

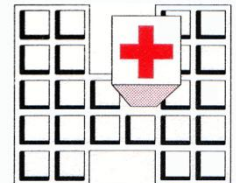
Carcinoma della prostata: quali novità per il 2015 ?



Negrar, 1 aprile 2015

IL TRATTAMENTO CHIRURGICO DELLA NEOPLASIA PROSTATICA LOCALMENTE AVANZATA

mauro pastorello



IL TRATTAMENTO CHIRURGICO DELLA NEOPLASIA PROSTATICA LOCALMENTE AVANZATA

IL TRATTAMENTO CHIRURGICO

The surgical treatment of prostate cancer (PCa) consists of radical prostatectomy (RP). This involves removal of the entire prostate gland between the urethra and bladder, and resection of both seminal vesicles, along with sufficient surrounding tissue to obtain a negative margin. Often, this procedure is accompanied by bilateral pelvic lymph node dissection.

NEOPLASIA PROSTATICA LOCALMENTE AVANZATA

Locally advanced prostate cancer:

cT3a	No :	High Risk
cT3b	No :	Very High Risk
cT4	No:	Very High Risk

correva l'anno 1981

a Genova

Progetto Obiettivo Nazionale per il Carcinoma Prostatico
«P.O.N.CA.P.»

PROTOCOLLO OBIETTIVO NAZIONALE PER IL CARCINOMA PROSTATICO
(P.O.N.CA.P.)

COORDINATORI: Prof. L. Giuliani (Genova)

Prof. L. Santi (Genova)

SEGRETERIA: Dott. F. Boccardo (Genova)

**IL
CARCINOMA
DELLA
PROSTATA**

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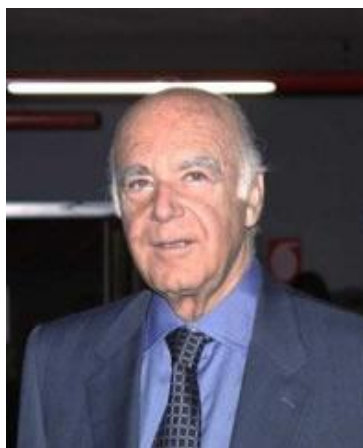
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Progetto Obiettivo Nazionale per il Carcinoma Prostatico
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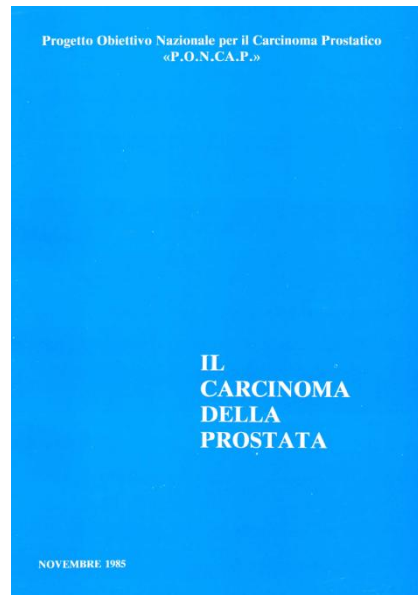
IL CARCINOMA DELLA PROSTATA

NOVEMBRE 1985

correva l'anno 1981

Al San Martino, a Santa Margherita ...

incontri di studio multidisciplinare tra oncologi, urologi, radioterapisti, farmacologi, ... per una elaborazione condivisa di protocolli diagnostici terapeutici e di follow-up sul carcinoma prostatico



correva l'anno 1981
sono trascorsi 34 aa

A quel tempo ... **epidemiologia**

La maggior parte dei casi, viene diagnosticata in stadio localmente avanzato e/o con metastasi a distanza: $T_3 - T_4$, N_{1-4} , M_{0-1} (Stadi C e D).
La tabella illustra la frequenza degli stadi avanzati al momento della diagnosi.

TABELLA N.1: Correlazione fra stadio e frequenza alla diagnosi

Estensione della neoplasia	Frequenza alla diagnosi
- Tumore non palpabile	5 - 10%
- Tumore intracapsulare	5 - 10%
- Tumore extracapsulare, assenza di metastasi clin. apprezzabili	40 - 45%
- Metastasi linfatiche o ematogene	30 - 35%




correva l'anno 1981

A quel tempo indicazioni terapeutiche

6.2 Prostatovesicuclectomia radicale

6.2.1 Indicazioni



In questo protocollo di base si è convenuto che la prostatovesicuclectomia sia oggi formalmente indicata solo per gli stadi a sviluppo realmente ed esclusivamente intraprostatico, comunque senza interessamento delle vescicole seminali. Una estensione dell'indicazione a tali casi è da considerarsi opzionale.


correva l'anno 1981

A quel tempo ...

..... In pratica, ad eccezione delle forme iniziali del tutto intraprostatiche e che sono estremamente rare all'osservazione clinica (meno del 20% dei casi), la terapia chirurgica si è rivelata troppo spesso insufficiente ai fini di una terapia veramente radicale.

correva l'anno 1981

A quel tempo ... **tecniche chirurgiche**

- 
- * exeresi dall'alto in basso con sezione e allacciatura preventiva e progressiva dei peduncoli vascolari nel corso dell'isolamento prostatico, in quanto è da ritenere che ciò diminuisca il rischio della diffusione ematogena e linfatica intraoperatoria;
 - * isolamento del blocco prostato-vescicolo-deferenziale su di un piano rigorosamente extra-aponeurotico, rispetto alla fascia di Denonvilliers e alle aponevrosi prostatiche laterali che devono essere comprese nella exeresi;
 - * sezione delle lamine di Delbet (porzione prostato-rettale dei ligamenti longitudinali laterali) del tutto rasente alla parete del retto;

Dopo trentaquattro anni

Progetto Obiettivo Nazionale per il Carcinoma Prostatico
«P.O.N.C.A.P.»

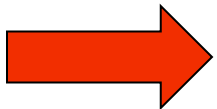
IL
CARCINOMA
DELLA
PROSTATA

NOVEMBRE 1985

- modificazione dei riscontri epidemiologici
- rilevante affinamento della diagnostica clinica e patologica

Dopo trentaquattro anni

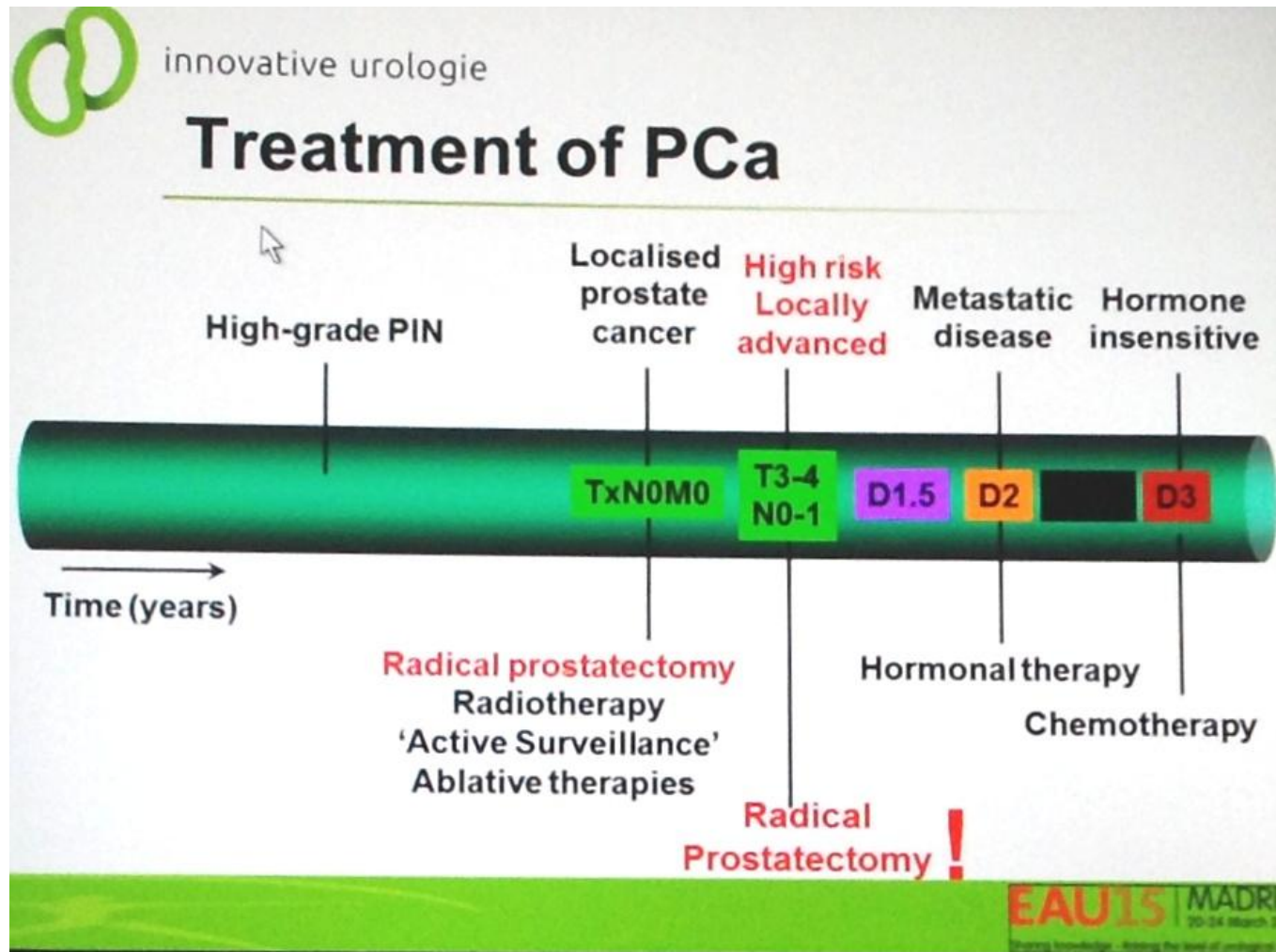
- modificazione dei riscontri epidemiologici
- rilevante affinamento della diagnostica clinica e patologica
- **evoluzione delle conoscenze in tema di anatomia chirurgica**
- **perfezionamento delle tecniche operative**
- **introduzione di supporti innovativi (dalla Laparoscopia al Robot)**



nuove prospettive terapeutiche

nuove prospettive terapeutiche

Hruby S, Janetschek G J Urol 2015



Ed oggi, nel 2015

**precocità diagnostica con
downstaging e downgrading ..**
(e conseguente alto rischio di overtreatment)

**ma ancora circa il 18% di paz diagnosticati in
avanzato stadio clinico**

O. Akre, et Al. *Eur Urol*, 60, 554–563, 2011.

Guidelines on Prostate Cancer

N. Mottet (chair), P.J. Bastian, J. Bellmunt,
R.C.N. van den Bergh, M. Bolla, N.J. van Casteren, P. Cornford,
S. Joniau, M.D. Mason, V. Matveev, T.H. van der Kwast,
H. van der Poel, O. Rouvière, T. Wiegel

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The widespread use of PSA testing has led to a significant migration in stage and grade of PCa with > 90% of men in the current era diagnosed with clinically localized disease (21). Despite the trends towards lower-risk PCa, 20-35% of patients with newly diagnosed PCa are still classified as high-risk based on either PSA > 20 ng/mL, GS \geq 8, or an advanced clinical stage (37). Patients classified with high-risk PCa are at an increased

21. Makarov DV, Trock BJ, Humphreys EB, et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. *Urology* 2007 Jun;69(6):1095-101.
37. Shao YH, Demissie K, Shih W, et al. Contemporary risk profile of prostate cancer in the United States. *J Natl Cancer Inst* 2009 Sep;101(18):1280-3.

Locally Advanced Prostate Cancer

Locally advanced prostate cancer is defined as a tumor that has extended clinically beyond the prostatic capsule, with invasion of the pericapsular tissue, apex, bladder neck or seminal vesicle, but without lymph node involvement or distant metastasis .

Boccon-Gobod L, Bertaccini A, Bono A, Dev Sarmah B, Holtl W, Mottet N *et al*: Management of locally advanced prostate cancer: a European consensus. *Int J Clin Pract* 57(3): 187-194, 2003.

It is estimated that 12% to 15% of prostate cancers are stage T3

Sullivan LD: Controversies in the management of clinical T3 carcinoma of the prostate. *Can J Urol* 1(3): 39-48, 1994.
van den Ouden D and Schroeder FH: Management of locally advanced prostate cancer. *World J Urol* 18: 194-203, 2000.

Overstaging or understaging of early prostatic cancer are common.

The correct staging of clinical T3 disease is even difficult, and both overstaging pT2 and understaging pT4 or pN+ are common.

Morgan WR, Bergstralh EJ and Zincke H: Long-term evaluation of radical prostatectomy as treatment in clinical stage C (T3) prostate cancer. *Urology* 41(2): 113-120, 1993.
Ward JF, Slezak JM, Blute ML, Bergstralh EJ and Zincke H: Radical prostatectomy for clinically advanced (cT3) prostate cancer since the advent of PSA testing: 15-year outcome. *BJU Int* 95(6): 751-756, 2005.

Locally Advanced Prostate Cancer

The overstaging of T3 prostate cancer occurs in about 13% to 27% of cases, meaning that these patients, who have organ-confined disease, can be cured with complete removal of the gland.

2006

TABLE 4: The percentage of overstaging and understaging in clinical locally advanced T3 prostate cancer.

Authors	pT2	pT4/N+
Van Poppel et al. [28]	13%	8%/11%
Van den Ouden et al. [29]	15%	3.4%/15.6%
Lerner et al. [16]	17%	—/33%
Morgan et al. [32]	22%	42% (stage D1)
Ward et al. [33]	27%	—/27%

Guidelines on Prostate Cancer

N. Mottet (chair), P.J. Bastian, J. Bellmunt, R.C.N. van den Bergh, M. Bolla, N.J. van Casteren, P. Cornford, S. Joniau, M.D. Mason, V. Matveev, T.H. van der Kwast, H. van der Poel, O. Rouvière, T. Wiegel



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TABLE 3: Comparison between positive surgical margins and pathologic staging after radical retropubic prostatectomy.

	Positive surgical margins
All patients	13.7%
pT2	4.8%
pT3a	17.4%
pT3b	18.2%
pT4	50%

Non vi è dubbio che la prostatectomia radicale (RP) sia il trattamento di elezione per il Ca Prost (PCa) localizzato

Currently, RP is the only treatment for localized PCa to show a benefit for OS and cancer-specific survival (CSS), compared with conservative management, as shown in one prospective randomized trial (5). After a follow-up of 15 years, the SPCG-4 trial showed that RP was associated with a reduction of all-cause mortality: relative risk (RR) = 0.75 (0.61-0.92).

Surgical expertise has decreased the complication rates of RP and improved cancer cure (6-10). If performed by an experienced surgeon, the patient's subsequent QoL should be satisfactory. Lower rates of positive surgical margins for high-volume surgeons suggest that experience and careful attention to surgical details, adjusted for the characteristics of the cancer being treated, can decrease positive surgical margin rates and improve cancer control with RP (11,12).

-
5. Bill-Axelsson A, Holmberg L, Ruutu M, et al. Radical prostatectomy versus watchful waiting in early prostate cancer. N Engl J Med 2011 May;364(18):1708-17.
<http://www.ncbi.nlm.nih.gov/pubmed/21542742>
 6. Wilt TJ, Brawer MK, Jones KM, et al. Radical prostatectomy versus observation for localized prostate cancer. N Engl J Med 2012 Jul 19;367(3):203-13.
<http://www.ncbi.nlm.nih.gov/pubmed/22808955>
 11. Eastham JA, Kattan MW, Riedel E, et al. Variations among individual surgeons in the rate of positive surgical margins in radical prostatectomy specimens. J Urol 2003 Dec;170(6 Pt 1):2292-5.
<http://www.ncbi.nlm.nih.gov/pubmed/14634399>
 12. Vickers AJ, Savage CJ, Hruza M, et al. The surgical learning curve for laparoscopic radical prostatectomy: a retrospective cohort study. Lancet Oncol 2009 May;10(5):475-80.
<http://www.ncbi.nlm.nih.gov/pubmed/19342300>

PCa localizzato:

Table 9.1: Oncological results of radical prostatectomy in organ-confined disease

Reference	Prospective/ retrospective	n	Year of RP	Median follow-up (months)	10-year PSA-free survival (%)	10-year CCS (%)	15-year CCS (%)	25-year CCS (%)
Bill-Axelsson et al. (2011) (5)	Prospective	347 randomized to RP	1989-99	153			85	
Wilt et al. (2012) (6)	Prospective	364 randomized to RP	1994- 2002	120		95.6 (12- year)		
Porter et al. (2006) (31)	Retrospective	752	1954-94	137	71	96	91	82
Isbarn et al. (2009) (32)	Retrospective	436	1992-97	122	60	94		
Han et al. (2001) (33)	Retrospective	2404	1982-99	75	74	96	90	
Roehl et al. (2004) (34)	Retrospective	3478	1983- 2003	65	68	97		
Hull et al. (2002) (35)	Retrospective	1000	1983-98	53	75	98		
Stephenson et al. (36)	Retrospective	6398	1987- 2005	48			88	

CCS = cancer-specific survival; n = number of patients; PSA = prostate-specific antigen; RP = radical prostatectomy.

e nel PCa avanzato? e nel Pca ad alto rischio?

9.4.1 *Locally advanced prostate cancer: cT3a*

Guidelines on Prostate Cancer

R. Hutter, J. Bostian, J. Behre, R.C.N. van den Bergh, M. Bolla, N.J. van Cuteren, P. Cornford, S. Jankov, M.D. Mason, V. Matveev, T.H. van der Kwast, H. van der Poel, O. Razvi, T. Wiegel

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Stage T3a cancer is defined as cancer that has perforated the prostate capsule. In the past, locally advanced PCa was seen in about 40% of all clinically diagnosed tumours. This figure is lower today; nevertheless its management remains controversial.

1990

The surgical treatment of clinical stage T3 PCa has traditionally been discouraged (39), mainly because patients have an increased risk of positive surgical margins and lymph node metastases and/or distant relapse (40,41).

40. Fallon B, Williams RD. Current options in the management of clinical stage C prostatic carcinoma. *Urol Clin North Am* 1990 Nov;17(4):853-66.
<http://www.ncbi.nlm.nih.gov/pubmed/2219582>
41. Boccon-Gibod L, Bertaccini A, Bono AV, et al. Management of locally advanced prostate cancer: a European Consensus. *Int J Clin Pract* 2003 Apr;57(3):187-94.
<http://www.ncbi.nlm.nih.gov/pubmed/12723722>

e nel PCa avanzato? e nel Pca ad alto rischio?

9.4 High-risk localized and locally advanced prostate cancer: cT3a or Gleason score 8-10 or prostate-specific antigen > 20 ng/mL

There is no consensus regarding the optimal treatment of men with high-risk PCa. Decisions on whether to elect surgery as local therapy should be based on the best available clinical evidence. **Provided that the tumour is not fixed to the pelvic wall, or that there is no invasion of the urethral sphincter, RP is a reasonable first step in selected patients with a low tumour volume.**

Extended LND should be performed in all high-risk PCa cases, because the estimated risk for positive lymph nodes is 15-40% (25). Limited LND should no longer be performed, because it misses at least half the nodes involved.

25. Briganti A, Larcher A, Abdollah F, et al. Updated Nomogram Predicting Lymph Node Invasion in Patients with Prostate Cancer Undergoing Extended Pelvic Lymph Node Dissection: The Essential Importance of Percentage of Positive Cores. Eur Urol 2012 Mar;61(3):480-7.

9.4.1 *Locally advanced prostate cancer: cT3a*

Several randomized studies of radiotherapy combined with ADT versus radiotherapy alone have shown a clear advantage for combination treatment but no trial has ever proven combined treatment to be superior to RP (42).

In recent years, there has been renewed interest in surgery for locally advanced PCa and several retrospective case series have been published. Although still controversial, it is increasingly evident that surgery has a place in treating locally advanced disease (43-45).

Overstaging of cT3 PCa is relatively frequent and occurs in 13-27% of cases. Patients with pT2 disease and those with specimen-confined pT3 disease have similarly good biochemical and clinical PFS (44,45). In 33.5-66% of patients, positive section margins are present, and 7.9-49% have positive lymph nodes (46). Thus, 56-78% of patients primarily treated by surgery eventually require adjuvant or salvage radiotherapy or HT (44,45).

42. Bolla M, Collette L, Blank L, et al. Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): a phase III randomised trial. *Lancet* 2002 Jul;360(9327):103-6.
<http://www.ncbi.nlm.nih.gov/pubmed/12126818>
43. Gerber GS, Thisted RA, Chodak GW, et al. Results of radical prostatectomy in men with locally advanced prostate cancer: multi-institutional pooled analysis. *Eur Urol* 1997;32(4):385-90.
<http://www.ncbi.nlm.nih.gov/pubmed/9412793>
44. Ward JF, Slezak JM, Blute ML, et al. Radical prostatectomy for clinically advanced (cT3) prostate cancer since the advent of prostate-specific antigen testing: 15-year outcome. *BJU Int* 2005 Apr;95(6): 751-6.
<http://www.ncbi.nlm.nih.gov/pubmed/15794776>
45. Hsu CY, Joniau S, Oyen R, et al. Outcome of surgery for clinical unilateral T3a prostate cancer: a single-institution experience. *Eur Urol* 2007 Jan;51(1):121-8;discussion 128-9.

Research Article

**Complications and Functional Results of Surgery for
Locally Advanced Prostate Cancer**

S. G. Joniau, A. A. Van Baelen, C. Y. Hsu, and H. P. Van Poppel

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Received 13 May 2011; Accepted 6 October 2011

Academic Editor: Paolo Gontero

2011

Records of 139 consecutive patients who underwent a radical prostatectomy (RP) for cT3 PCa with a mean follow-up of 8 years.

Our experience with 139 patients confirms the surgical feasibility of RP for cT3 PCa, showing **complication rates comparable with RP in organ-confined PCa and showing a **very low incidence of positive surgical margins** and associated failure of surgery. Improvement can be expected by further defining the patient population most suitable for surgery and by further optimising adjuvant treatments such as RT and HT.**

Continence rates were also comparable with those achieved after RP for localized PCa.

9.4.1 *Locally advanced prostate cancer: cT3a*

The problem remains the selection of patients before surgery. Nomograms, including PSA level, stage and Gleason score, can be useful in predicting the pathological stage of disease (21,46). In addition, nodal imaging with CT or MRI, and seminal vesicle imaging with MRI, or directed specific biopsies of the nodes or seminal vesicles can help to identify those patients unlikely to benefit from a surgical approach (47).

21. Makarov DV, Trock BJ, Humphreys EB, et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. *Urology* 2007 Jun;69(6):1095-101.
46. Joniau S, Hsu CY, Lerut E, et al. A pretreatment table for the prediction of final histopathology after radical prostatectomy in clinical unilateral T3a prostate cancer. *Eur Urol* 2007 Feb;51(2):388-96.
47. Van Poppel H, Ameye F, Oyen R, et al. Accuracy of combined computerized tomography and fine needle aspiration cytology in lymph node staging of localized prostatic carcinoma. *J Urol* 1994 May;151(5):1310-14.

9.4.1 *Locally advanced prostate cancer: cT3a*

Increased overall surgical experience must contribute to decreased operative morbidity and to improved functional results after RP for clinical T3 cancer (44,48). It has been shown that **continence can be preserved in most cases**, and in selected cases, **potency can also be preserved** (49).

48. Van Poppel H, Vekemans K, Da Pozzo L, et al. Radical prostatectomy for locally advanced prostate cancer: results of a feasibility study (EORTC 30001). *Eur J Cancer* 2006 May;42(8):1062-7.
49. Loeb S, Smith ND, Roehl KA, et al. Intermediate-term potency, continence, and survival outcomes of radical prostatectomy for clinically high-risk or locally advanced prostate cancer. *Urology* 2007 Jun;69(6):1170-5.

9.4.1 *Locally advanced prostate cancer: cT3a*

Recent studies demonstrate 5-, 10- and 15-year biochemical progression-free survival (BPFS) to range between 45-62%, 43-51% and 38-49%, respectively. RP may provide excellent tumour control in selected patients with cT3 disease, with 5-, 10- and 15-year CSS ranging between 90-99%, 85-92% and 62-84%, respectively.

Even though more than half of the patients received adjuvant HT and/or RT in most of the presented studies, the high CSS suggests that local cancer control remains especially important in men with locally advanced disease. Five- and 10-year OS ranged from 90-96% and 76-77%, respectively (Table 9.2). These survival rates surpass radiotherapy alone and similar to radiotherapy combined with adjuvant HT (42).

-
42. Bolla M, Collette L, Blank L, et al. Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): a phase III randomised trial. *Lancet* 2002 Jul;360(9327):103-6.

Table 9.2: Overall survival (OS) and cancer-specific survival (CSS) rates for high-risk localized and locally advanced PCa treated with RP as first treatment in a multimodal approach

Reference	n	Time span	OS			CSS			PSA-free survival		
			5-yr	10-yr	15-yr	5-yr	10-yr	15-yr	5-yr	10-yr	15-yr
cT3a											
Ward et al. (2005) (44)	841	1987-1997	90	76	53	95	90	79	58	43	38
Carver et al. (2006) (61)	176	1983-2003	-	-	-	94	85	76	48	44	-
Hsu et al. (2007) (45)	200	1987-2004	96	77	-	99	92	-	60	51	-
Freedland et al. (2007) (62)	62	1987-2003	-	-	-	98	91	84	62	49	49
Yossepowitch et al. (2008) (57)	243	1985-2005	-	-	-	96	89	-	-	-	-
Xylinas et al. (2009) (63)	100	1995-2005	-	-	-	90	-	-	45	-	-
Stephenson et al. (2009) (36)	254	1987-2005	-	-	-	-	85	62	-	-	-
Walz et al. (2010) (58)	293	1987-2005	-	-	-	-	-	-	52	44	-

CSS = cancer-specific survival; n = number of patients; PSA = prostate-specific antigen; RP = radical prostatectomy.

LA TERAPIA CHIRURGICA nel PCa localmente avanzato/"High Risk"

- il solo trattamento unimodale con realistiche possibilità di cura definitiva (ca 50%)

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- offre risultati funzionali sostanzialmente equivalenti alla P.R. dei pazienti con PCa organo-confinato (T1-T2)
- consente procedura "nerve-sparing" efficace sino al 64% dei casi (Briganti)

LA TERAPIA CHIRURGICA nel PCa localmente avanzato/"High Risk"

- risulta gravata, nel tempo, da minori complicanze rispetto alle terapie alternative multimodali oggi disponibili

rispetto alla RxT : dose escalated IMRT +
(long term) ADT in 100 of pts (Briganti, Eur Urol 2012)
rispetto alla ADT: CVD, diabetes, QoL,

**True Morbidity of
Multimodality Treatment**

Francesco Montorsi MD FRCS
Professor and Chair
Department of Urology
San Raffaele Hospital
Vita-Salute San Raffaele University
Milan, Italy



URI Urological
Research
Institute
Istituto di Ricerca Urologica

True morbidity of multimodality treatment: Conclusions

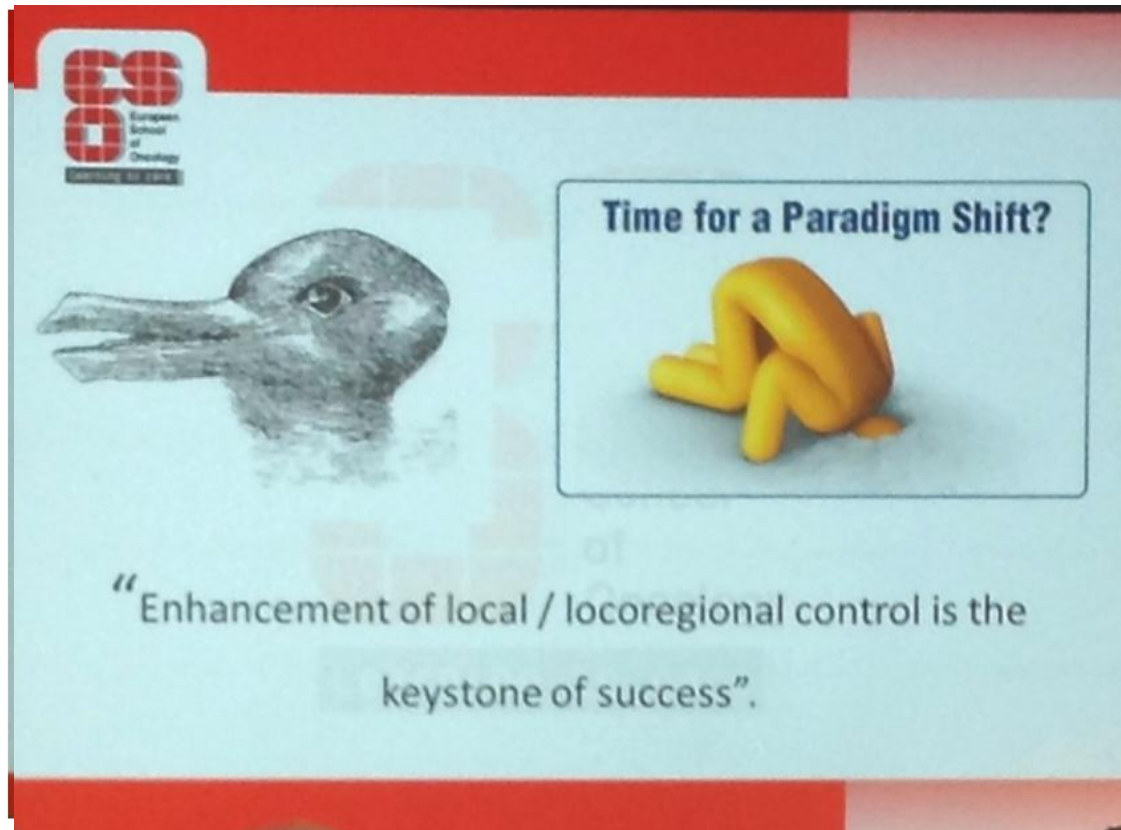
- The risk of short- and long-term side effects is **not negligible** among PCa patients receiving a multimodal approach
- Nonetheless, the harms of a multimodal approach **should not preclude its adoption when clinically indicated**
- **Baseline patient characteristics**, as well as the **type of treatment planned**, might help clinicians in the **identification of individuals at higher risk of morbidity**
- **Accurate patient selection is mandatory** in order to reduce the risk of short- and long-term adverse events associated with the administration of these treatment modalities


Montorsi et al 2015


The risk of short and long term side-effects is not negligible among PCa pts receiving an multimodal approach (RT + ADT).

Touijer:


**“ We have to put our heads together,
get out of our comfort zones and rethink the paradigm.”**



 European School of Oenology
Learning to Care



Time for a Paradigm Shift?



“Enhancement of local / locoregional control is the keystone of success”.

Counseling multidisciplinare pre-trattamento

- **sempre necessario**
- **indispensabile nel pt PCa LocAdv/HR (plurime variabili cliniche da ponderare)**
- **condizionato dai limiti attuali della diagnostica, in particolare dell'imaging, sia nei confronti del T che dell' N**

9.5.1 Locally advanced prostate cancer: cT3b-T4 N0

An US study has shown that 72 patients who underwent RP for cT4 disease had better survival than those who received HT or radiotherapy alone, and showed comparable survival to men who received radiotherapy plus HT (66).

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66. Johnstone PA, Ward KC, Goodman M, et al. Radical prostatectomy for clinical T4 prostate cancer. *Cancer* 2006 Jun;106:2603-9.
<http://www.ncbi.nlm.nih.gov/pubmed/16700037>

9.5.1 Locally advanced prostate cancer: cT3b-T4 N0

Another study has compared the outcomes of RP in very-high-risk PCa (T3-T4, N0-N1, N1, M1a) with those in localized PCa. The two groups did not differ significantly in surgical morbidity except for blood transfusion, operative time, and lymphoceles, which showed a higher rate in patients with advanced disease.

The OS and CSS at 7 years were 76.69% and 90.2% in the advanced disease group and 88.4% and 99.3% in the organ-confined disease group, respectively (65).

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65. Gontero P, Marchioro G, Pisani R, et al. Is radical prostatectomy feasible in all cases of locally advanced non-bone metastatic prostate cancer? Results of a single-institution study. *Eur Urol* 2007 Apr;51(4):922-9;discussion 929-30.

9.5.1 Locally advanced prostate cancer: cT3b-T4 N0

Another recent study assessed the outcomes of RP in 51 patients presenting with cT3b or cT4 PCa.

Intriguingly, overstaging in this group was still substantial, with approximately one-third of patients having either organ-confined disease (7.8%) or capsular perforation only (29.4%).

Overstaged patients were often cured by surgery alone: 35.3% of the whole group did not receive any form of (neo)adjuvant treatment and 21.6% remained free of additional therapies at a median follow-up of 108 months (64).

-
64. Joniau S, Hsu CY, Gontero P, et al. Radical prostatectomy in very high-risk localized prostate cancer: long-term outcomes and outcome predictors. Scand J Urol Nephrol 2012 Jun;46:164-71.

9.5.2 Advanced prostate cancer: any T, N1

The combination of RP and early adjuvant HT in pN+ PCa has been shown to achieve a 10-year CSS rate of 80% (67,68).

A retrospective observational study has shown a dramatic improvement in CSS and OS in favour of completed RP versus abandoned RP in patients who were found to be N+ at the time of surgery.

67. Ghavamian R, Bergstralh EJ, Blute ML, et al. Radical retropubic prostatectomy plus orchiectomy versus orchiectomy alone for pTxN+ prostate cancer: a matched comparison. J Urol 1999 Apr;161(4):1223-7;discussion 1277-8.
68. Messing EM, Manola J, Yao J, et al. Eastern Cooperative Oncology Group study EST 3886. Immediate versus deferred androgen deprivation treatment in patients with node-positive prostate cancer after radical prostatectomy and pelvic lymphadenectomy. Lancet Oncol 2006 Jun;7(6):472-9.

9.5.2 Advanced prostate cancer: any T, N1

These results suggest that RP may have a survival benefit and the abandonment of RP in N+ cases may not be justified (69). These findings have been corroborated in a contemporary retrospective analysis (70).

Radical prostatectomy resulted in superior survival of patients with N+ PCa after controlling for lymph node tumour burden. **The findings from these studies support the role of RP as an important component of multimodal strategies of N+ PCa.**

-
69. Engel J, Bastian PJ, Baur H, et al. Survival benefit of radical prostatectomy in lymph node-positive patients with prostate cancer. *Eur Urol* 2010 May;57(5):754-61.
 70. Steuber T, Budäus L, Walz J, et al. Radical prostatectomy improves progression-free and cancer-specific survival in men with lymph node positive prostate cancer in the prostate-specific antigen era: a confirmatory study. *BJU Int* 2011 Jun;107(11):1755-61.

Table 9.3: Overall survival (OS), cancer-specific survival (CSS) rates for very-high-risk PCa treated with RP as first treatment in a multimodal approach

Reference	n	Time span	OS			CSS			PSA-free survival		
			5-yr	10-yr	15-yr	5-yr	10-yr	15-yr	5-yr	10-yr	15-yr
cT3b-T4											
Johnstone et al. (2006) (66)	72	1995-2001	73	-	-	88	-	-	-	-	-
Joniau et al. (2012) (64)	51	1989-2004	88	71	-	92	92	-	53	46	-
Any T and N1											
Messing et al.(2006) (68) (*with vs without ADT)	98	1988-1993		55* 36 (11.5 yr)			85* 51 (11.5 yr)			53* 14 (11.5 yr)	
Schumacher et al. (2008) (72)	122	1989-2007	83	52	42	85	60	45	14	3	-
Da Pozzo et al. (2009) (74)	250	1988-2002	-	-	-	89	80	-	72	53	-
Engel et al. (2010) (69)	688	1988-2007	84	64	-	95	86	-	-	-	-
Steuber et al. (2011) (70)	108	1992-2004	79	69	-	84	81	-	-	-	-
Briganti et al. (2011) (73)	364	1988-2003	85	60	-	90	75	-	-	-	-

CSS = cancer-specific survival; n = number of patients; PSA = prostate-specific antigen; RP = radical prostatectomy.



2nd ESO Prostate Cancer Observatory 2015

MADRID, March 2015

OBIETTIVI per 2015

- **molecular imaging (optical biology) to improve staging**
- **biomarkers of disease aggressiveness / predictive models**
- **improve risk stratification and integration of genomic characterisation**



2nd ESO Prostate Cancer Observatory 2015

MADRID, March 2015

OBIETTIVI per 2015

- molecular imaging (optical biology) to improve staging
- biomarkers of disease aggressiveness / predictive models
- improve risk stratification and integration of genomic characterisation
- **INCREASE UTILISATION OF SURGERY**
- **multimodality approach with systemic therapy, surgery and radiation therapy**



2nd ESO Prostate Cancer Observatory 2015

MADRID, March 2015

K.Touijer (MSKCC)

"Urologists will play a central role in the managing PCa and they are going to start exploring -in a thoughtful and scientific way- the role of surgery in oligometastatic PCa.

"In other malignancies, we have seen great value in treating primary cancer through surgical excision," added Touijer.

OBIETTIVI MSKCC per 2015

K.Touijer

- AFFRONTARE IL PCa OLIGOMETASTATICO CON:

CHIRURGIA

RADIOTERAPIA

TERAPIA SISTEMICA docetaxol, cabazitaxel, radiun 223,
abiraterone acetate, enzalutamide

- RISERVARE LA ADT ALLA COMPARSA DI METASTASI CLINIC. SINTOMATICHE

available at www.sciencedirect.com
journal homepage: www.europeanurology.com



European Association of Urology



Platinum Opinion

Advancement of Technology and Its Impact on Urologists: Release of the da Vinci Xi, A New Surgical Robot

Timothy G. Wilson *

City of Hope Cancer Center, Duarte, CA, USA

It has forced us who do robotic surgery to specifically define our techniques and outcomes in a way that can be verified, reproduced, and examined critically as huge audiences watch by closed-circuit transmission [3]. Perhaps the future may include video revalidation of surgical skills [4]. As such, robotic technology has improved our field and has made us better surgeons and better doctors

- [3] Montorsi F1, Wilson TG, Rosen RC, et al., Pasadena Consensus Panel. Best practices in robot-assisted radical prostatectomy: recommendations of the Pasadena Consensus Panel. *Eur Urol* 2012;62:368–81.
- [4] Miller DC, Birkmeyer JD. Moving beyond the headlines: improving the technical quality of radical prostatectomy. *Eur Urol* 2014;65: 1020–2.

PROSTATECTOMIA RADICALE e LINFADENECTOMIA “ADEGUATA”

costituiscono ad oggi i migliori strumenti per un controllo locale - locoregionale di una malattia anche estesa

innovative urologie

Precision Medicine

Evolution of PLND in PCa

Extended PLND

Sentinel: ~~Tc 99m~~ → ICG

F – targeted → LN prostate

F – ultratargeted → LN PCa

targeted PLND



targeted PLND: the Salzburg Concept

EAU15 MADRID 20-24 March 2015

innovative urologie

Conclusions: PLND

- Targeted PLND: *better than blind e-PLND*
- Sentinel PLND: *Tc99m (γ-probe) and/or ICG (fluorescence, free or bound)*
- ICG targeted template dissection: *our current standard*
- Ultra-targeted PLND: LN of PCa *less lymph nodes removed, sensitivity ↓?*



Precision Medicine

EAU15 MADRID 20-24 March 2015

Sharing knowledge - Raising the level of urological care

The hidden fraction of the iceberg becomes smaller

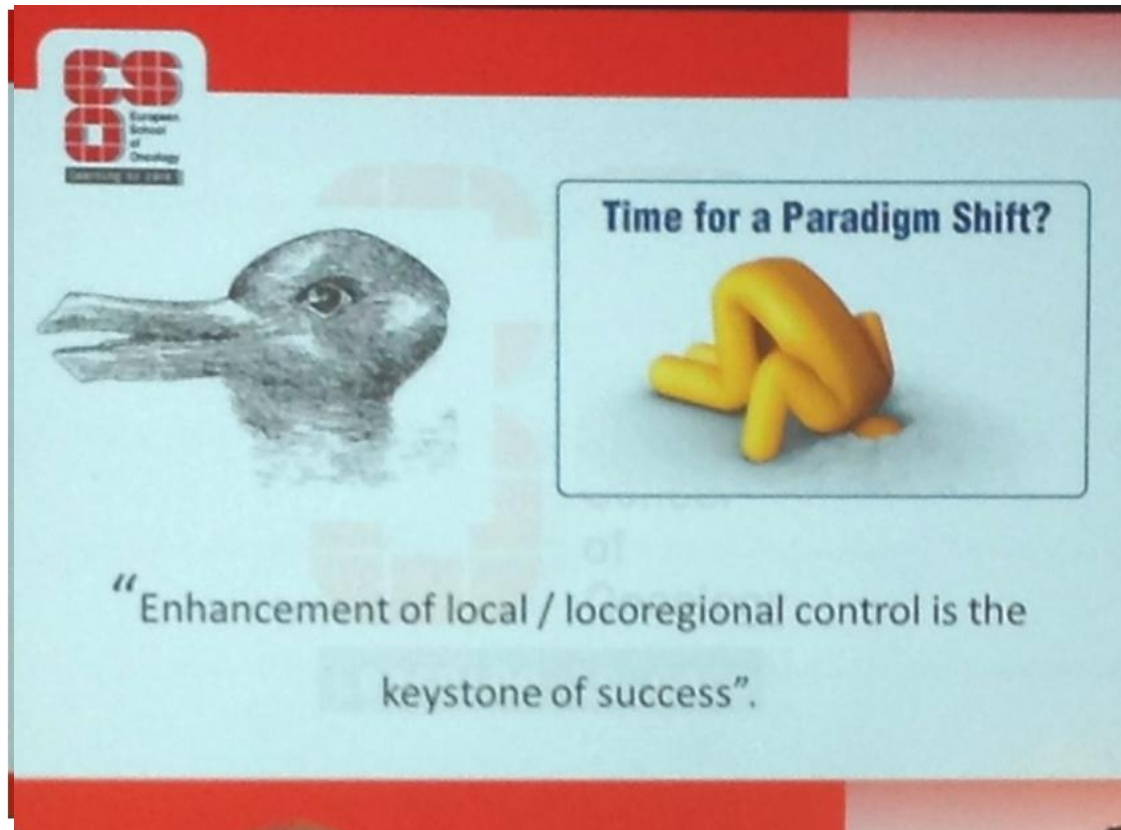
9.7 Recommendations for radical prostatectomy and eLND in low-, intermediate- and high-risk prostate cancer

	LE	GR
RP is a reasonable treatment option in selected patients with cT3a PCa, GS 8-10 or PSA > 20.	2b	B
Furthermore, RP is optional in highly selected patients with cT3b-4 N0 or any cT N1 PCa in the context of a multimodality approach.	3	C
Management decisions should be made after all treatments have been discussed by a multidisciplinary team (including urologists, radiation oncologists, medical oncologists and radiologists), and after the balance of benefits and side effects of each therapy modality has been considered by the patients with regard to their own individual circumstances.	1b	A
If RP is performed, pelvic eLND must be performed, because the estimated risk for positive lymph nodes is 15-40%.	2a	A
The patient must be informed about the likelihood of a multimodal approach.	1a	A
When nodal involvement is detected after surgery: <ul style="list-style-type: none"> • Adjuvant ADT is recommended when > 2 nodes are involved; • Expectant management is optional when the patient has undergone eLND and ≤ 2 nodes show microscopic involvement. 	1b 2b	A B
eLND is not necessary in low-risk PCa, because the risk for positive lymph nodes does not exceed 5%.	2b	A
eLND should be performed in intermediate-risk PCa if the estimated risk for positive lymph nodes exceeds 5%, as well as in high-risk cases. In these circumstances, the estimated risk for positive lymph nodes is 15-40%.	2b	A
Limited LND should no longer be performed, because it misses at least half the nodes involved.	2a	A

ADT = androgen deprivation therapy; eLND = extended lymph node dissection; GS = Gleason score; LND = lymph node dissection; PCa = prostate cancer; RP = radical prostatectomy;

Touijer:

**“ We have to put our heads together,
get out of our comfort zones and rethink the paradigm.”**



The slide features a red header and footer. In the top left corner is the logo for the European School of Oenology, which includes the letters 'ES' and 'O' in a stylized red font, with the text 'European School of Oenology' and 'Learning to Drink' below it. On the left side, there is a detailed pencil drawing of a duck's head. On the right side, a yellow, 3D-rendered duck-shaped object is shown in a curled-up, fetal-like position. A blue-bordered box contains the text 'Time for a Paradigm Shift?'. At the bottom, a quote is displayed: '“Enhancement of local / locoregional control is the keystone of success”'.

ES
European School of Oenology
Learning to Drink

Time for a Paradigm Shift?

“Enhancement of local / locoregional control is the keystone of success”.

available at www.sciencedirect.com
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European Association of Urology



Platinum Opinion

Prostate Cancer Outcomes: The Three Questions

Adam W. Glaser^{a,*}, Jessica L. Corner^{b,c}

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In particular, three key questions need to be answered for the patient:

1. Will I survive?
2. Will I be treated well?
3. What will I be like afterwards?

... it is imperative that the whole health economy (purchasers, providers, and the health charities) continue to actively embrace, promote, and support consumers in working to enhance the quality of care and survival of those affected by PCa.