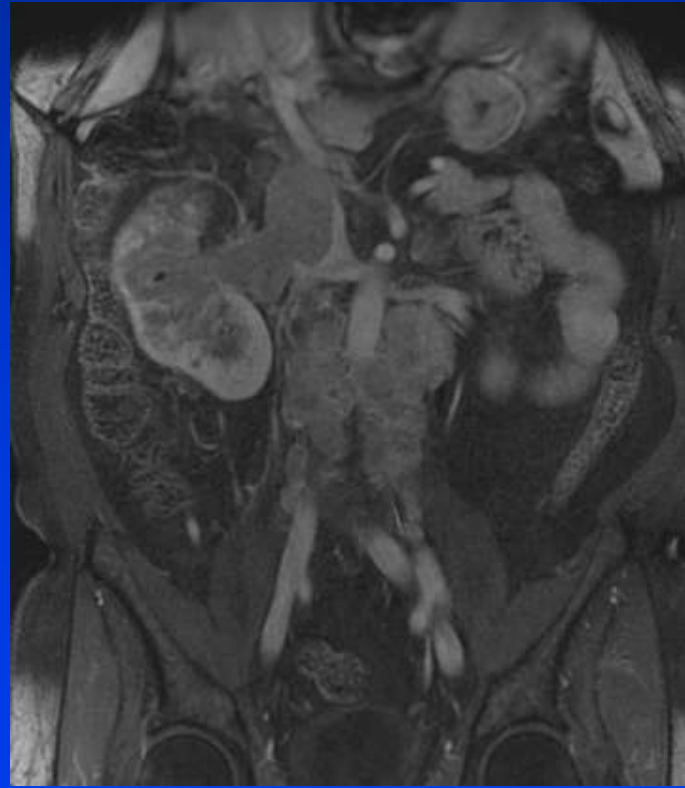
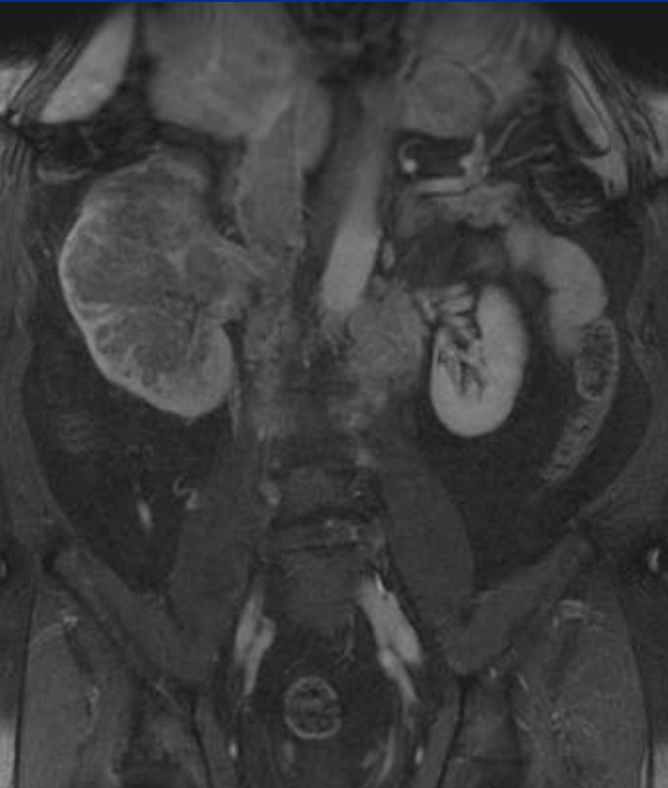


Lymphadenectomy and Metastasectomy in RCC

When I do and when I don't

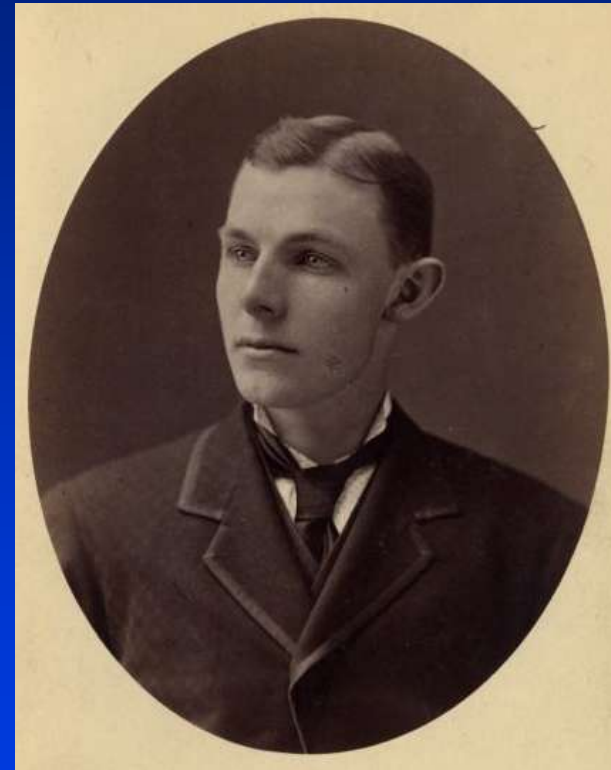
Bradley C. Leibovich, MD, FACS
Professor of Urology
Chairman, Department of Urology
Mayo Clinic, Rochester, MN



Concept of a Regional LND in Surgical Management of Malignancy

Introduced in the American literature by Halstead in 1886

Noted better survival in locally advanced breast cancer when treated with mastectomy and regional LND



LND in Urologic Malignancy

Known benefit to LND in:

Testis Cancer

Bladder Cancer

Upper Tract Urothelial Cancer

+/- Prostate Cancer

Benefit in RCC?

Staging accuracy

CT false negative 4%, false positive 58%

Studer, J Urol 1990

Therapeutic benefit?

Removal of overt or micrometastatic disease

**Removal of immunosuppressive antigen primed
nodes**

Nodal Involvement in RCC

	Total N	N+ (%)
Robson, 1967	88	20 (23%)
Giuliani, 1990	200	50 (25%)
Blom, 2009	336	11 (3.3%)
UCLA, 2003	960	43 (3.3%)
<u>Mayo, 2003</u>	<u>1965</u>	<u>107 (5.5%)</u>
Johnson/Helly (autopsy)	554	80 (14%)

Nodal involvement without hematogeneous mets is rare ~3-10%

Blute, J Urol 2004; Giuliani, J Urol 1990

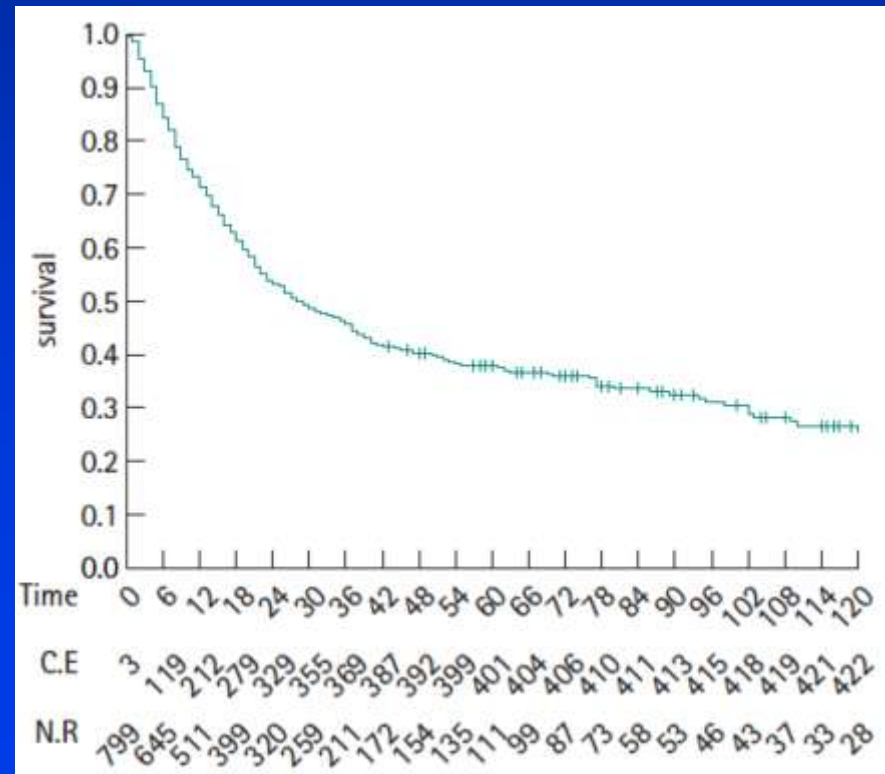
Node-positive renal cell carcinoma in the absence of distant metastases: predictors of cancer-specific mortality in a population-based cohort

Quoc-Dien Trinh[†], Jan Schmitges^{††}, Marco Bianchi[†], Maxine Sun[†], Shahrokh F. Shariat^{*}, Jesse Sammon, Claudio Jeldres[†], Kevin Zorn[†], Shyam Sukumar, Paul Perrotte[†], Markus Graefen^{†§}, Craig G. Rogers, James O. Peabody, Mani Menon and Pierre I. Karakiewicz[†]

2011 BJU INTERNATIONAL | 110, E21-E27

SEER data on 799 N1M0 RCC cases

<u>Time</u>	<u>CSS</u>
2 yrs	53%
5 yrs	38%
10 yrs	26%

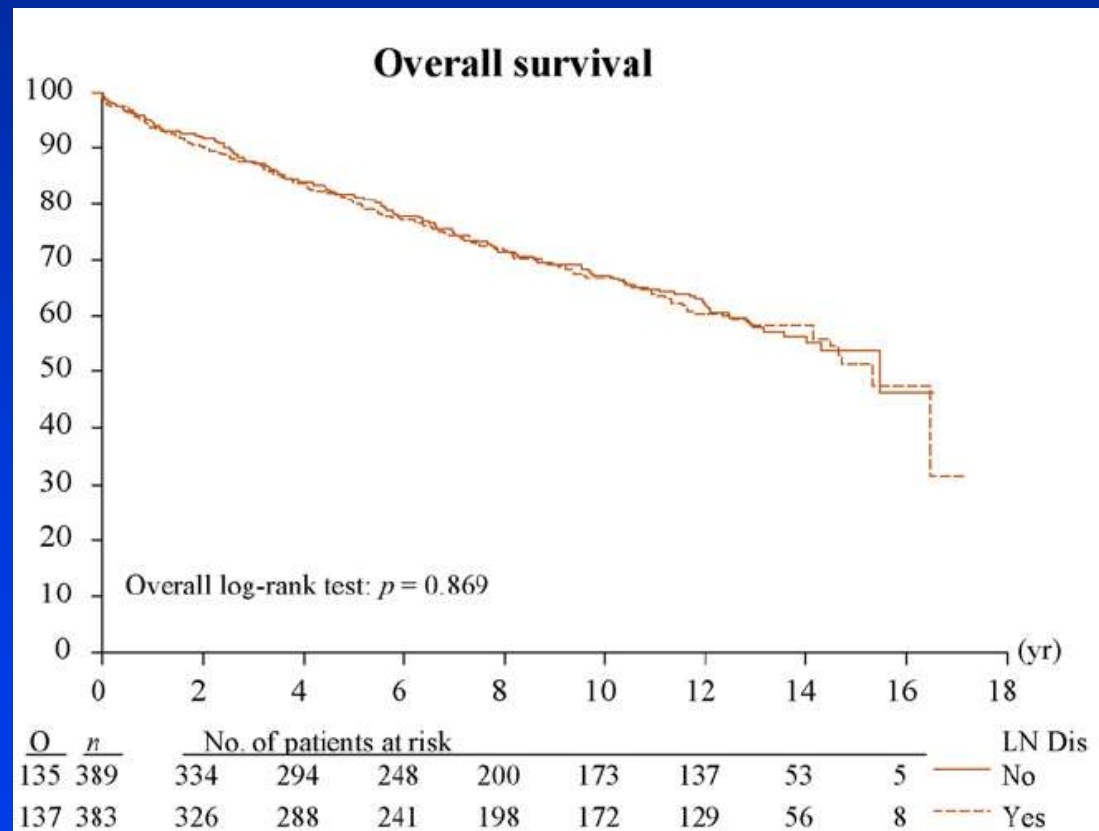


The Only RCT - EORTC 30881

Radical Nephrectomy with and without Lymph-Node Dissection:
Final Results of European Organization for Research and
Treatment of Cancer (EORTC) Randomized Phase 3 Trial 30881
Blom et al, Eur Urol 2009

1988-1991 enrolled 772 patients 732 eligible

Excluded clinical N+



Issues Regarding EORTC 30881

Extended LND

No data provided to
assess adequacy of
LND

4% LN+

Low stage patients

71% T0 - T2

Low grade patients

73% G0 - G2

Removal of palpable
adenopathy in no LND
group (9%), ?impact

	Without lymph- node dissection		With complete lymph-node dissection	
	n	%	n	%
pT category				
T0	5	1	4	1
T1	19	5	21	6
T2	230	65	221	63
T3	96	27	101	29
T4	2	1	3	1
TX	2	1	3	1
pN-category				
N0	-	-	332	96
N1	-	-	5	1
N2	-	-	6	2
N3	-	-	3	1
Grade				
G0	11	3	11	3
G1	98	28	78	22
G2	152	44	156	45
G3	49	14	67	19
G4	2	1	2	1
GX	37	11	34	10

Blom et al, Eur Urol 2009



Do Any RCC Patients Benefit From LND?

EORTC 30881 demonstrates that low risk patients do not benefit

5-year survival for N+M0 patients ranges from 5-40% with some suggestion that LND contributes to survival

Retrospective data supports resection of positive nodes in the setting of metastatic RCC

Role of LND in cN0M0

Risk stratification to determine surgical approach

Predicting Nodal Status

Blute, J Urol 2004

Reviewed 1652 radical nephrectomy cases for non-metastatic ccRCC

Determined features predictive of node positivity in MVA:

Nuclear grade 3 or 4

Sarcomatoid component

Tumor >10cm

Stage pT3 or pT4

Tumor necrosis

Prediction of LN+ RCC

Crispen, Eur Urol 2011

169 patients considered to be high risk (≥ 2 features)

Median # of LNs 6 (range 1-53)

38% (64/169) of patients LN+ disease

Median # of +LN 2 (range 1-20)

Median lymph node density 50% (range 4-100)

Prediction of LN+ RCC

Crispen, Eur Urol 2011

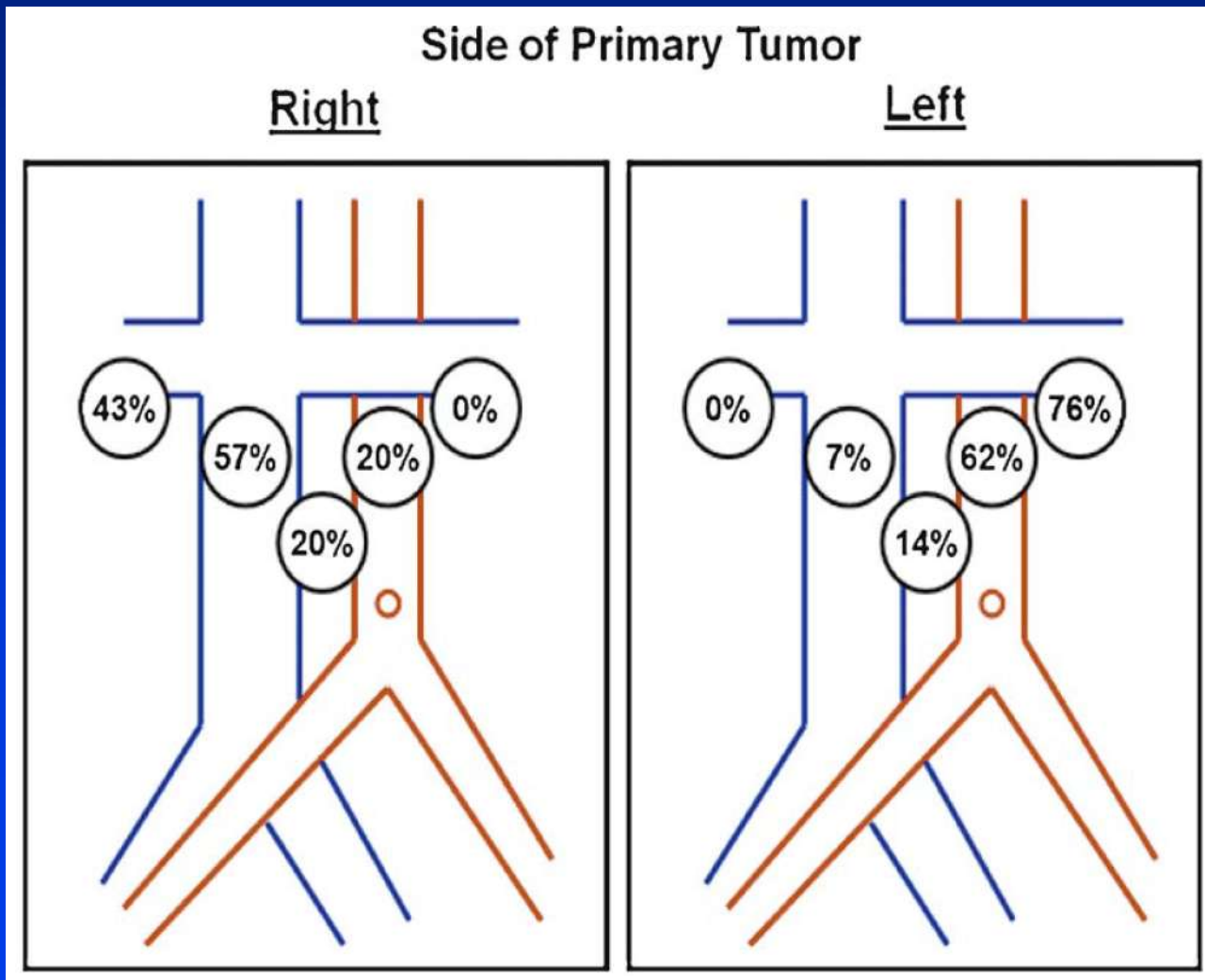
Positive risk factors, No.	Percentage of total patients	Percentage of patients with positive lymph nodes
2	21% (35/169)	20% (7/35)
3	42% (71/169)	37% (26/71)
4	31% (53/169)	49% (26/53)
5	6% (10/169)	50% (5/10)

**However, study included cN+ patients
42/64 N+ patients suspected preoperatively**

And there was no standardized LND

Location of Positive Nodes

29/64 N+ without hilar nodes involved



Preoperative Prediction of N+ RCC

Hutterer, Int J Cancer 2007

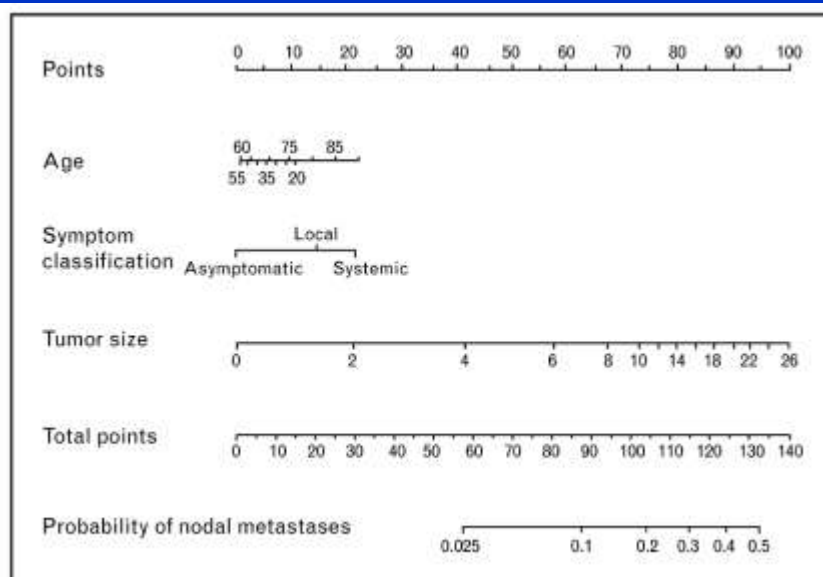
Pooled data from 12 institutions

4658 patients without mets treated with NSS or RN

Limited data analyzed

TABLE II – UNIVARIABLE AND MULTIVARIABLE LOGISTIC REGRESSION MODELS PREDICTING THE PROBABILITY OF NODAL METASTASES AT NEPHRECTOMY

Predictors	Univariable analyses or; <i>p</i> -value	Multivariable analyses	
		or; <i>p</i> -value	or; <i>p</i> -value
Age ¹	– ; 0.1	– ; 0.2	–
Tumor size ¹	– ; <0.001	– ; <0.001	– ; <0.001
Symptom classification	– ; <0.001	– ; <0.001	– ; <0.001
Local vs. asymptomatic	3.5; <0.001	2.0; 0.004	2.0; 0.004
Systemic vs. asymptomatic	6.1; <0.001	2.8; <0.001	2.9; <0.001



Role of LND in cN+M0

Guiliani, J Urol 1990

RN with extensive LND

5-year survival for 20 cases of N+M0 was 52%

Karakiewicz, Eur Urol 2006

171 N+M0 with variable LND

5-year survival 39%

Canfield, J Urol 2006

40 cases of N+M0 all with extensive LND

20 mos median survival, 30% NED at last f/u

Role of LND in mRCC

Pantuck et al J Urol 2003

Retrospective review of 1,087 RCC patients

Excluded bilateral, RCC syndrome

900 pts with RN for unilateral RCC

798 clinical and/or path data on nodes available

535 (59%) cN0M0 – no benefit to LND

129 (14%) cN+M0-1

236 (26%) cN0M1

No overall difference in outcome

No difference in complication rates

Role of LND in M1 RCC

Retrospective review of 1,087 RCC patients
MVA in subset of node + patients

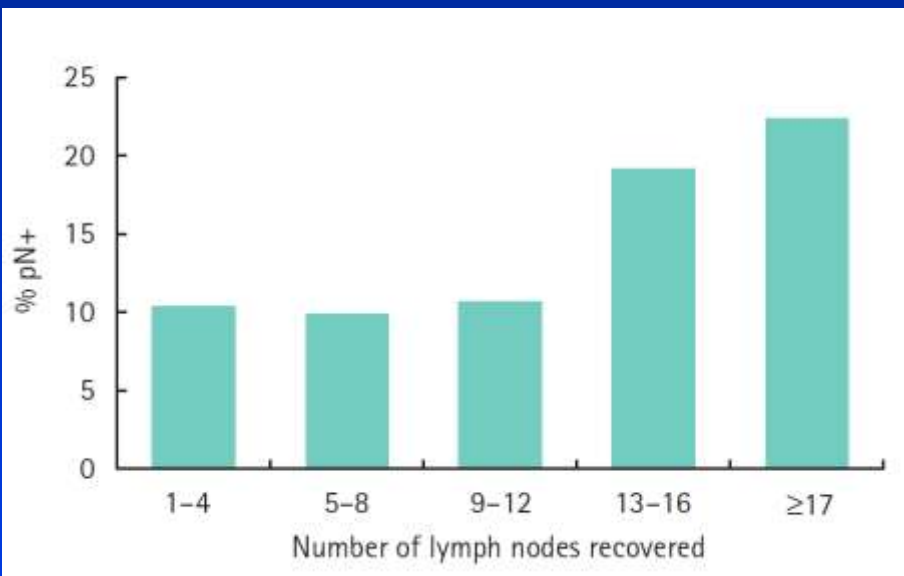
TABLE 3. *Cox multivariate survival analysis of patients with retroperitoneal lymph nodes treated with and without retroperitoneal lymph node dissection during cytoreductive nephrectomy*

Variable	HR ± SE (95% CI)	p Value
No dissection	3.11 ± 1.1 (1.48–6.11)	0.002
Grade	1.89 ± 0.41 (1.24–2.89)	0.003
ECOG performance status	1.36 ± 0.29 (0.89–2.07)	0.153
Immunotherapy	0.62 ± 0.16 (0.37–1.01)	0.057
Metastases	1.12 ± 0.32 (0.64–1.95)	0.678

Number of Nodes

Terrone, BJU Int 2003

Evaluated 608 RN patients with LND
13.6% Node positive



Variable	< 13	≥ 13
No. of patients	411	197
n (%):		
pT1	161 (39.1)	66 (33.5)
pT2	69 (16.7)	38 (19.2)
pT3	159 (38.6)	88 (44.6)
pT4	22 (5.3)	5 (2.5)
pN+	42 (10.2)	41 (20.8)*
M+	77 (18.7)	39 (19.7)
G1	30 (7.2)	9 (4.5)
G2	201 (48.9)	106 (53.8)
G3	117 (28.4)	62 (31.4)
G4	10 (2.4)	3 (1.5)
GX	53 (12.8)	17 (8.6)
Median (range) tumour size, cm	7 (1-30)	8 (3-20)

Number of Nodes

Whitson, J Urol 2011

SEER review of 9586 patients

8321 N0: number of nodes had no impact on survival

1265 N+: Increasing number of nodes in specimen associated with increased survival

This effect was independent of the number of positive nodes

Example 62 y/o with 9 cm RCC, G3, T3, 1 + node

5 nodes removed: 39% 5-year CSS

15 nodes removed: 49% 5-year CSS

Extent of lymph node dissection at nephrectomy affects cancer-specific survival and metastatic progression in specific sub-categories of patients with renal cell carcinoma (RCC)

Umberto Capitanio, Nazareno Suardi, Rayan Matloob, Marco Roscigno*, Firas Abdollah, Ettore Di Trapani, Marco Moschini, Andrea Gallina, Andrea Salonia, Alberto Briganti, Francesco Montorsi and Roberto Bertini

Institutional data from 1987-2011 totaling 1983 cases

Overall 120/1983 patients (6%) N+

14% of patients with LND (14%) N+

Mean #nodes removed

Limited LND:	3.1
Regional LND:	9.7
Extended LND:	14.8

Extent of lymph node dissection at nephrectomy affects cancer-specific survival and metastatic progression in specific sub-categories of patients with renal cell carcinoma (RCC)

Umberto Capitanio, Nazareno Suardi, Rayan Matloob, Marco Roscigno*, Firas Abdollah, Ettore Di Trapani, Marco Moschini, Andrea Gallina, Andrea Salonia, Alberto Briganti, Francesco Montorsi and Roberto Bertini

Patients' subgroup	All patients		Patients treated with LND	
	HR (95% CI)	P	HR (95% CI)	P
pT1a–pT1b pN _{any} M _{any}	1.05 (0.99–1.11)	0.1*	0.98 (0.71–1.35)	0.8*
pT2a–pT2b pN _{any} M _{any}	0.94 (0.89–0.99)	0.04*	0.91 (0.84–0.97)	0.008*
pT3a pN _{any} M _{any}	1.01 (0.98–1.03)	0.8*	1.01 (0.98–1.04)	0.5*
pT3b pN _{any} M _{any}	0.99 (0.94–1.06)	0.9*	1.04 (0.97–1.11)	0.3*
pT3c–pT4 pN _{any} M _{any}	0.91 (0.86–0.95)	<0.001*	0.89 (0.84–0.95)	<0.001*
Lymphadenopathies: cN1	0.98 (0.96–1.01)	0.2 [†]	0.98 (0.96–1.01)	0.2 [†]
Metastatic at diagnosis: cM1	0.98 (0.95–1.00)	0.09 [‡]	0.98 (0.95–1.01)	0.2 [‡]
Necrosis: any TNM	0.99 (0.98–1.02)	0.7 [†]	0.99 (0.98–1.02)	0.8 [†]
Sarcomatoid features: any TNM	0.84 (0.74–0.96)	0.008[†]	0.81 (0.69–0.94)	0.006[†]
Pathological tumour size >10 cm	0.97 (0.94–0.99)	0.03*	0.97 (0.94–0.99)	0.03*
Patients with metastatic disease only: cM1				
cM1 and pT1a–pT1b pN _{any}	1.0 (0.92–1.17)	0.6 [§]	1.0 (0.83–1.26)	0.8 [§]
cM1 and pT2a–pT2b pN _{any}	0.79 (0.64–0.97)	0.02[§]	0.74 (0.55–0.98)	0.04[§]
cM1 and pT3a pN _{any}	0.99 (0.96–1.03)	0.6 [§]	1.0 (0.96–1.04)	0.9 [§]
cM1 and pT3b pN _{any}	0.95 (0.85–1.05)	0.3 [§]	0.98 (0.86–1.11)	0.7 [§]
cM1 and pT3c–pT4 pN _{any}	0.88 (0.82–0.95)	0.002[§]	0.89 (0.83–0.97)	0.008[§]

Extent of lymph node dissection at nephrectomy affects cancer-specific survival and metastatic progression in specific sub-categories of patients with renal cell carcinoma (RCC)

Umberto Capitanio, Nazareno Suardi, Rayan Matloob, Marco Roscigno*, Firas Abdollah, Ettore Di Trapani, Marco Moschini, Andrea Gallina, Andrea Salonia, Alberto Briganti, Francesco Montorsi and Roberto Bertini

MVA showed # of nodes removed after adjusting for confounders was significant in patient subsets

Feature	HR	p value
pT2a-pT2b	0.91	0.008
pT3c-pT4	0.89	<0.001
Size >10 cm	0.97	0.03
Sarcomatoid features	0.81	0.006

CSS increased 3-19% for each additional node removed
Progression to M+ decreased 3-11% for each additional node removed



Extent of LND

Right tumors paracaval and interaortocaval

Left tumors paraaortic and interaortocaval

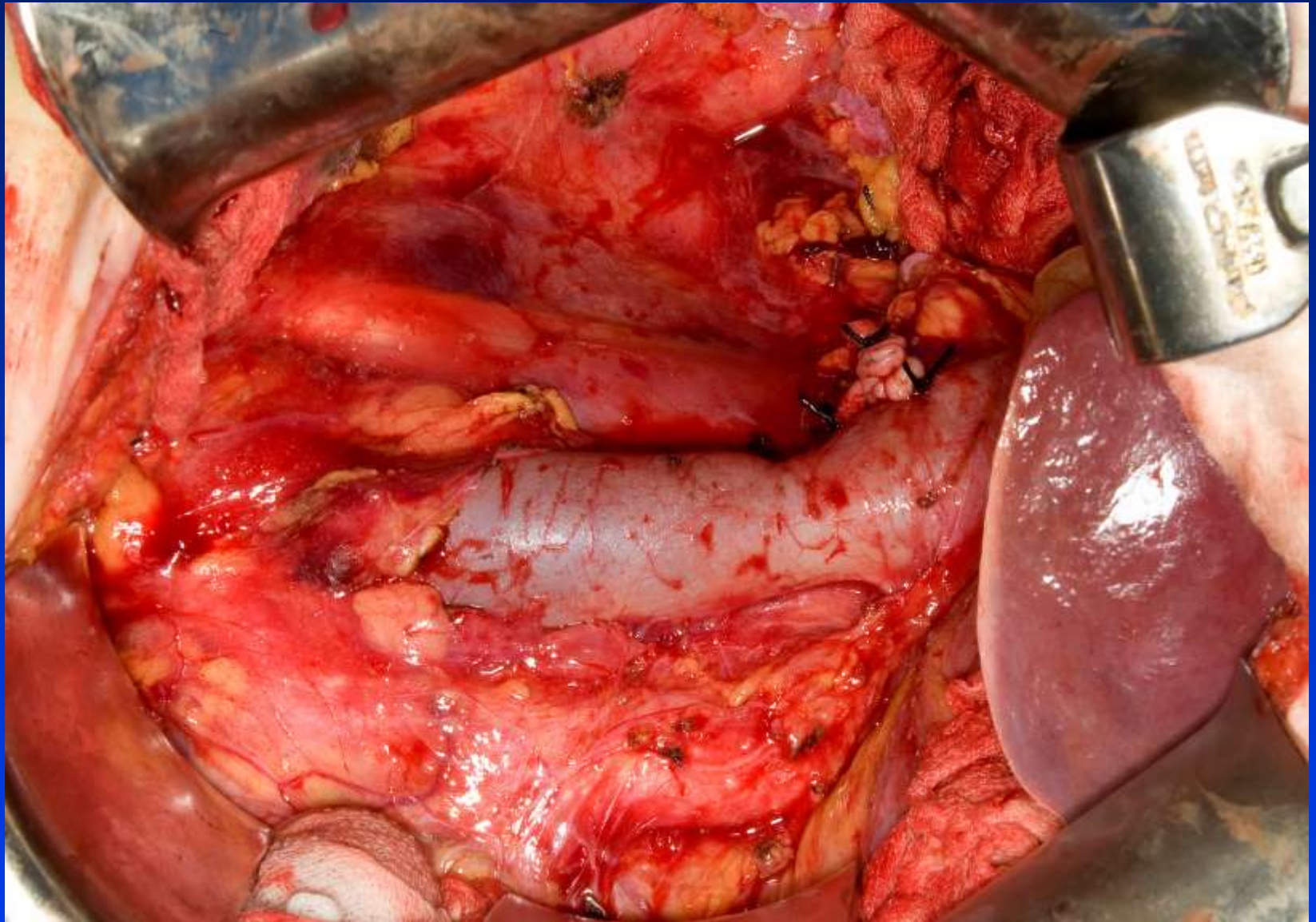
From diaphragm/adrenal to common iliac

Parker, Am J Anat 1935

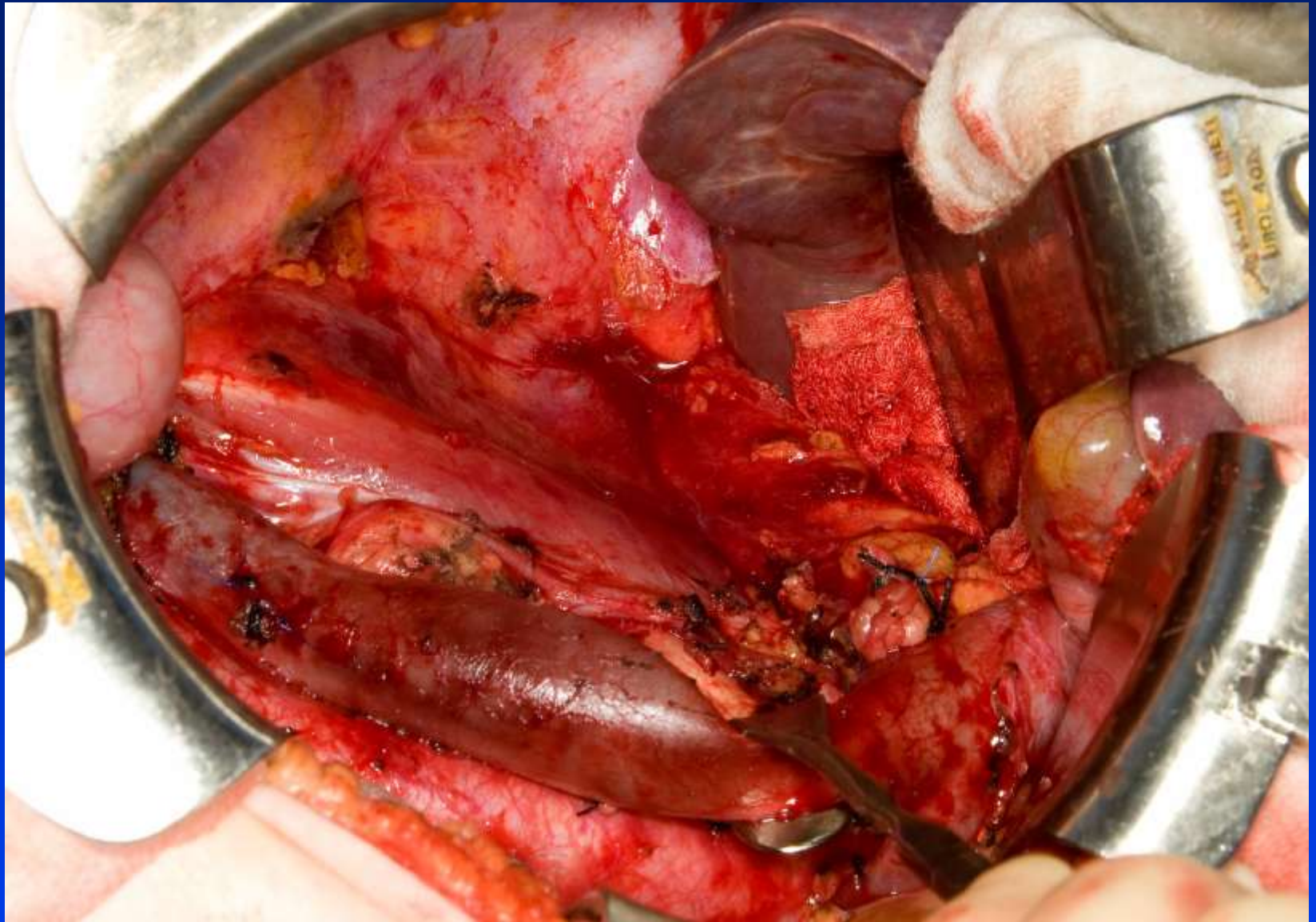
Hulten, Scand J Urol Nephrol 1969

Crispen, Eur Urol 2011









LND Recommendations

cT1N0M0: No LND

**cT2-4N0M0: +/- LND based on risk stratification,
surgeon, and patient preference**

cTanyN+M0: LND

**cM+: LND, however, no data in era of targeted
therapy**



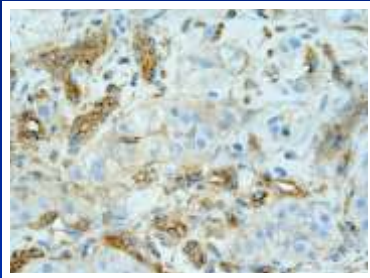
Benefit of Resection of mRCC

Maximal cytoreduction

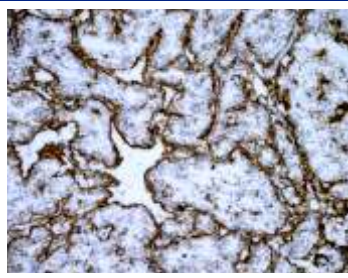


Increased B7-H3 or B7-H4 (B7x) Expression Predicts Aggressive Disease Course and Poor Survival for ccRCC Patients

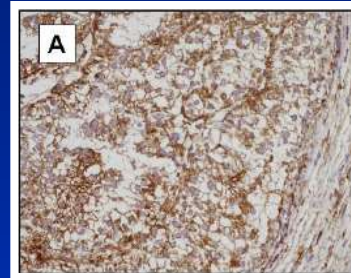
Tumor Cell
B7-H3+



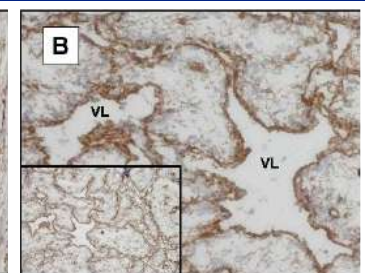
Tumor Blood
Vessel B7-H3+



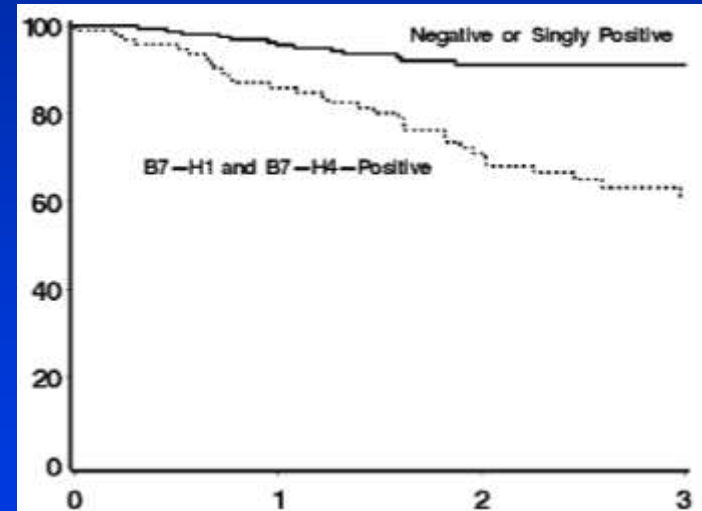
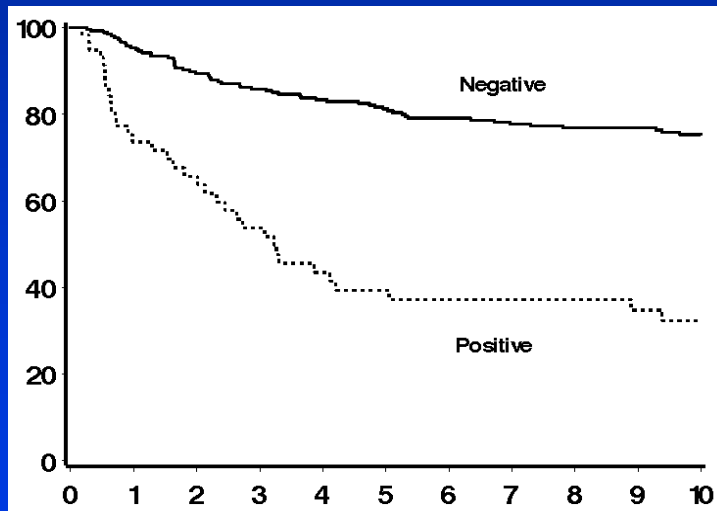
Tumor Cell
B7-H4+



Tumor Blood
Vessel B7-H4+



Cancer-Specific Survival



Years From Surgery to Last Follow-up



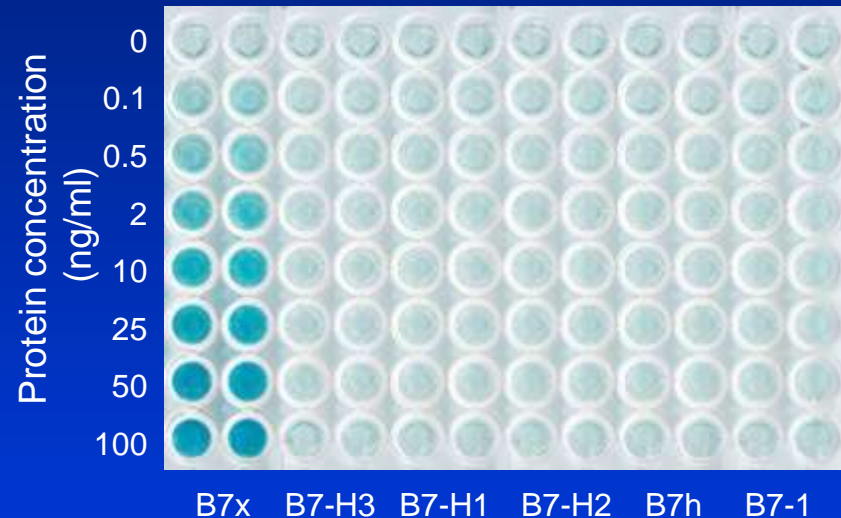
101 pts with clear cell RCC treated surgically at Mayo

100uL shipped to MSKCC



ELISA for sB7x

ELISA for serum soluble B7x



B7 family proteins

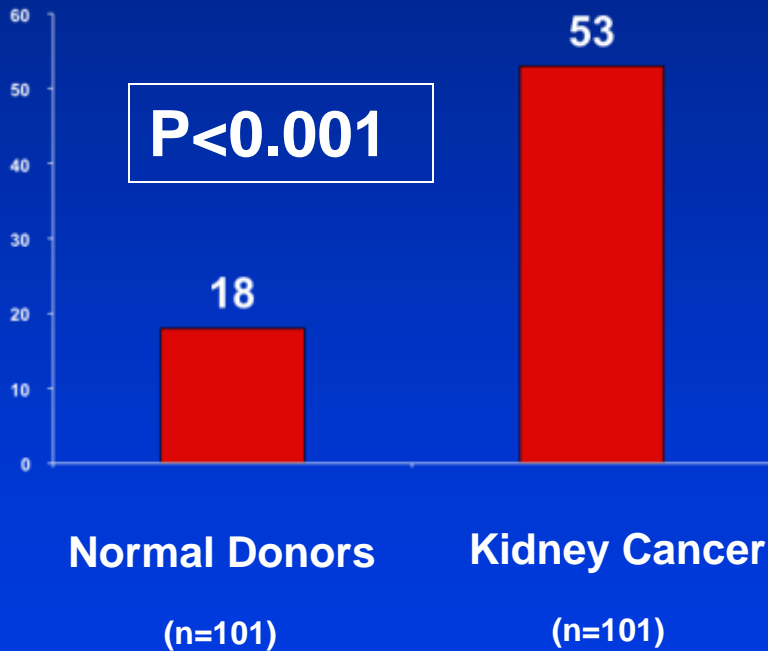
Baseline Features

Age	63
M:F	2:1
Low Grade	61
High Grade	40
pN+	7
pM+	12
Stage I	56
Stage II	8
Stage III	24
Stage IV	13

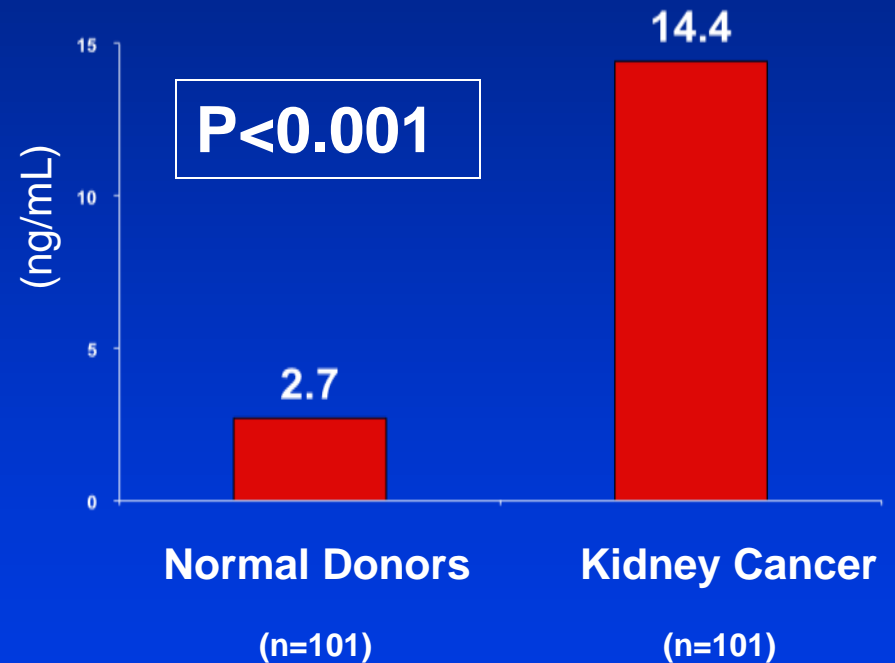
101 sex-matched controls within same age range

Serum soluble B7x

Percentage Positive

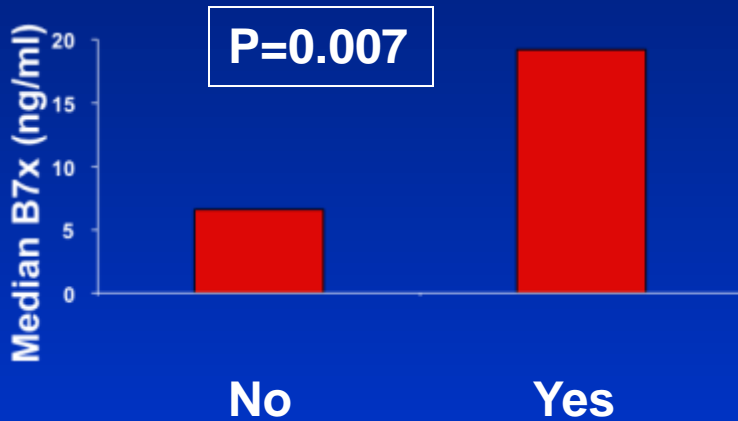


Median Concentration

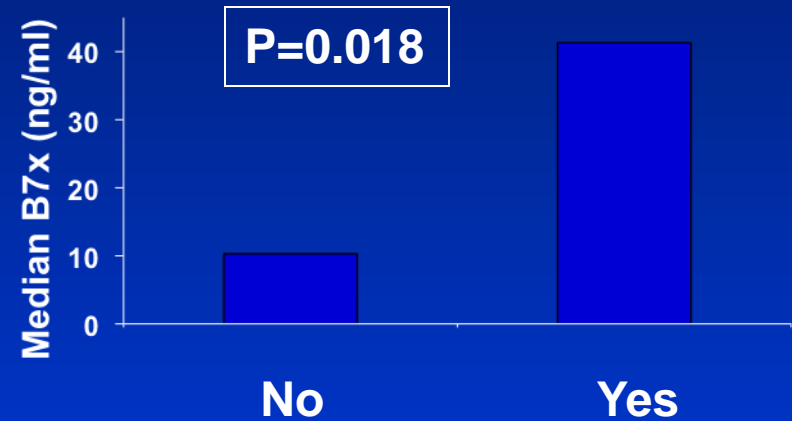


Serum B7x in RCC

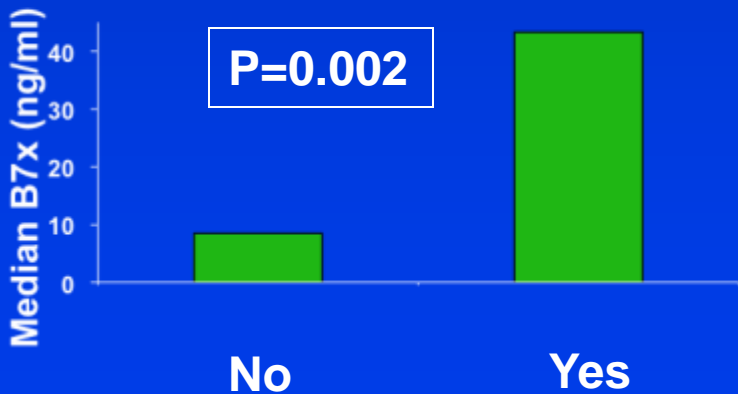
Tumor Thrombus (pT3b)



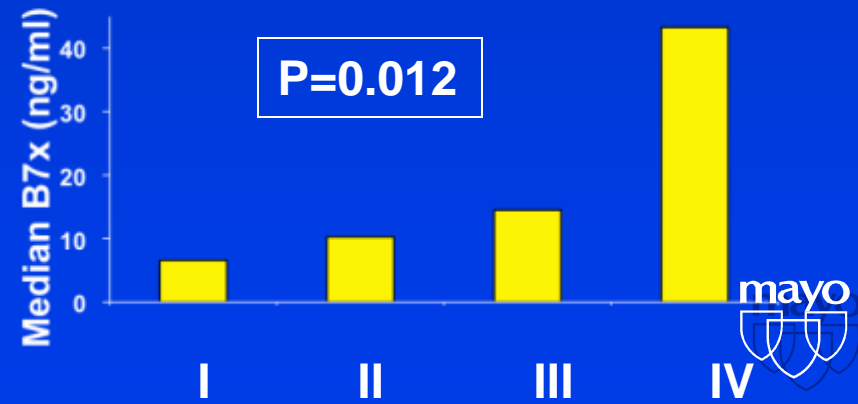
Positive Lymph Nodes (pN1)



Distant Metastases (pM1)



TNM Stage



Priority Report

Serum-Soluble B7x Is Elevated in Renal Cell Carcinoma Patients and Is Associated with Advanced Stage

R. Houston Thompson,¹ Xingxing Zang,² Christine M. Lohse,⁵ Bradley C. Leibovich,⁷ Susan F. Slovin,³ Victor E. Reuter,⁴ John C. Cheville,⁶ Michael L. Blute,⁷ Paul Russo,¹ Eugene D. Kwon,⁷ and James P. Allison²

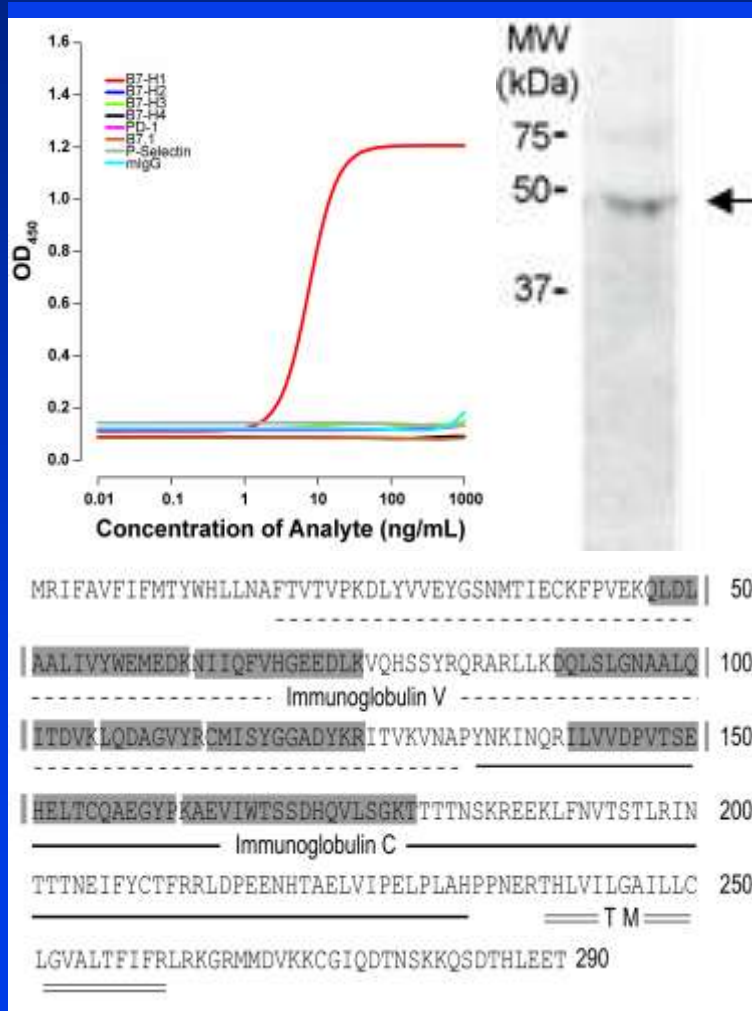
Cancer Res 2008; 68: (15). August 1, 2008

RCC patients are more likely to have detectable sB7x compared with controls

sB7x is elevated in patients with advanced disease

Serum-Soluble B7-H1 is Elevated in RCC Patients and is Associated with Advanced Stage of Disease and Predicts Poor Patient Survival

Frigola et al 2009



N = 179

Feature	Mean (Median; Range) sB7-H1	P-value
Age at Surgery (years)		
<65	0.32 (0.22; 0 – 3.00)	0.308
≥65	0.36 (0.26; 0 – 4.40)	
Gender		
Female	0.40 (0.24; 0 – 4.40)	0.438
Male	0.32 (0.22; 0 – 3.00)	
Tumor Size (cm)		
<5	0.28 (0.21; 0 – 2.25)	0.063
5 to <7	0.32 (0.24; 0.02 – 3.00)	
7 to <10	0.49 (0.26; 0 – 4.40)	
≥10	0.37 (0.29; 0 – 1.25)	
2002 Primary Tumor Classification		
pT1a, pT1b	0.29 (0.22; 0 – 3.00)	0.017
pT2	0.39 (0.21; 0 – 1.37)	
pT3a, pT3b, pT3c, pT4	0.42 (0.29; 0 – 4.40)	
Regional Lymph Node Involvement		
pNX/pN0	0.34 (0.23; 0 – 4.40)	0.232
pN1/pN2	0.34 (0.32; 0.14 – 0.86)	
Distant Metastases		
M0	0.34 (0.23; 0 – 4.40)	0.076
M1	0.34 (0.30; 0.13 – 0.86)	
2002 TNM Stage Groupings		
I	0.30 (0.22; 0 – 3.00)	0.079
II	0.39 (0.20; 0 – 1.37)	
III	0.47 (0.26; 0 – 4.40)	
IV	0.33 (0.29; 0.13 – 0.86)	
Tumor Thrombus		
None	0.31 (0.22; 0 – 3.00)	0.086
Level 0	0.40 (0.32; 0 – 1.63)	
Level I – IV	0.55 (0.27; 0 – 4.40)	
Nuclear Grade		
1, 2	0.26 (0.20; 0 – 1.66)	0.044
3, 4	0.40 (0.24; 0 – 4.40)	
Coagulative Tumor Necrosis		
Absent	0.30 (0.22; 0 – 3.00)	0.003
Present	0.46 (0.30; 0 – 4.40)	

Resection of Isolated Metachronous Nodal Metastases

Boorjian et al, J Urol 2008

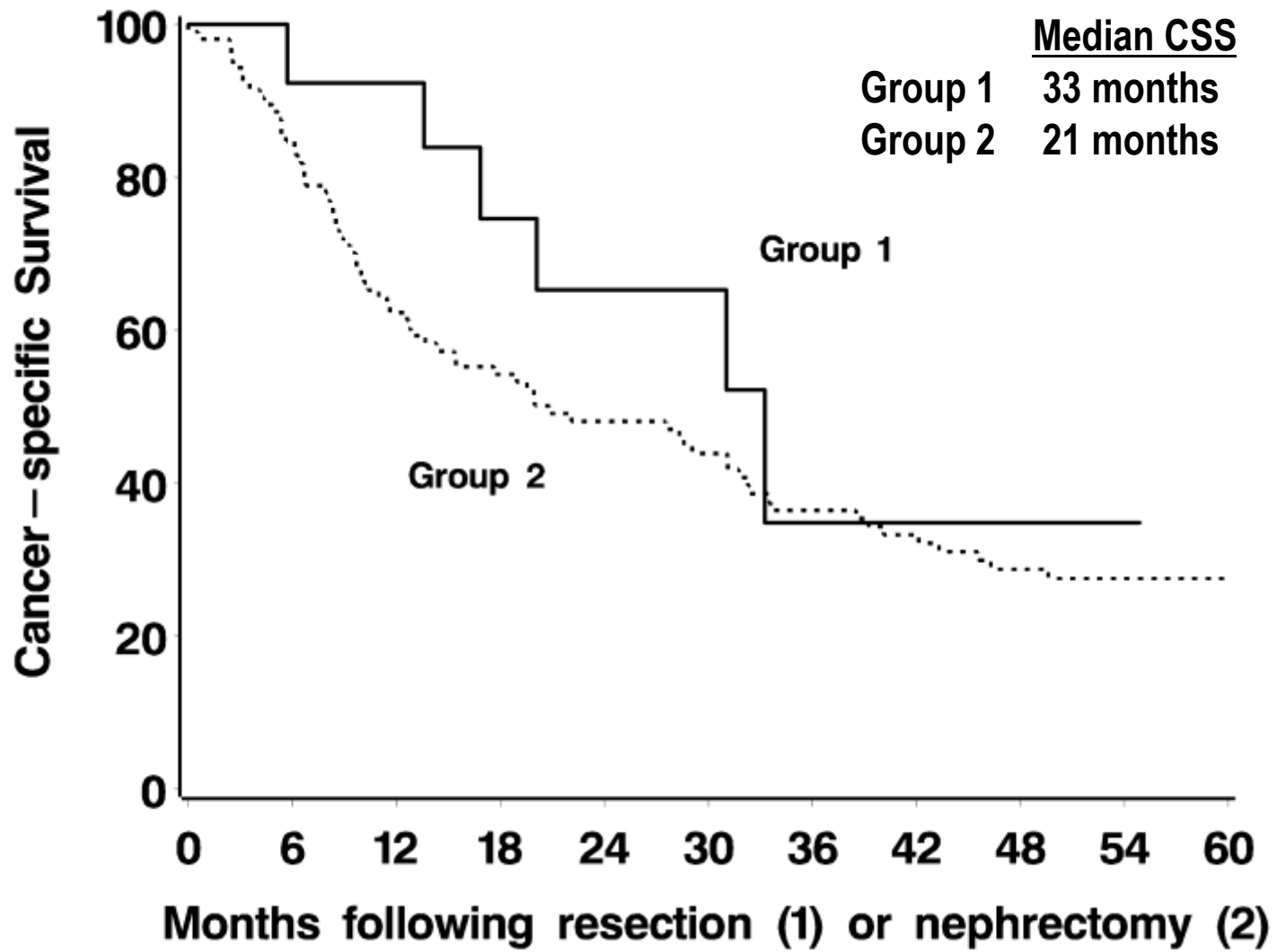
Reviewed 15 cases of isolated metachronous nodal resection post nephrectomy without neoadjuvant or adjuvant systemic therapy (group 1)

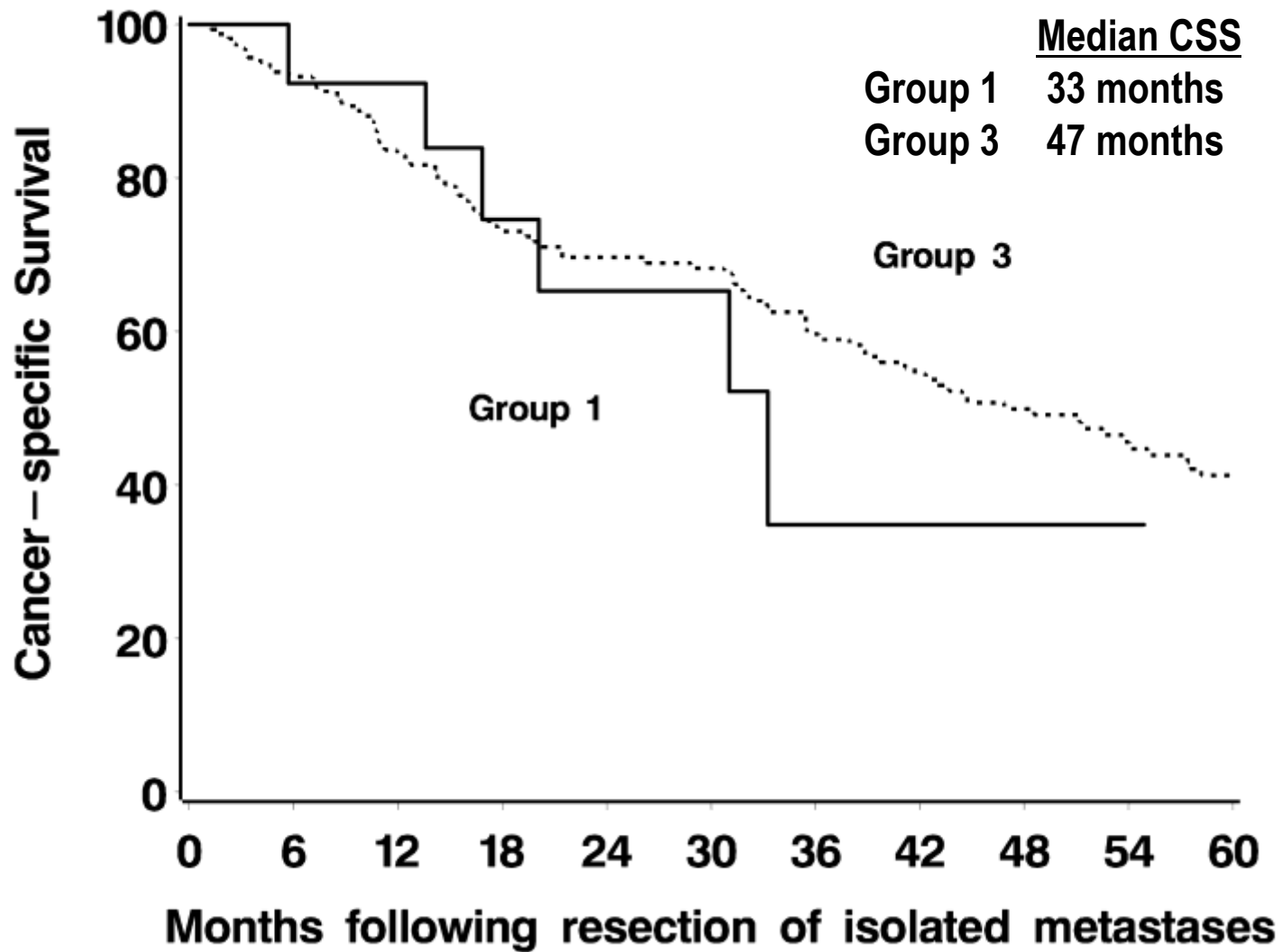
6 patients (40%) died of RCC at a median of 18 months (3-28) from resection

Compared with 107 patients with resection of synchronous N+ RCC (group2)

and

167 patients with complete resection of solitary metachronous metastasis (group 3)



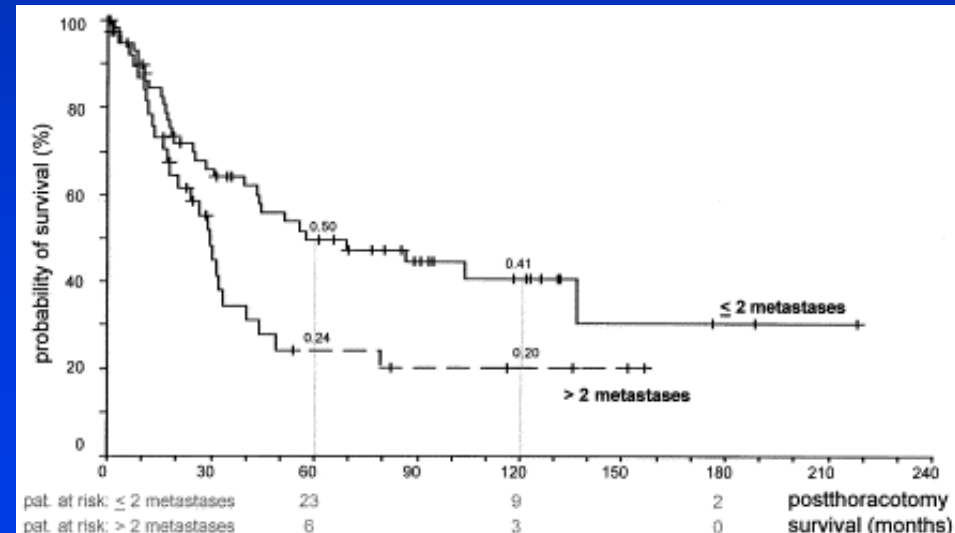
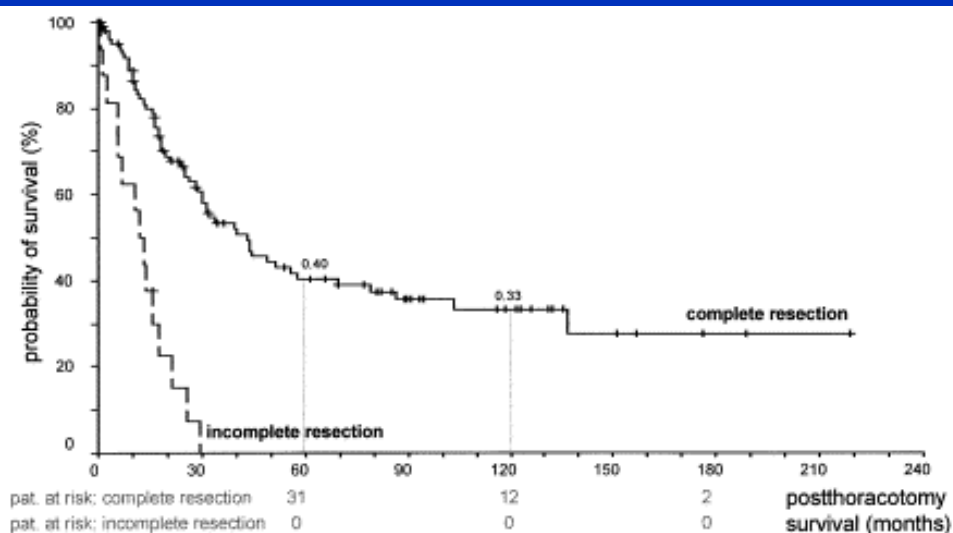


Benefit of Metastatectomy

Piltz et al, Ann Thor Surg 2002

105 patients with resection of pulmonary RCC metastases vs 17 with incomplete resection

Survival at 3, 5, and 10 years was 54%, 40%, and 33%, respectively



Metastatectomy

Kierny, Ann Surg Oncol 1994

Mayo series 41 patients with resection of solitary RCC metastasis

5 year survival 31%

Median 3.4 years

One patient alive and NED after 12 resections of mRCC over more than 7 years

Kavolius, JCO 1998

MSKCC 278 mRCC patients

Complete resection 44% 5 yr OS

Incomplete resection 14% 5 yr OS

Non-surgical therapy 11% 5 yr OS

Metastasectomy is Feasible

Lungs

Largest experience with RCC met rsxn

Author (study period)	N	No. (%) solitary Metastases	No. (%) Complete resection	5-year survival
Murthy et al (1986-2001)	92	35 (38%)	63 (68%)	Overall - 31% Complete resection - 42% Incomplete resection - 10%
Friedel et al (1980-1995)	77	35 (45%)	77 (100%)	Complete resection - 39%
Pfannschmidt et al (1985-1999)	191	NA	149 (78%)	Overall - 37% Complete resection - 42% Incomplete resection - 20%
Piltz et al (1980-2000)	105	49 (47%)	105 (100%)	Complete resection - 40%
Cerfolio et al (1965-1989)	96	48 (50%)	96(100%)	Complete resection - 36%
Hofmann et al (1975-2003)	64	NA	54 (84%)	Overall - 33%

Well tolerated

Approximately 10% incidence moderate-severe complications

Metastasectomy is Feasible

Bone

Lin et al, Bone Joint Surg Am, 2007

Palliative benefit (pain, impending fx)

Solitary bone met – 35% 5 yr survival

10% complication rate/7% “massive” (>5 L) blood loss/2% infection

Pancreas

Reddy et al, Lancet Oncol 2009

66% 5 yr survival after resection of isolated pancreatic lesion

6% risk of severe morbidity/2% perioperative mortality

Metastasectomy is Feasible

Adrenal

Antonelli et al, BJU 2006

60% 5-yr survival after resection of isolated adrenal metastasis

Severe complications rare

Renal fossa recurrence

Master, J Urol 2005

30% 5-yr survival after resection

42% overall complication rate

Retroperitoneal lymph nodes

Boorjian, J Urol 2008

33 months median CSS after RPLND for isolated recurrence

Impact of Metastasectomy on Survival

Author (study period)	N	Metastatic sites	No. (%) solitary met	Resection status	5-year survival	Risk factors for death
Leibovich et al (1970-2000)	727	54% lung 26% bone 10% liver 23% other	630 (87%)	Complete (26%)	15% (overall)	Symptoms (RR 1.28) Bone mets (RR 1.35) Liver mets (RR 1.69) DEI <2 years (RR 1.57) Complete resection (RR 0.5) Tumor thrombus (RR 1.43) Grade 4 (RR 1.53) Necrosis (RR 1.36)
Naito et al (1988-2002)	1463	62% lung 25% bone 9.3% liver 17% other	914 (70%)	Any metastasectomy (28%)	25% (overall) 44% (any metastasectomy)	DFI <12 mos (HR 1.6) ECOG PS >1 (HR 1.4) Anemia (HR 1.2) LDH (HR 2.8) Hypercalcium (HR 1.5) CRP (HR 2.1) Metastasectomy
Vogl et al (2001-2005)	99	62% lung 34% bone 23% liver 27% other	36 (36%)	Complete (21%) Incomplete (25%) No metastasectomy (53%)	50% (any metastasectomy) 38% (no metastasectomy)	high grade (RR 3.9) CRP (RR 2.7) Metastasectomy (RR 0.3) LDH (RR 3.3)
Eggerer et al (1989-2007)	129	64% lung 16% bone 10% liver 11% other	NA	Complete (31%) Incomplete (3%) No metastasectomy (66%)	27% (overall) 49% (any metastasectomy)	No metastasectomy (HR 2.7) Intermittent risk score (HR 3.0) Poor risk score (HR 12.4)
Kavolius et al (1980-1993)	278	57% lung 19% bone 18% other	155 (56%)	Complete (51%) Incomplete (25%) No metastasectomy (24%)	29% (overall) 44% (complete resection)	Short DFI Multiple tumors No metastasectomy Female

Risk Score and Metastectomy Independently Impact Prognosis of Patients With Recurrent Renal Cell Carcinoma

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129 patients with localized RCC who developed recurrence after nephrectomy

44 (34%) underwent metastectomy

Controlling for risk stratification:

Lack of metastectomy – 2.7 fold increased risk of all-cause mortality

Metastectomy benefited in all risk groups

Lung Metastasectomy

Largest experience with resection of mRCC

Author (study period)	N	No. (%) solitary Metastases	No. (%) Complete resection	5-year survival
Murthy et al (1986-2001)	92	35 (38%)	63 (68%)	Overall - 31% Complete resection - 42% Incomplete resection - 10%
Friedel et al (1980-1995)	77	35 (45%)	77 (100%)	Complete resection - 39%
Pfannschmidt et al (1985-1999)	191	NA	149 (78%)	Overall - 37% Complete resection - 42% Incomplete resection - 20%
Piltz et al (1980-2000)	105	49 (47%)	105 (100%)	Complete resection - 40%
Cerfolio et al (1965-1989)	96	48 (50%)	96 (100%)	Complete resection - 36%
Hofmann et al (1975-2003)	64	NA	54 (84%)	Overall - 33%

Approximately 10% incidence moderate-severe complications
Complete resection gives 36-42% 5 year survival without TKI

Impact of Metastasectomy on Survival

Author; study period	n	Metastatic sites ^a	Synchronous metastases	Solitary metastases	Resection status	Median survival (months) ^c	5-year survival ^f	Risk factors for death ^d
Leibovich <i>et al.</i> [10]	727	Lung 389 (54%); Bone 186 (26%); Liver 73 (10%); Other 165 (23%)	285 (39%)	630 (87%)	Complete 192 (26%); incomplete NA; no metastasectomy NA	NA	Overall 15%	Symptoms (RR 1.28); Bone mets (RR 1.35); Liver mets (RR 1.69); DFI <2 years (RR 1.57); Complete resection (RR 0.5); Tumor thrombus (RR 1.43); Grade 4 (RR 1.53); Necrosis (RR 1.50)
Alt <i>et al.</i> , unpublished data NA	887	Lung 647 (73%); Bone 328 (37%); Viscera 283 (32%); Other 305 (34.4%)	357 (40%)	0	Complete 125 (14%); incomplete 257 (29%); no metastasectomy 505 (57%)	Overall 17; complete resection 50	Overall 16%; Complete resection 44.5%	No metastasectomy; Incomplete metastasectomy; Extrapulmonary metastases
Naito <i>et al.</i> [11*]	1324	Lung 811 (62%); Bone 320 (25%); Liver 121 (9.3%); Other (219 (17%)	905 (62%)	914 (70%)	NA ^b	Overall 22; any metastasectomy 44	Overall 25%; any metastasectomy 44%	DFI <12 months (HR 1.6); ECOG PS >1 (HR 1.4); anemia (HR 1.2); LDH (HR 2.8); hypercalcemia (HR 1.5); CRP (HR 2.1); metastasectomy NA
Vogl <i>et al.</i> [12]	99	Lung 62 (62%); bone 34 (34%); liver 23 (23%); other 27 (27%)	65 (66%)	36 (36%)	Complete 21 (21%); incomplete 25 (25%); no metastasectomy 53 (53%)	Any metastasectomy 55; no metastasectomy 25	Any metastasectomy 50%; no metastasectomy 38%	High grade (RR 3.9); CRP (RR 2.7); Metastasectomy (RR 0.3); LDH (RR 3.3)
Eggner <i>et al.</i> [13]	129	Lung 82 (64%); bone 21 (16%); other 40	0	NA	Complete 40 (31%); incomplete 4 (3%); no metastasectomy 85 (66%)	Overall 28; any metastasectomy 45	Overall 27%; any metastasectomy 49%	No metastasectomy (HR 2.7); intermittent risk score (HR 3.0); poor risk score (HR 12.4)
Kavolius <i>et al.</i> [14]	278	Lung 158 (57%); bone 53 (19%); other 49 (18%)	129 (40%)	155 (56%)	Complete 141 (51%); incomplete 70 (25%); no metastasectomy 67 (24%)	Overall NA; complete resection 50	Overall 29%; Complete resection 44%	Short DFI, multiple tumors, no metastasectomy; female
van der Poel <i>et al.</i> [15]	95	Lung 39 (41%); bone 26 (27%); brain 8 (8%)	33 (35%)	40 (42%)	Complete 56 (59%); incomplete 39 (41%); no metastasectomy 0	Overall 24	Overall 23%	Bone metastases; Primary tumor stage
Daliani <i>et al.</i> [16]	38	Lung 201(55%); bone 4 (11%); other 4 (11%)	17 (45%)	NA	Complete 29 (76%); incomplete 9 (24%); no metastasectomy 0	Overall 57; complete resection 67	Overall 45%; Complete resection; 60%	Incomplete resection (RR 6.1); nonpulmonary mets (RR 1.8)
Kwak <i>et al.</i> [17]	93	Lung 42 (45%); bone 28 (30%); other 34 (37%)	45 (48%)	64 (69%)	Complete 93 (100%); incomplete 0; no metastasectomy 0	Overall 41	Immunotx 55%; no immunotx 25%	Multiple metastases (HR 3.7); nonpulmonary met (HR 2.1)
Kiemey <i>et al.</i> [18]	41	Lung 20 (49%); brain 7 (17%); other 14 (34%)	0	23 (56%)	Complete 36 (88%); incomplete 5 (12%); no metastasectomy 0	Overall 41	Overall 31%	Increased tumor grade of met

Metastasectomy 44-50% 5 year survival vs. ~12% for no resection

Significant predictor of survival in all series

Breau and Blute, Curr Opin Urol, 2010

A SCORING ALGORITHM TO PREDICT SURVIVAL FOR PATIENTS WITH METASTATIC CLEAR CELL RENAL CELL CARCINOMA: A STRATIFICATION TOOL FOR PROSPECTIVE CLINICAL TRIALS

BRADLEY C. LEIBOVICH,* JOHN C. CHEVILLE, CHRISTINE M. LOHSE, HORST ZINCKE,†
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Vol. 174, 1759–1763, November 2005

727 patients with metastatic clear cell RCC

TABLE 3. *Multivariate model for death from RCC for 727 patients with metastatic clear cell RCC*

Feature	Regression Coefficient	Risk Ratio (95% CI)	p Value
Constitutional symptoms at presentation	0.2430	1.28 (1.08–1.51)	0.005
Bone metastases	0.3005	1.35 (1.11–1.64)	0.003
Liver metastases	0.5221	1.69 (1.28–2.23)	<0.001
Multiple metastases	0.3015	1.35 (1.06–1.72)	0.015
Yrs from nephrectomy to metastases:			
Greater than 2		1.0 (reference)	
Less than 2	0.4490	1.57 (1.23–1.99)	<0.001
0 (metastases at nephrectomy)	0.2486	1.28 (1.02–1.62)	0.035
Complete resection of metastatic RCC	–0.6734	0.51 (0.42–0.62)	<0.001
Tumor thrombus level:			
0		1.0 (reference)	
I, II, III + IV	0.3588	1.43 (1.09–1.89)	0.011
Nuclear grade of primary tumor:			
1, 2 + 3		1.0 (reference)	
4	0.4228	1.53 (1.23–1.89)	<0.001
Coagulative tumor necrosis	0.3087	1.36 (1.14–1.63)	<0.001

Complete resection → 50% decrease in risk of death

Survival After Complete Surgical Resection of Multiple Metastases From Renal Cell Carcinoma

Angela L. Alt, MD¹; Stephen A. Boorjian, MD¹; Christine M. Lohse, MS²; Brian A. Costello, MD³; Bradley C. Leibovich, MD¹; and Michael L. Blute, MD⁴

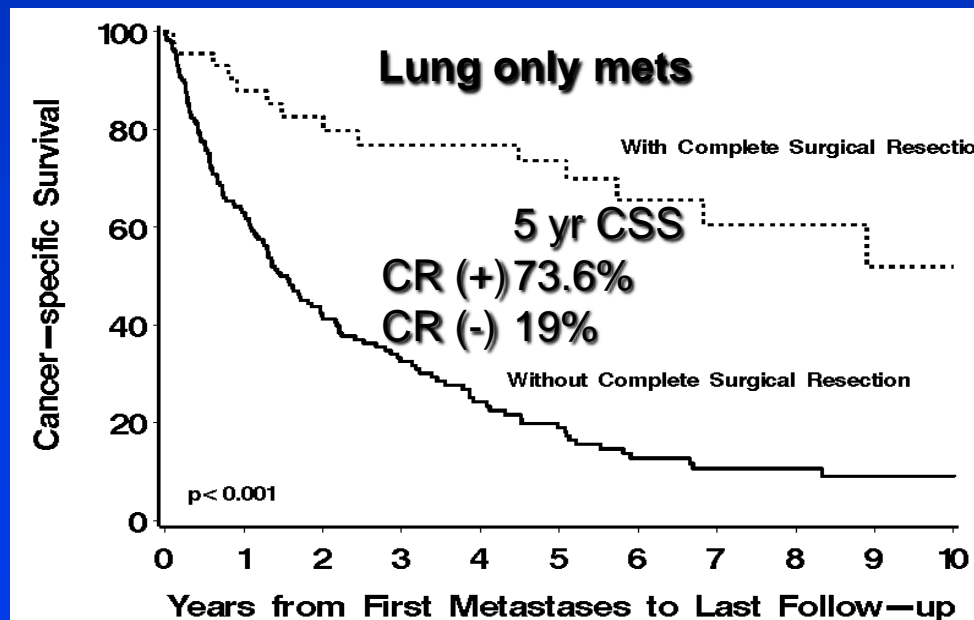
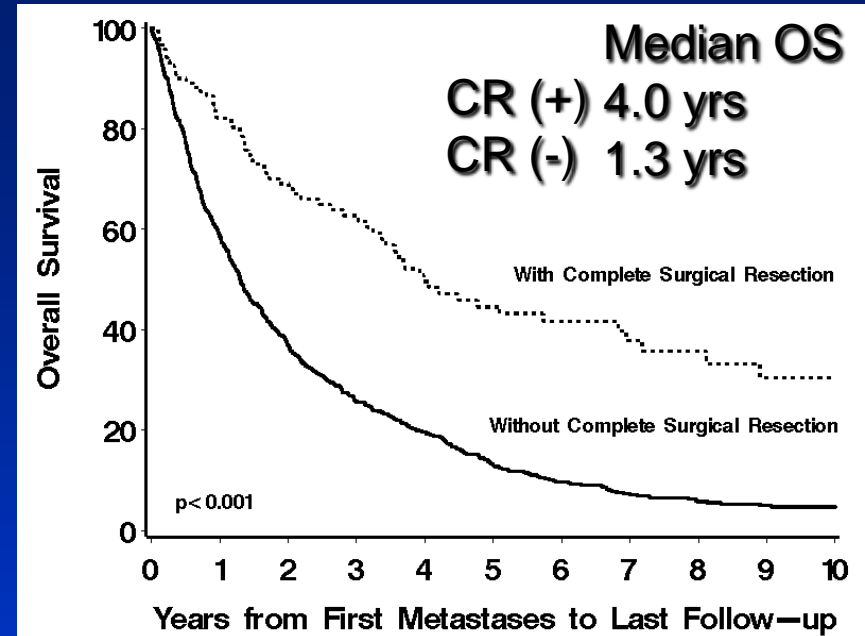
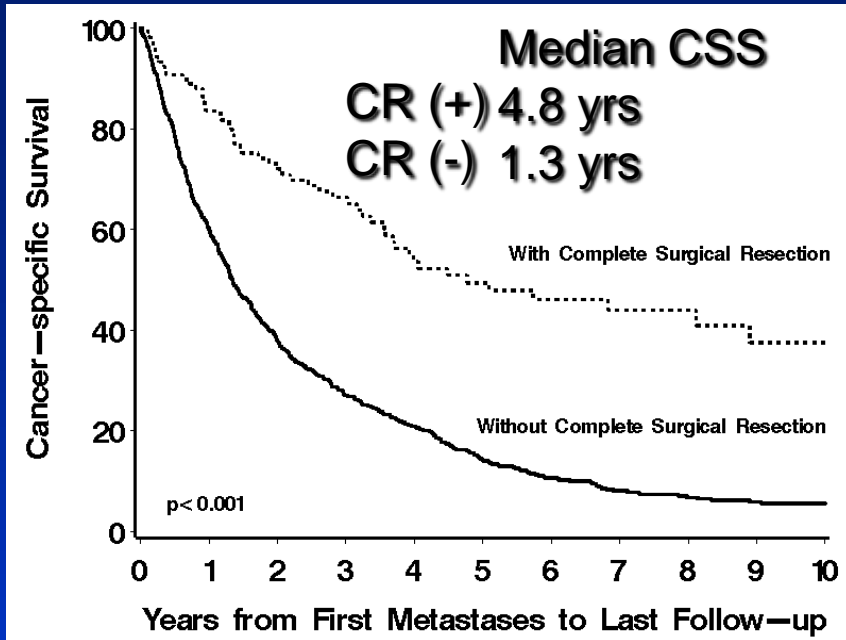
887 patients who underwent nephrectomy for RCC

Multiple mets at presentation or during follow-up

125 (14%) underwent complete resection

Median follow-up = 2.8 years

Complete Resection for Patients with Multiple Metastases



Complete Resection for Patients with Multiple Metastases

Complete resection associated with survival after adjusting for all other prognostic variables in MVA

Remained significant for patients with 3 or more metastatic lesions

Medical therapy for mRCC

Without complete metastasectomy:

Medical treatment 1.6 years

No medical treatment 1.1 years

($p=0.011$)

Complete metastasectomy:

Medical treatment 4.5 years

No medical treatment 5.7 years

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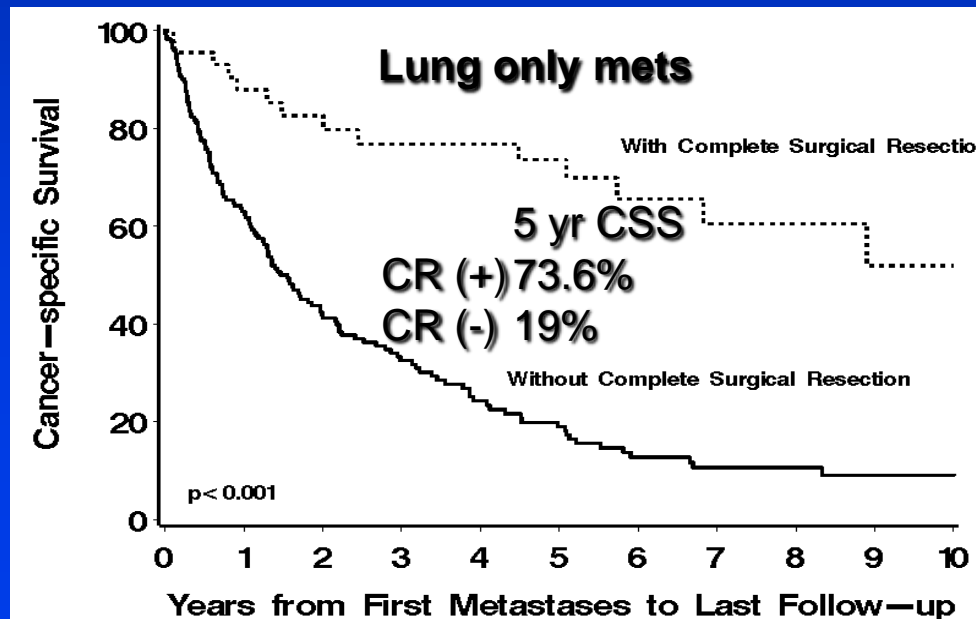
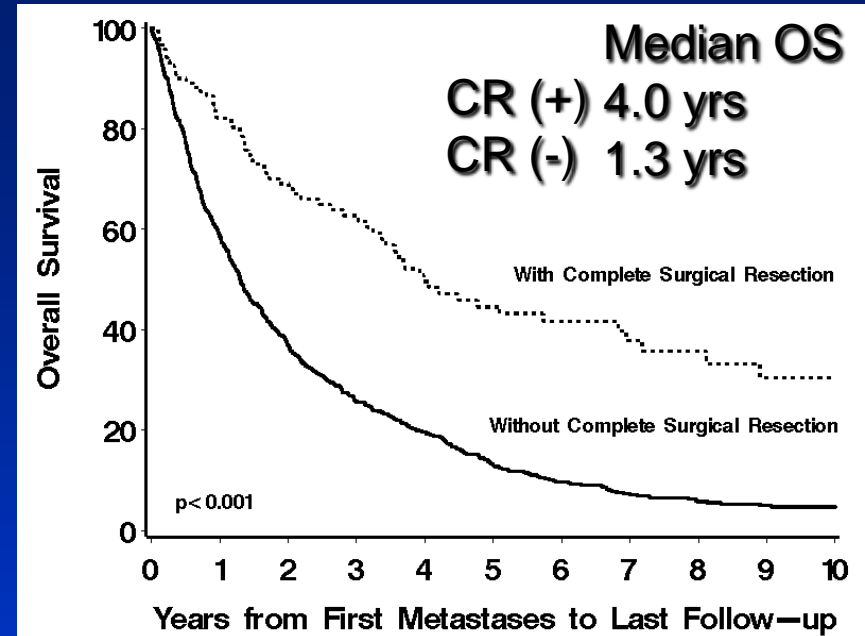
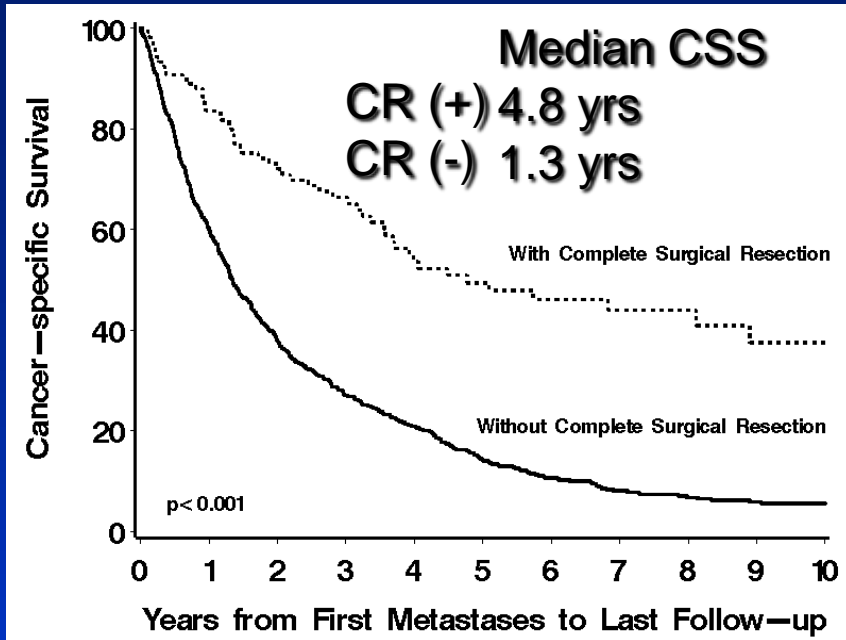
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Thank You For Your Attention

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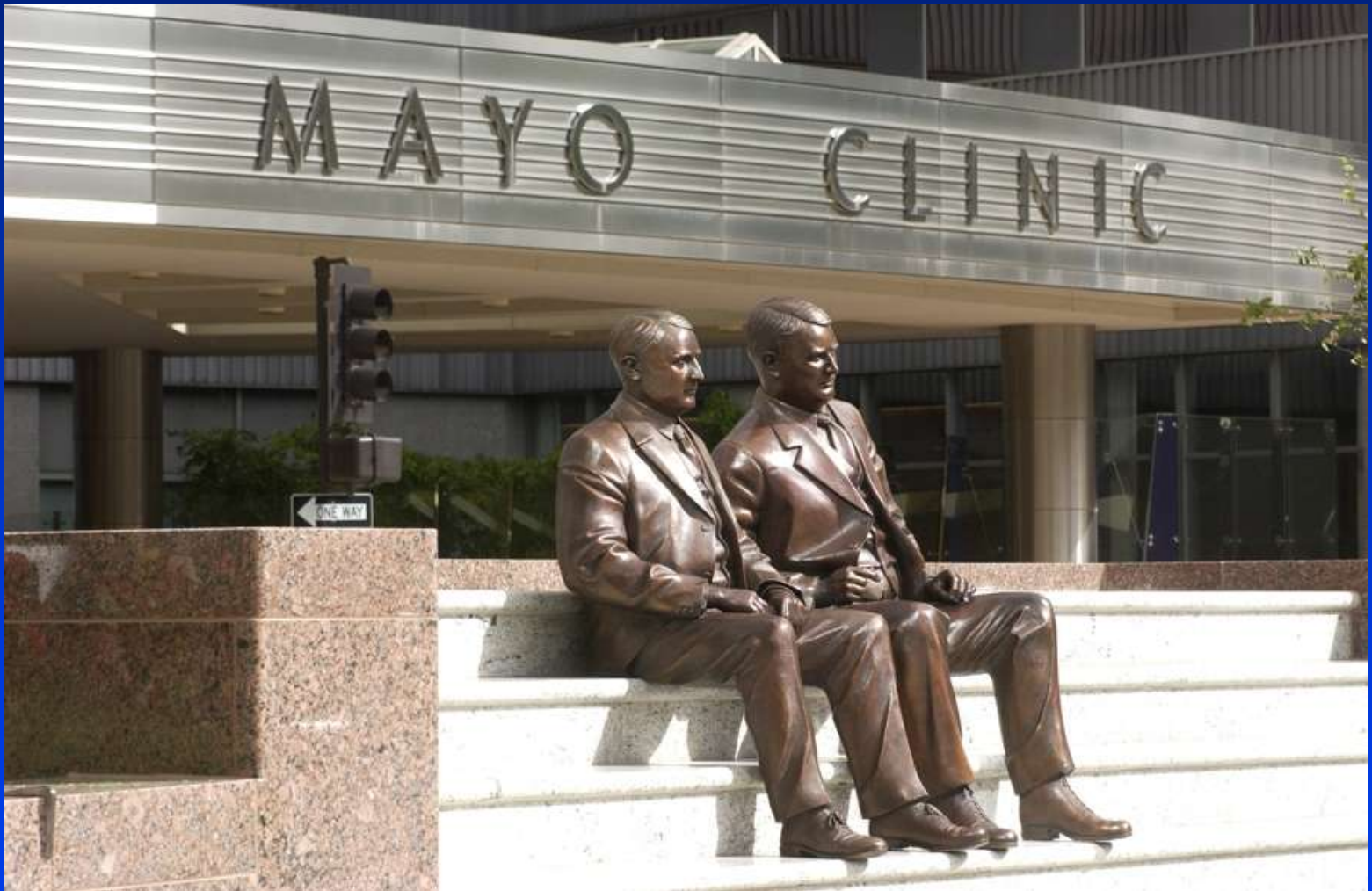
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Thank You

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