with prostate cancer can provide important information for susceptibility genes for prostate cancer and could have important clinical applications. Future studies will be required with more powerful GeneChips.

Continues on next page
**Poster #79**

**ACOMPARIISON OF NEPHRON-SPARING TECHNIQUES: PERCUTANEOUS RADIOFREQUENCY ABLATION (RFA) VS. OPEN AND LAPAROSCOPIC PARTIAL NEPHRECTOMY**

Adam S. Feldman, MD – Dept of Urology, Massachusetts General Hospital, Boston, MA
Debra Gervais, MD – Dept of Radiology, Massachusetts General Hospital, Boston, MA
Christopher J. Cutie, MD – Dept of Urology, Massachusetts General Hospital, Boston, MA
Peter R. Mueller, MD – Dept of Radiology, Massachusetts General Hospital, Boston, MA
W. Scott McDougal, MD – Dept of Urology, Massachusetts General Hospital, Boston, MA

**Introduction and Objective:** Nephrorn sparing techniques are now standard of practice in selected renal cases. We evaluated our experience with three treatment modalities over the past 7 years to compare procedural outcomes, cancer control and determine which patients would be most appropriate for what therapies.

**Methods:** We performed a retrospective analysis of all patients who underwent open partial nephrectomy (n=109), laparoscopic partial nephrectomy (n=18) and percutaneous RFA (n=95) for renal tumors treated from November 1998 to March 2005. All patients treated by RFA had biopsy proven renal cell carcinoma or an enlarging mass on serial CT. Ten open surgical patients, one laparoscopic patient and no RFA patients were lost to follow-up.

**Results:** The mean age for laparoscopy was 58.3 years, for open surgery 61.6 years and for RFA 69.4 years. The difference in age of patients treated surgically vs. by RFA was significant (p = 0.000002). RFA patients tended to have more severe medical comorbidities. Mean LOS was 3.2 days for laparoscopy and 5.4 days for open surgery. In RFA patients, 72 were treated as outpatients, 22 were admitted with a mean LOS of 2.7 days and 1 was an inpatient for other reasons. Four (4.2%) RFA patients underwent general anesthesia. Mean tumor size was 2.29cm (range 1 - 5.5) in laparoscopy, 2.87cm in open surgery (range 0.6 - 16) and 2.64cm (range 1 - 4) in RFA. A significant difference (p = 0.0037) in complication rate was observed between RFA (9.4%) and surgical patients (21% open, 22% laparoscopic). Perioperative blood transfusion was required in 2.1% of RFA, 5.5% of laparoscopic and 16.5% of open surgical patients. In the surgical group, 12 of 14 cardiovascular complications and 16 of 18 patients transfused were in patients aged 60 or older. Surgical patients with 3 or more medical comorbidities were more likely to have a major complication. Local recurrence was evident in 3 open surgical, no laparoscopic and 1 RFA patient. Metastatic disease developed in 1 open surgical patient, no laparoscopic patients and was already present in 4 RFA patients at the time of treatment. Of 127 surgical cases, 25 were benign tumors.

**Conclusions:** Our data demonstrate that RFA, laparoscopic partial and open partial nephrectomy have comparable short-term cancer control. Patients with large tumors, central tumors and tumors adjacent to the collecting system are better approached with surgical resection. Patients over the age of 60 with 3 or more medical comorbidities are better served by treatment with RFA.

**Funding** - None

**Poster #80**

**TREATMENT WITH TNF-A AND TPEN DECREASES NF-KB ACTIVITY AND INDUCES APOPTOSIS IN PC-3 CELLS**

Paul L. Crispen, Constantine Golovine, Peter Makhov, Alan Pollack, Eric M. Horwitz, Richard E. Greenberg, Robert G. Uzzo, Vladimir M. Kolenko, Fox Chase Cancer Center, Philadelphia, PA

**Introduction and Objectives:** Androgen dependent prostate cancer (CaP) responds poorly to current chemotherapeutic regimens, with only a two-month increase in overall survival. One of the characteristics of advanced CaP is resistance to apoptosis, a process that many chemotherapeutic agents utilize to induce tumor cell death. Associated with the resistance to apoptosis in advanced CaP is an increased level of the nuclear transcription factor NF-κB. Novel agents to overcome resistance to apoptosis are needed to either supplement or replace current therapeutic regimens. We investigated the ability of the zinc chelator, N,N,N',N'-tetrakis (2-pyridylmethyl) ethylenediamine (TPEN), to decrease NF-κB activity and increase TNF-α-induced apoptosis in the PC-3 cell line.
Methods: PC-3 cells were preincubated with TPEN (2-6μM) for one half hour prior to stimulating cells with TNF-a (10?g/ml) for 90 minutes. Nuclear extracts were harvested and NF-κB DNA binding activity was determined using a TransAmTM assay. Apoptosis was measured using TUNEL assay following six hours of incubation. Confirmation of apoptosis as the principle method of cell death was performed with the pan-caspase inhibitor Z-VAD (50μM) and PI staining to evaluate for cellular necrosis as a mechanism of cell death. Contributions of the intrinsic and extrinsic apoptotic pathways were assessed by measuring Caspase-3, -8, -9, cytochrome c, and Smac/DIABLO levels using western blots of whole cell lysates. Nuclear translocation of the NF-κB subunit RelA was then determined with western blots of nuclear and cytoplasmic extracts. Funding received from the WW Smith Foundation.

Results: Following incubation with TNF-a and TPEN alone a marked increase in NF-κB DNA binding was noted compared to untreated cells. Combination of TNF-a and TPEN demonstrated a significant reduction in NF-κB DNA binding compared to cells treated with TNF-a or TPEN alone. This reduction in NF-κB DNA binding was associated with a significant increase in apoptosis in PC-3 cells treated with the combination of TNF-a and TPEN. The increase in apoptosis was both dose and time dependent with a maximal response noted with TPEN 6μM at six hours. Preincubation with Z-VAD inhibited apoptosis at all concentrations of TPEN evaluated. PI staining revealed minimal cellular necrosis contributing to the observed cell death at six hours. Western blots of whole cell lysates demonstrated increased cleavage of caspase -3, -8, and -9 in cells treated with TNF-a and TPEN, but not with either agent alone. Mitochondrial release of cytochrome c and Smac/DIABLO, which was only noted in cells treated with the TNF-a and TPEN combination, further established of the involvement of the intrinsic pathway of apoptosis. Nuclear translocation of RelA was markedly diminished in cells treated with TNF-a and TPEN, but not with either agent alone. Conclusions: Advanced CaP is associated with a resistance to apoptosis and a poor response to current chemotherapeutic regimens. Are data demonstrates that the zinc chelator, TPEN, significantly decreases NF-κB activity and increases apoptosis in PC-3 cells after stimulation with TNF-a. Evaluation of caspase, cytochrome c, and Smac/DIABLO activity revealed the contribution of both the intrinsic and extrinsic pathways of apoptosis. Decreased nuclear translocation of RelA presents a potential mechanism of decreased NF-κB DNA binding activity noted in cells treated with both TNF-a and TPEN. These findings support the role of increased NF-κB levels as a mechanism of apoptosis resistance in advanced CaP. Future work on establishing agents which supplement current chemotherapeutic regimens in inducing apoptosis in advanced CaP may eventually lead to increased overall survival.

Poster #81

AGE ADJUSTED CHARLSON COMORBIDITY SCORE IS ASSOCIATED WITH TREATMENT DECISIONS AND CLINICAL OUTCOMES FOR PATIENTS UNDERGOING RADICAL CYSTECTOMY FOR BLADDER CANCER
Theresa M. Koppie, Angel Serio, Guido Dalbagni, Kinjal Vora, Ganesh V. Raj, Harry W. Herr, Bernard H. Bochner. Department of Urology, Memorial Sloan Kettering Cancer Center. New York, NY

Introduction and Objectives: Age and comorbidity have been associated with overall and disease specific outcomes in various cancers. Using the age-adjusted Charlson comorbidity index (ACCI), we sought to characterize the impact of age and comorbidity on progression and survival after radical cystectomy (RC) for TCC of the bladder. We also evaluated whether ACCI was associated with the clinicopathological and treatment characteristics of patients undergoing RC for TCC of the bladder.

Methods: Using an institutional RC database, we identified 1121 patients who underwent RC for the treatment of transitional cell carcinoma of the bladder. The ACCI was used to retrospectively quantify burden of comorbidity. Logistic regression was used to determine the relationship between ACCI scores and clinical features. To evaluate the association between age ACCI score and outcome, we used the Cox proportional hazards model of overall survival and progression free survival using stage and nodal status as covariates.

Results: ACCI scores of patients undergoing RC at a single cancer center rose from 1990 to 2004. (linear regression, p=0.02) Patients with higher ACCI scores were more likely to have extravesical disease (p=0.03) and more likely to be node positive (p<0.0005) at the time of RC. Patients with higher ACCI scores were less likely to have a formal node dissection (p=0.007), had fewer lymph nodes evaluated at radical cystectomy (p<0.0005), and were less likely to have post-operative chemotherapy (p=0.02) than patients with lower ACCI scores. When controlled for stage and nodal status, patients with higher ACCI scores had significantly lower progression free (p=0.001) and overall (p<0.0005) survival after RC.

Conclusions: Age and burden of comorbidity for patients undergoing RC at a cancer referral hospital are increasing. Patients with advanced age and comorbidity present with more advanced disease, yet they are less likely to be eligible for extensive surgical and chemotherapeutic treatments. When controlled for pathologic stage and nodal status, advanced age and more extensive comorbidity are associated with significantly lower progression free and overall survival after RC. Age and comorbidity are important clinical variables, which should be considered when comparing outcomes after bladder cancer treatment.

Funding Source: AFUD

Continues on next page
Poster #82

LACK OF PROGRESS - THE EARLY DIAGNOSIS OF BLADDER CANCER
Motoo Araki, Mrugesan Manoharan, Allen Neider, Mark Soloway. University of Miami, Miami, FL

Objectives: The Clinical stage of prostate cancer has changed dramatically over the last decade largely due to PSA and public awareness. In contrast there is little public awareness about bladder cancer and little use of urine based tumor markers. Has there been any stage migration in bladder cancer?

Methods: Total of 393 radical cystectomies were performed between Jan/1992 and Aug/2005 according to two interval. They are divided to two groups; Group 1; N= 139 (1992-1998), Group 2; N=254 (1999-2005). The characteristics of the patients (age, sex, T stage, pre- and post-op pathological grade and estimated blood loss) were compared between the two groups.

Results: Age (68.5±9.3, 69.4±8.9), sex (%male)(80.6, 80.3) and blood loss (662.6±608.3, 583.6±501.3) are similar in two groups. Pathological stage is the following (Fig. 1.)

Conclusion: There has not been any change in the stage of our radical cystectomy patients. Over 20 % have metastasis to regional nodes in both periods. Only a public awareness campaign, emphasizing the risk factors and early symptoms is likely to change this. In addition urologists must understand that failure to achieve a complete response after an initial bladder preservation approach should prompt radical cystectomy for the highgrade Ta-T1 urothelial cancer of the bladder.

Poster #83

BODY MASS INDEX AND IMPACT ON PSA SCREENING AND PROSTATE CANCER DETECTION IN THE PLCOTRIAL
*St. Louis, MO, +Rockville, MD, #Marshfield, WI, $Denver, CO

Introduction and Objective: Recent studies have shown an inverse relationship with serum PSA levels and body mass index (BMI). We examined the relationship of BMI and PSA levels and prostate cancer (CaP) detection among men enrolled in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

Methods: Between 1993 and 2001, 38,350 men aged 55-74 were randomized to undergo annual PSA and DRE screening. Of these men 32,997 had participated in at least one screening round and had complete information on BMI and other demographics, including family history of CaP. Mean age was 62.6 years. 89% of the subjects were white. Median BMI was 27; 26.6% of men had a normal BMI (< 25) and 23.5% were obese (BMI > 30). There was a family history of CaP in 7.7% of the subjects. We examined the association of BMI and serum PSA levels in the whole study population and we looked at the relationship of BMI and CaP detection among men who had undergone a prostate biopsy (n=3900).

Results: Mean PSA in the study population was 1.91 ng/mL. Mean PSA among men undergoing a biopsy was 5.79 ng/mL. Mean PSA at the initial screen decreased with increasing BMI (see table). Mean PSA increased with age, was higher in African American men (3.06 ng/mL) than in white men (1.87 ng/mL) and was higher in men with (2.05 ng/mL) than men without (1.90 ng/mL) a family history of CaP.
At the time of the first biopsy during the first 3 screening rounds PSA > 4.0 ng/mL (odds ratio 2.96) and suspicious DRE (OR 2.03) were most predictive of positive biopsy. African American race (OR 1.58) and BMI > 30 (OR 1.25) were also predictive of a positive biopsy than family history of CaP (OR 1.24, not significant) or age (not significant). Among men with PSA 2.5-4.0 ng/mL, cancer detection rates were similar among men with BMI < 30 (18.4%) and men with BMI > 30 (17.2%).

**Conclusions:** Data from the PLCO Trial confirms previous studies showing that serum PSA levels are inversely related to BMI. In the PLCO study, while controlling for PSA level, men with a BMI > 30 were 25% more likely to have a positive biopsy than men with a BMI < 30. Overall cancer detection rates were similar in men with BMI > 30 and BMI < 30, using the same PSA threshold for biopsy. Further study is needed to determine the optimal PSA biopsy thresholds for obese men.

<table>
<thead>
<tr>
<th>Mean PSA by BMI</th>
<th>N</th>
<th>PSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 24.9 (normal)</td>
<td>8764</td>
<td>2.12</td>
</tr>
<tr>
<td>25.0-29.9 (overweight)</td>
<td>16491</td>
<td>1.89</td>
</tr>
<tr>
<td>30.0-34.9 (obese – I)</td>
<td>6042</td>
<td>1.77</td>
</tr>
<tr>
<td>35.0-39.9 (obese – II)</td>
<td>1343</td>
<td>1.55</td>
</tr>
<tr>
<td>&gt; 40.0 (obese - III)</td>
<td>357</td>
<td>1.30</td>
</tr>
</tbody>
</table>

**Poster #84**

**INTRANVESICAL BCG AND INTERFERON-α2â THERAPY PRIOR TO CYSTECTOMY DOES NOT IMPACT NEGATIVELY ON SURVIVAL IN PATIENTS WITH RECURRENT SUPERFICIAL BLADDER CANCER**

Ihor S. Sawczuk1,2,3, Ravi Munver1,2, Debra L. Fromer1,2, Ilya A. Wolfsion1,2, Alexandra Sawczuk1, Bernadette Galli1, James M. McKiernan1, Eric T. Goluboff3, Gerald Hoke1, Guy Manetti2, and Mitchell C. Benson3

Hackensack University Medical Center, Hackensack, N.J.1
UMDNJ-New Jersey Medical School, Newark, N.J.2
College of Physicians and Surgeons, Columbia University, New York, N.Y.3

**Introduction and Objective:** Combined intravesical Bacillus Calmette-Guérin (BCG) and interferon-α2â has been utilized as a salvage therapy for recurrent superficial bladder cancer in patients who have failed primary treatment with other agents. There has been a concern that the time required to initiate and maintain BCG + interferon-α2â therapy may result in poor survival by delaying cystectomy in patients who ultimately recur. We report our survival outcomes in patients undergoing cystectomy after intravesical BCG + interferon-α2â.

**Methods:** Thirty-two patients with superficial bladder cancer (5 patients Ta, grade 1 or 2; 27 patients T1, grade 3 with or without CIS) underwent induction with 6 weekly treatments with full, 1/3, or 1/10 dose of BCG plus 50 or 100 MU of interferon-α2â based on prior BCG exposure and tolerance. Patients with no evidence of disease received maintenance therapy of 3 weekly treatments at 3 months followed by 2 additional maintenance cycles administered 6 months apart. Response was assessed by cystoscopy and biopsy every 3 months. Patients with biopsy proven recurrences underwent cystectomy.

**Results:** Eighteen of 32 patients (56%) were disease-free following the initial induction cycle. At a median follow-up of 16 months, 21 patients (66%) remain disease-free and 11 patients (34%) had disease recurrence. Five of 7 patients (71%) benefited from a second salvage induction course. Six of 9 patients (67%) ultimately failed combination therapy at the first 3 month evaluation. Of the 20 patients previously treated with BCG, 12 patients (60%) were disease-free following induction and subsequently received maintenance therapy. Fourteen of 32 patients (43.7%) underwent cystectomy. The mean time to cystectomy after initiation of therapy was 15 months (range 3 to 59 months). The mean survival time after cystectomy was 44.8 months with one non cancer related death.

**Conclusions:** The time required to initiate and maintain combination intravesical BCG + interferon-α2â therapy in patients with recurrent superficial bladder cancer does not appear to impact negatively on post cystectomy survival.

Funding Source: None
Poster Session

Continued from previous page

Poster #85

PROSPECTIVE SERIES COMPARING HAND ASSISTED LAPAROSCOPIC CYSTECTOMY WITH MINILAPAROTOMY ILEAL CONDUIT TO OPEN CYSTECTOMY
Hani H Rashid A, Grant D Taylor B, David A Duchene A, Kenneth S Koeneman A
A University of Minnesota, Minneapolis, Minnesota
B University of Texas, Southwestern Medical Center, Dallas, Texas.

Introduction and Objectives: Our initial experience with hand assisted laparoscopic (HAL) cystectomy was compared with our results of open cystectomy with ileal conduit diversion to determine HAL cystectomy feasibility in patients with invasive bladder cancer.

Methods: During an 18 month period, 36 cystectomies were performed by one surgeon (KSK), of which, 16 had ileal loop diversions (8 hand assist laparoscopic cystectomy, 8 open cystectomy). A prospective, non randomized comparison of these 16 patients was performed. Standard parameters were compared concerning patient operative and postoperative courses using 2-tailed t test statistical analysis.

Results: A total of 16 patients successfully underwent open (8) and HAL (8) cystectomy with an ileal conduit. Of the 16 cystectomies, 13 were performed for muscle invasive bladder cancer. Mean operative time did not differ significantly between the two groups (HAL 403 vs. Open 420 minutes). Mean estimated blood loss in the HAL and open groups was 637 and 957cc respectively (p=0.23). The mean postoperative parenteral analgesia administered was 31mg in the HAL group vs. 149mg in the open group (p=.01). Regular diet was resumed in 4.5 days in the HAL group vs. 7.9 days in the open group (p=.05). The HAL and open groups had a mean length of stay of 6.4 vs. 9.8 days (p=.06). Oncological efficacy was preserved in the short term.

Conclusions: Laparoscopic cystectomy with ileal loop diversion is a feasible surgical option for invasive bladder cancer. HAL cystectomy with ileal conduit appears to have less estimated blood loss and postoperative analgesic requirements, shorter length of stay and earlier return of bowel function than open cystectomy.

Poster #86

DISTANT METASTASIS OF BLADDER CANCERS: DISTRIBUTION AND ASSOCIATION WITH LYMPH NODE METASTASIS, PATHOLOGIC STAGE, AND LYMPHOVASCULAR INVASION
Steven Shen,1 Gilad E. Amiel,2 Shahrokh F. Shariat,3 Ganesh S. Palapattu,4 Yair Lotan5, Pierre I. Karakiewicz,5 Amnon Vazina,6 Craig G. Rogers,6 Patrick J. Bastian,6 Amit Gupta,3 Mark P. Schoenberg,4 Arthur I. Sagalowsky,3 and Seth P. Lerner2
1Department of Pathology, The Methodist Hospital, Houston, TX
2The Scott Department of Urology, Baylor College of Medicine, Houston, TX
3Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX
4The James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, MD
5Cancer Prognostics and Health Outcomes Unit, University of Montreal, Montreal, Quebec, Canada

Introduction and Objectives: Distant metastasis is considered the highest stage of cancer progression and strongest predictor of survival. Pathways and establishment of distant organ metastasis include lymphatic or blood vascular invasion. Our hypothesis is that patterns of distant organ metastasis may be predicted by histolopathologic parameters and has prognostic significance.

Design: A comprehensive review of a multicenter cystectomy database with 956 bladder cancer patients from three institutions was conducted to identify cases with distant organ metastasis. Relevant clinico-pathologic parameters were summarized and correlated with distant organ metastasis and overall survival using descriptive statistics and Kaplan-Meier analysis and log-rank test. Cox-regression method was used for multivariate analyses for prediction of distant metastasis.

Results: A total of 174 (18.2%) patients with progression to distant metastases were identified from 956 patients underwent cystectomy for bladder cancer. The mean patients’ age was 64 years (range 35-86) with a male to female ratio of 4.1:1. Ninety percent (n=156) were transitional cell carcinoma (TCC), and the remaining cases were adenocarcinoma (n=6), squamous cell carcinoma (n=5), small cell carcinoma (2), and others (5). The most common sites involved were: bone 52, lung 49, liver 36, lymph node 28 (retroperitoneal 11, periaortic 7, supraclavicular 4, mediastinum 3), brain 8, GI tract 7, and others. 96 of 174 (55%) had one metastasis and 51 (29%) had two or more sites of metastases. Time from
cystectomy to metastasis (n=157) ranged from 0 to 103.5 months with average of 17±19.1 months and median of 10.5 months. The 1-year, 2-year, and 5-year survival rates for patients with distant metastasis were 39%, 25%, 11%, respectively. The overall survival did not correlate with the numbers of metastasis (p=0.13). However, lymph node or lung metastasis only had better overall survival than bone metastasis (p=0.02). The 1-yr and 2-yr survival were 56% and 46% respectively, for patients with nodal metastasis alone, 53% and 34% for lung metastasis alone, 21% and 17% for bone metastasis alone. Multivariate analysis showed that pathologic stage, nodal metastasis and lymphovascular invasion are independent variables to predict distant metastasis.

Conclusion: The most frequent organ metastases of bladder cancer are bone, lung, liver, and lymph nodes. The average time to metastasis from cystectomy was 17 months. Distant metastases occur frequently in the absence of lymph node metastasis. The survival is more associated with the site, instead of the number of metastases. In addition to pathologic stage and nodal metastasis, lymphovascular invasion is an independent variable to predict distant organ metastasis.

Poster #87

HIGH CONCORDANCE OF GENE METHYLATION IN POST-DRE AND POST-BIOPSY URINE SAMPLES FOR PROSTATE CANCER DETECTION
Craig G. Rogers, Mark L. Gonzalgo, Gai Yan, Patrick J. Bastian, David Y. Chan, William G. Nelson, Christian P. Pavlovich
Brady Urological Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland (CGR, MLG, GY, DYC, WGN, CPP)
Klinik Und Poliklinik für Urologie, Rheinische Friedrich-Wilhelms Universität Bonn, Universitätsklinikum Bonn, Bonn, Germany (PJB)

INTRODUCTION AND OBJECTIVES: We evaluated the concordance between post-digital rectal exam (DRE) and post-prostate biopsy urine samples using conventional methylation-specific PCR (MSP) analysis of three different gene promoters in patients with suspected or confirmed prostate cancer (PCA).

METHODS: Voided urine specimens were collected from 17 men after 15-second DRE and again after transrectal ultrasound-guided biopsy of the prostate for suspected malignancy or for follow-up biopsy as part of an expectant management protocol. Urine sediment DNA was isolated and subjected to bisulfite modification. Methylation of GSTP1, EDNRB, and APC promoters was determined by conventional MSP analysis for both post-DRE and post-biopsy samples and correlated with clinical information.

RESULTS: PCA was detected on prostate biopsy in 12 of 17 (71%) patients. Promoter methylation was detected in post-DRE urine specimens for GSTP1 (29%), EDNRB (58%), and APC (12%). Promoter methylation was detected in post-biopsy urine specimens for GSTP1 (24%), EDNRB (83%), and APC (18%). The concordance between post-DRE and post-biopsy urine samples was 94% (GSTP1 and APC) and 84% (EDNRB). Overall, 100% of patients with biopsy-proven PCA had at least one gene methylated in the urine vs. 58% of patients without evidence of PCA on biopsy.

CONCLUSIONS: Gene analysis using conventional MSP is a reliable method for detecting abnormal DNA methylation in voided urine samples obtained following DRE or prostate needle biopsy. The concordance between post-DRE and post-biopsy urinary samples for promoter methylation is high (84-94%), suggesting that urine collected after DRE may be used for genetic analysis with similar results to post-biopsy urine samples.

Poster #88

PHASE I STUDY OF AN INTRAPROSTATIC VACCINE IN LOCALY RECURRING PROSTATE CANCER AFTER RADIOTHERAPY: RATIONALE AND PRELIMINARY RESULTS
Jean-Baptiste Lattouf, James Gulley, Philip Arlen, Jonathan Coleman, Peter A. Pinto

Introduction: Intratumoral vaccines have been shown to provide improved anti-tumor responses over systemic vaccinations in murine models. This may be due to the vaccine delivering human T-cell costimulatory molecules that are expressed on the surface of the tumor cell, and the ability to generate a polyvalent immune response. Previous studies with the same vaccine described here but given systemically in patients with metastatic disease have shown evidence of clinical benefit (PSA decline >50% or radiographic objective response) that correlates with immunologic response. We report herein a phase I safety study of an intra-prostatic vaccine regimen in patients with locally recurrent prostate cancer.

Continues on next page
Materials and Methods: Patients with biopsy proven locally recurrent prostate cancer, who have failed local radiation with curative intent are eligible. A priming sub-cutaneous vaccination with PROSTVAC®-V/TRICOM™ (vaccinia) 2x10^8 PFU and rF-GM-CSF 1x10^7 PFU is given subcutaneously in an extremity on day 1. An intra-prostatic boosting dose of PROSTVAC®-F/TRICOM™ (fowlpox) is given on days 29, 57 and 85. End of study sextant biopsies are done for comparison with pre-treatment biopsies. Baseline and end of study apheresis and blood samples are obtained to quantitate PSA specific T-lymphocytes production. 5 treatment groups of 3-6 patients are defined: Intra-prostatic fowlpox dose escalation is attempted from 4x10^7 PFU (cohort I) to 4x10^8 PFU (cohort II) and then with combination of the same vaccine doses as in cohort II with rF-GM-CSF 1x10^7 PFU (cohort III) to 1x10^8 PFU (cohort IV). Group V will receive maximal dose of PROSTVAC®-F/TRICOM™ and rF-GM-CSF intra-prostatic as well as subcutaneously.

Results: Four patients have been accrued to cohorts I and II. Toxicities were transient, self limited, and d' Grade 2. They included fever, urinary retention, and minor hematuria and hematochezia. There were no grade III-IV toxicities. Immunologic studies and pathologic studies are ongoing.

Conclusion: Intraprostatic vaccine injection is feasible and safe with the doses tested to date in our trial. Accrual is ongoing.

Poster #89

MANAGEMENT OF PATIENTS WITH SOLITARY LESIONS AT THE BLADDER DOME WITH WIDE LOCAL EXCISION PARTIAL CYSTECTOMY
David S Sharp*, Ganesh V. Raj, Anuradha Gopalan, Semra Olgac, Harry Herr. Memorial Sloan-Kettering Cancer Center, New York, NY

Introduction and Objective: Solitary lesions at the dome of the bladder are difficult to stage and manage, with partial cystectomy (PC) a treatment option for these tumors. The objective of this study was to evaluate the outcomes of patients with solitary dome lesions managed with PC.

Methods: A retrospective review of all patients treated for a solitary lesion at the bladder dome with partial cystectomy between 1979 and 2005 at our institution was performed. Patient characteristics, clinical features, and survival following surgery were analyzed using chi-square and Kaplan-Meier analysis.

Results: 69 patients who underwent primary surgical treatment at our institution for solitary dome lesions with a partial cystectomy comprise our study cohort. Median age of the cohort was 60.5 years and 71% of the patients were male. 89% of patients were symptomatic at time of presentation. Transurethral resection revealed urothelial carcinoma and adenocarcinoma in 58.0% and 37.7% of patients, respectively. Pathologic examination of PC specimens by a single pathologist revealed 30 patients with urachal carcinoma (UC) and 39 patients with a non-urachal bladder carcinoma (NUC). Pathologic stage was similar in both groups with 42% and 54% of patients with >pT2 disease in the NUC and UC groups, respectively. Compared to those in the UC group, patients in the NUC group were more likely to have CIS on final pathology (44% vs 10%, p=0.007.) Patients with NUC were more likely to recur within the bladder than those with UC (p<0.01). Local recurrence and metastases rates for the entire cohort were 17% and 28%, respectively and were not significantly different between NUC and UC. There was no difference in survival between NUC and UC of the bladder dome: median overall survival was 8.8 years, with 5 year actuarial survival of 61% for UC and 64% for NUC.

Conclusions: A high index of suspicion for urachal carcinoma should be entertained with any solitary lesion near the dome of the bladder. We recommend treatment with wide local excision including the urachus with any solitary lesion of the bladder dome. When completely resected, median survival exceeds 8 years and there is no difference in survival between urachal cancers and non-urachal solitary carcinomas of the bladder dome.

Funding Source: None
**Poster #90**

**ANALYSIS OF LAPAROSCOPIC PARTIAL NEPHRECTOMY FOR MULTIPLE RENAL TUMORS**

Kristian R. Novakovic, Manish A. Vira, Brian Keuer, S. Justin Lee, Jean-Baptiste Lattouf, Jonathan A. Coleman, McClellan Walther, W. Marston Linehan, Peter A. Pinto

**Introduction and Objective:** Laparoscopic nephron sparing surgery (LNSS) is increasingly employed as a treatment modality for renal tumors. A subset of patients with renal tumors may demonstrate multiple synchronous lesions, especially those with familial syndromes such as Von Hippel-Lindau (VHL), Birt-Hogg-Dube (BHD), hereditary papillary renal cell carcinoma (HPRC) and hereditary leiomyomatosis renal cell carcinoma (HLRCC), as well as patients with multiple sporadic tumors. To date, there is little data on the use of laparoscopic partial nephrectomy to treat multiple tumors. We report results of treating patients with multiple renal tumors using LNSS.

**Methods:** Since August 2002, 10 patients have undergone a total of 12 LNSS for multiple renal tumors at the National Cancer Institute. Eight patients were affected kindred of familial kidney cancer syndromes. Four procedures involved a hand assisted laparoscopic approach, while 6 and 2 underwent pure transperitoneal and retroperitoneal laparoscopy respectively. In eight of the 12 cases, hilar clamping was performed. Warm ischemia was reserved for removal of the largest tumor(s) in each case. Intracorporeal suturing was utilized when necessary for collecting system closure or hemostasis. Other techniques for hemostasis included use of an endoscopic monopolar dissector, and various hemostatic sealants.

**Results:** The median number of tumors removed was 4 (range, 2-12). The largest tumor in each case varied in size from 2-7cm (mean 3.2cm). Mean ischemia time in the relevant cases was 31 minutes (range, 19-67min). Mean pre and postoperative estimated creatinine clearances were 110.3 and 106.7 ml/min respectively. Mean overall change in serum creatinine was 0.04 with average follow up of 10 months (range 3days to 30mos). Mean estimated blood loss was 472cc (range, 100-1500cc). Two patients required peri-operative blood transfusion. There were no conversions to open procedures. One patient was treated for a postoperative urinary leak that resolved with internal stenting.

**Conclusions:** LNSS is a viable option for the treatment of multiple renal tumors. The relatively long operative times, potential for significant blood loss and warm ischemia do not appear to compromise overall renal function. Patients with familial cancer syndromes, who often require resection of multiple tumors are safely treated with LNSS and can therefore realize the benefits of minimally invasive surgery.

**Poster #91**

**IMPACT OF RENAL ARTERIAL OCCLUSION DURING LAPAROSCOPIC PARTIAL NEPHRECTOMY**

Manish Vira, Brian Keuer, Kristian Novakovic, S. Justin Lee, Jean-Baptiste Lattouf, McClellan Walther, W. Marston Linehan, Jonathan Coleman, and Peter Pinto

**Introduction:** Laparoscopic partial nephrectomy has shown to be a feasible and oncologically safe technique in the surgical management of renal tumors less than 4 cm in size. We evaluated our experience with laparoscopic partial nephrectomy with respect to changes in postoperative renal function.

**Methods:** We retrospectively reviewed the data from 45 patients who underwent laparoscopic partial nephrectomy for renal tumors between 1999 and 2005 at the National Cancer Institute. Our cohort was comprised of patients with both sporadic renal tumors as well as patients with hereditary renal cancer syndromes. Unique to our series was the inclusion of patients with multiple renal tumors (24.4% of the cohort). Renal function was assessed using serum creatinine, estimated creatinine clearance (using the Cockcroft and Gault equation), and differential renal function scans. Postoperative renal function studies were completed at least 1 month (median 3.5 months, range 1-12 months). Statistical differences in means were assessed using two tailed student t test.

**Results:** A total of 25 patients underwent laparoscopic partial nephrectomy without arterial clamping and 20 patients with arterial clamping. Mean clamp time in the latter group was 28.2 minutes (range 10-67 minutes). The average tumor size in each group was 2.35 cm (no clamping) and 2.75 cm (arterial clamping). There were no significant differences in estimated blood loss or total operative time between the two groups (p=0.08 and p=0.48, respectively). There was a mean increase of 3.3% (no clamping) and 6.4% (arterial clamping) in serum creatinine in the two groups. Among both groups 64% of the patients had a decrease in their estimated creatinine clearance. Among these patients, the group who underwent renal arterial clamping showed a small but significant difference in mean percentage change in estimated creatinine clearance (10.0% versus...
Continued from previous page

20.0%, p=0.04). However, there was no significant difference in the change in differential renal function in the affected renal unit by renal scintigraphy (8.3% versus 12.1%, p=0.38). Furthermore, among a small subset of patients (n=11), there was no significant difference in the change in measured creatinine clearance from 24 hour urine samples. **Conclusion:** We found no significant differences in the change in serum creatinine or differential renal function between patients who underwent no clamping and those who underwent renal arterial clamping during partial nephrectomy. However, we did find a small but significant difference in the decrease in the estimated creatinine clearance between these two groups. This result was not supported by measured creatinine clearance from 24 hour urine samples calling in to question the validity of estimated creatinine clearance in the evaluation of changes in renal function following laparoscopic partial nephrectomy. Laparoscopic partial nephrectomy with or without arterial occlusion was performed safely in our patient cohort, including those with multiple renal tumors.

**Poster #92**

**NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BLADDER CANCER: PERIOPERATIVE MORBIDITY, CLINICAL AND PATHOLOGICAL OUTCOMES, AND IMPLICATIONS FOR CYSTECTOMY AND URINARY DIVERSION**


**Introduction and Objective:** The objective of this study is to determine whether the perioperative morbidity and clinical outcomes following neoadjuvant chemotherapy and cystectomy has improved during the evolution of this approach; also, to evaluate whether the response to neoadjuvant chemotherapy can be used to determine the benefits of cystectomy and feasibility of orthotopic bladder reconstruction. **Method:** The survival of patients with locally advanced but operable urothelial carcinoma defined by the presence of lymphovascular invasion, a palpable 3-dimensional mass, or invasion of adjacent visceras (cT4a) is improved by neoadjuvant chemotherapy prior to cystectomy, and survival is tightly coupled to the absence of muscle-invasive tumor at cystectomy. We reviewed the clinical and pathological data from 148 patients enrolled in one of two prospective trials of neoadjuvant chemotherapy - methotrexate, vinblastine, adriamycin, cisplatin (MVAC) and taxol, methotrexate, cisplatin (TMP) and cystectomy between Jan 1989 and Dec 2004 to determine whether there have been marked differences in surgical morbidity, response to chemotherapy and disease specific survival as this approach has evolved. Also, to identify risk factors that correlates with pelvic recurrence that could be used to counsel patients regarding continent urinary diversion. **Results:** Mean patient age was 63.1±9.9 years, 98 were male and 37 female. Of the 148 patients, 75 (50.6%) patients received an ileal conduit diversion, 61 (41.2%) patients an orthotopic neobladder, and 12 (8.2%) patients a continent cutaneous diversion. There were no differences in patient demographics, performance status, median operative time (510 ± 122 minutes), intraoperative complications (n=4), incidence of perioperative complications (78 in 58 patients) or perioperative mortality (n=2) between the 2 groups. The most common complications were GI (26, ileus or small bowel obstruction), infectious (8, urosepsis, pneumonia), and wound complications (8). Three patients required reoperation. The mean time to regular diet was 8.7 ± 5.7 days and the length of hospital stay was 11.0 ± 5.7 days, with patients receiving TMP having a longer hospital stay (p< 0.001). Patients were followed for a mean duration of 43.1 months (range 1 to 203 months). Type of chemotherapy had no impact on pathologic downstaging to < pT2. 73 (49%) patients were downstaged to < pT2, and 35 (23.6%) patients were > pT3 following chemotherapy. The disease-specific survival (DSS) at 5 years was 60% with no significant difference noted between the chemotherapeutic regimens. Pelvic recurrence occurred in 21 patients (14.1%), 10 (6.1%) of which were isolated. Distant recurrence occurred in 30 (20.3%) patients. The absence of hydronephrosis at presentation, age < 65yrs, a favorable response to chemotherapy (<pT2), absence of non-TCC histology, and absence of positive lymph node disease at cystectomy correlated significantly with increased PFS and DSS (p<0.01). **Conclusion:** The feasibility of neoadjuvant chemotherapy for locally advanced but operable bladder cancer has been established, but the impact on survival has plateaued. It is important to be able to identify patients likely to respond favorably to neoadjuvant chemotherapy, and to consider other approaches for those not likely to respond. DSS and PFS in patients with locally advanced urothelial carcinoma treated by neoadjuvant chemotherapy and cystectomy can be predicted by the response to chemotherapy. Consideration should be given to performing cystoscopy and examination under anesthesia prior to cystectomy so that patients can be counseled with respect to the benefits of cystectomy and the feasibility of orthotopic bladder reconstruction.
**THURSDAY, DECEMBER 1, 2005**

7:00 p.m.

**BODY MASS INDEX AND IMPACT ON PSA SCREENING AND PROSTATE CANCER DETECTION IN THE PLCO TRIAL**
Robert L. Grubb*, David L. Levin†, Paul F. Pinsky‡, Jerome Mabie‡, Thomas L. Riley‡, Robert Greenlee*, Donald A. Urban†, Lawrence R. Ragard‡, E. David Crawford‡, and Gerald L. Andriole*

*St. Louis, MO, †Rockville, MD, ‡Marshfield, WI, §Denver, CO

**Introduction and Objective:** Recent studies have shown an inverse relationship with serum PSA levels and body mass index (BMI). We examined the relationship of BMI and PSA levels and prostate cancer (CaP) detection among men enrolled in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

**Methods:** Between 1993 and 2001, 38,350 men aged 55-74 were randomized to undergo annual PSA and DRE screening. Of these men 32,997 had participated in at least one screening round and had complete information on BMI and other demographics, including family history of CaP. Mean age was 62.6 years. 89% of the subjects were white. Median BMI was 27; 26.6% of men had a normal BMI (< 25) and 23.5% were obese (BMI > 30). There was a family history of CaP in 7.7% of the subjects. We examined the association of BMI and serum PSA levels in the whole study population and we looked at the relationship of BMI and CaP detection among men who had undergone a prostate biopsy (n=3900).

**Results:** Mean PSA in the study population was 1.91 ng/mL. Mean PSA among men undergoing a biopsy was 5.79 ng/mL. Mean PSA at the initial screen decreased with increasing BMI (see table). Mean PSA increased with age, was higher in African American men (3.06 ng/mL) than in white men (1.87 ng/mL) and was higher in men with (2.05 ng/mL) than men without (1.90 ng/mL) a family history of CaP.

At the time of the first biopsy during the first 3 screening rounds PSA > 4.0 ng/mL (odds ratio 2.96) and suspicious DRE (OR 2.03) were most predictive of positive biopsy. African American race (OR 1.58) and BMI > 30 (OR 1.25) were also predictive of CaP. BMI > 30 was more predictive of a positive biopsy than family history of CaP (OR 1.24, not significant) or age (not significant). Among men with PSA 2.5-4.0 ng/mL, cancer detection rates were similar among men with BMI < 30 (18.4%) and men with BMI > 30 (17.2%).

**Conclusions:** Data from the PLCO Trial confirms previous studies showing that serum PSA levels are inversely related to BMI. In the PLCO study, while controlling for PSA level, men with a BMI > 30 were 25% more likely to have a positive biopsy than men with a BMI < 30. Overall cancer detection rates were similar in men with BMI > 30 and BMI < 30, using the same PSA threshold for biopsy. Further study is needed to determine the optimal PSA biopsy thresholds for obese men.

<table>
<thead>
<tr>
<th>Mean PSA by BMI</th>
<th>N</th>
<th>PSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 24.9 (normal)</td>
<td>8764</td>
<td>2.12</td>
</tr>
<tr>
<td>25.0-29.9 (overweight)</td>
<td>16491</td>
<td>1.89</td>
</tr>
<tr>
<td>30.0-34.9 (obese –I)</td>
<td>6042</td>
<td>1.77</td>
</tr>
<tr>
<td>35.0-39.9 (obese – II)</td>
<td>1343</td>
<td>1.55</td>
</tr>
<tr>
<td>&gt; 40.0 (obese - III)</td>
<td>357</td>
<td>1.30</td>
</tr>
</tbody>
</table>

P < 0.0001 – test for trend

7:10 p.m.

**A PHASE I/II PROSPECTIVE DOSE ESCALATING TRIAL OF LYCOPENE IN PATIENTS WITH BIOCHEMICAL RELAPSE OF PROSTATE CANCER FOLLOWING DEFINITIVE LOCAL THERAPY**

Departments of *Urology, †Hematology and Oncology, ‡Radiation Oncology, and §Cancer Biology, and the Comprehensive Cancer Center of Wake Forest University Health Sciences, Winston-Salem, NC.

§: These authors contributed equally to this manuscript.

Continues on next page
PURPOSE: We report a prospective trial of lycopene supplementation in biochemically relapsed prostate cancer.

MATERIALS AND METHODS: 36 men with biochemically relapsed prostate cancer were enrolled in a dose escalating, phase I/II trial of lycopene supplementation. Six consecutive cohorts of six patients each received daily supplementation with 15, 30, 45, 60, 90, and 120 mg/day for one year. Serum levels of prostate specific antigen (PSA) and plasma levels of lycopene were measured at baseline and every three months. Primary endpoints were PSA response (defined as a 50% decrease in serum PSA from baseline), pharmacokinetics, and the toxicity/tolerability of this regimen.

RESULTS: 36 patients were enrolled. The median age was 74 (range 56–83) years with a median serum PSA at entry of 4.4 (range 0.8-24.9) ng/ml. There were no observed serum PSA responses. 37% of patients had PSA progression. The median time to progression was not reached. Toxicity was mild with one patient discontinuing therapy due to toxicity (diarrhea). Significant elevations of plasma lycopene were noted at three months and then appeared to plateau for all six dose levels. The plasma levels for doses between 15-90 mg/day were similar with further elevation only at 120 mg/day.

CONCLUSIONS: Lycopene supplementation in men with biochemically relapsed prostate cancer is safe and well tolerated. Plasma levels of lycopene are similar over a wide dose range (15-90 mg/day) and plateau by three months. Lycopene supplementation at the doses utilized in this study did not result in any discernible response in serum PSA.

Funding: Supported in part by NIH grant #: P30-CA12197-2751

7:20 p.m.

QUANTIFYING THE PUBLIC HEALTH IMPACT OF LOW HOSPITAL VOLUME ON OUTCOMES FOLLOWING CANCER SURGERY*
Brent K. Hollenbeck, David C. Miller, David A. Taub, Rodney L. Dunn, and John T. Wei
University of Michigan, Ann Arbor, MI

Context: Mounting evidence suggests the importance of hospital volume on outcomes following complex surgical procedures.
Objective: To estimate the potential benefit of regionalizing surgical services to top performing hospitals from low and very low volume centers treating 1 of 9 malignancies.

Design, Setting, and Participants: We estimated the likelihood of an in-hospital death or a prolonged length of stay following cancer surgery using a nationally representative sample of discharge abstracts collected within the framework of the Nationwide Inpatient Sample between the years 1988 and 2002. The 9 surgical procedures abstracted included: prostatectomy, adrenalectomy, cystectomy, nephrectomy, esophagectomy, pancreatectomy, lobectomy/pneumonectomy, liver resection, and rectal resection. The likelihood of an adverse event within hospital volume categories were used to estimate the percent attributable risk of very low and low volume hospitals on in-hospital mortality and prolonged length of stay (LOS) outcomes compared to top performing hospitals.

Main Outcome Measures: The percent attributable risk of very low and low hospital volume on in-hospital mortality and prolonged LOS, and the number of lives saved/earlier discharges.

Results: Relative to top performing hospitals, very low and low hospital volume was significantly associated with prolonged LOS and inhospital mortality for 8 and 7 cancer procedures, respectively, after adjusting for case mix and demographics. The magnitude of effect was greatest for patients undergoing prostatectomy for prostate cancer at very low volume hospitals—prolonged LOS: OR 4.2 (95% CI 4.0-4.4); in-hospital mortality: OR 5.3 (95% CI 3.7-7.5)—corresponding to 44,927 earlier discharges and 1,037 lives-saved if the procedure were to be regionalized to top performing hospitals. The greatest impact of volume on in-hospital mortality was noted for lobectomy/pneumonectomy for lung cancer in which up to 4,191 deaths (279 annually) could be attributed to the low volume. Despite a strong volume-outcome effect, regionalization of uncommon surgical procedures such as esophagectomy and liver resection would have relatively small impact on avoidable in-hospital deaths in the U.S. (59 and 38 lives-saved per year, respectively).

Conclusions: The public health impact of regionalizing patients undergoing cancer surgery to top performing centers is likely to be modest at best given the number of patients saved. Conversely, other clinical endpoints, such as prolonged LOS, may be more responsive to hospital volume and have broader implications to the U.S. public for volume-based initiatives.

*Source of funding: Institutional
**Branching Phenotype of Renal Cell Carcinoma Is Abrogated by Nox4 Silencing**

Jodi K Maranchie*, Ye Zhan, Worcester, MA.

**Introduction and Objective:** Inactivation of the von Hippel Lindau tumor suppressor (VHL) is an early event in 60-80% of sporadic clear cell renal cell carcinoma (RCC). VHL functions as a ubiquitin ligase for hypoxia-inducible transcription factors (HIF-alpha). We previously showed that generation of reactive oxygen species (ROS) by the kidney-specific NADPH oxidase, Nox4, is critical for expression and activity of HIF2-alpha. Knockdown results in dramatic reduction of HIF transcriptional activity even in the absence of VHL. VHL-deficient cells demonstrate a characteristic branching phenotype when exposed to hepatocyte growth factor-scatter factor (HGF-SF) that can be abrogated by re-expression of VHL. To determine the effect of Nox4 silencing on the branching phenotype of RCC, we examined VHL positive and negative cells after stable Nox4 knockdown.

**Methods:** Small inhibitory RNA able to knockdown Nox4 by at least 80% (siRNA) and a non-specific siRNA (scramble) were cloned into pSilencer™ 4.1-CMV puro (Ambion) as 54 nucleotide hairpin loops. The resulting vectors were used to transfet paired VHL-deficient human RCC cell lines expressing empty vector (786-0 pRC) or wild type VHL (786-0 WT). After selection with puromycin, single cell clones were screened for reduced production of ROS using a 2',7'-dichlorofluorescin diacetate fluorescent assay. Stable transfectants and parental 786-0 cells were suspended in matrigel and incubated with recombinant HGF-SF at 37°C, for 72 hours. Triplicate wells were evaluated by counting non-branching cells in 3 high power fields per well.

**Results:** Cells expressing VHL were rounded with minimal branching. No differences were seen between 786-0 WT cells expressing siRNA or scramble. VHL-deficient cells expressing pSilencer-scramble developed marked branching of the majority of cells, and were indistinguishable from parental 786-0 cells. However, after stable knockdown of Nox4 in 786-0-PRC, both the number of branching cells and the average number of branches per cell were decreased by greater than 50%.

**Conclusions:** ROS production by Nox4 is necessary for the full branching phenotype of VHL-deficient RCC cells. The branching phenotype, commonly seen following malignant transformation, correlates with increased mitogenesis, morphogenesis and motility in cancer cells. These results suggest that branching in response to HGF-SF occurs downstream of HIF activation, consistent with our earlier finding that constitutive expression of mutant HIF-alpha resulted in branching of VHL positive cells. Branching represents yet another established RCC phenotype down-regulated by inhibition of Nox4 activity, further supporting Nox4 as a candidate for molecularly targeted RCC therapy.

**Funding:** NIDDK064887.

---

**Risk of Death Due to Prostate Cancer and Competing Causes Amongst African American Men Choosing Watchful Waiting**

Ashutosh Tewari*, New York, NY; George Divine, Mani Menon, Detroit, MI

**Introduction and Objective:** African Americans (AA) have twice the mortality of White Americans (WA) when diagnosed with prostate cancer. Most previous studies have focused on differences in PSA recurrence and few have studied long term survival and impact of competing medical conditions on this racial disparity. This study was aimed at comparing the 10 year mortality rate due to prostate cancer and competing causes among AA men choosing Watchful Waiting (WW).

**Methods:** This analysis involved data from Prostate Outcomes Consortium (POC) and included 3000 patients with clinically localized prostate cancer. The data-points included vital statistics, serum PSA, TNM Stage, Gleason, co-morbidities, treatment received and demographic data such as age, race and socio-economic status. Survival curves were constructed with the Kaplan-Meier method. All P-values were two-sided. Using Cox Proportional model, we have constructed tables for patients undergoing watchful waiting. **Results:** 10 years % mortality estimates due to prostate cancer and competing risk among healthy men with PSA less than 10 ng/ml

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;60</th>
<th>61-70</th>
<th>&gt;70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCA</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Competing cause</td>
<td>12</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>AA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCA</td>
<td>2</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Competing cause</td>
<td>10</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

**Conclusions:** As can be seen in the table and figure African American men have significant probability of death due to prostate cancer if they choose watchful waiting.
7:50 p.m.

**LAPAROSCOPIC PELVIC LYMPH NODE DISSECTION FOR PROSTATE CANCER: EXTENDED VS. LIMITED DISSECTION AND VALUE OF PARTIN TABLES IN SELECTING PATIENTS FOR LYMPHADENECTOMY**

Karim Touijer, Farhang Rabbani, Javier Romero, Bertrand Guillonneau

**Objectives:** To evaluate the value of the Partin tables’ prediction of lymph node invasion in selecting patients for pelvic lymphadenectomy during radical prostatectomy.

To compare the results of an extended vs. limited pelvic lymphadenectomy (PLND) during radical prostatectomy

**Material and Methods:** A total of 485 patients with clinically localized prostate cancer underwent a laparoscopic radical prostatectomy. In the first 362 patients, a cutoff of 1% on the Partin tables’ predicted probability of lymph node invasion (PPLNI) was used to select patients for a limited PLND (external iliac nodes only). In the following 123 patients, all patients underwent an extended PLND (external iliac, obturator and hypogastric nodes).

Patients were classified into 4 groups: Group I, 185 patients with a PPLNI <1% who underwent LRP without node dissection, Group II, 64 patients with PPLNI < 1%, who underwent LRP with extended node dissection, Group III, 177 patients with PPLNI >1% underwent LRP with limited node dissection and Group IV, 59 patients with PPLNI>1% who underwent LRP with extended node dissection.

We compared Group I and II to assess the value of the Partin tables in selecting low risk patients for nodal metastasis. Logistic regression analysis was performed to compare the node positivity rate between groups III and IV, controlling for preoperative and pathological parameters.

**Results:** None of the patients in group II had a positive lymph node after an extended PLND. On multivariate logistic regression analysis, controlling for preoperative PSA, biopsy Gleason sum, clinical stage, pathological Gleason sum, pathologic stage, and seminal vesicle invasion, the extended PLND independently impacted the rate of positive lymph nodes retrieved with a relative risk (RR) of 21.2 (95% CI 3.4 – 133, p=0.001) vs a limited PLND. Other independent predictors of node positivity were seminal vesicle invasion (RR: 42.6, 95% CI: 3.9 – 462, p=0.002) and clinical stage T3 vs T1c (RR 14.7, 95% CI 1.99 – 109, p=0.008). The median (mean) number of lymph nodes retrieved was 9 (10) and 14 (15) after limited and extended PLND respectively (p=0.001, 95% CI: 2.8-6.4).

**Conclusions:** A lymph node dissection including the external iliac, obturator and hypogastric lymph node groups yields positive nodes more frequently and detects significantly more positive lymph nodes, retrieving a higher total nodal count than the often-performed lymphadenectomy limited to the external iliac nodes.

Forgoing a lymph node dissection in low risk patient may be safe; however, this selective omission of lymphadenectomy in low-risk patients needs to be validated by long-term biochemical recurrence data.

8:00 p.m.

**RISK OF DIABETES MELLITUS IN MEN UNDERGOING ANDROGEN DEPRIVATION THERAPY FOR PROSTATE CANCER**

Ithaar H Derweesh, M.D.,1 Matt C. Kincade, M.D.,1 John Malcolm, M.D.,1 Kimberly D. Lamar, M.D.,1 Anthony L. Patterson, M.D.,1 Abbas E. Kitabchi, M.D., Ph.D.,1 and Robert Wake, M.D.1

From the Departments of Urology,1 Preventive Medicine,2 and Internal Medicine,3 University of Tennessee Health Science Center, Memphis, Tennessee

**Introduction and Objective:** Androgen deprivation therapy (ADT) is the mainstay of treatment for advanced prostate cancer (CaP). Anecdotal reports have raised concerns about the risks of insulin resistance due to male hypogonadism. We investigated the incidence of de novo Diabetes Mellitus (DM) and of worsening glycemic control in established diabetics following induction of ADT for prostate cancer.

**Methods:** We retrospectively reviewed the medical records of 394 patients who underwent ADT (LhRH agonist therapy, combined androgen blockade, or bilateral orchiectomy) for prostate cancer (CaP) at our center between 1/2000 and 7/2005. Variables included age, race, and body mass index (BMI, kg/m²), duration and type of ADT, pre-existing DM, and pre- and post-treatment serum glucose and HbA1c levels. Data were analyzed using Student’s t-test and Logistic Regression.

**Results:** Median age at initiation of treatment was 72 (range 49-94) and mean duration of treatment and follow up was 59 ± 40 months. 58.5% were African American and 41.5% were Caucasian/other. 24.8% had BMI>30 and 75.2% had BMI <30. There was an 11.4% incidence of de novo DM
(dnDM) after ADT initiation. In existing diabetics (n=77), worsening of glycemic control (> 5% increase from baseline for fasting serum glucose and HbA1c) was noted in 34% and 42%, respectively. Mean pre-treatment BMI in patients who developed dnDM was significantly higher than BMI for non-DM patients (dnDM BMI 28.1 ± 5.9 vs. non-DM BMI 25.9 ± 5.9, p=0.04). Pre-treatment BMI in patients with pre-existing DM (29.9 ± 6.7) was also significantly greater than BMI for non-diabetics (p<0.001). Logistic regression analysis demonstrated that BMI >30 (OR 4.647, 95% CI 4.608-4.686, p=0.031) had a significant predictive value for de-Novo diabetes, while Vitamin D supplementation may have a significant protective effect (OR 5.748, 95% CI 5.111-6.385, p=0.017).

**Conclusions:** The overall de novo DM rate for men on ADT for CaP was 11.4%. In established diabetics, induction of ADT led to worsening of HbA1c and blood glucose in 42% and 34%, respectively. BMI >30 was associated with onset of post ADT DM, while Vitamin D supplementation may be protective. While further investigation into these relationships is needed, patients on prolonged ADT for CaP should be followed closely with respect to DM and glycemic control, and appropriate preventive and treatment measures should be undertaken to prevent worsening of glycemic parameters.

**Source of Funding:** None

---

**REDOX REGULATION OF INVASION AND MIGRATION IN BLADDER CANCER**

Badar Mian, MD, James Belarmino, MD, Xiao Fang Ha and J. Andre Melendez, PhD (Presented By: Badar Mian, MD)

**Introduction and Objective:** Reactive oxygen species (ROS) have long been implicated in the process of carcinogenesis. Superoxide dismutases-2 catalyzes the dismutation of O$_2^-$ to H$_2$O$_2$ and H$_2$O, while catalase converts H$_2$O$_2$ to O$_2$ and H$_2$O. It appears that intracellular oxidative stress may play an important role in tumor progression. Increased expression of SOD-2 was noted in metastatic esophageal, gastric and colorectal cancers. The relationship between SOD-2 or Catalase expression and bladder cancer progression, with respect to invasion and migration, has not been reported previously. Our goal was to evaluate the role of intracellular redox status on the invasion and migration of bladder cancer cells.

**Methods:** Poorly tumorigenic bladder cancer cells, 253J, (low SOD-2; high Catalase) and tumorigenic and metastatic cells, UMUC-3, (high SOD-2; low Catalase) were used. We transfected 253J-P cells were transfected to upregulate SOD-2 activity (253J-SOD2) and the UMUC-3 cells were transfected to overexpress Catalase (UMUC-3-Cat). The control, vector control and transfected cells were then plated, in triplicates, at a density of 1.0x10$^5$ cells/well in a Matrigel Invasion Chamber and incubated at 37°C in 5% CO$_2$ for 22 hours. The cells were allowed to degrade and invade through a layer of Matrigel and then migrate through a membrane with 8-micron pores towards a chemoattractant. Using a fluorescent stain (Hoechst 33258 stain), the cells which had migrated to the opposite side of the membrane were counted in five high power fields from each membrane. Zymography was performed to determine the effect of SOD-2 and Catalase on MMP activity.

**Results:** Overexpression of SOD-2 in 253J cells resulted in a significant increase in the expression and activity of MMP-9 and MMP-2. The 253J-SOD2 cells were highly invasive as evident from the significantly increase number of migrating cells when compared to the control cells (214 ± 34 vs. 62± 9, p < 0.005). Conversely, the UMUC-3-Cat cells exhibited a lower level of MMP activity and were significantly less likely to invade and migrate (33 ± 5 vs. 69 ± 17, p < 0.005).

**Conclusion:** Both SOD-2 and Catalase play a role in the expression of MMPs and the invasive phenotype of various bladder cancer cells, possibly through intracellular hydrogen peroxide. The role of hydrogen peroxide as a signal transducer warrants further study.

**Source of Funding:** NE-AUA section, VAMC

**Keywords:** Superoxide dismutase, bladder cancer, invasion

---

**IMPACT OF FLOURESCENT IN SITU HYBRIDIZATION OF RENAL TUMORS AND HISTOPATHOLOGIC DIAGNOSIS**

Jeffrey Bassett, Glenn M. Cannon, Jr., James Catroppo, Rajiv Dhir, Ronald L. Hrebinko, and Michael E. Franks

University of Pittsburgh, Pittsburgh, PA

**Introduction:** Although pathologists can usually diagnose renal masses in a definitive manner, some renal masses are difficult to categorize even with current techniques. Fluorescent in situ hybridization (FISH) is a technique in which DNA probes are labeled with fluorescent molecules that
can be visualized with microscopy to detect chromosomal abnormalities from tumor specimens. We examine the relationship of FISH results to pathologic diagnosis in patients after nephrectomy for renal masses.

**Methods:** The medical records of all patients undergoing radical or partial nephrectomy for renal masses at our institution December 2003 to May 2005 were reviewed. The routine pathologic diagnosis was noted in each case. DNA probes from chromosomes 1, 2, 7, 17 were used for FISH analysis, and were selected based on prior analysis in renal tumor subtypes. The relationship between histopathology and FISH results were recorded with particular attention to cases where FISH findings were inconsistent with pathologic diagnosis.

**Results:** During the 18-month period, 324 nephrectomies were performed. FISH was performed on 79 masses. All patients after December 2004 underwent FISH analysis, and no cases of familial RCC were included. Of these 79 cases, FISH results were inconsistent with the pathologic diagnosis in 16 (20%) in such a way that would potentially alter clinical management. An additional 9 (11%) had the pathologic diagnosis clarified by FISH. Of particular interest was that of 9 patients with the pathologic diagnosis of oncocytoma who underwent FISH analysis, 6 (67%) were reclassified to have chromophobe renal cell carcinoma based on chromosomal changes.

**Conclusion:** FISH analysis has potential utility in the molecular diagnosis of renal tumors after routine histopathological evaluation. Although this needs to be studied in a prospective fashion, the potential impact on decisions regarding adjuvant therapy and reclassification of a benign subtype (oncocytoma) to renal cell carcinoma warrants further evaluation, and may be clinically relevant.

**Funding:** none

---

**PATTERNS OF CARE FOR MEN WITH PROSTATE CANCER FOLLOWING FAILURE OF PRIMARY TREATMENT**

Tracey Krupski, MD, MPH, Christopher Saigal, MD, MPH, Janet Hanley, MS and Mark Litwin, MD, MPH (Presented By: Tracey Krupski, MD, MPH)

**Purpose:** We sought to determine trends in patterns of care following failure of primary prostate cancer treatment and to determine whether nonclinical factors influenced the receipt of secondary treatment.

**Methods:** We identified 65,885 patients treated for nonmetastatic prostate cancer in the years 1991-1999 from the linked databases of Surveillance, Epidemiology, and End Results and Medicare. The outcome of interest was receipt of secondary therapy. We performed logistic regression analysis to investigate a link between the likelihood of receiving secondary treatment after either surgery or radiation and demographic information.

**Results:** Of 65,716 patients who met our inclusion criteria, 10,200 (15%) received some form of secondary therapy. For patients undergoing initial surgical therapy, tumor grade and geographic region were the only factors associated with secondary therapy. For patients undergoing initial radiation therapy, not only were tumor grade and geographic region significant; but also age, year of diagnosis, marital status, and ethnicity were associated with receipt of secondary therapy.

**Conclusion:** Patterns of care following primary prostate cancer radiotherapy vary to a great degree. Despite dissemination of standardized definitions variation by geographic and sociodemographic variables persist for all prostate cancer patients suggesting a need for large scale trials in order to promote evidence-based, high quality care.

---

**THE NATURAL HISTORY OF RESIDUAL AND RECURRENT DISEASE FOLLOWING RENALABLATIVE THERAPY: A MULTICENTRAL STUDY**

Surena F. Matin, Kamran Ahrar (University of Texas M. D. Anderson Cancer Center, Houston, TX); Jeffrey A. Cadeddu (University of Texas Southwestern Medical Center, Dallas, TX); Debra A. Gervais, Francis J. McGovern (Massachusetts General Hospital, Boston, MA); Ronald J. Zagoria (Wake Forest University Baptist Medical Center, Winston-Salem, NC); Robert G. Uzzo (Fox Chase Cancer Center, Philadelphia, PA); John Haaga, Martin I. Resnick (Case Western Reserve University, Cleveland, OH); Jihad Kaouk, and Inderbir S. Gill (The Cleveland Clinic Foundation, Cleveland, OH)

**Introduction:** There are no standard guidelines for determining how or when follow-up abdominal imaging should be performed after renal energy ablative therapy. The purpose of this study was to examine the natural history of residual and recurrent disease after radiofrequency
Ablation (RFA) or cryoablation of a renal mass and, using this information, to determine reasonable minimum recommendations for when to perform surveillance imaging in the first year after treatment.

**Methods:** We reviewed treatment and follow-up information of patients who underwent RFA or cryoablation as treatment for a renal mass at 7 institutions. These cases were monitored using a variety of surveillance schedules.

**Results:** A total of 63 out of 616 patients were found to have residual or recurrent disease after primary RFA or cryoablation, or a median of 8.7% over 7 institutions. Most incomplete treatments (69.8%) were detected within the first 3 months. After salvage ablative therapy was rendered, only 4.2% had failed therapy. At a mean follow-up duration of 24.2 months, patients with residual or recurrent disease had an overall survival rate of 82.5%, and a 2-year cancer-specific survival rate of 97.4% for those with localized, unilateral renal tumors.

**Conclusions:** In most cases, initial-treatment failure was detected within the first 3 months post-treatment. Our findings support a minimum of 3 imaging studies in the first year after ablative therapy, at month 1, month 3 or 6, and month 12.

---

**2:40 p.m.**

**PERIOPERATIVE QUALITY CARE INDICATORS OF RETROPUBIC, LAPAROSCOPIC, AND ROBOTIC PROSTATECTOMY: RESULTS FROM A NATIONAL, MULTI-CENTER, PROSPECTIVE COHORT**


Harvard Medical School (JCH, DD, MGS), University of Michigan (DW, BKH, JEM, JTW), Washington University (ASK, GA), UCLA (CSS, MSL), MD Anderson Cancer Center (LP) Cleveland Clinic (EK)

**Background:** Individual case series have reported outcomes of retropubic (RRP), laparoscopic (LRP), or robotic-assisted prostatectomies (RAP). However, prospective, multi-center comparisons using clinical trials methods to evaluate concurrently conducted RRP, LRP and RAP are lacking.

**Methods:** The PROST-QA Consortium is an NIH-funded, prospective study of 1,074 men enrolled prior to treatment for early stage prostate cancer at 8 high volume centers from 3/03 to 10/05. Clinical report forms were used to collect patient demographics, cancer severity, complications, histopathologic features, and clinical outcomes with > 95% subjects having follow-up. This analysis evaluates effects of surgical technique on perioperative quality care indicators such as operative blood loss (EBL), operative time (ORT), transfusion, infection, thromboembolic events, lengths of stay (LOS), urinary retention, and surgical margin status.

**Results:** Analysis was based on intent-to-treat. 517 patients participating in the study planned radical prostatectomy; via traditional RRP in 71% and via laparoscopy in 29%. Among laparoscopic cases, 43% underwent standard LRP while 57% underwent RAP. There were no differences in age, body mass index, or prostate size between prostatectomy techniques. Pretreatment PSA was highest for RRP (mean RRP 7.1, RAP 6.7, LRP 5.9; p<0.01), while RAP had the lowest Gleason scores (p=0.04). Racial differences in prostatectomy utilization were evident (white subjects comprising 93% RP vs. 97% LRP vs. 84% of RAP; p=0.02). EBL was higher for RRP vs. LRP vs RAP (median EBL RRP 700, LRP 350, RAP 150 mL; p <0.01), while ORT was lower for RRP vs. LRP or RAP (mean ORT RRP 198, LRP 227, RAP 219 minutes; p<0.01). Differences were also evident in LOS (mean RRP 2.0, LRP 1.8, RAP 1.3 days; p<0.01). The table shows perioperative complication and positive margin rates. Heterologous transfusion rates were higher for RRP versus the two lap groups combined (p=0.01) whereas no differences were detected among the other care quality indicators:

<table>
<thead>
<tr>
<th>Event occurrence (%)</th>
<th>RRP</th>
<th>LRP</th>
<th>RAP</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterologous Transfusion</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0.07</td>
</tr>
<tr>
<td>Wound or UTI</td>
<td>11</td>
<td>8</td>
<td>9</td>
<td>0.88</td>
</tr>
<tr>
<td>Thromboembolic event</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>0.77</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>10</td>
<td>8</td>
<td>15</td>
<td>0.52</td>
</tr>
<tr>
<td>Unplanned admit or ER visit</td>
<td>4</td>
<td>10</td>
<td>2</td>
<td>0.14</td>
</tr>
<tr>
<td>Positive surgical margin</td>
<td>18</td>
<td>20</td>
<td>26</td>
<td>0.28</td>
</tr>
</tbody>
</table>

**Conclusion:** Selection bias complicates comparison between RP techniques, even among a concurrent, prospective cohort with uniform entry criteria. ORT was shortest for RRP while RRP had higher EBL, transfusion rates, and LOS. However, practitioner preferences may affect LOS, and sample power was limited in evaluating low frequency events. Modest differences in EBL and LOS between LRP and RAP were statistically significant but of uncertain clinical impact.

Continues on next page
Introduction and Objective: New susceptibility genes are needed for prostate cancer to improve methods for prostate cancer detection. High throughput DNA microarray methods that examine for single nucleotide polymorphisms (SNPs) across the whole-genome have been used to identify new genes for many diseases. We conducted a genome-wide association study for new gene discovery for prostate cancer among 40 cases and 40 controls and then genotyped positive SNPs from this analysis among 2169 men who underwent a prostate biopsy.

Methods: We conducted a case-control study and used the 10,000 (10K) Affymetrix GeneChip to examine for SNPs across the genome. Cases were 40 patients diagnosed with high grade cancer (Gleason score 8 or more), PSA <10 ng/mL, cT1c, and of Caucasian background. Controls were 40 patients with no evidence of prostate cancer by biopsy, matched by PSA, DRE and ethnicity. We then genotyped positive SNPs found by the 10K GeneChip among 2169 men who underwent a prostate biopsy for an abnormal PSA to determine the odds ratio for prostate cancer detection.

Results: Among the 40 cases and 40 controls, we found 237 SNPs across the genome to be positively associated with prostate cancer using the Affymetrix GeneChip. The p-values for these SNPs associated with prostate cancer ranged from p=0.05 to p=0.00001. Using the NCBI builds to correlate these SNPs to the described genome, we selected 16 SNPs to genotype 2169 men who underwent a prostate biopsy for prostate cancer. Among the 2169 men who underwent one or prostate biopsies, 1073 (49.5%) were diagnosed with cancer. Among the 16 SNPs, we found one SNP, rs552895, to be strongly associated with increased prostate cancer risk. This SNP is a Cytosine for Guanine polymorphism and we found that 56.4% of cases had the variant homozygous genotype compared to 44.5% in the controls (p=0.0003, chi-square=15.9). The adjusted odds ratio for prostate cancer for patients with the CC genotype and the CG genotype compared to the GG genotype was 1.67 (95% C.I.: 1.3 - 2.1, p<0.0001) and 1.31 (95% C.I.: 1.1 - 1.6, p=0.006), respectively. This SNP maps to chromosome 9p22.3 (Build 88, NCBI).

Conclusions: Genome-wide association studies for prostate cancer are feasible using high throughput DNA microarray chips. These SNPs found to be associated with prostate cancer can provide important information for susceptibility genes for prostate cancer and could have important clinical applications. Future studies will be required with more powerful GeneChips.