SEMINARIO: "EPIDEMIOLOGÍA, PREVENCIÓN, DIAGNÓSTICO Y TRATAMIENTO DEL CÁNCER DE PRÓSTATA"

AVANCES EN LA RADIOTERAPIA DEL CA DE PROSTATA

Universidad Rey Juan Carlos

Cátedra de Innovación Y Gestión Sanitaria

Consorci Hospitalari Provincial de Castelló

CARLOS FERRER ALBIACH

ESTADO ACTUAL Y PERPECTIVAS DE FUTURO

- BAJO RIESGO
- INTERMEDIO
- ALTO
- OTRAS INDICACIONES
- NUEVOS RETOS

CALIDAD DE VIDA/ESCALAS DE COMORBILIDAD

Modified Charlson Index

PATHOLOGY	SCORE
Coronary disease	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Peptic ulcer	1
Mild liver disease	1
Diabetes	1
Hemiplegia	2
Moderate-severe renal disease	2
Diabetes with damage to target organs	2
Any tumor, leukemia, lymphoma	2
Moderate-severe liver disease	3
Solid metastasic tumor	6
AIDS	6

In addition, for each decade > 50 years 1 extra point is added.

Source: *Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-databases. J Clin Epidemiol. 1992; 45(6):613-619.*

Table 14.1: The Geriatric 8 (G8) frailty screening method

	Items	Possible responses (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing, or swallowing difficulties?	0 = severe decrease in food intake
		1 = moderate decrease in food intake
		2 = no decrease in food intake
B	Weight loss during the last 3 months?	0 = weight loss > 3 kg
		1 = does not know
		2 = weight loss between 1 and 3 kg
		3 = no weight loss
C	Mobility?	0 = bed or chair bound
		1 = able to get out of bed/chair but does not go out
		2 = goes out
E	Neuropsychological problems?	0 = severe dementia or depression
		1 = mild dementia
		2 = no psychological problems
F	BMI? (weight in kg)/(height in m^2)	0 = BMI < 19
		1 = BMI 19 to < 21
		2 = BMI 21 to < 23
		3 = BMI ≥ 23
H	Takes more than three prescription drugs per day?	0 = yes
		1 = no
P	In comparison with other people of the same age, how does the patient consider his/her health status?	0.0 = not as good
		0.5 = does not know
		1.0 = as good
		2.0 = better
	Age	0: > 85
		1: 80-85
		2: < 80
	Total score	0-17

BMI = body mass index

Leve 3-5 MODERADA 6 y 7 SEVERA 8 o superior
>5 MORTALIDAD EN 3 AÑOS >80%

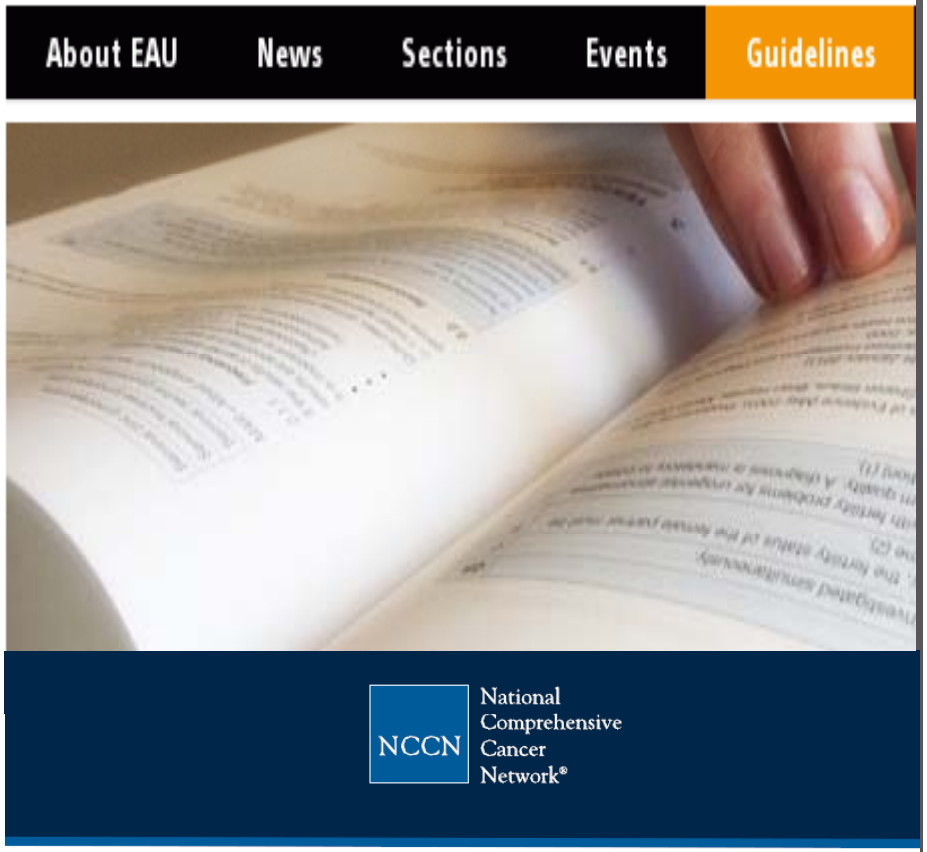
American Urological Association

2007, ACTUALIZADAS 2011

Guidelines on Prostate Cancer

European Association of Urology

JUNIO 2014

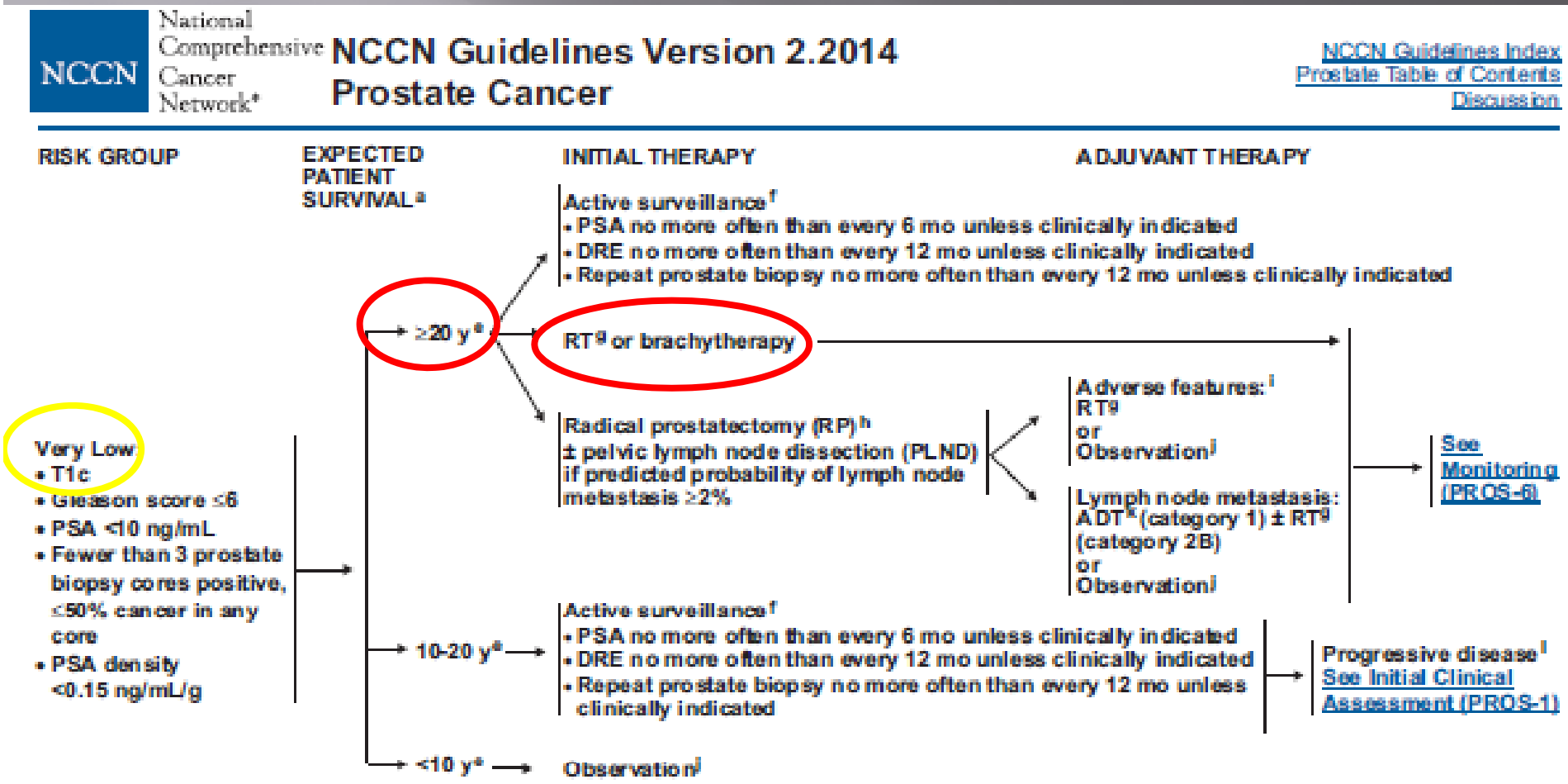


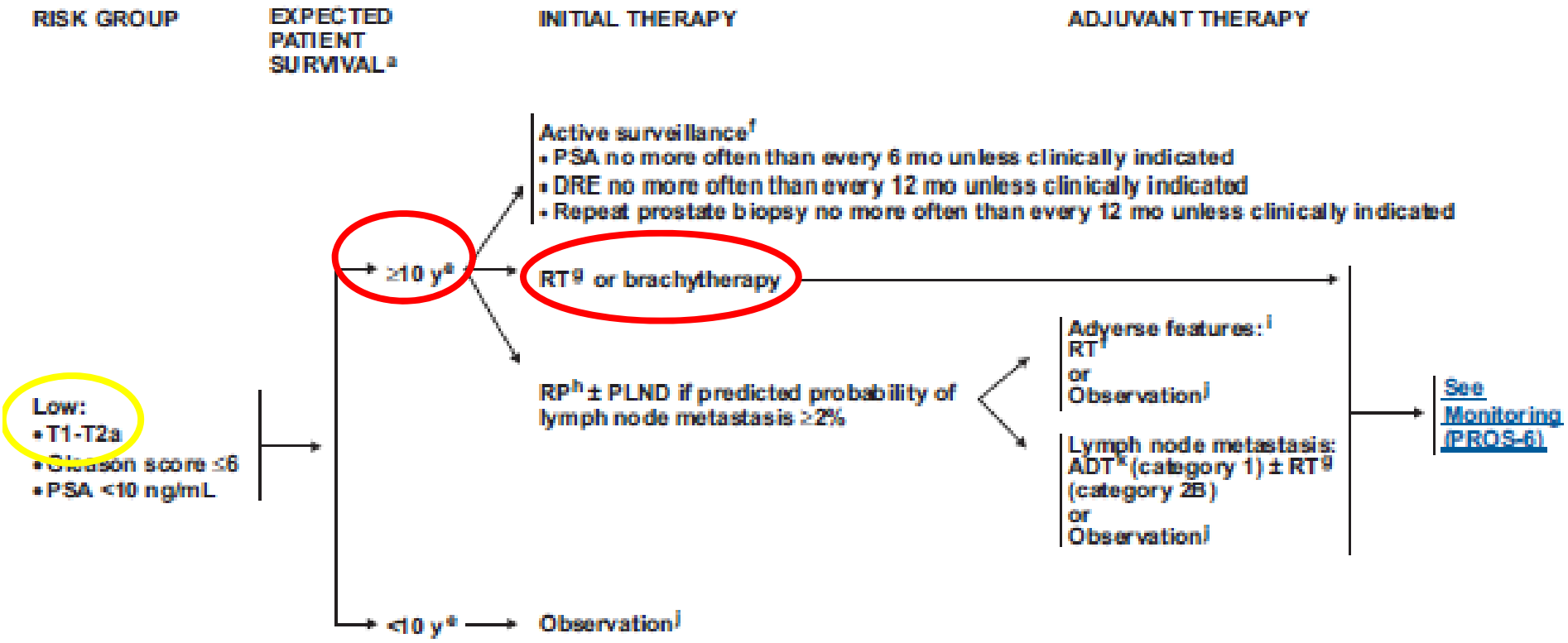
NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®)

Prostate Cancer

Version 2.2014

BAJO Y MUY BAJO RIESGO




RISK GROUP
EXPECTED PATIENT SURVIVAL[a]
INITIAL THERAPY
ADJUVANT THERAPY
Low:
• T1-T2a
• Gleason score ≤6
• PSA <10 ng/mL
≥10 y*
<10 y*
Active surveillance[f]
• PSA no more often than every 6 mo unless clinically indicated
• DRE no more often than every 12 mo unless clinically indicated
• Repeat prostate biopsy no more often than every 12 mo unless clinically indicated
RT[g] or brachytherapy
RP[h] ± PLND if predicted probability of lymph node metastasis ≥2%
Adverse features:[i]
RT[j]
or
Observation[j]
Lymph node metastasis:
ADT[k] (category 1) ± RT[g] (category 2B)
or
Observation[j]
Observation[j]
See Monitoring (PROS-6)

BAJO RIESGO EUA

10.3.5 ***Proposed EBRT treatment policy for localized PCa***

10.3.5.1 Low-risk PCa

Intensity-modulated radiotherapy with escalated dose and without ADT is an alternative to brachytherapy (see below).

10.5 Transperineal brachytherapy

Transperineal brachytherapy is a safe and effective technique. There is a consensus on the following eligibility criteria:

- Stage cT1b-T2a N0, M0;
- A Gleason score ≤ 6 assessed on an adequate number of random biopsies;
- An initial PSA level of ≤ 10 ng/mL;
- ≤ 50% of biopsy cores involved with cancer;
- A prostate volume of < 50 cm^3;
- An International Prostatic Symptom Score (IPSS) ≤ 12 (43).

BAJO RIESGO AUA

Treatment Alternatives

Standard: A patient with clinically localized prostate cancer should be informed about the commonly accepted initial interventions including, at a minimum, active surveillance, radiotherapy (external beam and interstitial), and radical prostatectomy. A discussion of the estimates for benefits and harms of each intervention should be offered to the patient.

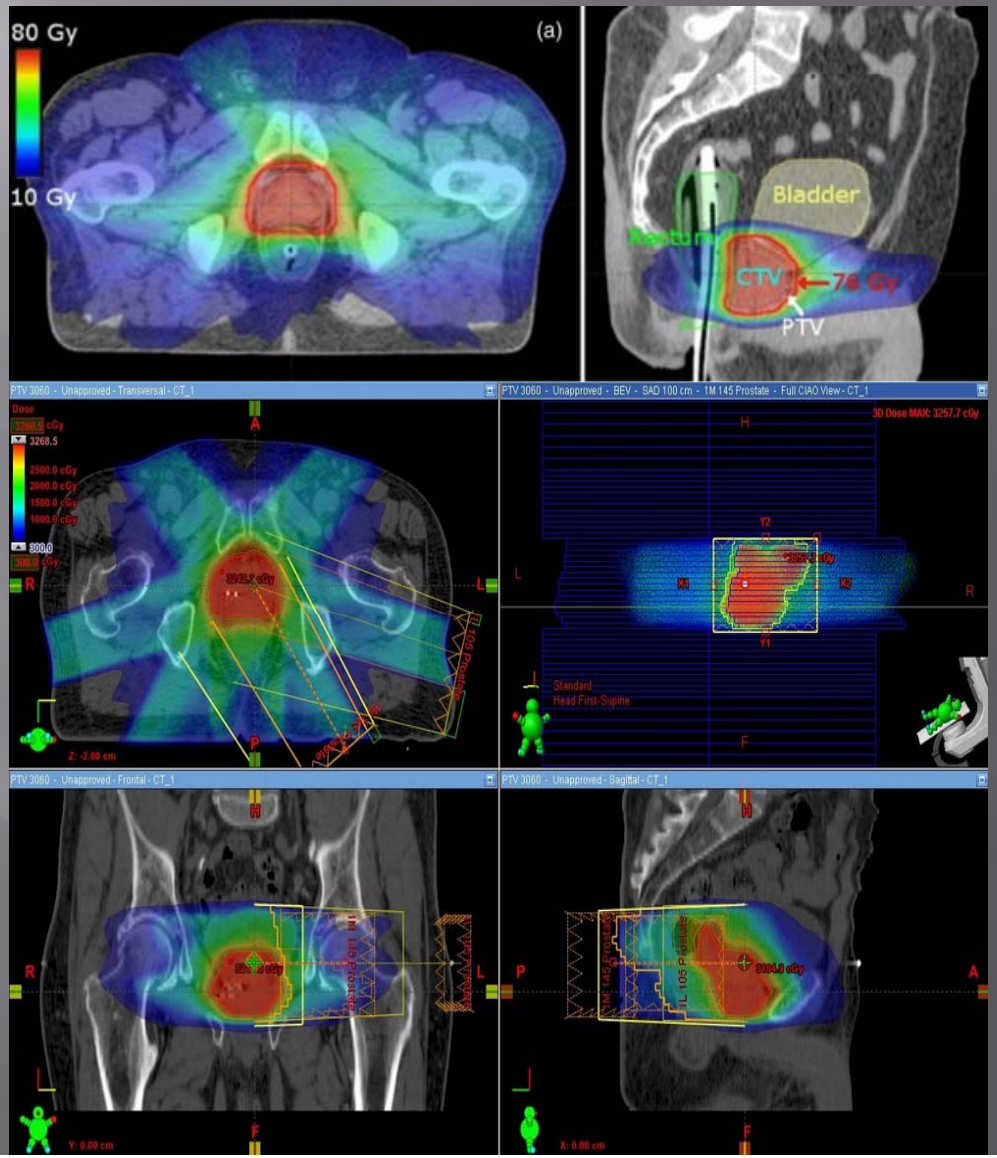
[Based on Panel consensus.]

Standard: Patient preferences and health conditions related to urinary, sexual, and bowel function should be considered in decision making. Particular treatments have the potential to improve, to exacerbate or to have no effect on individual health conditions in these areas, making no one treatment modality preferable for all patients.

¿COMO ES LA RT DEL SIGLO XXI?

IGRT-VMAT

IMRT



¿Y..... QUE DOSIS ADMINISTRAR?

VOLUME 23 · NUMBER 27 · SEPTEMBER 20 2005

JOURNAL OF CLINICAL ONCOLOGY

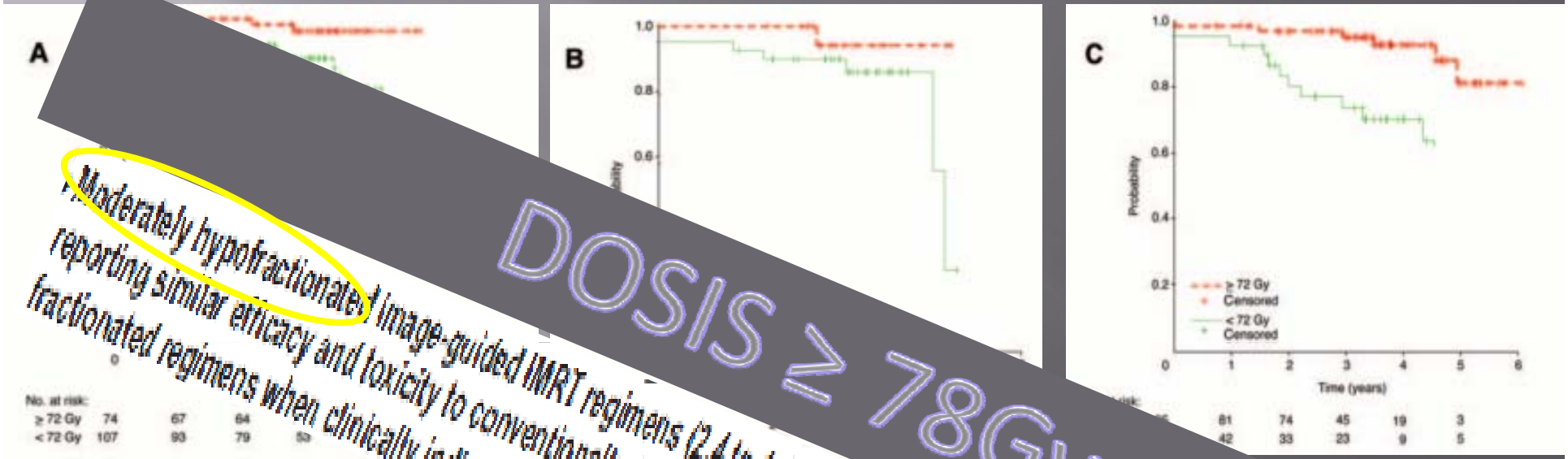
ORIGINAL REPORT

Risk-Adapted Androgen Deprivation and Escalated Three-Dimensional Conformal Radiotherapy for Prostate Cancer: Does Radiation Dose Influence Outcome of Patients Treated With Adjuvant Androgen Deprivation? A GICOR Study

Almudena Zapatero, Francisco Valcárcel, Felipe A. Calvo, Rosa Algás, Amelia Béjar, Javier Maldonado, and Salvador Villá

Patients and Methods

Between October 1999 and October 2001, 416 eligible patients with prostate cancer were assigned to one of three treatment groups according to their risk factors: 181 low-risk patients were treated with 3DCRT alone; 75 intermediate-risk patients were allocated to receive neoadjuvant AD (NAD) 4-6 months before and during 3DCRT; and 160 high-risk patients received NAD and adjuvant AD (AAD) 2 years after 3DCRT. Stratification was performed for treatment/risk group and total radiation dose.



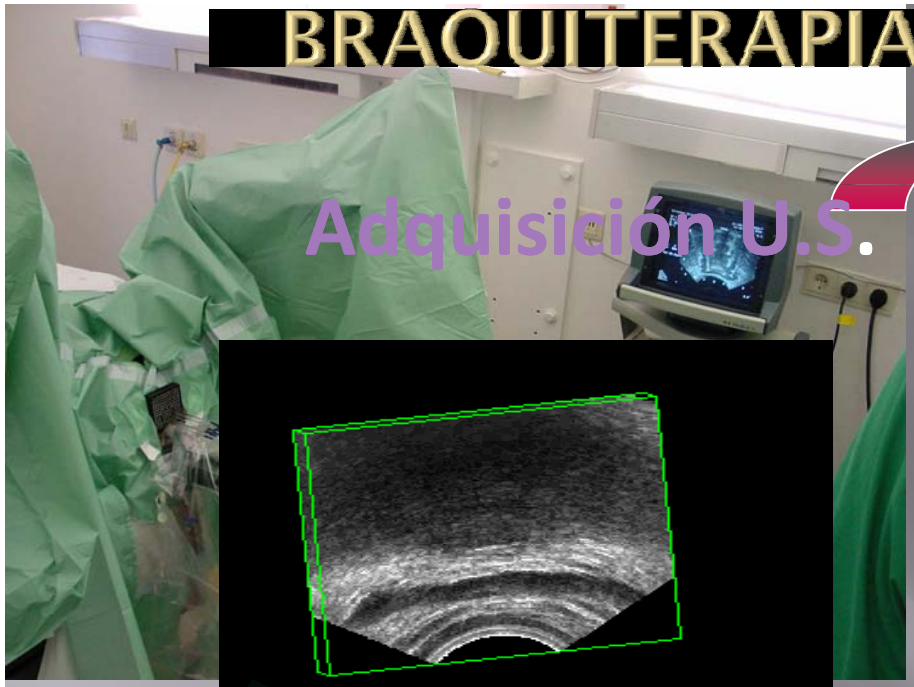
DOSIS ≥ 78Gy

Moderately hypofractionated image-guided IMRT regimens (2.4 to 4 Gy per fraction over 4-6 weeks) have been tested in randomized trials reporting similar efficacy and toxicity to conventionally fractionated IMRT. They can be considered as an alternative to conventionally fractionated regimens when clinically indicated.

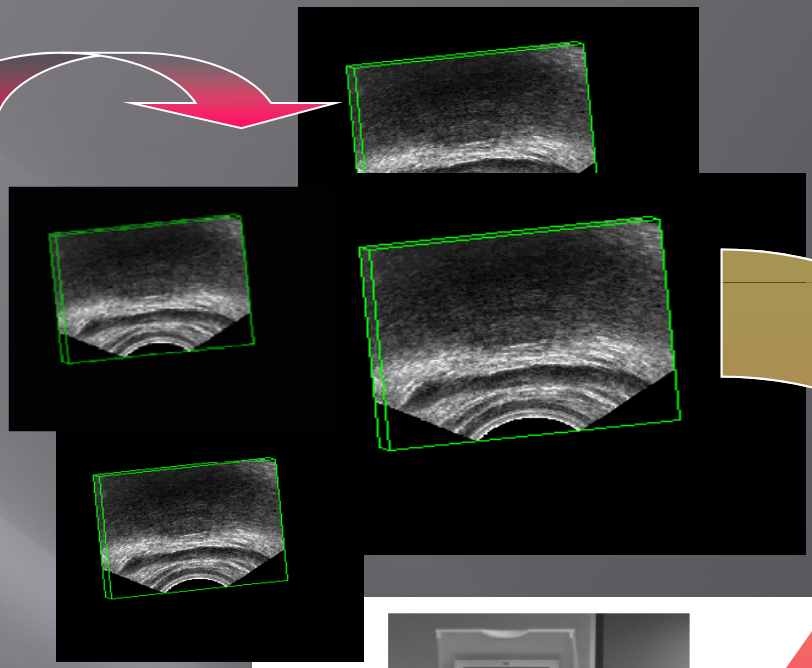
Results

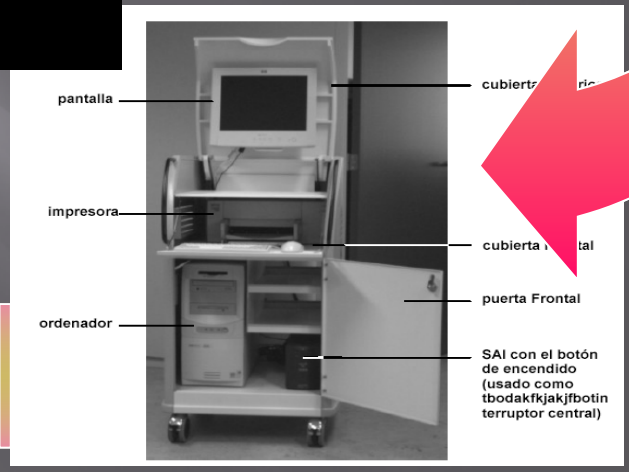
After a median follow-up of 36 months (range, disease-free survival (bDFS) at 5 years for all patients for low-risk, intermediate-risk, and high-risk disease were (P = .847). Univariate analysis showed that higher radiation dose factor associated with bDFS for all patients (P = .0004). When stratified by this benefit was evident for low-risk patients (P = .009) and, more interesting, patients treated with AAD. The 5-year bDFS for high-risk patients treated with AAD 53% for radiation doses less than 72 Gy and 84% for those ≥ 72 Gy (P = .003).

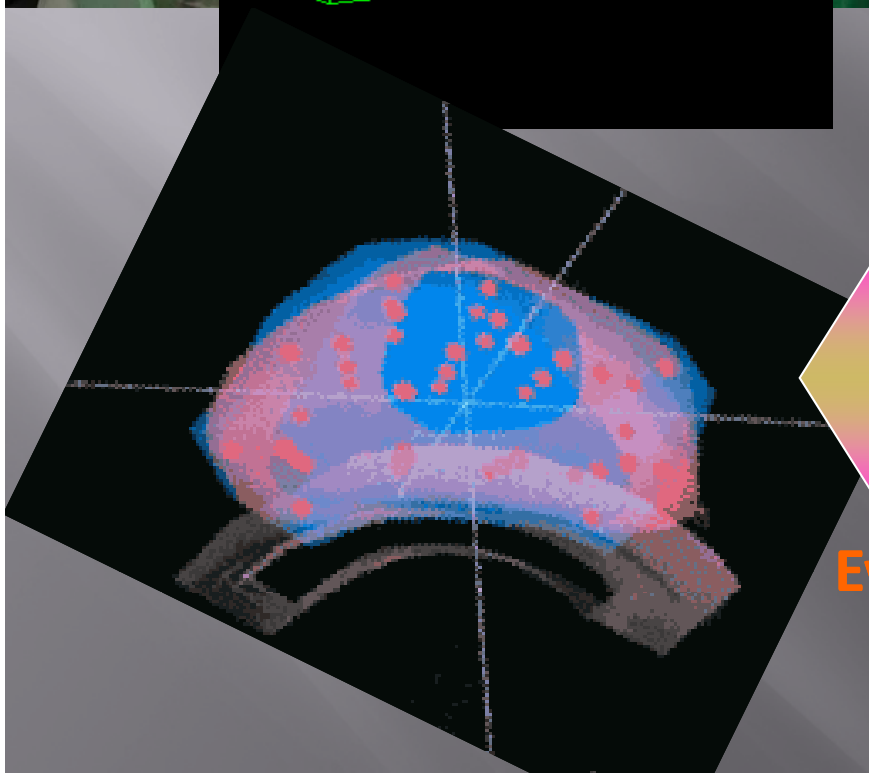
BRAQUITERAPIA CON SEMILLAS



Adquisición U.S.



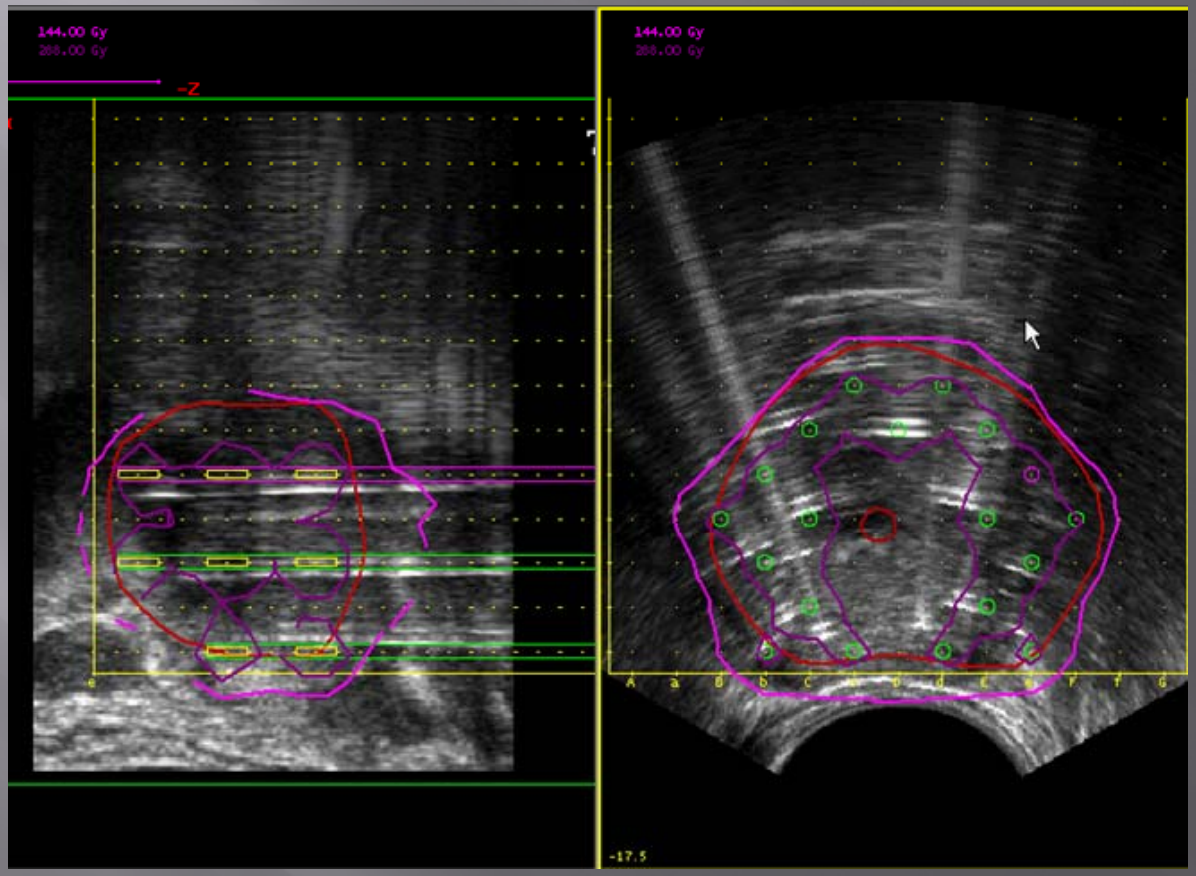




Evaluación.

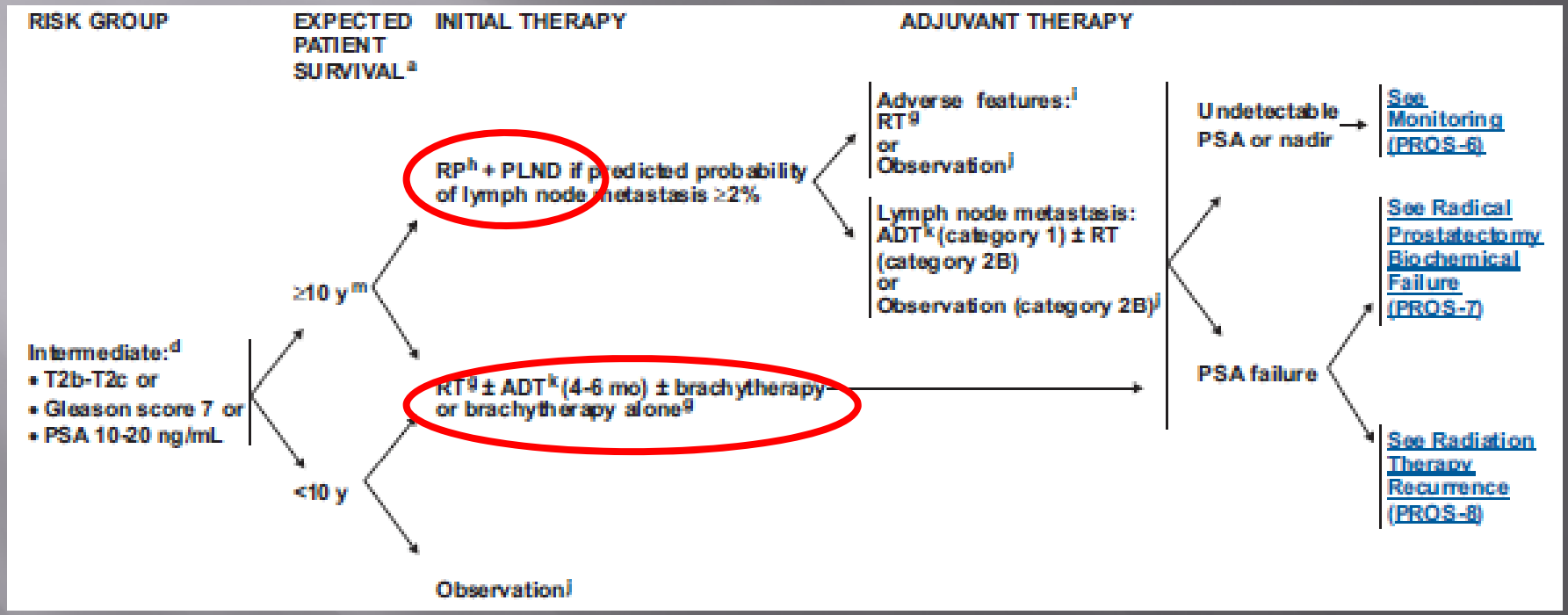
Contorneo del blanco y órganos a riesgo

BRAQUITERAPIA CON SEMILLAS EN TIEMPO REAL



DOSIS 145 Gy

RIESGO INTERMEDIO



RIESGO INTERMEDIO EUA

10.3.5.2 Intermediate-risk PCa

Patients suitable for ADT can be given combined IMRT with short-term ADT (4-6 months) (26,27). For patients unsuitable for ADT (e.g. due to comorbidities) or unwilling to accept ADT (e.g. to preserve their sexual health), the recommended treatment is IMRT at an escalated dose (80 Gy) or a combination of IMRT and brachytherapy.

RIESGO INTERMEDIO AUA

Option: Active surveillance, interstitial prostate brachytherapy, external beam radiotherapy, and radical prostatectomy are appropriate treatment options for the patient with intermediate-risk localized prostate cancer.

[Based on review of the data and Panel consensus.]

Active surveillance, interstitial prostate brachytherapy, external beam radiotherapy, and radical prostatectomy are all options for the treatment of intermediate-risk localized prostate cancer. Study outcomes data do not provide clear-cut evidence for the superiority of any one treatment.

Y…… SIN EMBARGO SE MUEVE

Dear Dr. Zapatero,

Congratulations! On behalf of the Annual Meeting Scientific Program Committee of the American Society for Radiation Oncology (ASTRO), it is my pleasure to inform you that your abstract has been selected for presentation in an **ORAL** Scientific Session during the 2014 Annual Meeting being held September 14-17 in San Francisco.

Your abstract details are:

Presentation #: PL-02

Abstract Title: Randomized Phase III Trial of Adjuvant Androgen Deprivation in Combination with High-dose Conformal Radiotherapy in Intermediate and High Risk Localized Prostate Cancer

Presenter: Almudena Zapatero

Author Block: A. Zapatero[1], A. Guerrero[2], J. Maldonado[3], A. Alvarez[4], C. Gonzalez San Segundo[4], M. Cabeza Rodriguez[5], V. Macias[6], A. Pedro-Olive[7], F. Casas[8], A. Boladeras[9], C. Martin de Vidales[10], M. Vazquez de la Torre[11], F. A. Calvo[12], *[1]Hospital Universitario de La Princesa, Madrid, Spain, [2]Hospital Son Dureta, Palma de Mallorca, Spain, [3]Hospital Vall d'Hebron, Barcelona, Spain, [4]Hospital Universitario Gregorio Marañón, Madrid, Spain, [5]Hospital Universitario 12 de Octubre, Madrid, Spain, [6]Hospital General de Catalunya-Hospital Universitario Salamanca, Salamanca, Spain, [7]Clinica Plato, Barcelona, Spain, [8]Hospital Clinic, Barcelona, Spain, [9]Instituto Catala de Oncología, Barcelona, Spain, [10]Hospital Universitario de la Princesa, Madrid, Spain, [11]Hospital Do Meixoeiro, Vigo, Spain, [12]Hospital General Universitario Gregorio Maranon, Madrid, Spain*

Scientific Session Title: Plenary

Abstract:

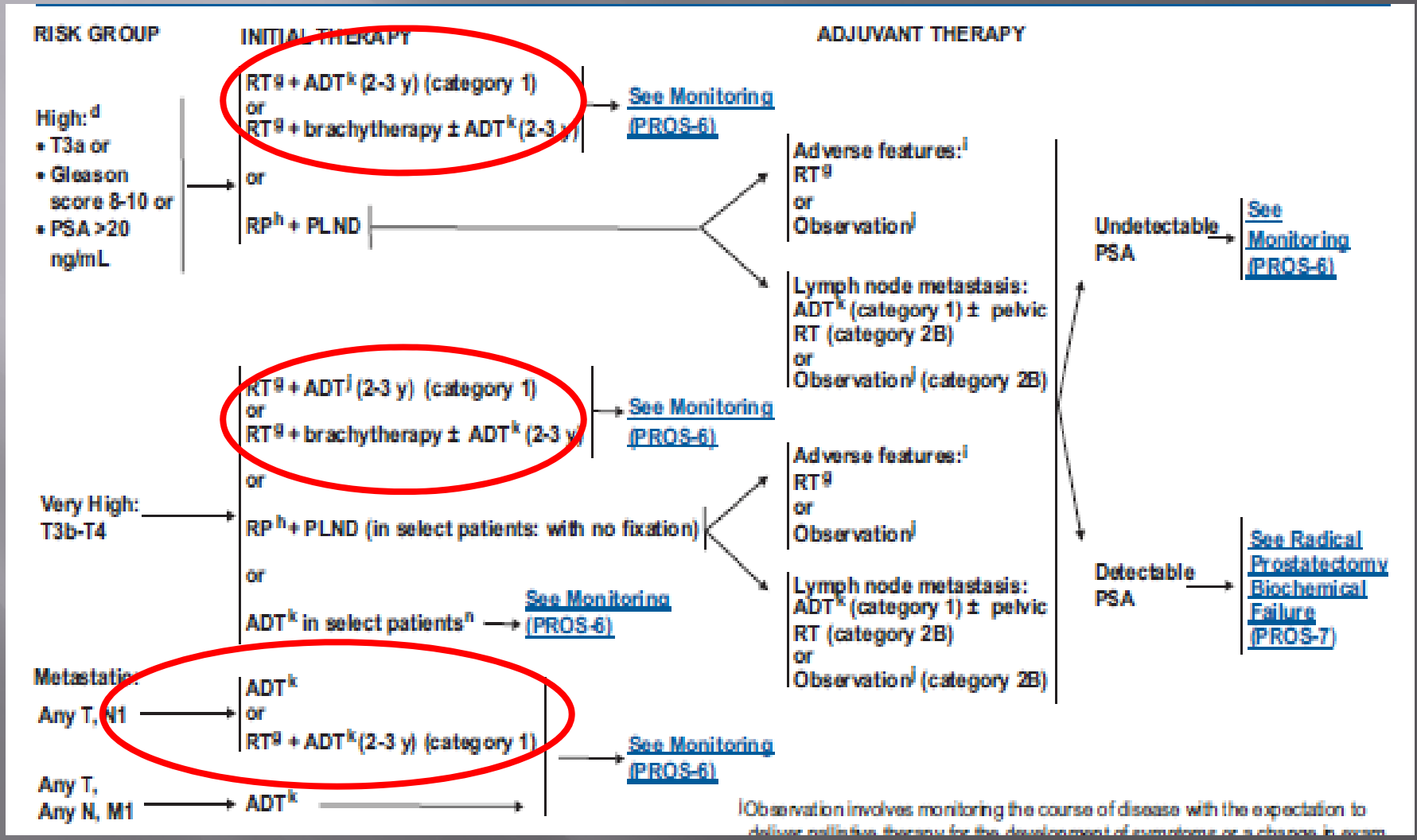
Purpose/Objective(s):Although androgen deprivation (AD) combined with radiotherapy significantly decreases mortality of patients with locally advanced prostate cancer (PCa), controversy remains about the optimal duration of AD associated with dose escalation RT. This trial was designed to evaluate whether long-term AD (LTAD) improves outcome compared to short-term AD (STAD) in patients treated with high-dose radiotherapy (HDRT).

Materials/Methods:Between 2006 and 2010, 362 assessable patients were enrolled. Eligibility included patients with cT1c-T3aN0M0 PCa with intermediate and high risk factors according to NCCN criteria and PSA less than 100 ng/ml. All patients received 4 months of neoadjuvant and concomitant AD (STAD) + HDRT (median dose to the prostate 78.0 Gy) before randomization to adjuvant goserelin (LTAD) for two years. Stratification was performed according to risk group (intermediate risk [IR] versus high risk [HR]). Primary endpoints were biochemical-disease free survival (bDFS) and toxicity scores. Secondary endpoints included metastasis free survival (MFS), overall survival (OS) and cancer specific survival (CSS).

Results:Three hundred and fifty two patients (STAD =177, LTAD=175) were eligible with 57 months median follow-up. There were 188 HR patients (STAD = 97, LTAD = 91) and 164 IR patients (STAD = 80, LTAD = 84) (p=0.669). Twenty-three patients in the STAD group and 7 patients in the LTAD group had biochemical failure according to Phoenix Consensus definition (p=0.003). At 5 years bDFS was significantly improved in the LTAD group (95.4%, 95% CI: 93.2-97.6, compared to the STAD group (86.1%%, 95% CI: 83.5-88.7). Five-year MFS was 85.5% (95% CI: 82.9-88.1) for STAD and 93.2% (95% CI: 91.0-95.4) for LTAD, and OS was 88.8% (95% CI: 86.3-91.3) for STAD and 94.0% (95% CI: 91.9-96.1) for LTAD. Grade ≥ 2 radiation related adverse effects in both groups were not significantly different.

Conclusions:This study shows that the combination of LTAD plus HDRT provides superior bDFS compared with STAD + HDRT. Further follow-up is needed to confirm these findings and to estimate precisely the impact on OS and CSS.

ALTO RIESGO


RISK GROUP
INITIAL THERAPY
ADJUVANT THERAPY
High:[d]
• T3a or
• Gleason score 8-10 or
• PSA >20 ng/mL
RT[g] + ADT[k] (2-3 y) (category 1)
or
RT[g] + brachytherapy ± ADT[k] (2-3 y)
See Monitoring (PROS-6)
or
RP[h] + PLND
Adverse features:[l]
RT[g]
or
Observation[j]
Lymph node metastasis:
ADT[k] (category 1) ± pelvic RT (category 2B)
or
Observation[j] (category 2B)
Undetectable PSA
See Monitoring (PROS-6)
Very High: T3b-T4
RT[g] + ADT[j] (2-3 y) (category 1)
or
RT[g] + brachytherapy ± ADT[k] (2-3 y)
See Monitoring (PROS-6)
or
RP[h] + PLND (in select patients: with no fixation)
Adverse features:[l]
RT[g]
or
Observation[j]
Lymph node metastasis:
ADT[k] (category 1) ± pelvic RT (category 2B)
or
Observation[j] (category 2B)
Detectable PSA
See Radical Prostatectomy Biochemical Failure (PROS-7)
or
ADT[k] in select patients[n]
See Monitoring (PROS-6)
Metastatic:
Any T, N1
ADT[k]
or
RT[g] + ADT[k] (2-3 y) (category 1)
See Monitoring (PROS-6)
Any T, Any N, M1
ADT[k]
[l]Observation involves monitoring the course of disease with the expectation to

RIESGO ALTO AUA

Standard: High-risk patients who are considering specific treatment options should be informed of findings of recent high-quality clinical trials, including that:

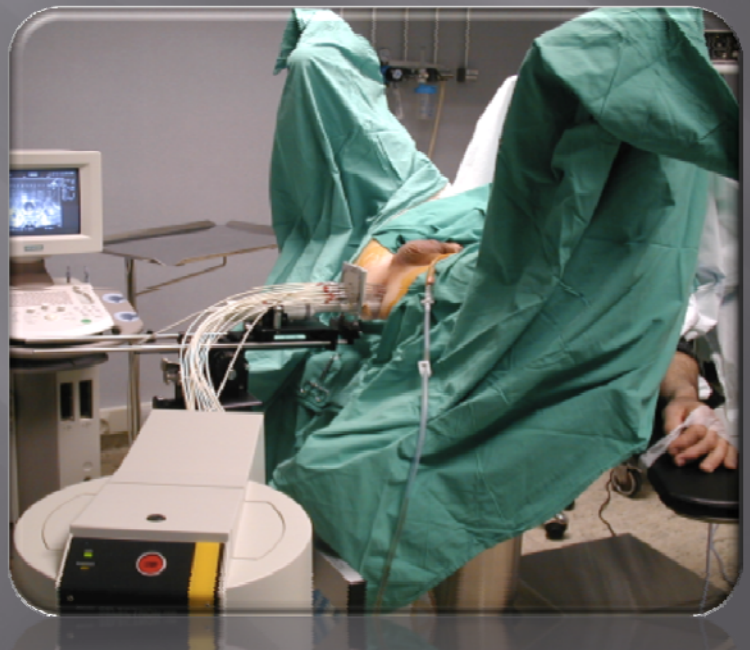
- **When compared with watchful waiting, radical prostatectomy may lower the risk of cancer recurrence and improve survival[10]; and**
- **For those considering external beam radiotherapy, use of hormonal therapy combined with conventional radiotherapy may prolong survival.[11, 14]**

RIESGO ALTO EUA

RADIOTERAPIA

In patients with locally advanced PCa T3-4 N0 M0, concomitant and adjuvant hormonal therapy for a total duration of 3 years, with external-beam irradiation for patients with WHO 0-2 performance status, is recommended, as it improves the overall survival.	1b	A
In a subset of patients with T2c-T3 N0-X and a Gleason score of 2-6, short-term ADT before and during radiotherapy can be recommended, as it may favourably influence the overall survival.	1b	A
In patients with very high-risk PCa c-pN1 M0, with no severe comorbidity, pelvic external irradiation and immediate long-term adjuvant hormonal treatment is recommended, as it may improve the overall survival, disease-specific failure rate, metastatic failure rate, and biochemical control.	2b	B

BT DE ALTA TASA HDR



ELSEVIER

BRACHYTHERAPY

Brachytherapy 11 (2012) 20–32

American Brachytherapy Society consensus guidelines for high-dose-rate prostate brachytherapy

Yoshiya Yamada[1,*], Leland Rogers[2], D. Jeffrey Demanes[3], Gerard Morton[4], Bradley R. Prestidge[5], Jean Pouliot[6], Gil'ad N. Cohen[7], Marco Zaider[7], Mihai Ghilezan[8], I-Chow Hsu[6]

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ABSTRACT

PURPOSE: A well-established body of literature supports the use of high-dose-rate (HDR) brachytherapy as definitive treatment for localized prostate cancer. Most of the articles describe HDR as a boost with adjuvant external beam radiation, but there is a growing experience with HDR monotherapy.

METHODS AND MATERIALS: The American Brachytherapy Society has convened a group of expert practitioners and physicists to develop guidelines for the use of HDR in the management of prostate cancer. This involved an extensive literature review and input from an expert panel.

RESULTS: Despite a wide variation in doses and fractionation reported, HDR brachytherapy provides biochemical control rates of 85–100%, 81–100%, and 43–93% for low-, intermediate-, and high-risk prostate cancers, respectively. Severe toxicity is rare, with most authors reporting less than 5% Grade 3 or higher toxicity. Careful attention to patient evaluation for appropriate patient selection, meticulous technique, treatment planning, and delivery are essential for successful treatment.

CONCLUSION: The clinical outcomes for HDR are excellent, with high rates of biochemical control, even for high-risk disease, with low morbidity. HDR monotherapy, both for primary treatment and salvage, are promising treatment modalities.

Keywords: High-dose-rate brachytherapy; Prostate cancer; American Brachytherapy Society; Guidelines

Introduction

There is mounting evidence that the outcome of patients with localized prostate cancer is related directly to local tumor control, even for patients with high-risk features (1). For example, the risk of distant metastasis is closely tied to local control (2). Dose-escalation strategies, particularly with intermediate- and high-risk prostate cancer, have improved local control, and higher doses of radiation, whether with brachytherapy, external beam radiation, or a combination, have consistently demonstrated improved outcomes (2–11).

High-dose-rate (HDR) brachytherapy is a vehicle for absolute and radiobiologic dose escalation that has resulted in high tumor control and low toxicity rates. As with all advanced technology, meticulous treatment planning and carefully executed methods are essential to the accurate delivery of high-dose radiation to complex volumes such as the prostate and seminal vesicles while avoiding excessive dose to the rectum, bladder, and urethra. The following

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Continuing Medical Education Institute Speakers Bureau.
No other disclosures for any of the other authors.
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E-mail address: yamadaj@mskcc.org (Y. Yamada).

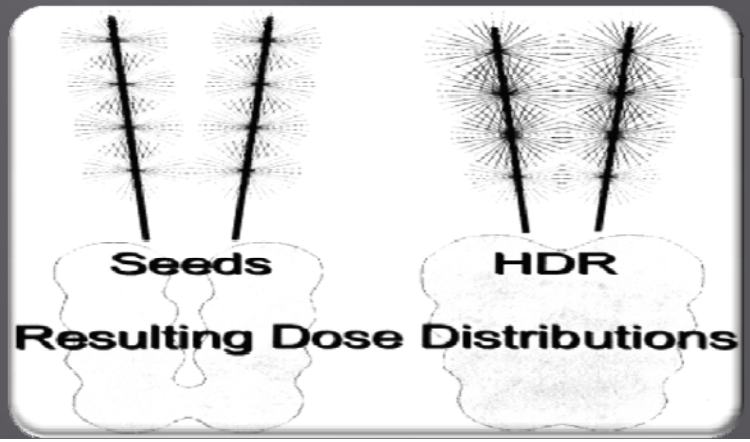
1538-4721/$ - see front matter © 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.
doi:10.1016/j.brachy.2011.09.008

PROSTATE HDR

"IMRT en Braquiterapia":
podemos modular la intensidad de RT (tiempo y espacio) +ventaja RB del Hipofraccionamiento.
•ES EL MEDIO PARA ESCALAR DOSIS QUE HA CONSEGUIDO:

-> CONTROL TUMORAL.

-Y MENOR TOXICIDAD.



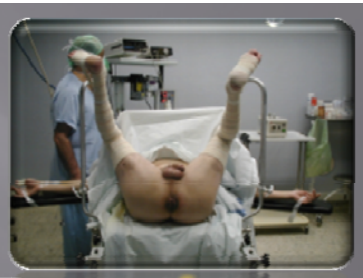
INDICACIONES

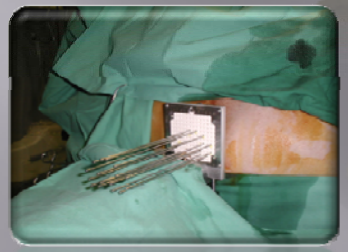
- **EBRT +HDR (Sobreimpresión o Boost):**
  - *Alto Riesgo: PSA > 20 ó GL >7 ó T2c (ó 2 criterios de RI)*
  - *Riesgo Intermedio: PSA 11-20 ó GL 7 ó T2b*

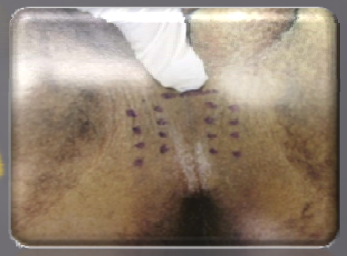
Control Bioquímico 5 años:
85-100% Bajo Riesgo
83-98% Riesgo Intermedio
51-96% Alto Riesgo

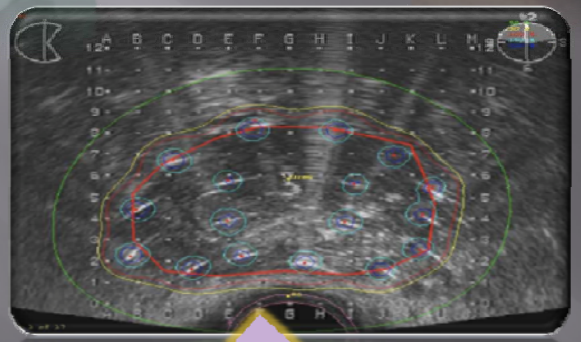
- **MONOTERAPIA:**
  - *Bajo Riesgo: PSA <10 ó GL 6 ó T2*
    Tumores Agresivos:
    - *N.º y % de cilindros afectos*
    - *Aumento PSA >2 ng / año*
  - *Riesgo Intermedio: PSA 11-20 ó GL 7 (3+4) ó T2b*
    Casos Seleccionados:
    - *La velocidad del PSA debe ser <2ng / año.*
    - *Número y % cilindros, +*
    - *Gleason (3 + 4).*

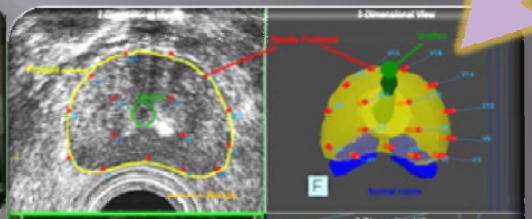
Quirófano
Raquianestesia
Pos. Litotomía
Eco Transrectal

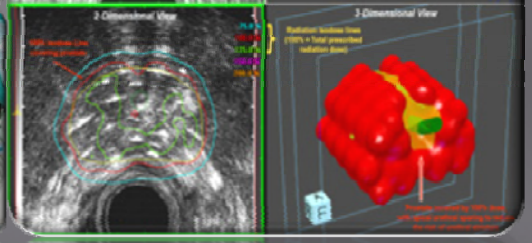


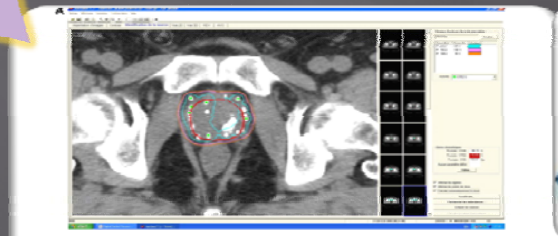


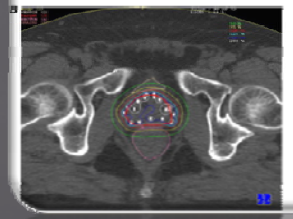


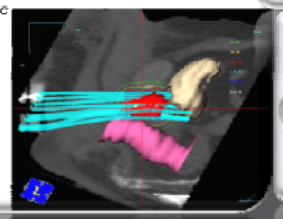


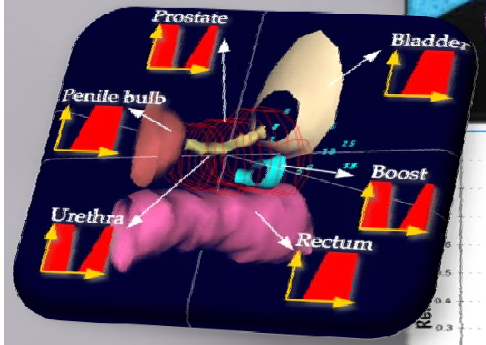


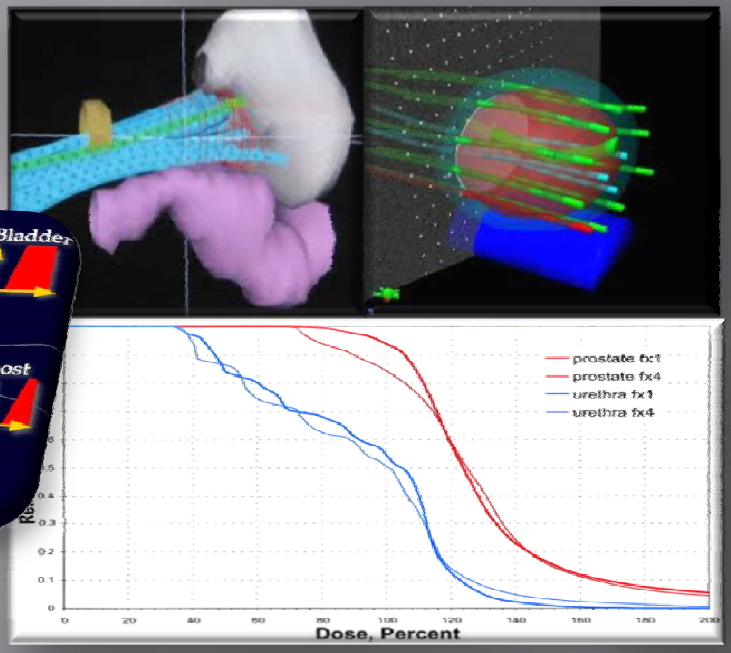












SOBREIMPRESIÓN

ALTO RIESGO

RT. EXT. → 46 Gy /2Gy/23 ses. o HIPOF.
HDR → 5ª y 15ª de la Rt. ext.
DOSIS HDR → 1.150 cGy x 2

RIESGO INTERMEDIO

RT. EXT. → 46 Gy /2Gy/23 ses. o HIPOF.
HDR → 5ª de la Rt. ext.
DOSIS HDR → 1.500 cGy x 1

MONOTERAPIA

1 DOSIS EN 1 FRACCIÓN

20.5 Gy

Prescripción de dosis

CTV:
V100 ≥ 95%
V150 15% ± 5% del CTV
V200 5% ± 5%
D90 > 100% de la dosis

Órganos a riesgo

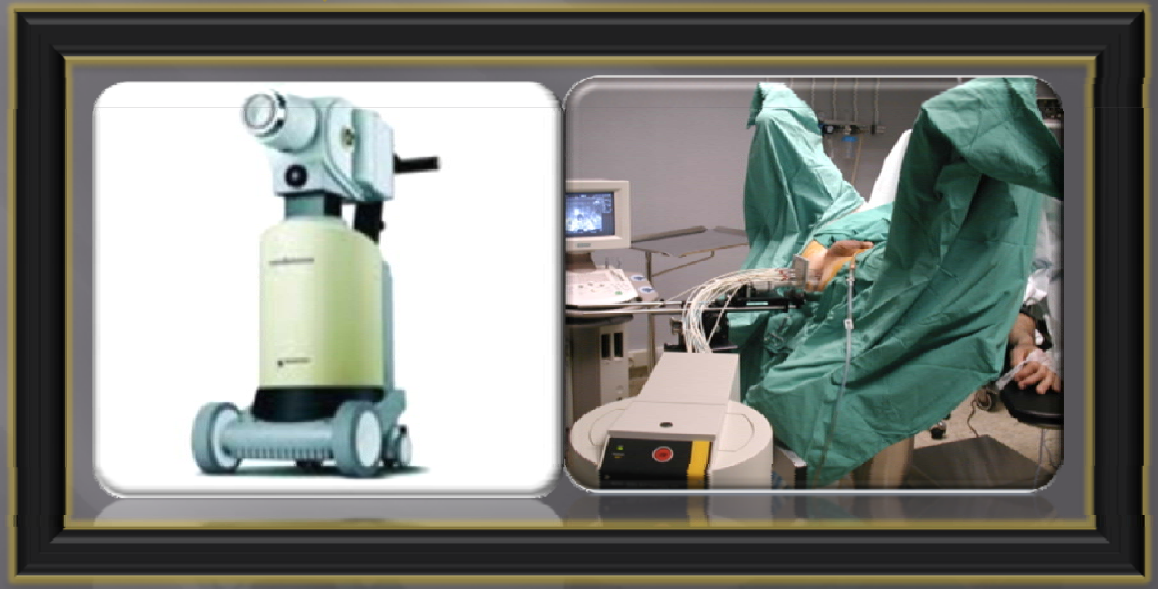
Recto: Dmax < 100% de la dosis
Uretra: Dmax < 110% de la dosis

Prescripción de dosis

CTV:
V100 ≥ 95%
V150 15% ± 5% del CTV
V200 5% ± 5%
D90 > 100% de la dosis

Órganos a riesgo

Recto: Dmax ≤ 90% de la dosis
Uretra: Dmax < 110% de la dosis

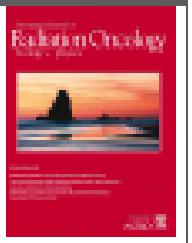


OTRAS INDICACIONES…..ADYUVANTE Y RESCATE

American Urological Association

ASTRO

CME ASTRO



J Urol 2013;190(2):441-9

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Guidelines

Adjuvant and Salvage Radiation Therapy After Prostatectomy: American Society for Radiation Oncology/American Urological Association Guidelines

Richard K. Valicenti, MD, MBA,* Ian Thompson Jr., MD,† Peter Albertsen, MD, MS,‡ Brian J. Davis, MD, PhD,§ S. Larry Goldenberg, MD,‖ J. Stuart Wolf, MD,¶ Oliver Sartor, MD,# Eric Klein, MD,** Carol Hahn, MD,†† Jeff Michalski, MD, MBA,‡‡ Mack Roach III, MD,§§ and Martha M. Faraday, PhD‖‖

INDICACIONES DE TRATAMIENTO ADYUVANTE/RESCATE

- Algunos pacientes con RB vivos a los 10 años y PSA estable.
- Doblamiento PSA< 3 meses mal pronóstico
- Algunos subgrupos se benefician especialmente: >Gleason >T
- Los pacientes con PSA<1 mejor pronostico

Y …cual es el resultado?

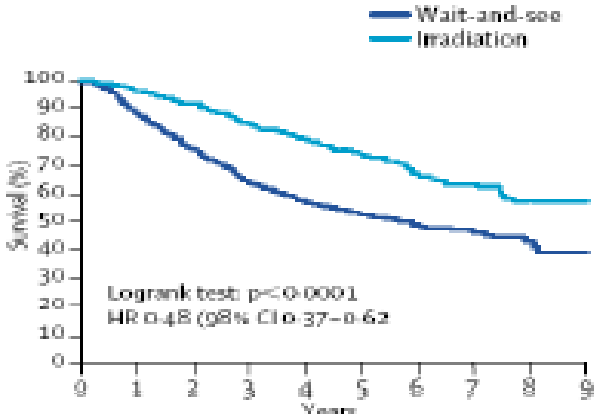
Postoperative radiotherapy after radical prostatectomy: a randomised controlled trial (EORTC trial 22911)

Michel Bolla, Hein van Poppel, Laurence Collette, Paul van Cangh, Kris Vekemans, Luigi Da Pozzo, Theo M de Reijke, Antony Verbaeys, Jean-François Bosset, Roland van Velthoven, Jean-Marie Maréchal, Pierre Scalliet, Karin Haustermans, Marianne Piérart, for the European Organization for Research and Treatment of Cancer

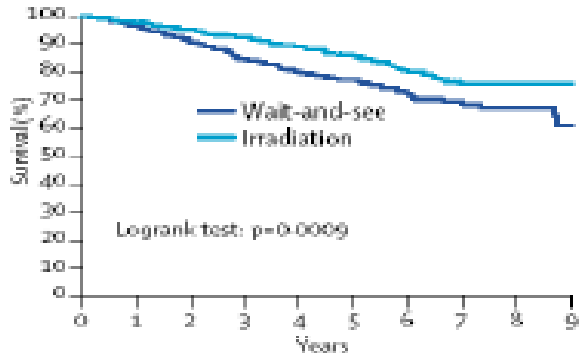
Lancet 2005; 366: 572–78

5 años	RT	Observación	p
SLRBQ	**74%**	**52.6%**	<0.0001
SLRclínica	**85.1%**	**77.5%**	<0.0009

SLRBQ



SLRclin



No diferencias en SLM+ ,en SG, ni en toxicidad

RADICALS

Radiotherapy and androgen deprivation in combination after local surgery
A randomised controlled trial in prostate cancer

MRC Clinical Trials Unit | CANCER RESEARCH UK | NCIC Clinical Trials Group / NCIC Groupe des essais cliniques | NCRI

Tuesday, 03 June 2014

- Home
- About RADICALS
  - Overview and aims
  - Radiotherapy Timing Comparison
  - Hormone Duration Comparison
  - Eligibility Criteria
- News
- Information for Patients
  - Patient Information Sheets
  - Patient Information Booklet

About RADICALS

RADICALS is a large clinical trial which is taking place in the UK, Canada, Denmark and the Republic of Ireland at the moment.

It is a phase III randomised controlled trial that will recruit approximately 3000 men to help answer two important questions for men who have had surgery for prostate cancer:

- Which is the best way to use radiotherapy after surgery?
- Which is the best way to use hormone treatment with any radiotherapy given after surgery

In breast cancer, surgery is followed by radiotherapy and hormone treatment, because the combination is better than surgery alone. In prostate cancer, surgery alone is a standard treatment, and we are not sure how best to use radiotherapy and hormone treatment after surgery.

The trial may be suitable at some point for most men who have a radical

Latest Updates

Accrual

22/05/14
Latest Accrual figures

News

08/11/13
1st Canadian centre to recruit 100 patients!

Videos

01/10/10
YouTube Video: Hormone Duration Randomisation - Q&A Section Part 1

Overview and aims

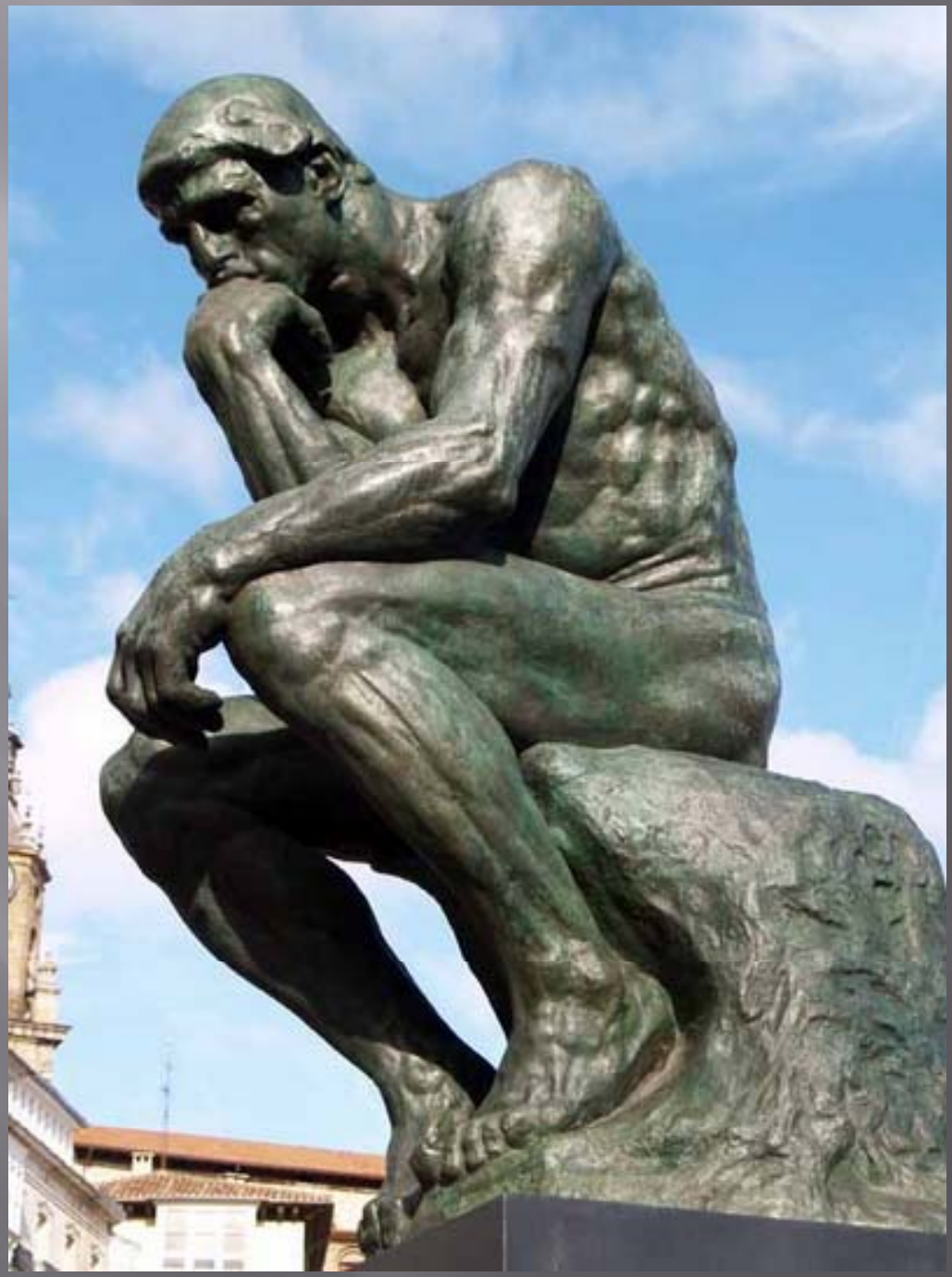
RADICALS is a large clinical trial which is taking place in the UK, Canada, Denmark and the Republic of Ireland at the moment. It is a phase III randomised controlled trial that will recruit approximately 3000 men to help answer two important questions for men who have had surgery for prostate cancer:

- Which is the best way to use radiotherapy after surgery?
- Which is the best way to use hormone treatment with any radiotherapy given after surgery

In breast cancer, surgery is followed by radiotherapy and hormone treatment, because the combination is better than surgery

RADICALS
RT Rescate +/- 6 m vs 2 años HT (análogos/Bic 150)
RT Adyuvante +/- 6 m vs 2 años HT(análogos/Bic 150)

Men for whom there is uncertainty about whether radiotherapy is needed straight after the operation can join the Radiotherapy Timing Comparison. If they wish to, they can also join the Hormone Duration Comparison.



¿QUE PAPEL JUEGA LA RNM?

Table 4 3T mMRI studies of prostate cancer staging

References	No. of patients	BPA	ERC	MR technique	Sensitivity (%)	Specificity (%)	Accuracy (%)
[14]	32	Yes	Yes	T2 and T1 weighted	88	96	94
[15]	27	Yes	No	T2 weighted	ECE in 67	ECE in 100	ECE in 85
[16]	46	Yes	Yes	T2 weighted	PPA: 13	BPA: 100	BPA: 70
					ERC: 80	ERC: 100	ERC:93
[17]	42	Yes	No	T2 and T1 weighted	ECE in 69	ECE in 92	ECE in 83
[19]	54	Yes	No	T2 weighted	ECE in 81	ECE in 67	ECE in 72
					SVI in 75	SVI in 100	SVI in 98
2013	118	Yes	Yes	T2 and T1 weighted, DCE, DWI	ECE in 28	ECE in 91	ECE in 75
					SVI in 50	SVI in 99	SVI in 95
2013	60	No	Yes	T2 and T1 weighted, DCE	ECE in 35	ECE in 90	ECE in 62
Present study	47	Yes	No	T2 and T1 weighted, DCE, DWI	ECE in 57	ECE in 95	ECE in 89

ECE extracapsular extension, *ERC* endorectal coil, *BPA* body phased array, *SVI* seminal vesicle invasion, *DCE* dynamic contrast enhanced, *DWI* diffusion weighted imaging

NCCN

Magnetic Resonance Imaging

- The strengths of MRI include high soft tissue contrast and characterization, multiparametric image acquisition, multiplanar imaging capability, and advanced computational methods to assess function.
  - MRI can be performed with or without the administration of intravenous contrast material
  - Resolution of MR images in the pelvis can be augmented with the use of an endorectal coil
- Standard MRI techniques can be considered for initial evaluation of high-risk patients.
  - T3 or T4 disease
  - Patients with T1 or T2 disease and nomogram indicated probability of lymph node involvement >10% may be candidates for pelvic imaging, but the level of evidence is low.
- MRI may be considered in patients after RP when PSA fails to fall to undetectable levels or when an undetectable PSA becomes detectable and increases on 2 or more subsequent determinations, or after RT for rising PSA or positive DRE if the patient is a candidate for additional local therapy

EAU

Given its low sensitivity to microscopic invasion, MRI is not recommended in the local staging of low-risk patients, but MRI may be useful in selected patients with intermediate- to high-risk cancers (44,46,47).

6.4.3 ***Recommendation for imaging***

	LE	GR
When available, mMRI of the prostate can be used to trigger a (targeted) repeat prostate biopsy.	2b	B

mMRI = multiparametric magnetic resonance imaging

Clin Transl Oncol
DOI 10.1007/s12094-014-1186-6

RESEARCH ARTICLE

Role of 3.0 T multiparametric MRI in local staging in prostate cancer and clinical implications for radiation oncology

F. Couñago · M. Recio · E. del Cerro · L. Cerezo · A. Díaz Gavela · F. J. Marcos · R. Murillo · J. M. Rodriguez Luna · I. J. Thuissard · J. L. R. Martin

Received: 15 March 2014 / Accepted: 23 April 2014

t al.

Table 3 Modification of risk groups and treatment by 3TMRI in all 103 patients treated with radiotherapy

Risk group modification by changes in local tumor stage	No. of patients (%)	Initial treatment	New treatment
Low risk → Intermediate risk	21 (20.1)	CTV: prostate;	CTV: prostate + SSVV;
T1c or T2a and GS ≤6 and PSA <10 ng/mL → T2b or T2c and GS ≤6 and PSA ≤10 ng/mL		doses: 78 Gy HT: none	doses: 80 Gy HT: none
Low Risk → High Risk	1 (0.9)	CTV: prostate;	CTV: prostate + SSVV;
T1c or T2a and GS ≤6 and PSA <10 ng/mL → T3 or T4 and GS ≤6 and PSA ≤10 ng/mL		doses: 78 Gy HT: none	doses: 80 Gy; HT × 24 months
Intermediate risk → Intermediate-high risk	5 (3.8)	CTV: prostate + SSVV	CTV: prostate + SSVV
T1c or T2a + PSA 10–20 + GS = 7 → T2b or T2c + PSA 10–20 ng/mL + GS = 7		doses: 80 Gy HT: none	doses: 80 Gy HT × 6 months
Intermediate risk → High Risk	8 (7.6)	CTV: prostate + SSVV	CTV: prostate + SSVV
T1c-T2c → T3 or T4 (T2b-T2c or GS = 7 or PSA 10–20 ng/mL)		doses: 80 Gy HT: none	doses: 80 Gy HT × 24 months

CTV clinical target volume, *GS* Gleason score, *HT* hormone therapy, *SSVV* seminal vesicles

Y .....la FORMULA DE ROACH: la Rt PELVICA?????

Paul L. Nguyen Anthony V. D'Amico

- Aplicando la misma fórmula a los pacientes de la encuesta epidemiológica (SEER) en 2004, con PSA <100 ng/mL que tenían ganglios positivos examinados anatomopatológicamente muestra que solo el 8% de los pacientes con una puntuación según la fórmula de Roach >= 15 tuvieron ganglios positivos.
- La fórmula de Roach sobreestima el riesgo de afectación nodal en la época actual.

Table 1. Patient Data From the 2004 SEER Data Set With PSA Less Than 100 ng/mL

Risk by Roach Score (%)	Observed Node-Positive Rate (%)	No. of Patients	No. with Positive Nodes
80-89.9	14	7	1
70-79.9	0	6	0
60-69.9	18	39	7
50-59.9	23	83	19
40-49.9	17	207	35
30-39.9	14	601	84
20-29.9	7	927	68
15-19.9	3	1,154	37
10-14.9	2	2,956	45
5-9.9	0.3	742	2
0-4.9	0.4	2,713	10
> 15	8	3,024	251
< 15	1	6,411	57

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; PSA, prostate-specific antigen.

J Clin Oncol. 2008 Apr 20;26(12):2055-6; author reply 2056-7. doi: 10.1200/JCO.2007.15.9939.

Targeting pelvic lymph nodes in men with intermediate- and high-risk prostate cancer despite two negative randomized trials.

Nguyen PL, D'Amico AV.

AUTHOR	YEAR	JOURNAL	SUPPORT ROACH FORMULA	NOT SUPPORT ROACH FORMULA
PAUL L. NGUYEN, M.D.,*	2008	JCO		X
PAUL L. NGUYEN, M.D.,*	2009	IJROBF		X
YU JB. M.D.	2011	IJROBF		X
DESERNO WM, M.D.	2011	IJROBF		X
SOPHIA RAHMAN, M.D	2012	IJROBF		X
COOKE EW, M.D.	2012	AJCO		X
YU JB. M.D.	2012	IJROBF		X

- *Updated analysis of RTOG 94-13*
  - **NO existen diferencias en SLE entre los pacientes con RT pelvis completa vs sólo próstata.**
  - **TIENE SENTIDO LA IRRADIACIÓN PELVICA????**

SUPERVIVENCIA MEJORABLE

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	-	-	-	-

EUA GUIDELINES 2014

NUEVOS RETOS……

- TERAPIA FOCAL

Recommendations	GR
In patients who are unfit for surgery or radiotherapy, CSAP can be an alternative treatment for PCa.	C
If HIFU is offered, the lack of long-term comparative outcome data (> 10 y) should be discussed with the patient.	C
Focal therapy of PCa is still in its infancy and cannot be recommended as a therapeutic alternative outside clinical trials.	A

- TRATAMIENTOS COMBINADOS

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

  - Abiraterona 8 ensayos F II-III
  - Enzalutamida 4 ensayos

Clinical Investigation: Genitourinary Cancer

Prospective Randomized Phase 2 Trial of Intensity Modulated Radiation Therapy With or Without Oncolytic Adenovirus-Mediated Cytotoxic Gene Therapy in Intermediate-Risk Prostate Cancer

MEJOR SELECCIÓN DE PACIENTES

- PLATAFORMAS MOLECULARES

- EUA
- Jun-2014

16. SUMMARY OF GUIDELINES ON PRIMARY TREATMENT OF PCA

Stage	Treatment	Comment	GR
T1a	Watchful waiting	In patients with < 10-year life expectancy standard treatment for Gleason score ≤ 6 and 7 adenocarcinomas.	B
	Active surveillance	In patients with > 10-year life expectancy, re-staging with TRUS and biopsy is recommended.	B
	Radical prostatectomy	Optional in younger patients with a long life expectancy, especially for Gleason score ≥ 7 adenocarcinomas.	B
	Radiotherapy	Optional in younger patients with a long life expectancy, in particular in poorly differentiated tumours. Higher complication risks after TURP, especially with interstitial radiation.	B
	Hormonal	Not an option.	A
	Combination	Not an option.	B
T1b-T2b	Watchful waiting	Patients with a life expectancy < 10 years.	B
	Active surveillance	Treatment option in patients with cT1c-cT2a, PSA < 10 ng/mL, biopsy Gleason score ≤ 6, ≤ 2 biopsies positive, ≤ 50% cancer involvement of each biopsy.	B
		Patients with a life expectancy > 10 years once they are informed about the lack of survival data beyond 10 years.	
		Patients who do not accept treatment-related complications.	
T1a-T2c	Watchful waiting	Patients with life expectancy < 10 years and Gleason score < 7. Patients with life expectancy < 10 years and Gleason score = 7.	A B
	Radical prostatectomy	Optional in patients with pT1a PCa. Standard treatment for patients with a life expectancy > 10 years who accept treatment-related complications.	A
	Radiotherapy	Patients with a life expectancy > 10 years who accept treatment-related complications.	B
		Patients with contraindications for surgery.	
		Unfit patients with 5-10 years of life expectancy and poorly differentiated tumours (combination therapy is recommended; see below).	
	Brachytherapy	Low-dose rate brachytherapy can be considered for low risk PCa patients with a prostate volume ≤ 50 mL and an IPSS ≤ 12.	B
	Hormonal	Symptomatic patients, who need palliation of symptoms, unfit for curative treatment.	C
		Anti-androgens are associated with a poorer outcome compared to 'watchful waiting' and are not recommended.	A
	Combination	For high-risk patients, neoadjuvant hormonal treatment and concomitant hormonal therapy plus radiotherapy results in increased overall survival.	A

T3-T4	Watchful waiting	Option in asymptomatic patients with T3, Gleason score ≤ 7, and a life expectancy < 10 years who are unfit for local treatment.	C
	Radical prostatectomy	Optional for selected patients with T3a, PSA < 20 ng/mL, biopsy Gleason score ≤ 8 and a life expectancy > 10 years.	C
		Patients have to be informed that RP is associated with an increase risk of positive surgical margins, unfavourable histology and positive lymph nodes and that, therefore, adjuvant or salvage therapy such as radiation therapy or androgen deprivation might be indicated.	
	Radiotherapy	T3 with > 5-10 years of life expectancy. Dose escalation of > 74 Gy seems to be of benefit. A combination with hormonal therapy can b recommended.	A
	Hormonal	Symptomatic patients, extensive T3-T4, high PSA level (> 25-50 ng/ mL), PSADT (DT) < 1 year.	A
		Patient-driven, unfit patients.	
		Hormone monotherapy is not an option for patients who are fit enough for radiotherapy.	
	Combination	Overall survival is improved by concomitant and adjuvant hormonal therapy (3 years) combined with external beam radiation.	A
		NHT plus radical prostatectomy: no indication.	B
N+, M0	Watchful waiting	Asymptomatic patients. Patient-driven (PSA < 20-50 ng/mL), PSADT > 12 months. Requires very close follow-up.	B
	Radical prostatectomy	Optional for highly selected patients with a life expectancy of > 10 years as part of a multimodal treatment approach.	C
	Radiotherapy	Optional in highly selected patients with a life expectancy of > 10 years, combination therapy with adjuvant androgen deprivation for 3 years is mandatory.	C
	Hormonal	Standard treatment after extended node dissection if > 2 positive nodes (irrespective of the local treatment: surgery or radiotherapy). Hormonal therapy should only be used as monotherapy in patients who are unfit for any type of local therapy.	A
	Combination	No standard option. Patient-driven.	B
M+	Watchful waiting	No standard option. May have worse survival/more complications than with immediate hormonal therapy. Requires very close follow-up.	B
	Radical prostatectomy	Not a standard option.	C
	Radiotherapy	Not an option for curative intent; therapeutic option in combination with androgen deprivation for treatment of local cancer-derived symptoms.	C
	Hormonal	Standard option. Mandatory in symptomatic patients.	A

DT = doubling time; NHT = neoadjuvant hormonal treatment; IPSS = International Prostatic Symptom Score; PSA = prostate specific antigen; TRUS = transrectal ultrasound; TURP = transurethral resection of the prostate

PATIENT DRIVE CARE

15.6 Recommendations on QoL in PCa management

	LE	GR
Patients with low risk prostate cancer should be informed on the fact that functional outcome of AS is better than for local active treatment.	2	B
Patients should be informed that functional outcome after Sex Med and open prostatectomy will be similar.	2	B
Patients should be informed that the long-term (15 year) QoL outcomes EBRT and RP will be similar.	2	B

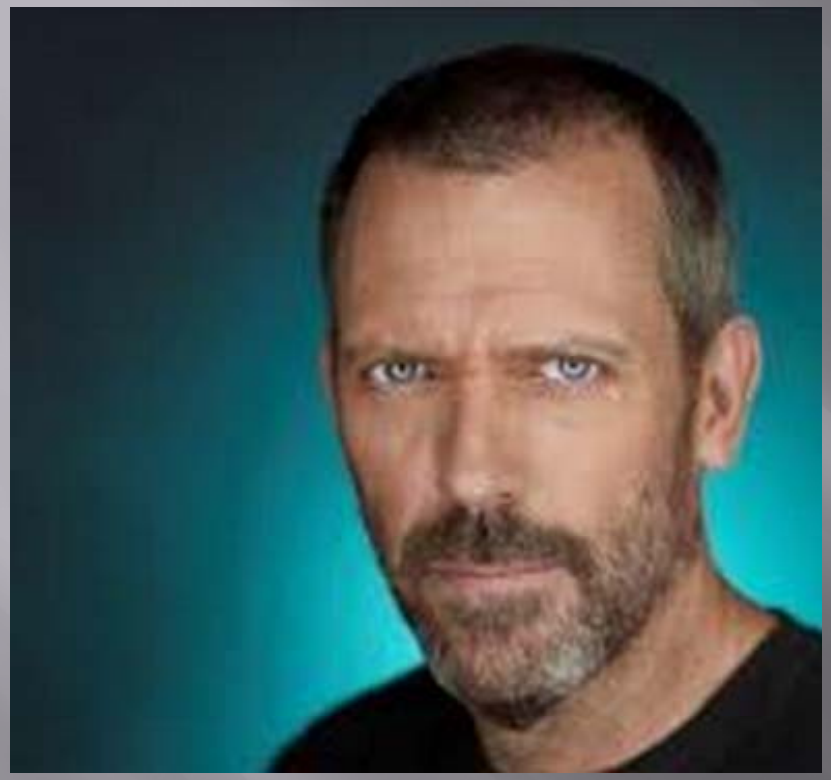
AS = active surveillance; EBRT = external beam radiation therapy; QoL = quality of life; RP = radical prostatectomy.

Mira JJ, Aranaz J. La satisfacción del paciente como una medida del resultado de la atención sanitaria. Medicina Clínica 2000;114 (Supl 3):26-33

La satisfacción del paciente como una medida del resultado de la atención sanitaria

José Joaquín Mira, Jesús Aranaz

Universidad Miguel Hernández



GRACIAS