SMALL RENAL MASSES: THE ROLE OF BIOPSY AND ACTIVE SURVEILLANCE

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DEPARTMENT OF UROLOGY
MEDICAL UNIVERSITY OF VIENNA
MALE, 76 YRS
ASYMPTOMATIC

2.4cm
OPEN PARTIAL NEPHRECTOMY FOR RCC
SURVIVAL vs. TU DIAMETER

Ca. specific survival %

- ≤ 4 cm 310 PATS.
- > 4 cm 175 PATS.

HAFEZ, J.UROL. 162:1930, 1999
ARE SMALL RENAL TUMORS HARMLESS ?
DIAMETER OF SOLID RENAL MASSES IN 688 KIDNEYS TREATED 1993 - 2003

PEARSON p=0.04

REMZI J.UROL.176:896,2005
CAN BENIGN TUMORS BE IDENTIFIED BY IMAGING?
76 OF 614 TUMORS REMOVED WERE HISTOLOGICALLY BENIGN

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Oncocytoma</td>
<td>47%</td>
</tr>
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<td>37%</td>
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REMZI, BJU Int. 99:1002, 2007
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**Review of Preop CT***

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<th>Classification</th>
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<tr>
<td>Benign Tu.</td>
<td>17%</td>
</tr>
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<td>Indeterminate</td>
<td>58%</td>
</tr>
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<td>Malignant</td>
<td>25%</td>
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*2 Blinded Radiologists

Remzi, BJU Int. 99:1002, 2007
WITH BIOMARKERS ?
TOTAL CELL - FREE DNA

BENIGN
43 PATS.

RCC
157 PATS.

p < 0.001

De MARTINO, CANCER, Epub 2011
METHYLATED CELL-FREE DNA

- VHL: RCC 50%, BENIGN 9%
- RASSF1A: RCC 41%, BENIGN 7%

p < 0.001
DIAMETER OF SOLID RENAL MASSES IN 688 KIDNEYS TREATED 1993 - 2003

79% RCC T1a

PEARSON p=0.04

REMZI J. UROL. 176:896, 2005
ARE SMALL RENAL CELL CANCERS LESS AGGRESSIVE?
## SMALL (T1A) RCC REMOVED SURGICALLY

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<td>&lt; 2 cm</td>
<td>65</td>
<td>4%</td>
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<td>2.1 – 2.9 cm</td>
<td>103</td>
<td>5%</td>
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> 3 cm SIGN. MORE AGGRESSIVE!
IN 24 PATIENTS WITH TU. MED. Ø 3.3cm ONLY 5 GREW WITH 31.6 MOS. MEAN FOLLOW-UP WITHOUT TU. GROWTH RISK OF METASTASES LIMITED

KASSOUF, J. UROL. 171:111, 2004
## ERROR IN CT MEASUREMENT OF SMALL RENAL TUMORS

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<tr>
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<th>INTER READER</th>
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<td>x (mm)</td>
<td>± 2.3</td>
<td>± 3.1</td>
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<td>y (mm)</td>
<td>± 2.5</td>
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<td>z (mm)</td>
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29 T.U.S, 5mm COLLIMATION, 2.5mm INTERVAL

PINNEN, J. UROL. 176:2386, 2006
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<tr>
<td>Vol (mm³)</td>
<td>± 2.075</td>
<td>± 2.515</td>
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29 T.U.S, 5mm COLLIMATION, 2.5mm INTERVAL

PINNEN, J. UROL. 176:2386, 2006
106 SMR UNDER SURVEILLANCE

- NO DEFINABLE CHARACTERISTICS TO PREDICT GROWTH

- SIMILAR MALIGNANCY RATES BETWEEN GROWING AND NOT GROWING SMR

KUNKLE, J. UROL. 177:849, 2007
THE SOBERING FACTS

- T1A RENAL TUMORS INCREASING, ESPECIALLY IN ELDERLY, MULTIMORBID PATIENTS
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- T1A RENAL TUMORS INCREASING, ESPECIALLY IN ELDERLY, MULTIMORBID PATIENTS

- ~20% BENIGN, IMAGING UNRELIABLE, BIOMARKERS PROMISING, NOT THERE YET
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- ~80% RCC, BUT ONLY ~1/5 AGGRESSIVE
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- ~20% BENIGN, IMAGING UNRELIABLE, BIOMARKERS PROMISING, NOT THERE YET

- ~80% RCC, BUT ONLY ~1/5 AGGRESSIVE

- NO CORRELATION BETWEEN GROWTH PATTERN, MALIGNANCY AND AGGRESSIVE POTENTIAL
IDEAL WOULD BE A BIOMARKER FOR
MALIGNANT vs. BENIGN
AGGRESSIVE vs. NON-AGGRESSIVE

...BUT WE ARE NOT THERE YET
RCC: TOTAL CELL-FREE DNA vs. DISEASE SPECIFIC SURVIVAL

*CUT-OFF: 2400 GE/ml

HR 15.03
95% CI 3.52 - 64.21

P < .001

De MARTINO, CANCER, Epub 2011
THE SOLUTION FOR NOW:
PERCUTANEOUS BIOPSY WHENEVER IT HAS THERAPEUTIC CONSEQUENCES
PRONE
LOCAL ANESTH.
CT-FLUOROSCOPY
17G SHEATH ON TUMOR
18G CORE Bx AND FINE NEEDLE ASPIRATION Bx TROUGH SHEATH
## RENAL CORE BIOPSIES

### FROZEN SECTION AS COMPARED TO DEFINITIVE HISTOLOGY

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<tr>
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<td>Non-Diagnostic</td>
<td>17%</td>
</tr>
<tr>
<td>Diagnostic Accuracy</td>
<td>75%</td>
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DECHET, J. UROL. 162:1282, 1999
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**PROSPECTIVE CT GUIDED BIOPSY OF SMALL RENAL MASSES → SURGERY**

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<td><strong>4%</strong>&lt;sup&gt;*&lt;/sup&gt;</td>
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*1 PERIPHERAL PNEUMOTHORAX, 4 MINOR HEMATOMAS

SCHMIDBAUER, EUR UROL 53: 1003, 2008
PROSPECTIVE CT GUIDED BIOPSY OF SMALL RENAL MASSES → SURGERY

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ACCURACY IN DEFINING
- MALIGNANCY

92%  97%

*1 PERIPHERAL PNEUMOTHORAX, 4 MINOR HEMATOMAS

SCHMIDBAUER, EUR UROL 53: 1003, 2008
Ø 3.7cm
CHROMOPHOBEBE DIFFERENTIATION
CK7 POSITIVE

ONCOCYTOMA
CK7 NEGATIVE
## PROSPECTIVE CT GUIDED BIOPSY OF SMALL RENAL MASSES → SURGERY

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<tr>
<td>- MALIGNANCY</td>
<td>92%</td>
<td>97%</td>
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<tr>
<td>- RCC SUBTYPE</td>
<td>86%</td>
<td>92%</td>
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<td>- RC GR 1/2 vs. 3/4</td>
<td>28%</td>
<td>74%</td>
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*1 PERIPHERAL PNEUMOTHORAX, 4 MINOR HEMATOMAS

SCHMIDBAUER, EUR UROL 53: 1003, 2008
Bx  CLEAR CELL RCC G2
PARTIAL NEPHRECTOMY: CLEAR CELL RCC WITH FOCI OF G3
RT Bx: CLEAR CELL RCC G2
HE 100x
LT TUMOR PARTIAL NEPHRECTOMY
PURE ONCOCYTOMA
HE 40x
RT TUMOR PART. N´ECTOMY
CLEAR CELL RCC G2
HE 200x
HAVING A SPECIFIC Bx PROVEN TUMOR DOES NOT RULE OUT TUMORS OF OTHER HISTOLOGY ELSEWHERE
CT GUIDED NEEDLE BIOPSY CORRECTLY IDENTIFIES:

- BENIGN TUMOR WITH 100% SENSITIVITY AND 95% SPECIFICITY
- RCC WITH 93.5% SENSITIVITY AND 100% SPECIFICITY
- RCC SUBTYPE AND GRADE WITH 91% AND 76% RSP DIAGNOSTIC ACCURACY
DO SMALL RENAL CELL CANCERS REALLY HAVE TO BE TREATED AGGRESSIVELY?
**MORTALITY OF RENAL TUMORS < 4cm***

*SEER, AGE, DIAMETER, TX YEAR CORRECTED

ZINI, BJU Int. 2009; 03:899
MORTALITY OF RENAL TUMORS < 4cm*

CA. SPEC.

8% DIFF. AFTER 5YRS.

NO SURGICAL THERAPY

N´ECTOMY

*SEER, AGE, DIAMETER, TX YEAR CORRECTED

ZINI, BJU Int. 2009; 03:899
MORTALITY OF RENAL TUMORS < 4cm*

*SEER, AGE, DIAMETER, TX YEAR CORRECTED

ZINI, BJU Int. 2009; 03:899
OA MORTALITY : RENAL TUMORS < 4cm*

*SEER, AGE, DIAMETER, TX YEAR CORRECTED

ZINI, BJU Int. 2009; 03:899
FOR SMALL RENAL MASSES < 4 cm (SMRS) DETECTED INCIDENTALLY

"ACTIVE SURVEILLANCE IS A REASONABLE OPTION FOR PATIENTS WITH LIMITED LIFE EXPECTANCY OR FOR THOSE WHO ARE UNFIT FOR AN INTERVENTION . . ."

AUA GUIDELINES FOR MANAGING STAGE I RENAL MASS, 2009

www.auanet.org/content/guidelines/renalmass09.pdf
"ACTIVE SURVEILLANCE"
THE PROSPECTIVE TORONTO TRIAL

151 RENAL MASSES < 4cm
MEAN FOLLOW-UP 28 MOS

JEWETT, EUR UROL 60:39, 2011
"ACTIVE SURVEILLANCE"
THE PROSPECTIVE TORONTO TRIAL

151 RENAL MASSES < 4cm
MEAN FOLLOW-UP 28 MOS

16% LOCAL PROGRESSION, 1.3% M2

JEWETT, EUR UROL 60:39, 2011
IS THIS A POTENTIALLY AGGRESSIVE TUMOR (IN VIEW OF A LIMITED LIFE EXPECTANCY)?
IS THIS A POTENTIALLY AGGRESSIVE TUMOR (IN VIEW OF A LIMITED LIFE EXPECTANCY) ?

INDIVIDUAL RISK ASSESSMENT ?
• **IS THIS A POTENTIALLY AGGRESSIVE TUMOR (IN VIEW OF A LIMITED LIFE EXPECTANCY) ?**

• **INDIVIDUAL RISK ASSESSMENT ?**

• **IF LOW RISK RCC, HOW IS PATIENT FOLLOWED – UP WITH ACT. SURVEILLANCE?**
• IS THIS A POTENTIALLY AGGRESSIVE TUMOR 
  (IN VIEW OF A LIMITED LIFE EXPECTANCY ) ?

• INDIVIDUAL RISK ASSESSMENT ?

• IF LOW RISK RCC, HOW IS PATIENT 
  FOLLOWED – UP WITH ACT. SURVEILLANCE? 
  - SEQUENTIAL CT / MRI / US ? 
  - EVERY 6 , 12 , 18 MONTHS … ?
IS THIS A POTENTIALLY AGGRESSIVE TUMOR (IN VIEW OF A LIMITED LIFE EXPECTANCY) ?

INDIVIDUAL RISK ASSESSMENT ?

IF LOW RISK RCC, HOW IS PATIENT FOLLOWED – UP ?

(COST-BENEFIT RATIO COMPARED TO STANDARD THERAPY ?)
A VERY THEORETICAL MODEL:
COST EFFECTIVENESS OF SRM MANAGEMENT
BASED ON PATIENT AGE* AND TUMOR SIZE

CALCULATED FOR AGE 65, US$ 50,000.- COST THRESHOLD,
MARKOV MODEL ESTIMATE

CHANG, J. UROL. 185:1591, 2011
IS THERE A PLACE FOR "ACTIVE SURVEILLANCE"?
IS THERE A PLACE FOR "ACTIVE SURVEILLANCE"?

YES, BUT LIMITED TO

- BIOPSY PROVEN BENIGN TUMORS < 4cm IN DIAMETER
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YES, BUT LIMITED TO

- BIOPSY PROVEN BENIGN TUMORS < 4cm IN DIAMETER
- BIOPSY PROVEN LOW GRADE RCC < 3 cm IN PATIENTS AT HIGH SURGICAL RISK (CCM > 2)
IS THERE A PLACE FOR "ACTIVE SURVEILLANCE"?

YES, BUT LIMITED TO

- BIOPSY PROVEN BENIGN TUMORS < 4cm IN DIAMETER
- BIOPSY PROVEN LOW GRADE RCC < 3 cm IN PATIENTS AT HIGH SURGICAL RISK (CCM > 2)

MANY REMAINING UNCLEAR ISSUES