

Robot-assisted laparoscopic radical prostatectomy

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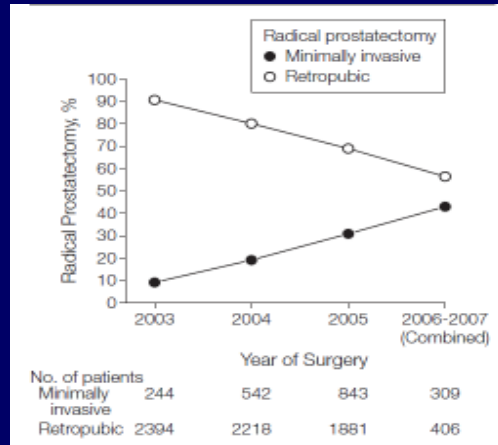


Radical Prostatectomy History

- HH Young, 1904
 - Radical Perineal Prostatectomy
- P. Walsh, 1983
 - Radical Retropubic Prostatectomy with preservation of sexual function
- WW Schuessler, 1992
 - Laparoscopic Radical Prostatectomy
- J Binder, 2000
 - Robot assisted laparoscopic radical prostatectomy

Use of Minimally Invasive vs Open Retropubic Radical Prostatectomy

SEER registries: 2003-2007



Hu JC, et al. JAMA 2009; 302: 1557-1564

Learning curve of conventional laparoscopic radical prostatectomy

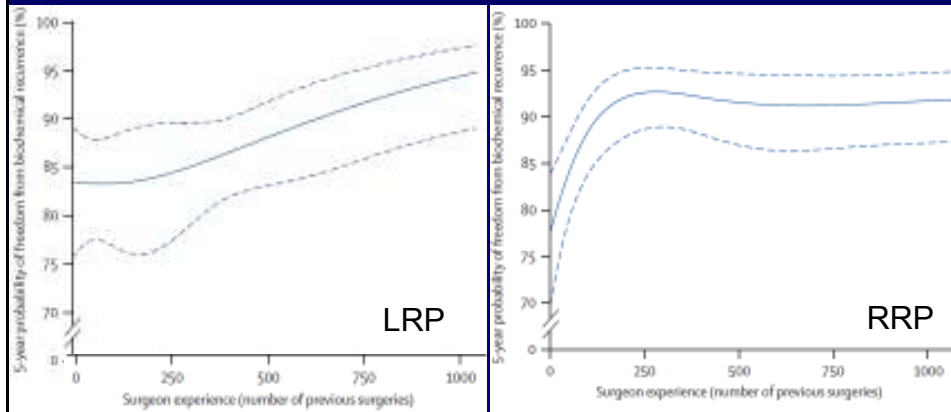
- 4-h proficiency standard
- Learning curve of LRP is estimated to range between 40 to 100 cases according to different surgeons
- It has been shown that surgeons continued to improve in terms of operative time, even after 300 cases

Guillonneau B. et al J Urol 2000; 163: 1643

Martina GR et al Urology 2005; 65: 959

Stolzenburg JU et al World J Urol 2006; 65: 959

The limitations of traditional laparoscopic surgery: learning curve



Vickers A. et al Lancet Oncology 2009; 10: 475-80

The limitations of laparoscopic surgery

- Rigidity of the instrument shaft and fixed position of the trocar
- Reduction of range of motion (only four degrees of freedom)
- Two-dimensional vision
- Impaired eye-hand coordination
- Reduced haptic sense (only minimal tactile feedback)

Potential advantages for the surgeon: 3-D Vision



- Twin optical paths, fused to give 3-D image
- Magnification up to x12



Potential advantages for the surgeon: laparoscopic instruments with 7 degree of freedom

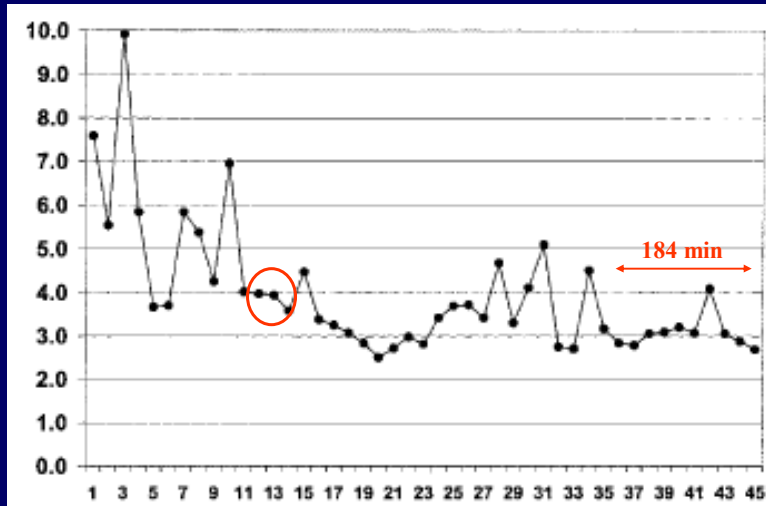


Traditional laparoscopy



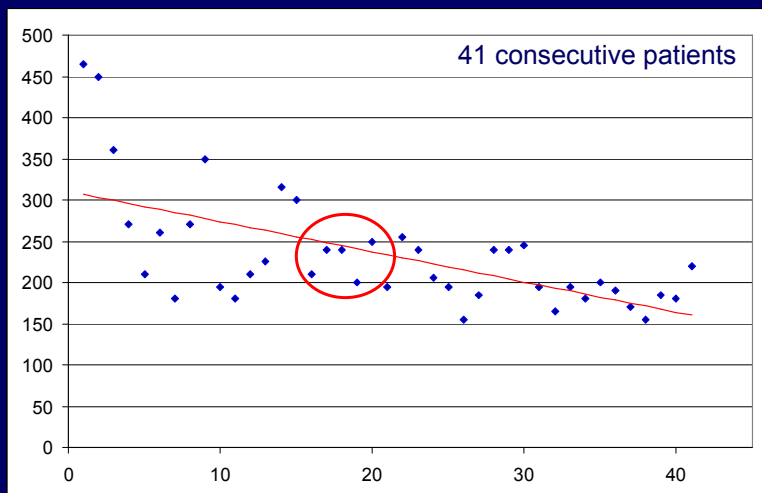
Endowrist[®] Instrument
which duplicates the dexterity
of the surgeon

Robot-assisted Laparoscopic Radical Prostatectomy: Learning curve



Ahlering et al, J Urol 170: 1738-1741, 2003

Robot-assisted Laparoscopic Radical Prostatectomy: Learning curve



Artibani W. et al. Urol Intern, 2008; 80:237-244

Learning curve: Personal experience and comparison with literature

Author	Year	Cases	Time (min)	Blood loss (ml)	Transfusion (%)	Conver. (%)	Complic. (%)	In-hospital stay (days)	Catheter (day)
Menon	2002	40	274	256	0%	0%	5%	1	n. r.
Menon	2002	30	288	329	7%	3%	20%	1,5	10,7
Bentas	2003	41	498	570	32%	5%	41,70%	17	16,7
Ahlering	2003	45	225	145	0%	0%	8,80%	1,5	7
Sim	2004	17	247	494	18%	0%	6%	2,7	9,8
Chien	2005	56	354	356	2%	0%	9%	1,9	6,6
Patel	2005	50	202	151	0%	0%	1%	n. v.	n. v.
Artibani	2006	41	226	608	9,8%	4,9%	9,7%	8,2	9
Analysis			330	415	9,8%	2%	14%	1-17	9

Ficarra V. et al Eur Urol 2007; 51: 45-55

Robot-assisted Laparoscopic Radical Prostatectomy: Learning curve

- Acceptable PSM rates
- 20 cases (Artibani W. et al Urol Inter, 2008)
- 30 cases (Atug F et al Eur Urol, 2006)
- 50 cases (Ahlering TE et al Urology, 2004)
- 80 cases (Weizer AZ et al Urology, 2007)

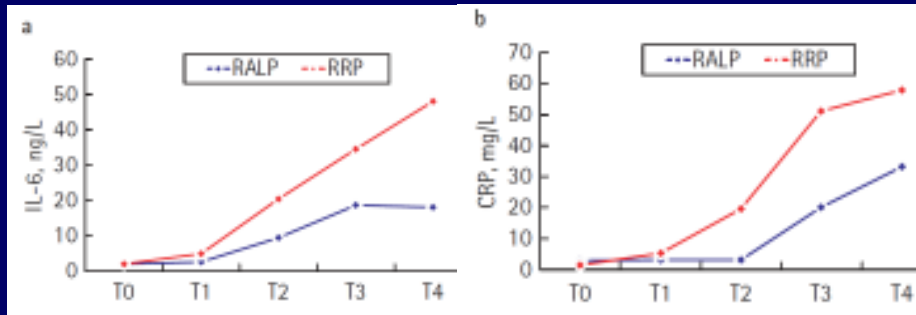
Potential advantages for the surgeon and for the patient

- RALP simplifies the learning process, allowing quicker reduction in the operative time compared to LRP
- Classical advantages of laparoscopy
- **Ultraprecise dissection possible**

Outcomes evaluated

- **Intraoperative and perioperative**
 - tissue damage, operative time, blood loss, transfusion rate, in-hospital stay, catheter time, overall complication rates
- **Functional**
 - anastomotic stricture, urinary continence and potency recovery
- **Oncological**
 - positive surgical margins, bDFS, OS and CSS

Invasiveness and evaluation of tissue damage (RALP Vs RRP)



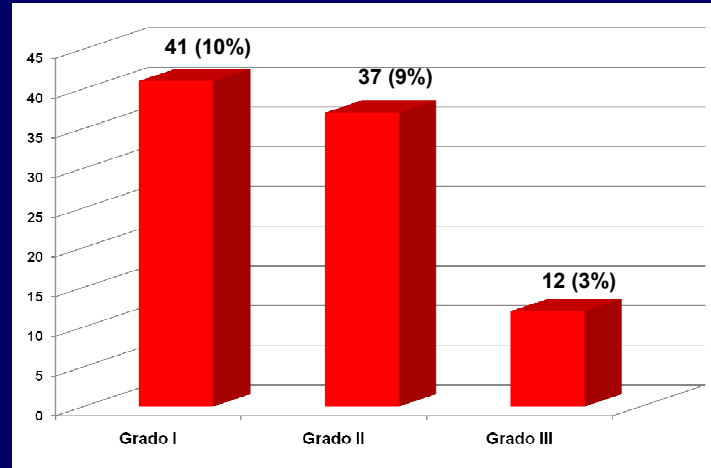
T0 = Baseline T1= during surgery T2= end of anaesthesia
 T3 = 12 h POD T4 = 24 h POD

Fracalanza S. et al. BJU Inter 2008; 101: 1145-49

Perioperative data: non comparative RALP series

Authors	Cases	OR	BL	Transf (%)	Compl (%)	In-hospital stay
Chatelineau, 2004	105	155	500	6%	7%	5,5
Bhandari, 2005	300	177	109	0%	5,7%	1,2
Costello, 2005	122			3%	15%	2
Hu, 2006	322	186	250	1,6%	17%	
Farnham, 2006	176		191	0,5%		
Joseph, 2006	325	180	196	1,3%	10%	1
Van Appledorn, 2006	150	191		2,6%	3,3%	3,4
Borin, 2007	400		103			1
Menon, 2007	2652	154	142	0%	2,3%	1,14
Mottrie, 2007	184	171	200		12%	
Patel, 2007	500	130	50	0	4%	1
Zorn, 2007	300	282	273	1,7%	9%	1,4
Nelson, 2007	629				17%	1,17
Badani, 2007	2766	154	142	1,5%	12%	1,14
Jaffe, 2008	278	158	533	5%		5
Krambeck, 2009	286	236		5%	4,8%	
Padua series	415	184	300	5%	21%	6
Analysis		181 (130-282)	224 (50-533)	2% (0-5%)	9% (1-21%)	2 (1-6)

Perioperative complications according to Clavien



Novara G. et al. Eur Urol (in press)

Device failure and adverse events related to the da Vinci surgical system

Author	Study design	System failure (%)	Adverse events
Patel, 2007	Single Center	0.2%	
Borden, 2007	Single Center	2.6%	
Lavery, 2008	Multi-institutional	0.4%	
Andonian, 2008	MAUDE 2000-2007	0.4%	4.8%

MAUDE: Manufacturer and User Facility Device Experience

Patients should be counseled preoperatively about this possibility and alternatives should be discussed

Murphy D. et al. Eur Urol (in press)

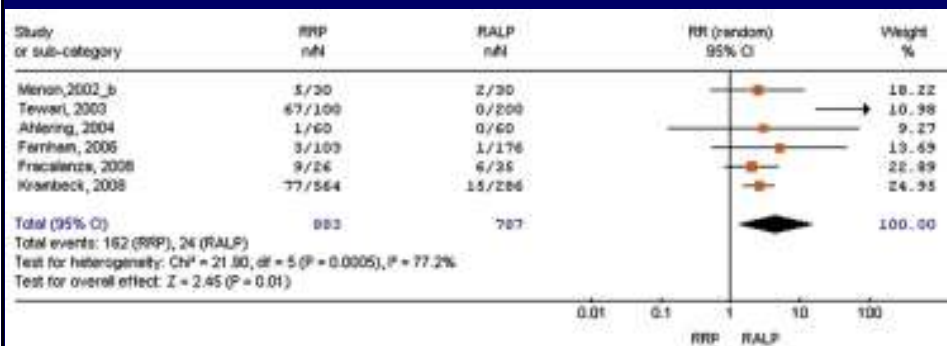
Operative time and blood loss: RRP Vs RALP

Cumulative analyses of operative time and blood loss were not possible

Level	Study	No. of cases, type	Median/mean operative time, min	Median/mean blood loss, ml	Transfusion rate, %
2b	Menon et al [45]	30 RRP	138*	970	17
		30 RALP	288	329*	7*
	Tewari et al [46]	100 RRP	163	930	67
		200 RALP	160	153*	0*
	Farnham et al [48]	103 RRP	-	664	12.9
		176 RALP	-	191*	0.5*
	Nelson et al [50]	174 RRP	-	-	-
		629 RALP	-	-	-
	Fracalanza et al [51]	26 RRP	127*	500	34
		35 RALP	195	300*	17*
Krambeck et al [53]	564 RRP	204	-	13.1	
	286 RALP	236	-	5.1	
	60 RRP	214	438	2	
4	Ahlering et al [54]	60 RRP	214	438	2
		60 RALP	231	109*	0

Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

Transfusion rate: RRP Vs RALP



Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

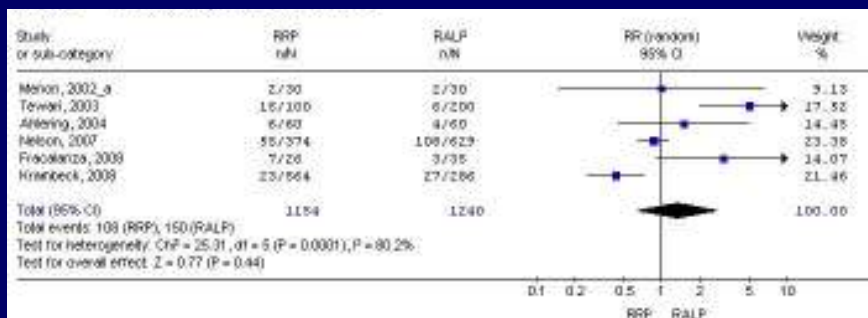
Catheterisation and in-hospital stay : RRP Vs RALP

Cumulative analyses of catheterisation time an in-hospital stay were not possible

Level	Study	No. of cases, type	Catheterisation duration, d	In-hospital stay, d	Overall complication rate, %
2b	Menon et al [45]	30 RRP	14	56 h	6
		30 RALP	11	36 h*	6
	Tewari et al [46]	100 RRP	15.8	3.5	15
		200 RALP	7*	1.2*	3*
	Farnham et al [48]	103 RRP	-	-	-
		176 RALP	-	-	-
	Nelson et al [50]	374 RRP	-	1.23	15
		629 RALP	-	1.17	17
	Fracalanza et al [51]	26 RRP	-	8	27
		35 RALP	-	5*	9
Kranbeck et al [53]	564 RRP	-	-	8	
	286 RALP	-	-	4.8	
4	Ahlering et al [54]	60 RRP	9	2	10
		60 RALP	7	1*	6.7

Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

Overall complication rate: RRP Vs RALP



Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

RALP Vs RRP: non randomized, comparative, prospective study

Variables	RALP	RRP	P value
Cases	103	105	
Operative time	185	135	< 0.001
Blood loss	300	500	< 0.001
Transfusion rate	2%	14%	< 0.001
Complications	10%	13%	0.85

Ficarra V et al BJU Inter 2009; 104: 534-539

Outcomes evaluated

- **Intraoperative and perioperative**
 - tissue damage, operative time, blood loss, transfusion rate, in-hospital stay, catheter time, overall complication rates
- **Functional**
 - anastomotic stricture, urinary continence and potency recovery
- **Oncological**
 - positive surgical margins, bDFS, OS and CSS

RALP: Anastomotic strictures

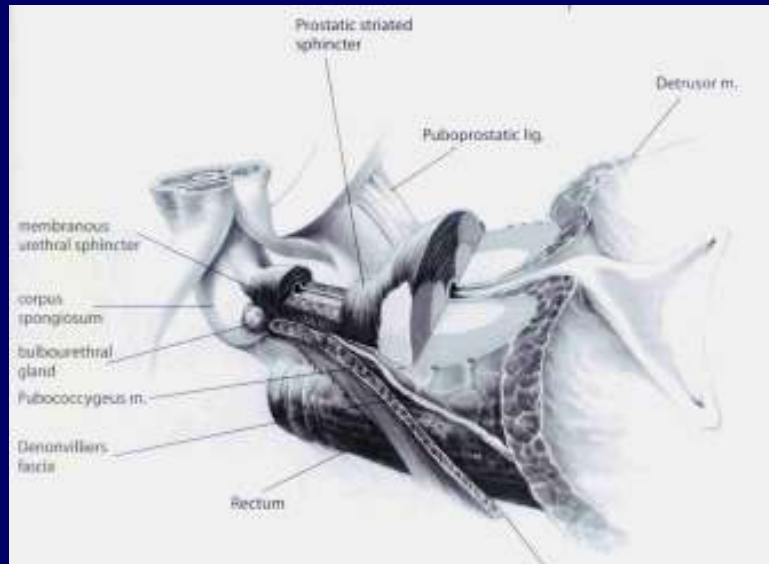
Authors	Cases	Strictures (%)
Costello, 2005	122	4.2
Joseph, 2006	325	2.1
Zorn, 2007	300	1.4
Krambeck, 2009	286	4.6
Artibani, 2009	416	3

Anastomotic strictures: RALP Vs RRP or LRP

Procedural types	Level of evidence	Study	No. of cases, type	Anastomosis strictures, %
RRP vs RALP	3b	Krambeck et al [53]	564 RRP	4.6
			286 RALP	1.2
LRP vs RALP	3b	Hu et al [58]	358 LRP	1.4
			322 RALP	0.3
	4	Joseph et al [57]	50 LRP	2
			50 RALP	6

Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

Anatomy of the Sphincter



Urinary continence recovery after RALP

Authors	Origin	Cases	Follow-up	Definition	Continence (%)
Chatelineau, 2004	Europe	105	6 months	0 pads	70%
Costello, 2005	Australia	122	6 months	0-1 pads	82%
Joseph, 2006	USA	325	6 months	0 pads	96%
Menon, 2007	USA	2652	12 months	0 pads	84%
Mottrie, 2007	Europe	184	6 months	0 pads	85%
Patel, 2007	USA	500	12 months	0 pads	97%
Zorn, 2007	USA	300	12 months	0 pads	90%
Badani, 2007	USA	1110	12 months	0 pads	93%
Krambeck, 2009	USA	286	12 months	0 pads	92%
Padua series	Europe	248	12 months	No leak	94%
Analysis					92% (84-97%)

Urinary continence: RALP Vs RRP

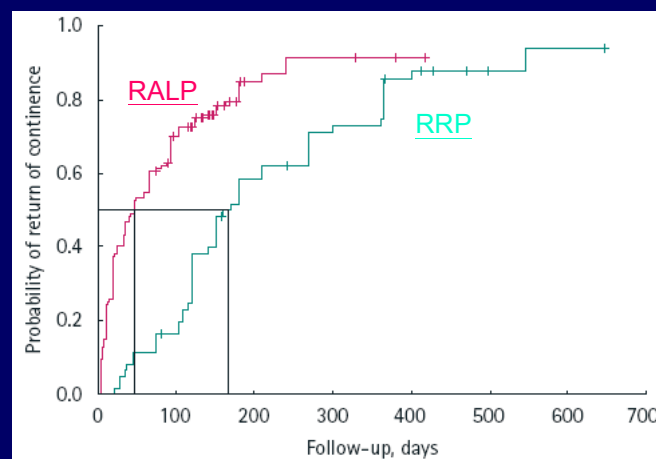
Procedural types	Level of evidence	Study	No. of cases, type	Method	Criterion	6 mo, %	12 mo, %	24 mo, %
RRP vs RALP	B	Tewari et al [44]	100 RRP 200 RALP	Interview	No pad	100 d* 44 d*	-	-
	B	Kramerloch et al [33]	584 RRP 286 RALP	Nonvalidated questionnaire	No leak	-	81.7	91.8
	A	Ahlering et al [36]	80 RRP 60 RALP	Nonvalidated questionnaire	No pad	73	-	-
LRP vs RALP	A	Joseph et al [37]	50 LRP 50 RALP	Physician	No pad	81	-	90

* p < 0.05

Cumulative analysis was not possible because the studies reported the results in different formats.

Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

Urinary continence: RALP Vs RRP



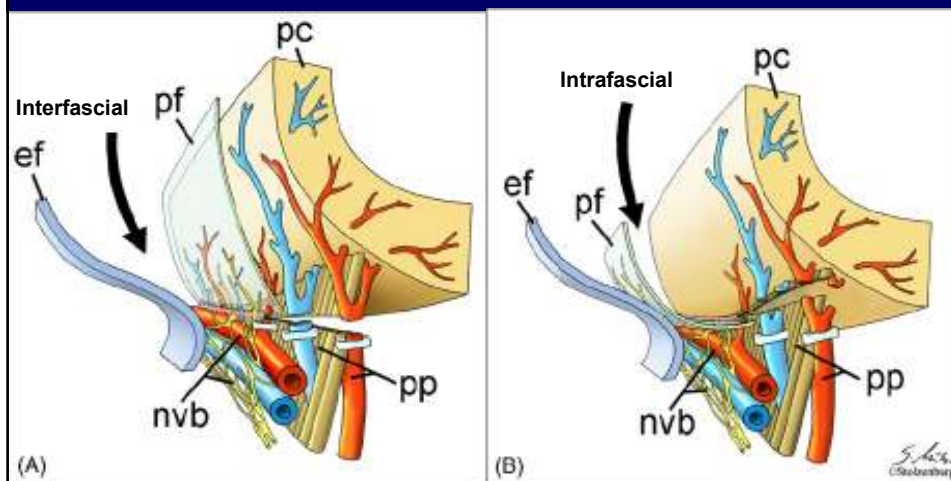
Tewari et al BJU Inter 2003; 92: 205-210.

Urinary continence: RALP Vs RRP

Definition	RRP	RALP	p value
Cases	105	103	
Early continence	41%	69%	<0.001
Time to continence	75 days	25 days	< 0.001
12-month continence	88%	97%	0.01

Ficarra V et al BJU Inter 2009; 104: 534-539

Interfascial and intrafascial nerve-sparing radical prostatectomy



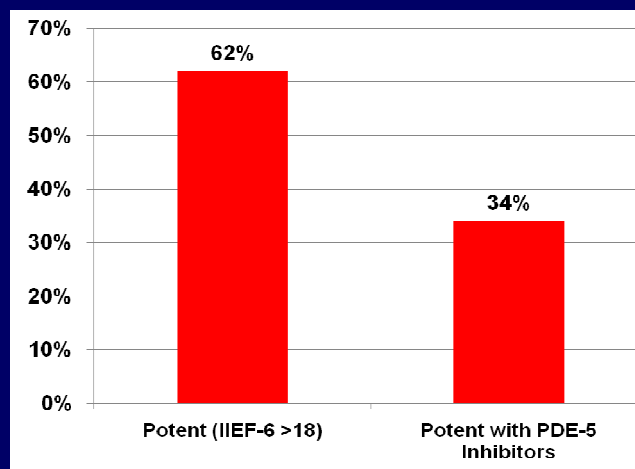
Stolzenburg JU et al, Eur Urol 2007;51(3):629-39

Potency recovery after RALP

Authors	Origin	Cases	Follow-up	Definition	Potency (%)
Chatelineau, 2004	Europe	105	12 months	Intercourse	79%
Joseph, 2006	USA	325	12 months	Intercourse	81%
Menon, 2007	USA	2652	12 months	Intercourse	70%
			24 months	Intercourse	86%
			48 months	Intercourse	100%
Motrie, 2007	Europe	184	6 months	Intercourse	70%
Patel, 2007	USA	500	12 months	Intercourse	78%
Zorn, 2007	USA	300	12 months	Intercourse	80%
Badani, 2007	USA	1110	12 months	Intercourse	79%
Krambeck, 2009	USA	286	12 months	Intercourse	70%
Padua series	Europe	216	12 months	Intercourse	62%
Analysis					76% (62-80%)

12-month potency recovery after RALP

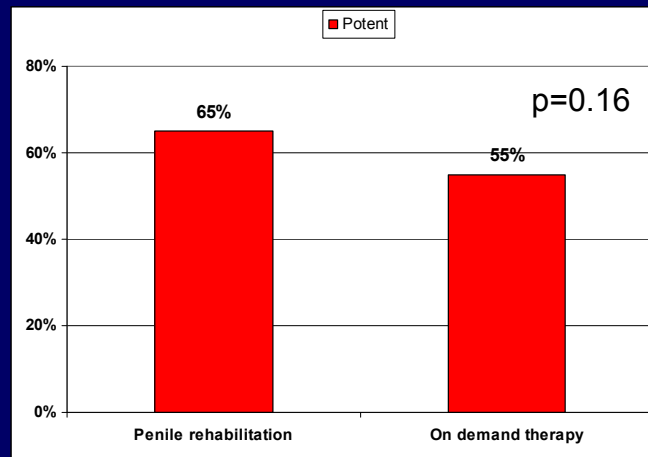
Median Follow-up 14 months (IQR 12 – 15)



Novara G, Ficarra V. et al J Sex Med (in press)

12-month potency recovery after RALP

Median Follow-up 14 months (IQR 12 – 15)



Novara G, Ficarra V. et al J Sex Med (in press)

12-month potency recovery after RALP

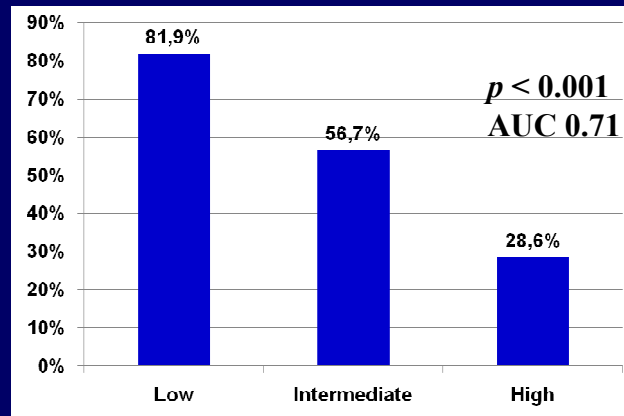
Median Follow-up 14 months (IQR 12 – 15)

Multivariate analysis

Variables	Caterories	HR	95% CI	p value
Age (yrs)	≤60 VS > 60	2.828	1.591 - 5.027	< 0.001
Charlson score	0 VS ≥1	2.992	1.358 - 6.588	0,007
Baseline IIEF-5 score		0,843	0.799 - 0.889	< 0.001

Novara G, Ficarra V. et al J Sex Med (in press)

Selection criteria: the San Raffaele risk group external validation



Low risk: age ≤ 65 years, baseline IIEF-6 > 21 , Charlson score ≤ 1
 Intermediate risk: age 66–69 years, IIEF-6 score 11–21, Charlson score ≤ 1
 High risk: age ≥ 70 , baseline IIEF-6 score ≤ 10 , Charlson score ≥ 2

Novara G, Ficarra V. et al J Sex Med (in press)

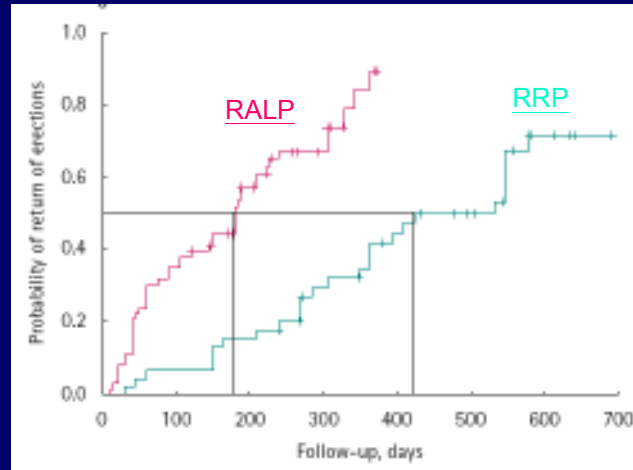
Potency recovery: comparative studies

Procedural types	Level of evidence	Study	No. of cases, type	Method	Criteria	3 mo, %	12 mo, %	24 mo, %
RRP vs LRP	2b	Anagnostou et al [23]	70 RRP	Nonvalidated questionnaire	Erection sufficient for intercourse	–	73	–
			130 LRP	IIEF	Erection sufficient for intercourse	33.3	–	–
		Sourragiers et al [25]	26 LRP	Nonvalidated questionnaire	Erection sufficient for intercourse	–	–	54.5
			101 LRP	Interview	Presence of erection	440 d*	–	–
RRP vs BARP	2b	Toward et al [46]	100 RRP	Interview	Intercourse	200 d†	–	–
			100 BARP	Interview	Intercourse	200 d†	–	–
			RRP 504	Nonvalidated questionnaire	Intercourse	–	62.8	–
LRP vs BARP	4	Joseph et al [57]	50 LRP	IIEF	Erection sufficient for intercourse	36	–	–
			50 BARP	IIEF	Erection sufficient for intercourse	46	–	–

Cumulative analyses were not possible because the studies reported the results in different formats.

Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

Potency recovery: RALP Vs RRP



Tewari et al BJU Inter 2003; 92: 205-210.

Potency recovery: RALP Vs RRP

Definition	RRP	RALP	p value
Cases	105	103	
Overall Potency recovery	32%	61%	< 0.001
Potency (Bilateral NS)	49%	81%	< 0.001
Potency bilat NS + < 65 years)	59%	84%	< 0.001
Time to reach potency	7 months	3 months	< 0.001

Ficarra V et al BJU Inter 2009; 104: 534-539

Outcomes evaluated

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 - positive surgical margins, bDFS, OS and CSS

Positive Surgical Margin rates

- PSMs are an independent risk factor for bDFS, local recurrence and need for salvage therapy and may used as a surrogate for good surgical technique
- Tumor biology
 - extraprostatic extension
 - high-grade tumour
- Surgical factors
 - type of procedure and surgical technique
 - surgeon volume and experience
- Different pathologic protocols used to process the prostatectomy specimen

Positive Surgical Margin rates after RALP

Authors	Origin	Cases	Overall PSM (%)	pT2 PSM (%)	pT3 PSM (%)
Chatelineau, 2004	Europe	105	22%	12%	43%
Costello, 2005	Australia	122	16%		
Atug, 2006	USA	140	26%	18%	
Joseph, 2006	USA	325	13%	10%	27-37%
Van Appledorn, 2006	USA	150	17%		
Borin, 2007	USA	400	12,5%	6%	19-40%
Menon, 2007	USA	2652	13%	1,5%	
Mottrie, 2007	Europe	184	16%	2,5%	
Patel, 2007	USA	500	9,4%	2,5%	23-46%
Zorn, 2007	USA	300	21%	15%	52%
Badani, 2007	USA	2766	13%		
Jaffe, 2008	Europe	278	20%		
Ficarra, 2009	Europe	322	29%	10%	57%
Analysis			18% (9-29%)	9% (1,5-18%)	19-57%

Positive Surgical Margin rates after RALP

Variables	Categories	HR	95% CI	P value
Clinical Model				
Prostatic volume (TRUS)	≤ 40 vs > 40 cc	0.420	0.240 – 0.734	0.002
Clinical Stage T	cT1 vs cT2	2.217	1.229 – 3.998	0.008
Bioptical Gleason Score				0.316
-7 vs ≤ 6		1.266	0.650 – 2.465	0.488
-8-10 vs ≤ 6		2.131	0.758 – 5.991	0.152
Pathological Model				
Prostate volume	≤ 40 vs > 40 cc	0.621	0.330 – 1.165	0.138
Pathological stage T	pT2 vs pT3-4	11.852	6.172 – 22.757	<0.001
Perineural invasion	Absent vs present	1.370	0.591 – 3.177	0.463
Lymphatic invasion	Absent vs present	1.023	0.415 – 2.524	0.961
Gleason Score				0.717
-7 vs ≤ 6		0.911	0.446 – 1.861	0.798
-8-10 vs ≤ 6		0.649	0.222 – 1.891	0.428

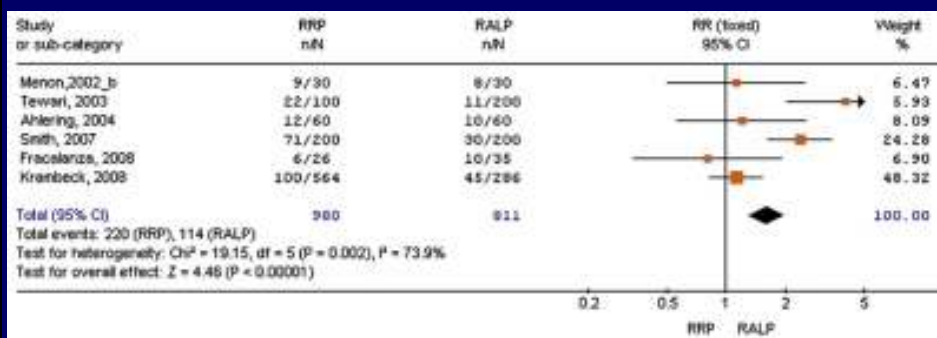
Ficarra V. et al. J Urol 2009 (in press)

Positive Surgical Margin rates after RALP in organ-confined disease

Variables	Negative margins (n = 177)	Overall PSM (n = 21)	Analisi univariata P value	Analisi multivariata
Prostate Volume (cc)			0.04	-
- ≤ 40				
- > 40	95 (85.6%)	16 (14.4%)		
Perineural invasion			0.01	HR 4.1; p=0.02
- Absent	73 (96.1%)	3 (3.9%)		
- Present	104 (85.2%)	18 (14.8%)		

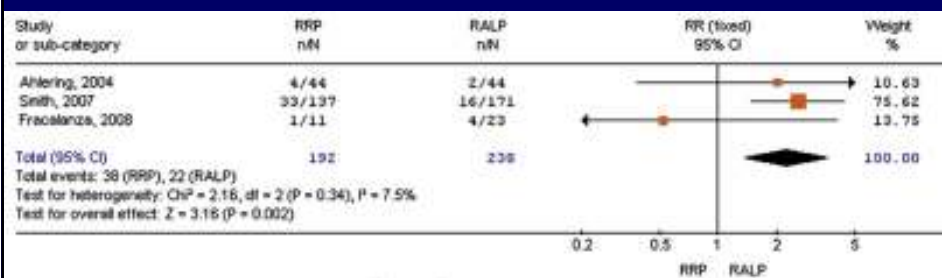
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Positive surgical margins: RALP Vs RRP



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Positive surgical margins (pT2): RALP Vs RRP



- millimetric surgery ?
- selection bias of patients ?
- few patients analysed ?

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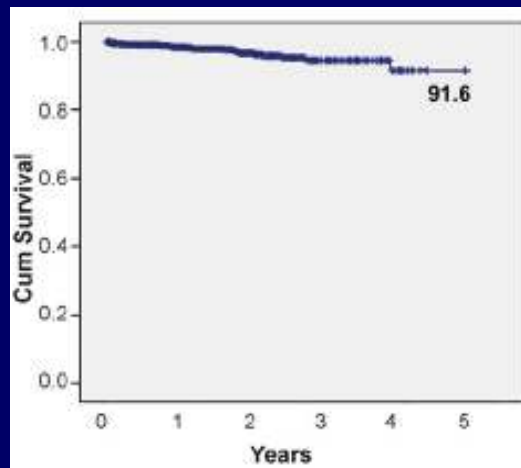
Salvage therapy after LRP/RALP

Outcomes	MRP	RRP	MRP vs RRP, Ratio (95% Confidence Interval) ^a	P Value
Length of stay, median (IQR) ^b	2 (1-2)	3 (2-4)	0.67 (0.58-0.72)	<.001
Heterologous blood transfusion, %	2.7	20.8	0.11 (0.06-0.17)	<.001
30-Day complications, %				
Overall	22.2	23.2	0.95 (0.77-1.16)	.98
Cardiac	2.4	2.9	0.81 (0.49-1.33)	.37
Respiratory	4.3	6.6	0.63 (0.46-0.87)	.004
Genitourinary	4.7	2.1	2.28 (1.61-3.22)	.001
Wound	2	1.9	1.05 (0.61-1.82)	.86
Vascular	3.4	3.9	0.85 (0.55-1.35)	.50
Miscellaneous medical	10	8.5	1.19 (0.89-1.6)	.26
Miscellaneous surgical	4.3	5.6	0.75 (0.56-0.99)	.03
Death	0.1	0.2	0.31 (0.07-1.28)	.05
Anastomotic stricture, % ^c	5.8	14.0	0.39 (0.28-0.52)	<.001
Incontinence per 100 person-years ^d				
Diagnosis	15.9	12.2	1.3 (1.05-1.61)	.02
Procedures	7.8	8.9	0.87 (0.69-1.1)	.24
Erectile dysfunction per 100 person-years ^d				
Diagnosis	26.8	19.2	1.40 (1.14-1.72)	.009
Procedure	2.3	2.2	1.05 (0.74-1.51)	.78
Additional cancer therapy per 100 person-years				
Overall	8.2	6.9	1.19 (0.84-1.69)	.35
Radiation	5.1	4.9	1.05 (0.84-1.32)	.67
Hormone	5.3	3.7	1.42 (0.88-2.32)	.21
Death during the study period per 100 person-years	0.8	0.9	0.91 (0.53-1.57)	.72

Hu JC. et al. JAMA 2009; 302: 1557-1564

Oncological Results: bDFS after RALP

1.142 patients undergoing VIP



Menon M et al Eur Urol 2007; 51: 648-58

Oncological Results: bDFS

- Further studies on primary oncological endpoints are necessary
- Confirms on large series with strong endpoints and adequate follow-up are needed

Potential disadvantages of RALP: Costs

- Installation cost is approximately:
Euro 1.8 million
- Maintenance costs about:
Euro 100,000/year
- Robotic instrument costs about:
Euro 1.500/case
- Lack of competitor in this area has contributed to costs remaining prohibitively high for many hospitals

Potential disadvantages of RALP: Costs

- To date, cost equivalence with RRP can be achieved only at higher volume centres
- An institution must perform about 75 cases per year with an average operative time of 3 h per case to be cost effective in the United States.

Ficarra V. et al. Eur Urol 2009; 55: 1037-1063

RALP and more complex cases

- Obese patients
- Previous TURP / Median lobe
- Large size prostates
- Salvage RALP after radiation therapy or cryotherapy or HIFU

Murphy D. et al. Eur Urol (in press)

RALP and more complex cases

- More complex cases should be avoided within the early robotic experience of any centre
- Such cases are equally challenging with attendant morbidity when performed by an open or conventional laparoscopic approach
- Patients must be informed regarding the increased morbidity and should understand that RALP does not negate the increased likelihood of morbidity

Murphy D. et al. Eur Urol (in press)

Conclusions

- The urologic community missed the windows of opportunity to test novel approaches within an evidence-based frame.
- RALP is the evolution of traditional laparoscopic surgery and currently is considered as the most relevant alternative to open surgery

Conclusions

- RALP is followed by significantly lower blood loss and transfusion rates and have all traditional advantages of a minimally invasive procedure
- Data from the literature seems to prove superiority of RALP in terms of functional outcomes with similar early oncological outcomes
- Further studies on primary oncological endpoints are necessary