The Andrew C. Novick Lecture:

Tribute to a Mentor

Robert G. Uzzo, M.D.

Willing G. Pepper Chairman of Surgery
Fox Chase Cancer Center
Temple University School of Medicine
Chair, Department of Urology
Urological Institute at Einstein Healthcare Network
Philadelphia, PA USA
Why do students choose urology?

1. Family role model
2. Personal Experience
3. People you meet along the way
Finding my way to Urology
How can I be like him?
Three Mentors

How can I be like him?
Three Mentors

Here is what Andy is best known for

- Renovascular surgery
- Renal Transplantation
- Management of RCC
  - Partial Nephrectomy
  - Renal Preservation techniques
Three Mentors

- Clinical /Technical Excellent
- Emphasis on Process
- Advancing the field through research
- Vision and Leadership - Institute model
- Pay it forward (training promising new professionals)

“How helping patients, doing research,
  defining the state-of-the-art,
  molding young minds, training
  promising new professionals...
  that’s the formula for success.”

~ Dr. Andrew C. Novick
Clinical and Technical Excellence

1985
- 7 Urologists
- No labs

2008
- 74 Urologists
- 8 urology labs
- $130 million Institute
- 591 peer reviewed papers
- 104 book chapters
- >150 trainees
- only individual to serve as
  - President ABU
  - Chairman Exam Committee
  - Chairman of the Urology RRC
Clinical and Technical Excellence

Bench nephron sparing surgery → Open NSS → MIS NSS

- The difference is in the details
- “Step toward the table”
• Brought Andy great distinction and acclaim

• He treated every operative case with the same attention to detail with an intent to cure
Emphasis on Process and Performance
The Evolution of Integrated Medical Systems

"A patient is the most important person in this institution. A patient is not dependent on us — we are dependent on him. A patient is not an interruption of our work — he is the purpose of it. A patient is not an outsider to our business — he is part of it. A patient is a person and not a statistic. It is our job to satisfy him."

- Dr. William E. Lawee
The Clinic’s Department of Urology is consistently rated one of the top two in the United States
You can’t manage what you don’t measure
Advancing the Field through Research
Basic Science with Novick, Bukowski and Finke
Combined Classical Cytogenetics and Microarray-Based Genomic Copy Number Analysis Reveal Frequent 3;5 Rearrangements in Clear Cell Renal Cell Carcinoma


Identification of Novel Target Genes by an Epigenetic Reactivation Screen of Renal Cancer


A global profile of gene promoter methylation in treatment-naive urothelial cancer


Promoter Hypermethylation of Tumor Suppressor Genes in Urine from Kidney Cancer Patients


Elevated Expression of Stromal Palladin Predicts Poor Clinical Outcome in Renal Cell Carcinoma


Lymphopenia is an Independent Predictor of Inferior Outcome in Clear Cell Renal Carcinoma


Detection of Bladder Cancer in a Tumor Suppressor Gene Hypermethylation Panel


The genetics of renal oncogenetics: a possible model for neoplastic progression

Vision and Leadership to “Mold Young Minds”

“It behooves all urologists to be actively aware of the confusions, inconsistencies, and inadequacies existing at the present time in the education and standardization of urological specialists.”

~ Dr. Charles C. Higgins
Andy’s Disciples

Teach, inspire, contribute
Putting it Together

Finding my way
June 2001 Case A:  
Fellowship + 11mo

- 62 yo male with complicated history of Crohns
- Incidental 1.5 cm right enhancing mass noted
- PMHx: Stable angina, COPD, CVA, HTN, IBD
- PSHx: Appy, perirectal abscess
- SHx: 1ppd
- Meds: Prednisone, flagyl, metoprolol, Asacol, hydralazine, clonidine, Cartia, famotidine
- PE: 145 lbs, 134/86, PS 1-2
- Labs: Sr 1.3 mg/dl
Enhancing 1.5cm mass.....kidneys otherwise clear
July 2001 Case Z:  
Fellowship + 12 mo

- **77 yo male** with incidental enhancing right renal mass (2.0 cm)
- **PMHx:** HTN (RAS), chol, CAD, NIDDM, CRI
- **PSHx:** CABG then stents, TURP
- **FHx:** negative
- **PE:** 180 lbs, 140/92, PS=0
- **Labs:** Scr = 1.9 mg/dl GFR 45cc/min
- **MAG-3 scan notes** 58% right 42% left split fx
77 yo male with incidental enhancing right renal mass (2.5 cm)

Performance status = 0
Case A

- CT 6/01 – 1.5 cm enhancing lesion
- November 01 – CVA and aspiration, recovered
- CT 1/02 – 1.5 cm solid renal mass unchanged
- CT 6/02 – 1.5 cm solid renal mass unchanged
- CT 12/02 – 1.5 cm mass unchanged
- CT 7/03 – 1.5 cm mass unchanged
- CT 2/04 – 1.5 cm mass unchanged
- CT 5/05 – 1.5 cm mass unchanged
- CXR and further extent of disease negative

• Expired 2007 of other causes
July 2001 Case Z: Fellowship + 12 mo

- CT 7/01 – 2.0 cm enhancing lesion with simple cysts
- CT 9/01 – 2.0 cm and unchanged
- US 12/01 – 2.2 cm solid renal mass
- US 4/02 – 1.8 cm solid renal mass
- CT 7/02 – 2.5 cm mass
- CT 12/02 – 2.6 cm mass

- Inexperienced doctor with new toys = pretty worried
- Inexperienced family = very worried
Dec 2002:

Fellowship + 30 mo

- 79 yo CAD (s/p CABG and stents) – cleared
- 2h 30min lap partial, min EBL, NSM = SUCCESS!!
- When closing skin = arrested = immediate to cath lab

Died in cath lab secondary to acute stent occlusion
Plus–minus (+/−, plus/minus) is a sports statistic used to measure a player's impact on the difference between their team's total scoring versus their opponent's.

The statistic is directly affected by overall team performance, influenced by both the offensive and defensive performance of the team as a whole.

- Wiki /plus-minus
Active Surveillance = +1
Active Treatment = -1
<table>
<thead>
<tr>
<th></th>
<th>Good</th>
<th>Bad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>+1 Dr and patient claim the “win”</td>
<td>-1</td>
</tr>
<tr>
<td>Bad</td>
<td>-1</td>
<td>-1 Dr blames the disease, patient feels the “loss”</td>
</tr>
</tbody>
</table>
SEER: Latent class analysis with Principal Stratification and propensity score matching

Latent Class Approach

<table>
<thead>
<tr>
<th>Description of Class of Patients</th>
<th>Percent of Population in Class</th>
<th>Life Expectancy Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery helps, but relatively poor outcomes overall</td>
<td>4.2%</td>
<td>+4.1 years</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Surgery highly beneficial</td>
<td>11.5%</td>
<td>+8.8 years</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Surgery is Harmful</td>
<td>13.7%</td>
<td>-2.1 years</td>
<td>p=0.004</td>
</tr>
<tr>
<td>Surgery helps, but relatively better outcomes overall</td>
<td>70.6%</td>
<td>+3.6 years</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

Egleston, Wong and Uzzo, JASA (in press)
My Risk Model

- Tumor Risk (Inherent Biology)
- Physician Risk (Skill Set)
- Pt Risk (Co-morbidity)
- Hospital Risk (Process)

Understand/Manage Variability
Observations on the Growth of Renal Neoplasms

Bernard A. Birnbaum, MD • Morton A. Bosniak, MD • Alec J. Megibow, MD • Edward Lubat, MD • Richard B. Gordon, MD

Radiology 1990; 176:695–701

Abstract

A retrospective review of the imaging results of 11 patients with 13 solid renal parenchymal neoplasms was performed, allowing analysis of the linear growth rates of these tumors. The study sample included seven pathologically proved renal adenocarcinomas and six lesions that were indicative of a neoplasm radiologically (enhancing parenchymal mass on computed tomographic [CT] scans with documented interval growth), which were followed up for 2-7.8 years. Variable interval tumor growth was demonstrated in every case except one and ranged from 0 to 1.6 cm/yr, with an overall mean linear growth rate of approximately 0.5 cm/yr. Ten of 11 “small renal neoplasms” (less than or equal to 3.0 cm in diameter) displayed interval growth, with five ultimately measuring greater than 3.0 cm (size range, 3.5-7.0 cm). While the results are preliminary and reflect observations on a very small study sample, it was noted that five of the seven pathologically proved adenocarcinomas appeared homogeneous and well margined, and all were low-grade, low-stage carcinomas. These grew more slowly and were generally smaller at initial presentation than higher-grade lesions, which demonstrated a more heterogeneous appearance on CT scans.

N = 11 patients
So my score was 0

What next?

Observation of Small Incidentally Detected Renal Masses
Morton A. Bosniak, MD

Growth Rate and Behavior of Small Renal Neoplasms

In a series of 43 small renal tumors (in 40 patients) that were less than 3.0 cm in size when initially seen and were followed-up for at least two years (2 to 8 years; mean 3.5 years), none developed metastasis while being followed-up. Also, metastasis...
$N = 286$

$0.25 - 0.45 \text{ cm/y}$
Active Surveillance of Incidental Renal Mass

Enhancing Renal Masses With Zero Net Growth During Active Surveillance
David A. Kunkle, Paul L. Crispen, David Y. T. Chen, Richard E. Greenberg and Robert G. Uzzo* From the Department of Urologic Oncology, Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, Pennsylvania

Excise, Ablate or Observe: The Small Renal Mass Dilemma—A Meta-Analysis and Review
David A. Kunkle, Brian L. Egleston and Robert G. Uzzo* From the Departments of Urologic Oncology and Nephrology, Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, Pennsylvania.

Tumor Size Predicts Synchronous Metastatic Renal Cell Carcinoma: Implications for Surveillance of Small Renal Masses
David A. Kunkle,* Paul L. Crispen,* Tianyu Li* and Robert G. Uzzo* From the Departments of Urologic Oncology and Nephrology, Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, Pennsylvania.

Competing Risks of Death in Patients with Localized Renal Cell Carcinoma: A Comorbidity Based Model
Alexander Kutikov,* Brian L. Egleston,* Daniel Canter, Marc C. Smaldone, Yu-Ning Wong and Robert G. Uzzo*.

Natural History, Growth Kinetics, and Outcomes of Untreated Clinically Localized Renal Tumors Under Active Surveillance
Paul L. Crispen, MD; Rosalia Viterbo, MD; Stephen A. Boorjian, MD; Richard E. Greenberg, MD; David Y-T. Chen, MD; and Robert G. Uzzo, MD.

Evaluating Overall Survival and Competing Risks of Death in Patients With Localized Renal Cell Carcinoma Using a Comprehensive Nomogram
Alexander Kutikov, Brian L. Egleston, Yu-Ning Wong, and Robert G. Uzzo

Is anatomic complexity associated with renal tumor growth kinetics under active surveillance?

Delayed Intervention of Sporadic Renal Masses Undergoing Active Surveillance
Paul L. Crispen, MD; Rosalia Viterbo, MD; Eric B. Fox; Richard E. Greenberg, MD; David Y. T. Chen, MD; and Robert G. Uzzo, MD.
I thought you would enjoy the attached article I found while recently taking an on-line course RNtoBSN at Ohio University. There are two especially interesting items here. I enjoyed the quote for the refrain of the Irish folk song which goes (bottom of page 196), “The older you are the sooner you’ll bloody well die”. This idea of course shown not to be true. Also the discussion of the Bertrand’s Box Paradox, (Left middle of page 196) ((also known as the Monte Hall Problem)). See http://en.wikipedia.org/wiki/Monty_Hall_problem. Now, I’ve taken semester courses in Statistics and in Probability and I have a difficult time accepting what is the consensus.

Thanks so much for the care and the guidance you have given us regarding Mom’s kidney cancer. And thank you for the book and the advice about the wait and see approach as it so proved to be our best choice.
Argument for initial AS in low risk tumors...

The More you know....

The Monty Hall or Three Prisoners Problem or the older Bertrand’s box paradox

Bayes Theorem or Rule

...the better you choose
What would my Mentors Do?

Tried to contribute in additional ways:

1. Nephrometry
2. Objectifying Risk
3. Process and Safety
4. Adjuvant therapy
5. Clinical trials
6. Education

"It behooves all urologists to be actively aware of the confusions, inconsistencies, and inadequacies existing at the present time in the education and standardization of urological specialists."

~ Dr. Charles C. Higgins

"A patient is the most important person in this institution. A patient is not dependent on us — we are dependent on him. A patient is not an interruption of our work — he is the purpose of it. A patient is not an outsider to our business — he is part of it. A patient is a person and not a statistic. It is our job to satisfy him."

~ Dr. William E. Lowes
Who I am

Three mentors

What I am

We are, each of us, a multitude
- Within us is a little universe

What I do
Thanks to the entire GU Team at Fox Chase

• Colleagues:
  - Alex Kutikov
  - Mark Smaldone
  - Betsy Plimack
  - Richard Greenberg
  - David Chen
  - Lia Viterbo
  - Dan Geynisman
  - Matt Zibelman
  - Ning Wong
  - Eric Ross
  - Brian Egleston
  - James Helstrom
  - Richard Fisher
  - Eric Horwitz

• Nurses/PAs:
  - Sue Burke
  - Lisa Hicks
  - Jill Schreiber
  - Mike McCurry
  - Marcel Knotek
  - Lois Malizzia
  - Fellows and Residents

• Administrators:
  - Shelly Smith
  - Pat O’Brian
  - Beth Bromberg
  - Lisa Erickson
  - Karen Comsa

• Lab Scientists:
  - Vlad Kolenko
  - Paul Cairns
  - Joe Testa
  - Al Knudsen
  - John Chernoff
  - Eti Cukierman
  - Erica Golemis

• Data Managers:
  - Deb Kister
  - Michelle Collins

• Many others:
  - Wafik El-Diery
  - Al Bellacosa
  - Tahseen Al-Saleem
  - Essel Al-Saleem

• Many others