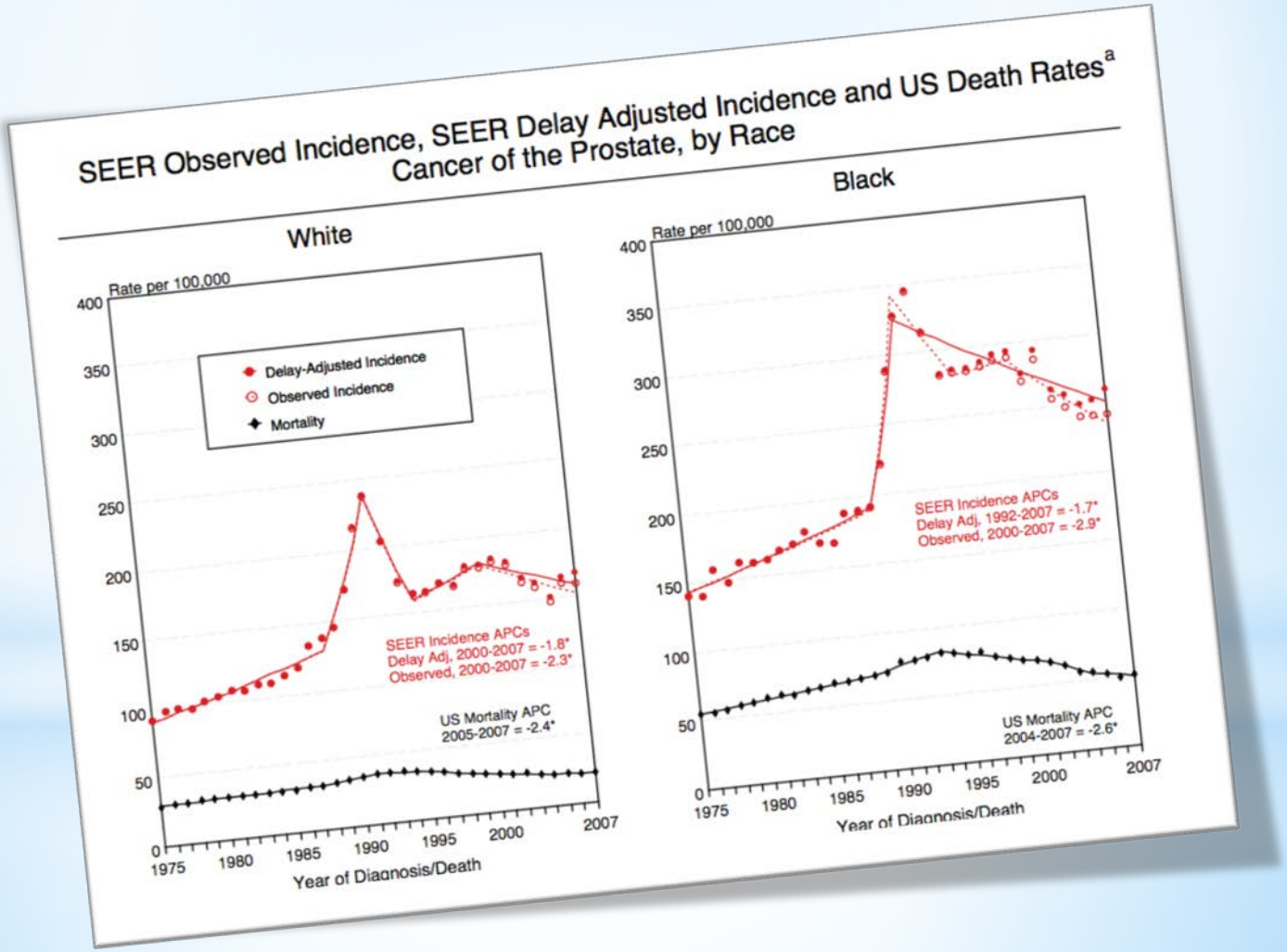
4OS ENCONTROS DE ANDROLOGIA

ONCO-ANDROLOGIA

* FOCAL THERAPY OF PROSTATE CANCER

Luis Campos Pinheiro

* The changing epidemiology of prostate cancer



* The changing epidemiology of prostate cancer

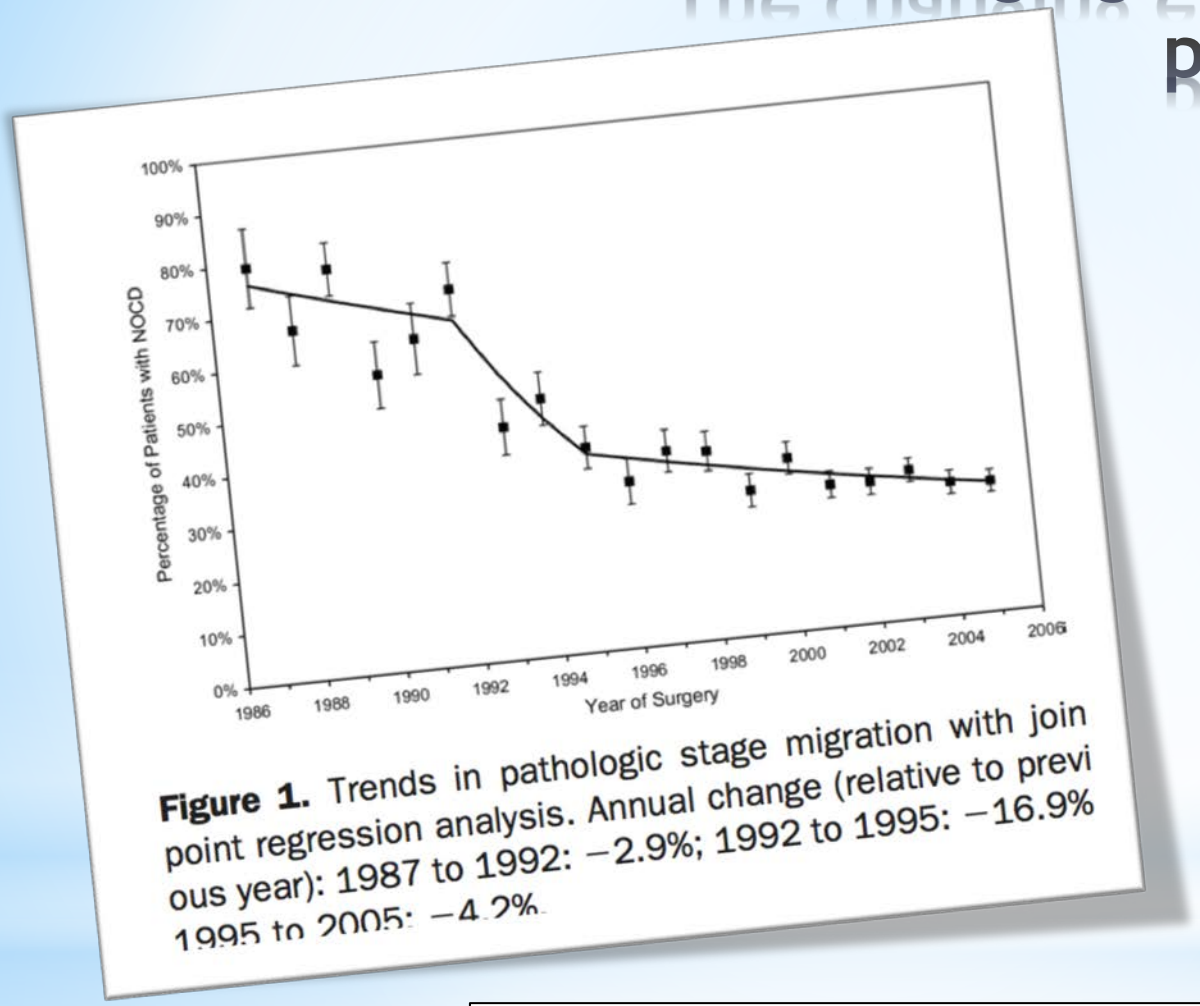
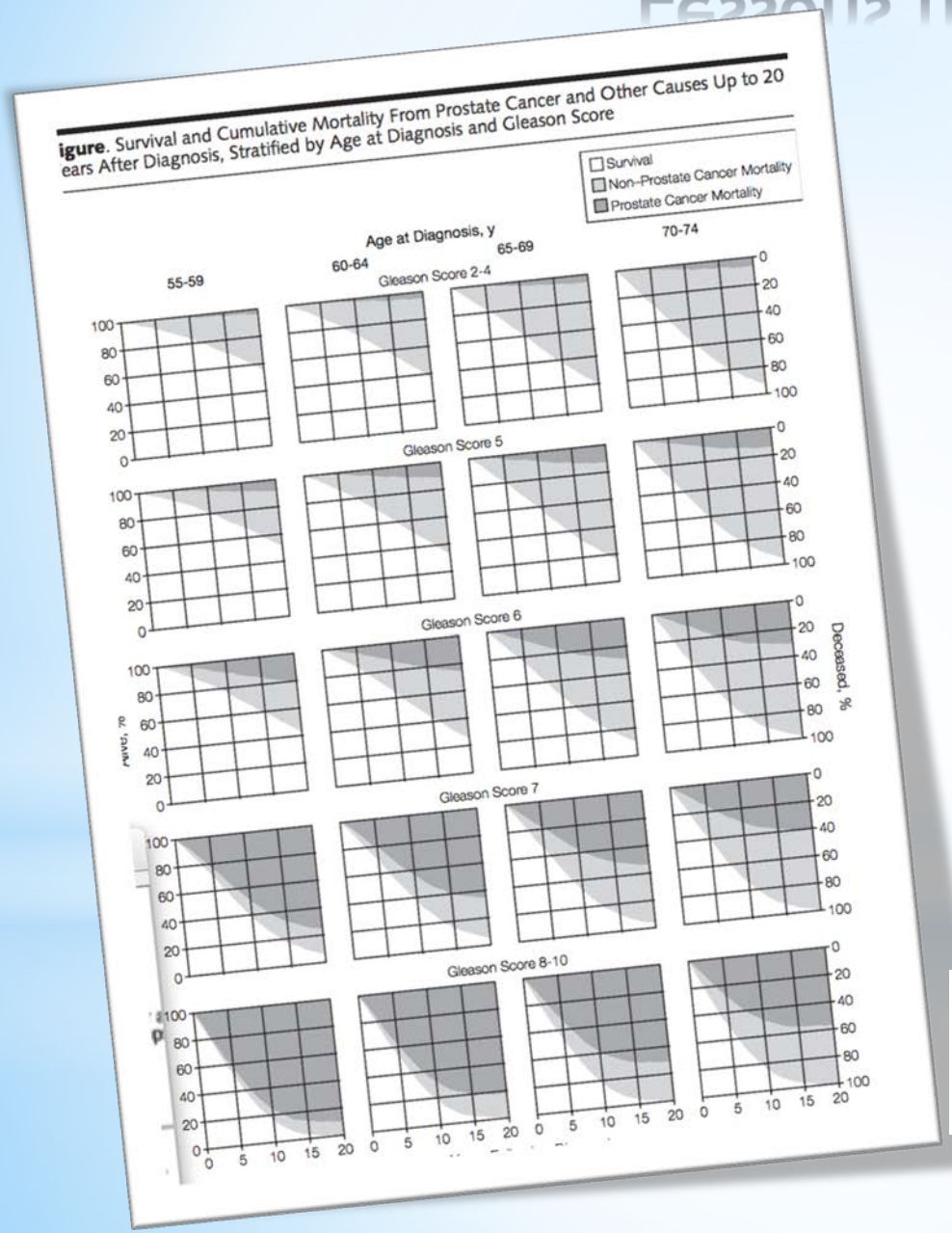


Figure 1. Trends in pathologic stage migration with join point regression analysis. Annual change (relative to previ ous year): 1987 to 1992: −2.9%; 1992 to 1995: −16.9% 1995 to 2005: −4.2%.

Pathologic Stage Migration Has Slowed in the Late PSA Era

Fei Dong, Alwyn M. Reuther, Cristina Magi-Galluzzi, Ming Zhou, Patrick A. Kupelian, and Eric A. Klein

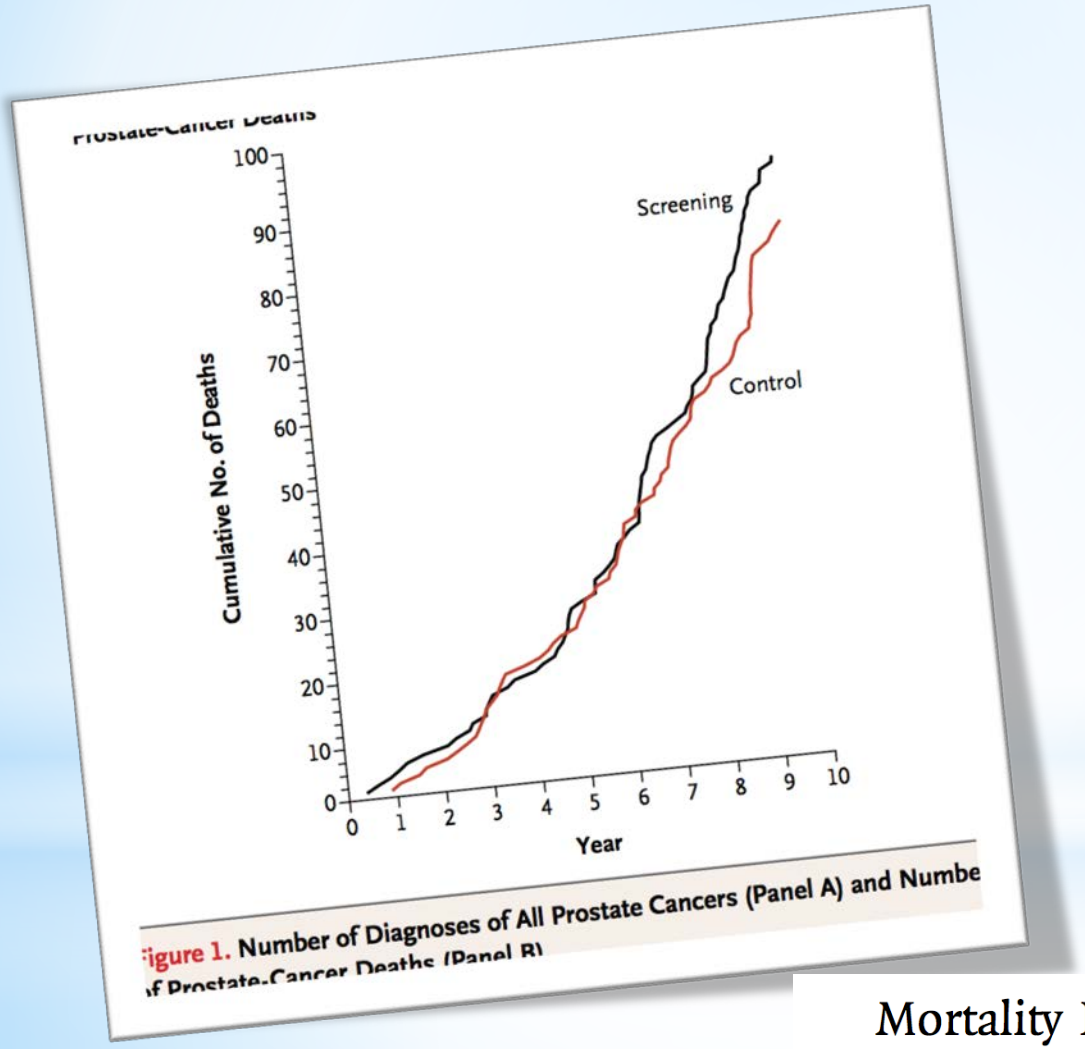
* Lessons from mortality studies



Peter C. Albertsen, MD, MS
James A. Hanley, PhD
Judith Fine, BA

20-Year Outcomes Following Conservative Management of Clinically Localized Prostate Cancer

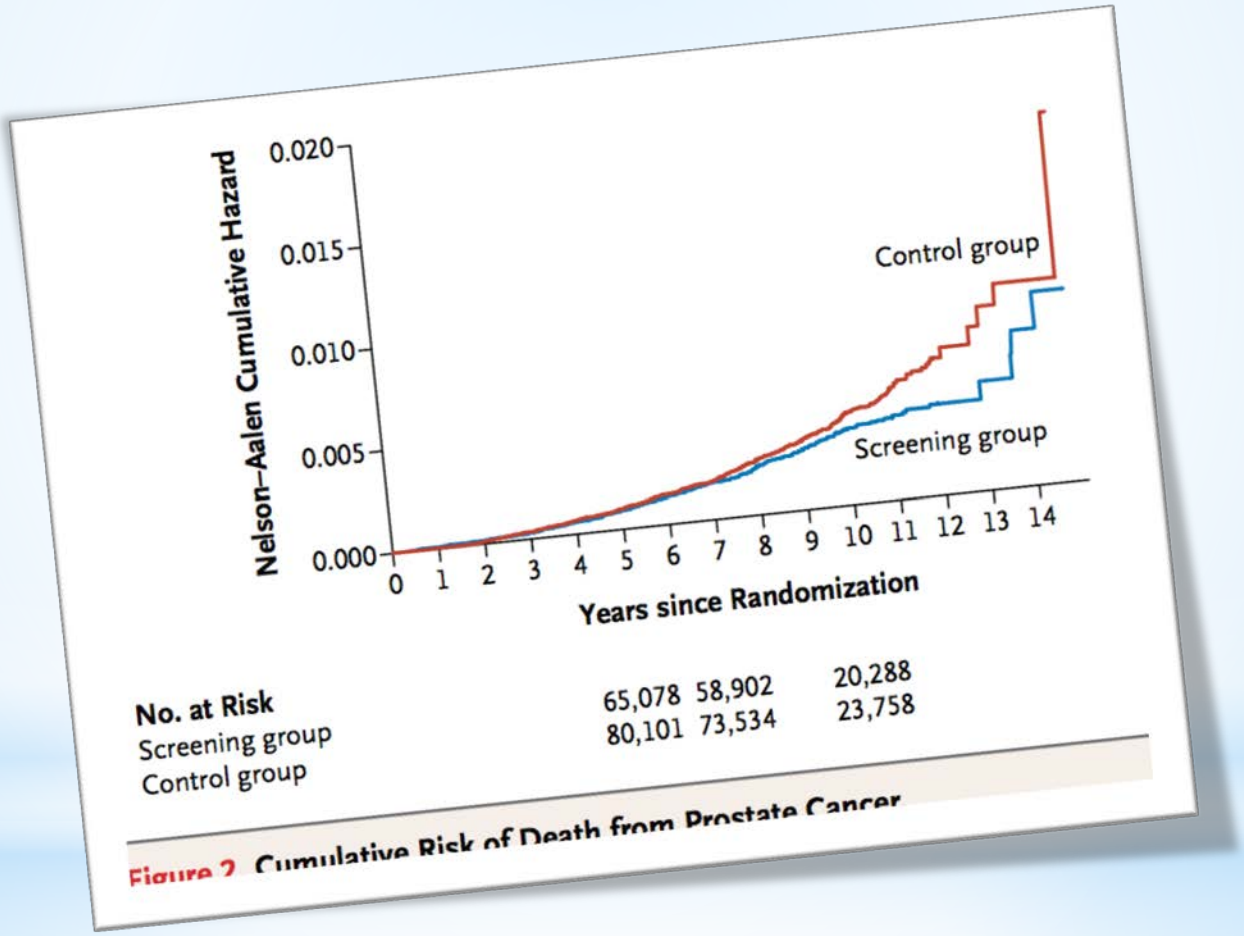
* Lessons from mortality studies



Mortality Results from a Randomized Prostate-Cancer Screening Trial

Gerald L. Andriole, M.D., E. David Crawford, M.D., Robert L. Grubb III, M.D.,

* Lessons from mortality studies



Screening and Prostate-Cancer Mortality in a Randomized European Study

Fritz H. Schröder, M.D., Jonas Hugosson, M.D., Monique J. Roobol, Ph.D.,

* Lessons from mortality studies

Lead Time and Overdiagnosis in Prostate-Specific Antigen Screening: Importance of Methods and Context

Gerrit Draisma, Ruth Etzioni, Alex Tsodikov, Angela Mariotto, Elisabeth Wever, Roman Gulati, Eric Feuer, Harry de Koning

The time by which prostate-specific antigen (PSA) screening advances prostate cancer diagnosis, called the lead time, has been reported by several studies, but results have varied widely, with mean lead times ranging from 3 to 12 years. A quantity that is closely linked with the lead time is the overdiagnosis frequency, which is the fraction of screen-detected cancers that would not have been diagnosed in the absence of screening. Reported overdiagnosis estimates have also been variable, ranging from 25% to greater than 80% of screen-detected cancers.

We used three independently developed mathematical models of prostate cancer progression and detection that were calibrated to incidence data from the Surveillance, Epidemiology, and End Results program to estimate lead times and the fraction of overdiagnosed cancers due to PSA screening among US men aged 54–80 years in 1985–2000. Lead times were estimated by use of three definitions. We also compared US and earlier estimates from the Rotterdam section of the European Randomized Study of Screening for Prostate Cancer (ERSPC) that were calculated by use of a microsimulation screening analysis (MISCAN) model.

The models yielded similar estimates for each definition of lead time, but estimates differed across definitions. Among screen-detected cancers that would have been diagnosed in the patients' lifetimes, the estimated mean lead time ranged from 5.4 to 6.9 years across models, and overdiagnosis ranged from 23% to 42% of all screen-detected cancers. The original MISCAN model fitted to ERSPC Rotterdam data predicted a mean lead time of 7.9 years and an overdiagnosis estimate of 66%; in the model that was calibrated to the US data, these were 6.9 years and 42%, respectively.

* Two alternative strategies to overcame screening overdiagnosis

Active surveillance

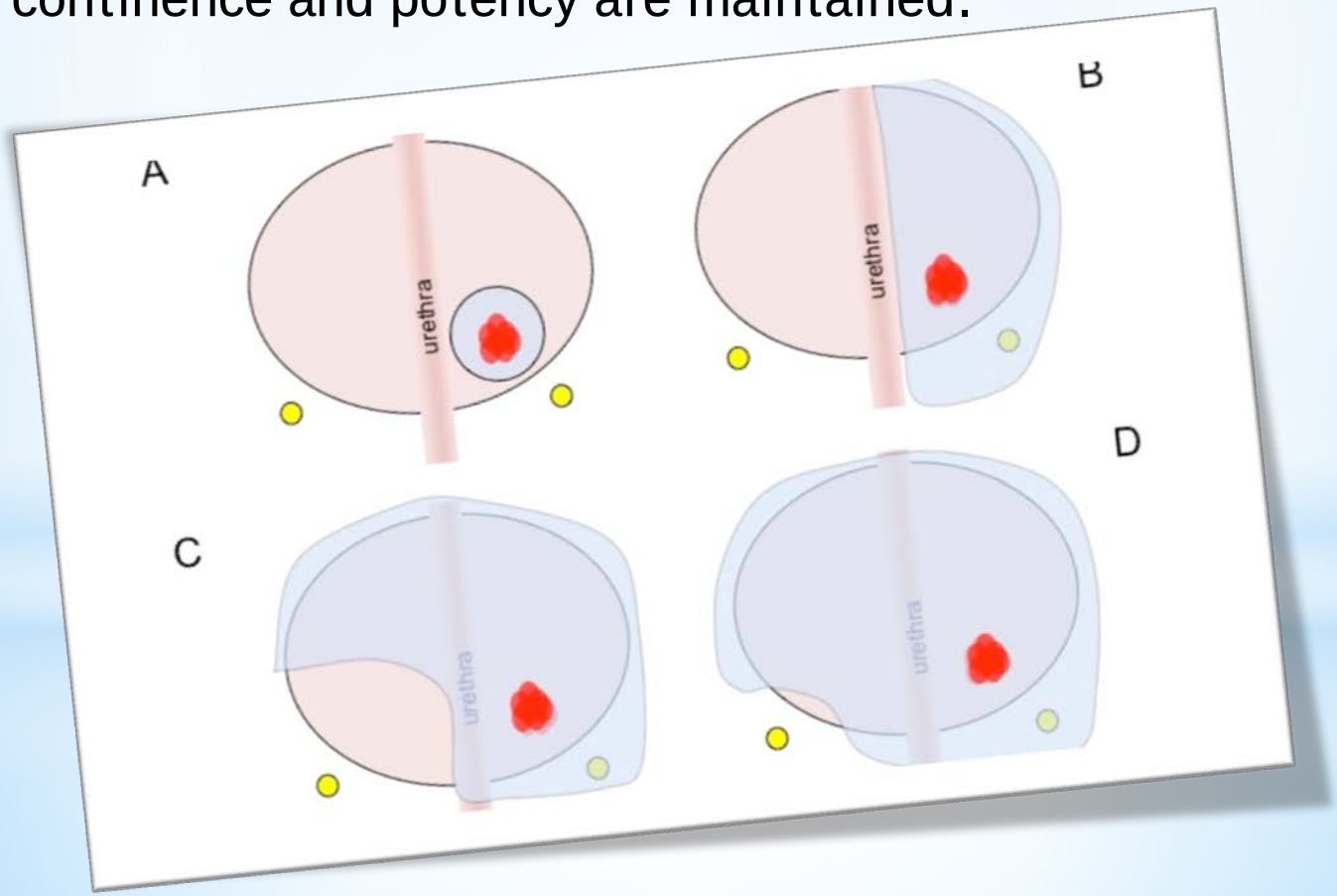
Focal therapy

* Active surveillance outcomes

	n	Median age	Follow up (M)	Cancer specific survival	% remaining on As
Carter	407	66	41	100	59
Van As	326	67	22	100	73
Khatami	270	64	63	100	61
Roemeling	278	70	41	100	71
Dall'Era	321	64	43	100	76
Eggener	262	69	29	100	84
Van den Bergh	533	70	48	99	50
Klotz	450	70	81	97	53
total	2849	64-70	22-81	97-100	50-84

* Focal therapy

Goal of destroying known areas of cancer while still organ confined and sparing uninvolved tissue so that urinary continence and potency are maintained.



* Multifocality of prostate cancer

Preoperative Prediction of Multifocal Prostate Cancer and Application of Focal Therapy: Review 2007

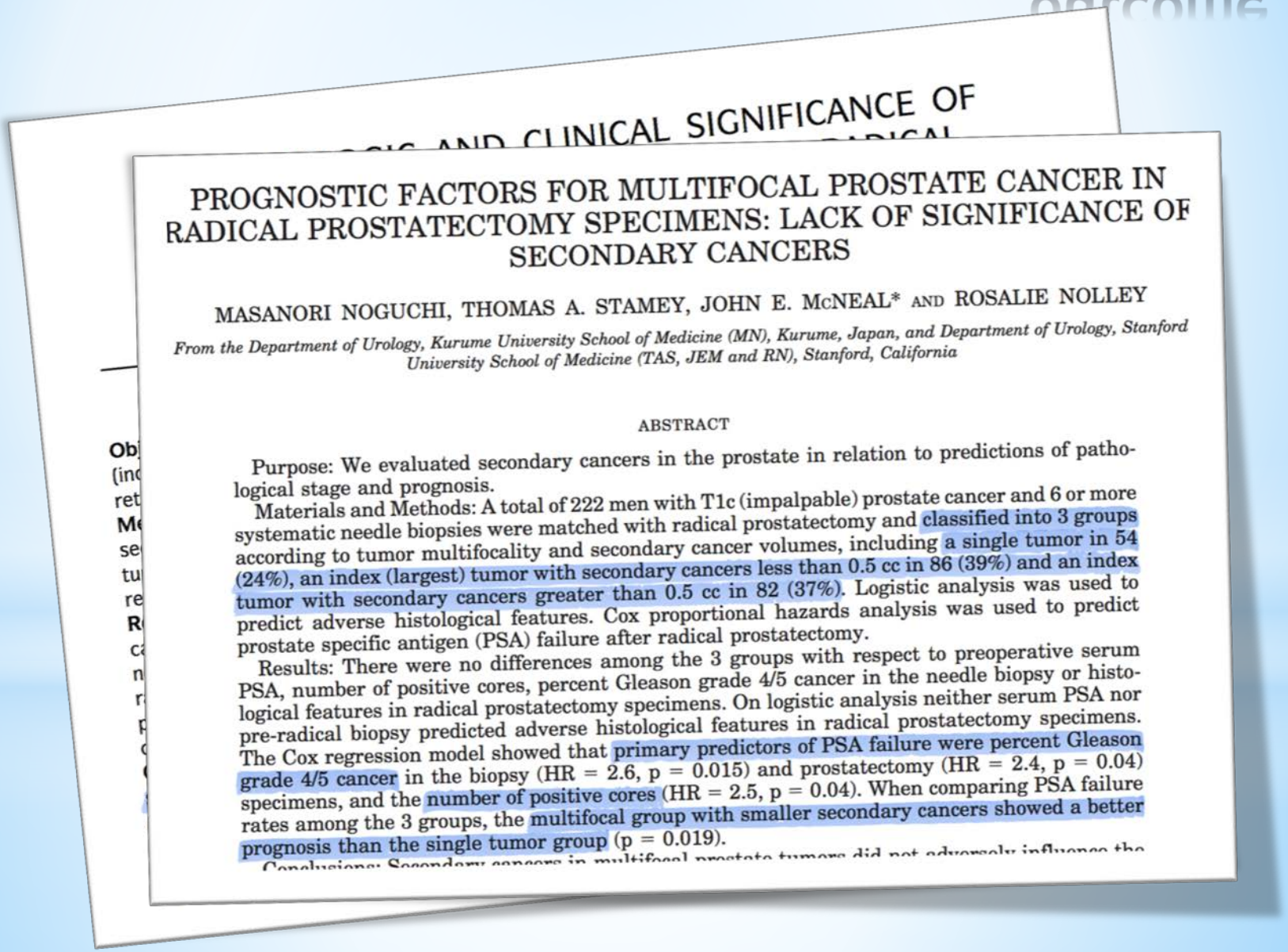
David G. Bostwick

Table 1. Incidence of multifocal prostate cancer in radical prostatectomies

Study	Radical Prostatectomy	N	Multifocality (%)
Villers *et al.*[10] (1992)	Stanford protocol*	234	50
Miller *et al.*[11] (1994)	Whole-mounted	151	56
Djavan *et al.*[12] (1999)	4-mm specimen sections	308	67
Noguchi *et al.*[13] (2003)	Stanford protocol*	222	76
Song *et al.*[14] (2003)	Whole-mounted	132	33
Ng *et al.*[15] (2004)	Whole-mounted	364	85
Eichelberger *et al.*[16] (2004)	Whole-mounted	312	85
Horninger *et al.*[17] (2004)	4-mm specimen sections	80	65
Cheng *et al.*[18] (2005)	Whole-mounted	62	69
Torlakovic *et al.*[19] (2005)	Stanford protocol*	46	65
Magi-Galluzzi *et al.*[20] (2006)	Not stated	130	87
Muezzinoglu *et al.*[21] (2006)	Whole-mounted	947	73

* Stanford protocol uses serial transverse sections at 3-mm intervals.[10,22]

* Index lesion drives PCA biology and outcome



PROGNOSTIC FACTORS FOR MULTIFOCAL PROSTATE CANCER IN RADICAL PROSTATECTOMY SPECIMENS: LACK OF SIGNIFICANCE OF SECONDARY CANCERS

MASANORI NOGUCHI, THOMAS A. STAMEY, JOHN E. McNEAL* AND ROSALIE NOLLEY

From the Department of Urology, Kurume University School of Medicine (MN), Kurume, Japan, and Department of Urology, Stanford University School of Medicine (TAS, JEM and RN), Stanford, California

ABSTRACT

Purpose: We evaluated secondary cancers in the prostate in relation to predictions of pathological stage and prognosis.

Materials and Methods: A total of 222 men with T1c (impalpable) prostate cancer and 6 or more systematic needle biopsies were matched with radical prostatectomy and classified into 3 groups according to tumor multifocality and secondary cancer volumes, including a single tumor in 54 (24%), an index (largest) tumor with secondary cancers less than 0.5 cc in 86 (39%) and an index tumor with secondary cancers greater than 0.5 cc in 82 (37%). Logistic analysis was used to predict adverse histological features. Cox proportional hazards analysis was used to predict prostate specific antigen (PSA) failure after radical prostatectomy.

Results: There were no differences among the 3 groups with respect to preoperative serum PSA, number of positive cores, percent Gleason grade 4/5 cancer in the needle biopsy or histological features in radical prostatectomy specimens. On logistic analysis neither serum PSA nor pre-radical biopsy predicted adverse histological features in radical prostatectomy specimens. The Cox regression model showed that primary predictors of PSA failure were percent Gleason grade 4/5 cancer in the biopsy (HR = 2.6, p = 0.015) and prostatectomy (HR = 2.4, p = 0.04) specimens, and the number of positive cores (HR = 2.5, p = 0.04). When comparing PSA failure rates among the 3 groups, the multifocal group with smaller secondary cancers showed a better prognosis than the single tumor group (p = 0.019).

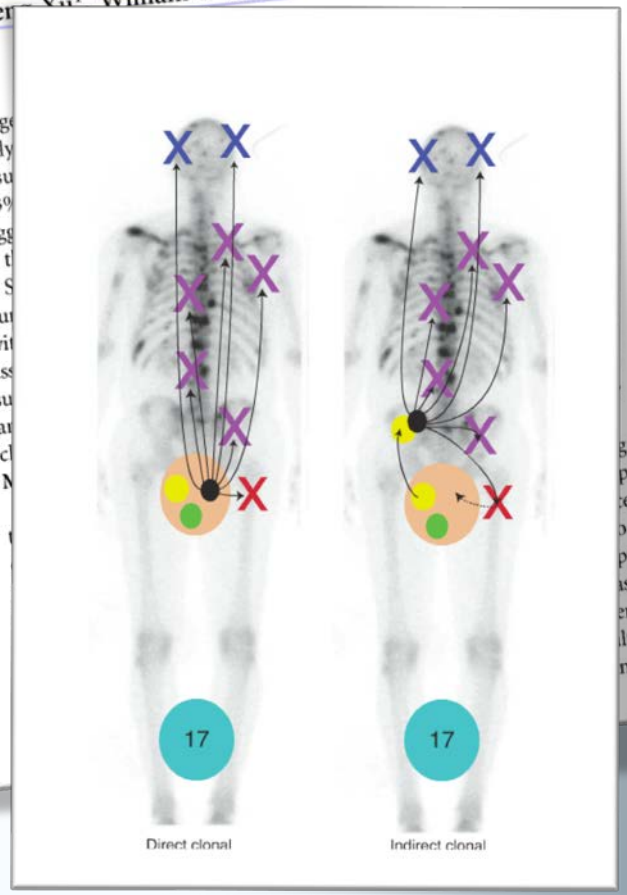
Conclusions: Secondary cancers in multifocal prostate tumors did not adversely influence the

* Index lesion drives PCA biology and outcome

Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer

Wennuan Liu[1,9], Sari Laitinen[2,9], Sofia Khan[3], Mauno Vihinen[3], Jeanne Kowalski[4], Guoqiang Yu[5], Li Chen[5], Charles M Ewing[6], Mario A Eisenberger[7], Michael A Carducci[7], William G Nelson[7], Srinivasan Yegnasubramanian[7], Jun Luo[6,7], Yue Wang[5], Jianfe... Xu[1], William B Isaacs[6,7], Tapio Visakorpi[2] & G Steven Bova[6–8]

Many studies have shown that primary prostate cancers are multifocal[1–3] and are composed of multiple genetically distinct cancer cell clones[4–6]. Whether or not multiclonal primary prostate cancers typically give rise to multiclonal or monoclonal prostate cancer metastases is largely unknown, although studies at single chromosomal loci are consistent with the latter case. Here we show through a high-resolution genome-wide single nucleotide polymorphism and copy number survey that most, if not all, metastatic prostate cancers have monoclonal origins and maintain a unique signature copy number pattern of the parent cancer cell while also accumulating a variable number of separate subclonally sustained changes. We find no relationship between anatomic site of metastasis and genomic copy number change pattern. Taken together with past animal and cytogenetic studies of metastasis[7] and recent single-locus genetic data in prostate and other metastatic cancers[8–10], these data indicate that despite common genomic heterogeneity in primary cancers, most metastatic cancers arise from a single precursor cancer cell. This study establishes that genomic archeology of multiple anatomically separate metastatic cancers in individuals can be used to define the salient genomic features of a parent cancer clone of proven lethal metastatic phenotype.



* Identifying the Index Lesion

Evaluating Localized Prostate Cancer and Identifying Candidates for Focal Therapy

A. Oliver Sartor, Hedvig Hricak, Thomas M. Wheeler, Jonathan Coleman, David F. Penson, Peter R. Carroll, Mark A. Rubin, and Peter T. Scardino

Can focal therapy successfully control prostate cancer? Also, if so, which patients should be considered eligible? With limited data available from relatively few patients, these questions are difficult to answer. At this writing, the most likely candidates for focal therapy are patients with low-risk, small-volume tumors, located in 1 region or sector of the prostate, who would benefit from early intervention. The difficulty lies in reliably identifying these men.

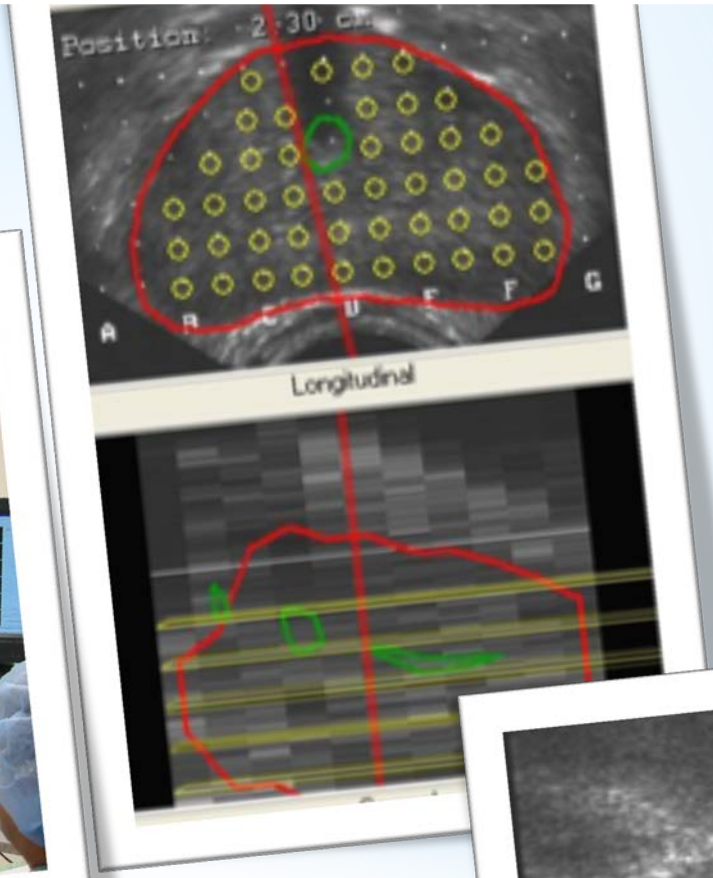
The larger number of cores obtained in each needle biopsy session has increased both the detection of prostate cancer and the potential risk of overtreating many patients whose cancers pose very little risk to life or health. Urologists typically perform at least a 12-core template biopsy. Although the debate continues about the optimal template, laterally and peripherally directed biopsies have been shown to improve the diagnostic yield. However, as many as 25% of tumors arise anteriorly and can be missed with peripherally directed techniques.

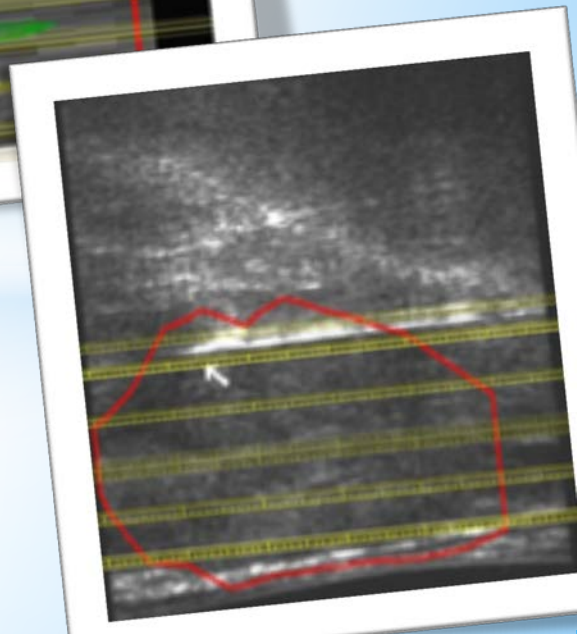
Prostate cancer tends to be multifocal, even in its earliest stages. However, the secondary cancers are usually smaller and less aggressive than the index cancer. They appear similar to the incidental cancers found in cystoprostatectomy specimens and appear to have little effect on prognosis in surgical series. When a single focus of cancer is found in 1 core, physicians rightly suspect that more foci of cancer are present in the prostate. Assessing the risk in these patients is challenging when determined by the biopsy data alone.

To predict the presence of a very low-risk or "indolent" cancer, nomograms have been developed to incorporate clinical stage, Gleason grade, prostate-specific antigen levels, and prostate volume, along with the quantitative analysis of the biopsy results. Transperineal "mapping" or "saturation" biopsies have been advocated to detect cancers missed or underestimated by previous transrectal biopsies. This approach could provide the accurate staging, grading, and tumor localization needed for a focal therapy program. Nevertheless, for men with minimal cancer who are amenable to active surveillance or focal therapy, consensus about the most accurate biopsy strategy has not yet been reached.

Imaging, particularly magnetic resonance imaging and magnetic resonance spectroscopic imaging, has been used to assess men with early-stage prostate cancer. Large-volume cancers can be seen reasonably well, but small lesions have been difficult to detect reliably or measure accurately. Factors such as voxel resolution, organ movement, biopsy artifact, and benign

Transperineal Template-Guided Prostate Mapping Biopsy





Transperineal Template-Guided Prostate Mapping Biopsy

The Role of 3-Dimensional Mapping Biopsy in Decision Making for Treatment of Apparent Early Stage Prostate Cancer

Al B. Barqawi,*,† Kyle O. Rove, Saeed Gholizadeh, Colin I. O'Donnell, Hari Koul‡ and E. David Crawford§

Materials and Methods: We prospectively performed 3-dimensional mapping biopsy on 180 consecutive men who presented to our clinic between 2006 and 2009 with early stage, organ confined prostate cancer based on transrectal ultrasound guided 10 to 12-core biopsy, and on 35 with prior negative transrectal ultrasound biopsies.

Results: At presentation median patient age was 60.5 years (range 43 to 77), median prostate specific antigen was 4.8 ng/ml (range 0.5 to 72.4) and median prostate volume was 35 cc (range 9 to 95). The median number of cores acquired by transrectal ultrasound and 3-dimensional mapping biopsy was 12 and 56, and the median number of positive cores was 1 and 2, respectively. We documented Gleason score upgrade in 49 of 180 cases (27.2%) and up-stage in 82 (45.6%). The incidence of urinary retention catheter requirement of greater than 48 hours was 3.2% and the

* Multiparametric MRI

Diffusion-Weighted Magnetic Resonance Imaging in Patients With Unilateral Prostate Cancer on Extended Prostate Biopsy: Predictive Accuracy of Laterality and Implications for Hemi-Ablative Therapy

In Gab Jeong, Jeong Kon Kim, Kyoung-Sik Cho, Dalsan You, Cheryn Song, Jun Hyuk Hong, Hanjong Ahn and Choung-Soo Kim*

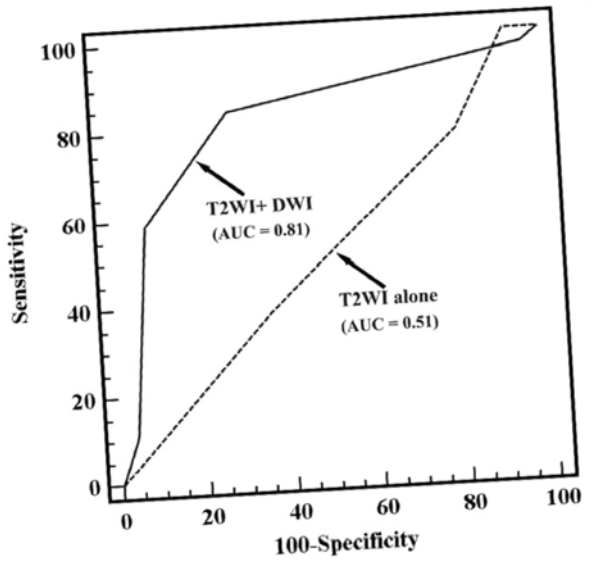
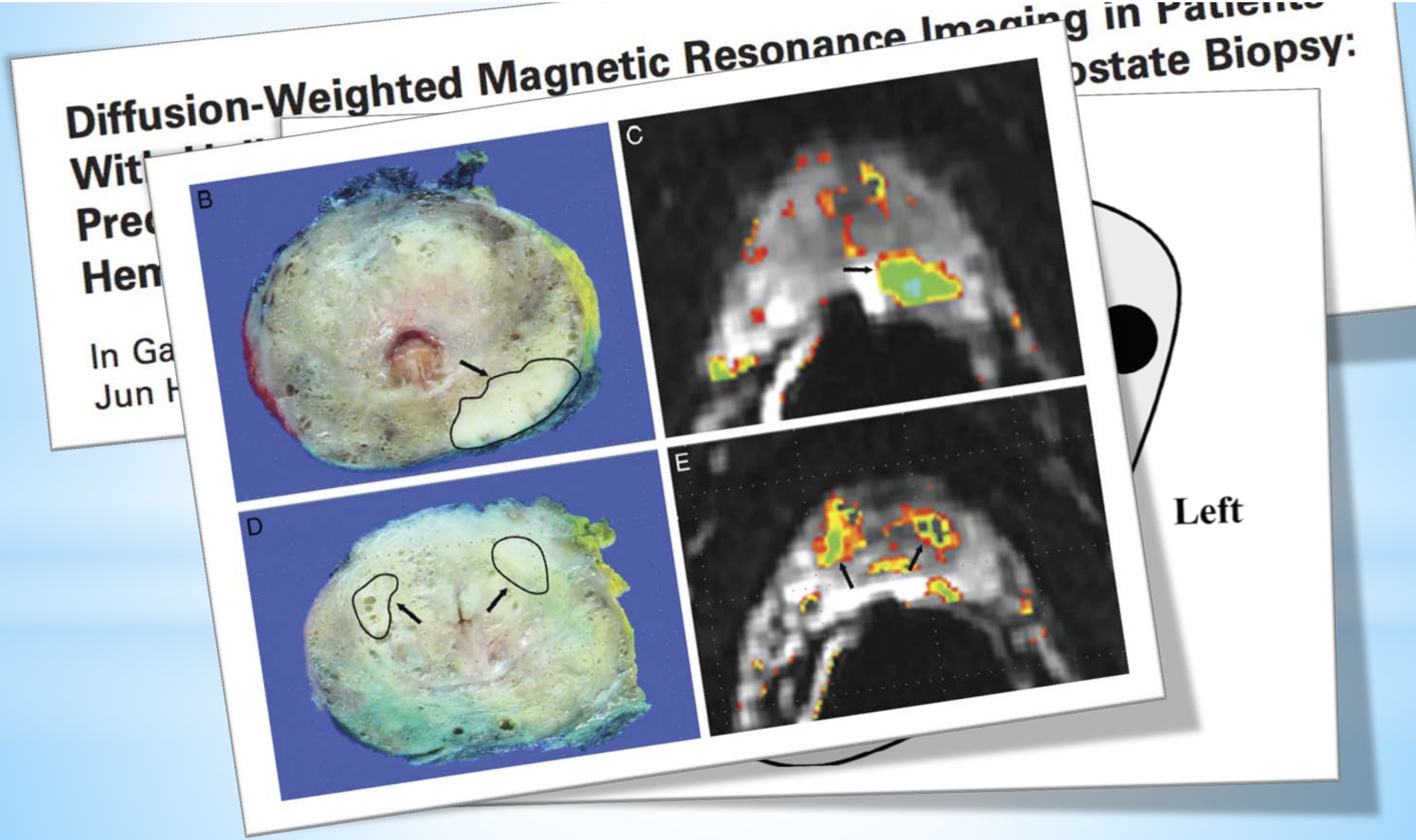


Figure 2. ROC curves to detecting prostate tumors in lobes

Figure 3. Representative data on 72-year-old man with prostate cancer with preoperative PSA 6.9 ng/ml, clinical stage T1c and Gleason score 4 + 3. *A*, 12-core prostate biopsy sites. Black circles indicate 6 positive cores. *B*, histological step section of prostate base shows single cancer area (outline) in peripheral zone of left lobe (arrow). *C*, closest ADC map corresponding to pathological slice reveals decreased area of diffusion (arrow). *D*, histological step section of mid prostate reveals 2 cancer areas (outlines) in bilateral transitional zone (arrow). *E*, closest ADC map corresponding to pathological slice shows decreased diffusion areas (arrows).



* Multiparametric MRI

Diffusion-Weighted Magnetic Resonance Imaging in Patients With Unilateral Prostate Cancer on Extended Prostate Biopsy: Predictive Accuracy of Laterality and Implications for Hemi-Ablative Therapy

In Gab Jeong, Jeong Kon Kim, Kyoung-Sik Cho, Dalsan You, Cheryn Song, Haniong Ahn and Choung-Soo Kim*

Table 2. *Ability of T2W M*

	ve biopsy	
	V (95% CI)	p Value
% Sensitivity	7–92.1)	0.003
% Specificity	6–87.9)	0.004
% Pos predictive value	–95.2)	
% Neg predictive value	–81.3)	
Pos likelihood ratio*	–5.68)	
Neg likelihood ratio†	–0.41)	

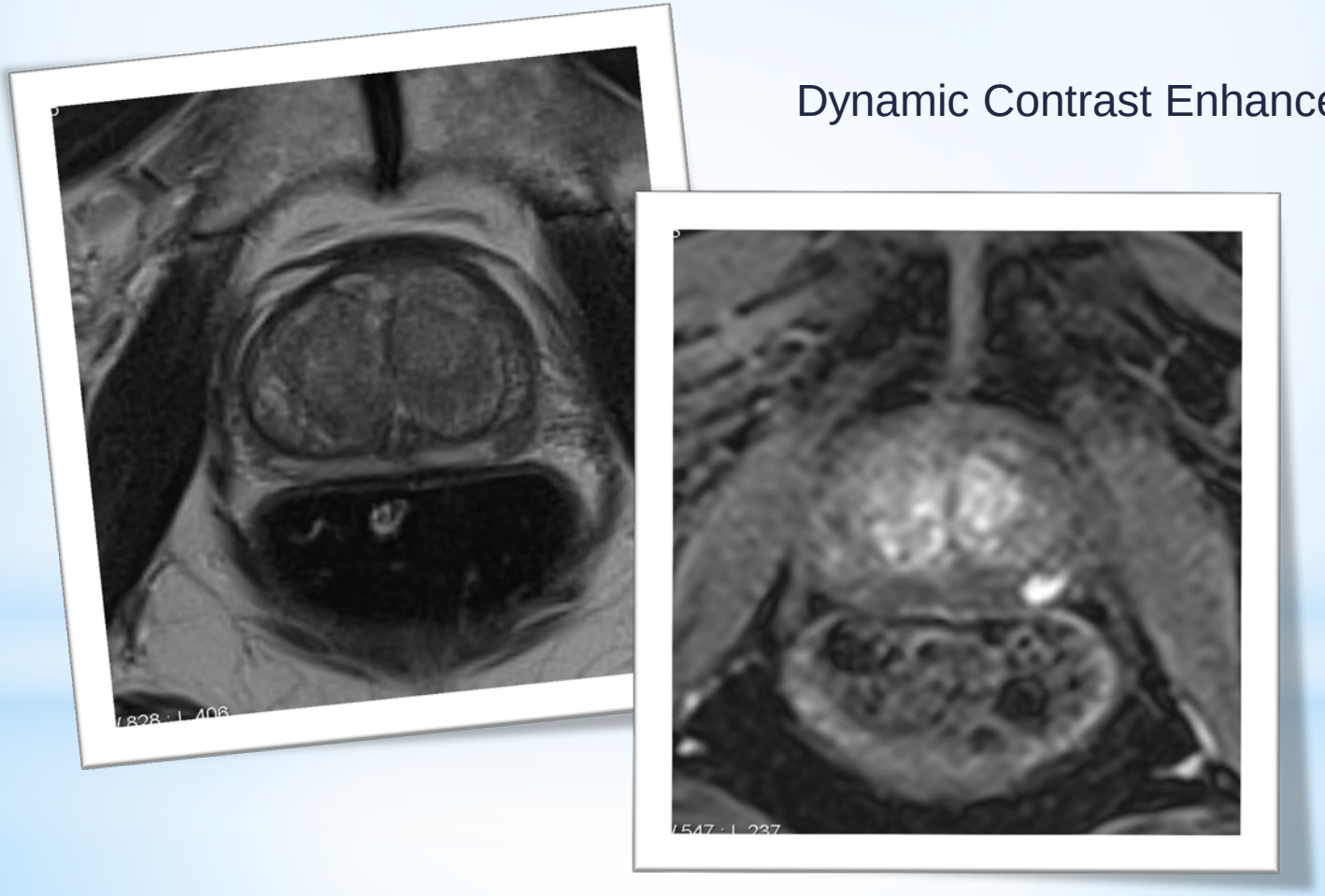
* Sensitivity/1 — specificity

CONCLUSIONS

Results show that extended prostate biopsy does not provide accurate information on prostate cancer unilaterality. DW MRI combined with T2W MRI had an incremental diagnostic benefit to predict unilateral disease. These results suggest that the combination of DW and T2W MRI along with prostate biopsy may help select candidates for hemi-ablative focal therapy for prostate cancer.

* Multiparametric MRI

T2-Weighted



Dynamic Contrast Enhanced

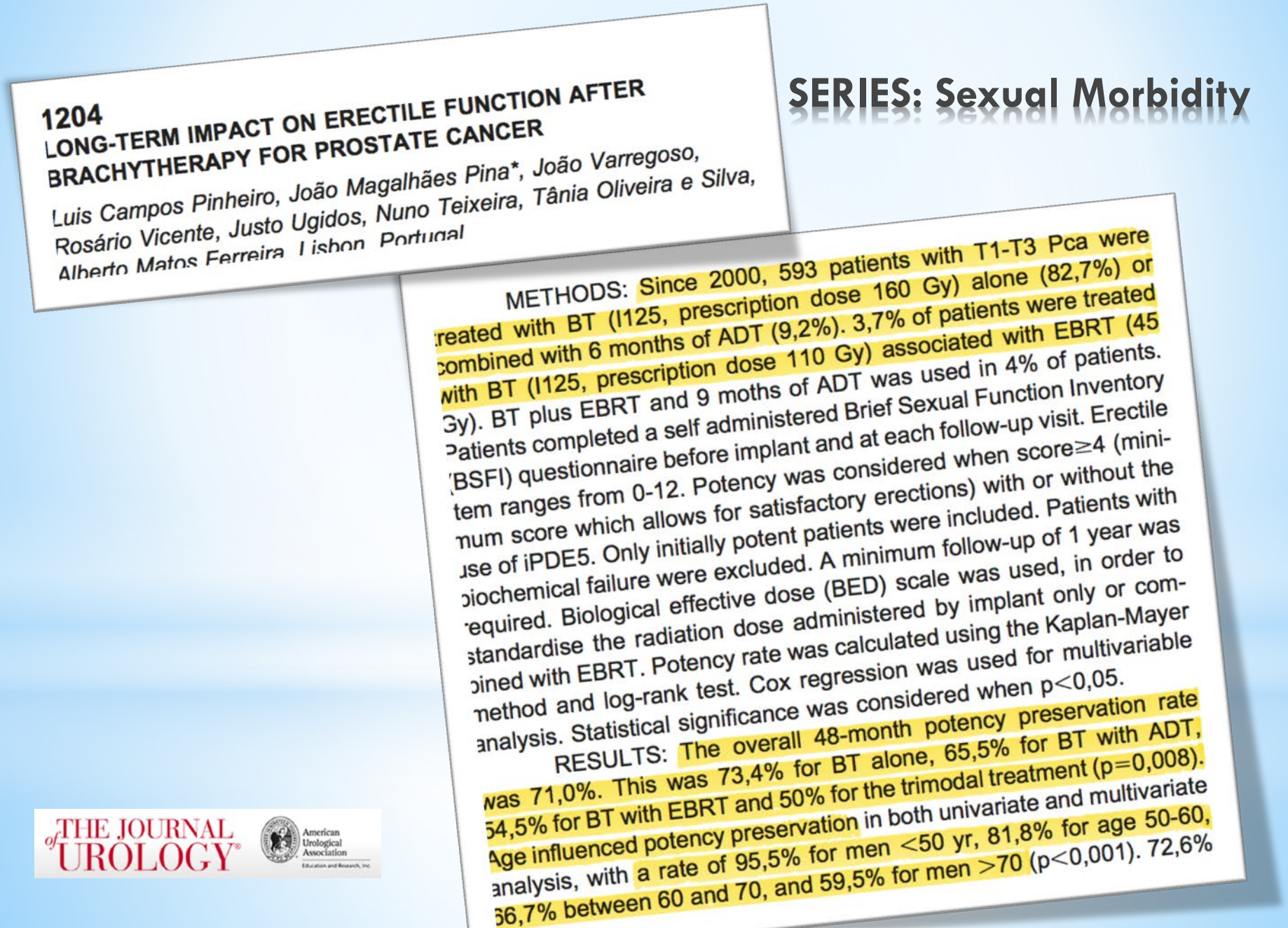
* Modalities for Focal Therapy

Cryotherapy
High Intensity Focused Ultrasound
Photodynamic therapy
Electroporation
…

* Outcomes of Focal Cryotherapy

	n	Mean follow up	Biochemical RFS (%)	Potency (%)	Incontinence (%)
Bahn	31	70	93	89	0
Ellis	60	15	80	71	4
Lambert	25	28	88	71	0
Onik	55	43	95	86	5
Total	171	15-70	80-95	71-89	0-5

SERIES: Sexual Morbidity



1204
LONG-TERM IMPACT ON ERECTILE FUNCTION AFTER BRACHYTHERAPY FOR PROSTATE CANCER

Luis Campos Pinheiro, João Magalhães Pina*, João Varregoso, Rosário Vicente, Justo Ugidos, Nuno Teixeira, Tânia Oliveira e Silva, Alberto Matos Ferreira, Lisbon, Portugal

METHODS: Since 2000, 593 patients with T1-T3 Pca were treated with BT (I125, prescription dose 160 Gy) alone (82,7%) or combined with 6 months of ADT (9,2%). 3,7% of patients were treated with BT (I125, prescription dose 110 Gy) associated with EBRT (45 Gy). BT plus EBRT and 9 moths of ADT was used in 4% of patients. Patients completed a self administered Brief Sexual Function Inventory (BSFI) questionnaire before implant and at each follow-up visit. Erectile item ranges from 0-12. Potency was considered when score≥4 (minimum score which allows for satisfactory erections) with or without the use of iPDE5. Only initially potent patients were included. Patients with biochemical failure were excluded. A minimum follow-up of 1 year was required. Biological effective dose (BED) scale was used, in order to standardise the radiation dose administered by implant only or combined with EBRT. Potency rate was calculated using the Kaplan-Mayer method and log-rank test. Cox regression was used for multivariable analysis. Statistical significance was considered when $p<0,05$.

RESULTS: The overall 48-month potency preservation rate was 71,0%. This was 73,4% for BT alone, 65,5% for BT with ADT, 54,5% for BT with EBRT and 50% for the trimodal treatment ($p=0,008$). Age influenced potency preservation in both univariate and multivariate analysis, with a rate of 95,5% for men <50 yr, 81,8% for age 50-60, 66,7% between 60 and 70, and 59,5% for men >70 ($p<0,001$). 72,6%

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* Challenges of Focal Cryotherapy

Patient selection – Intermediate risk patient

Identification of index lesion accurately

Advances in MRI

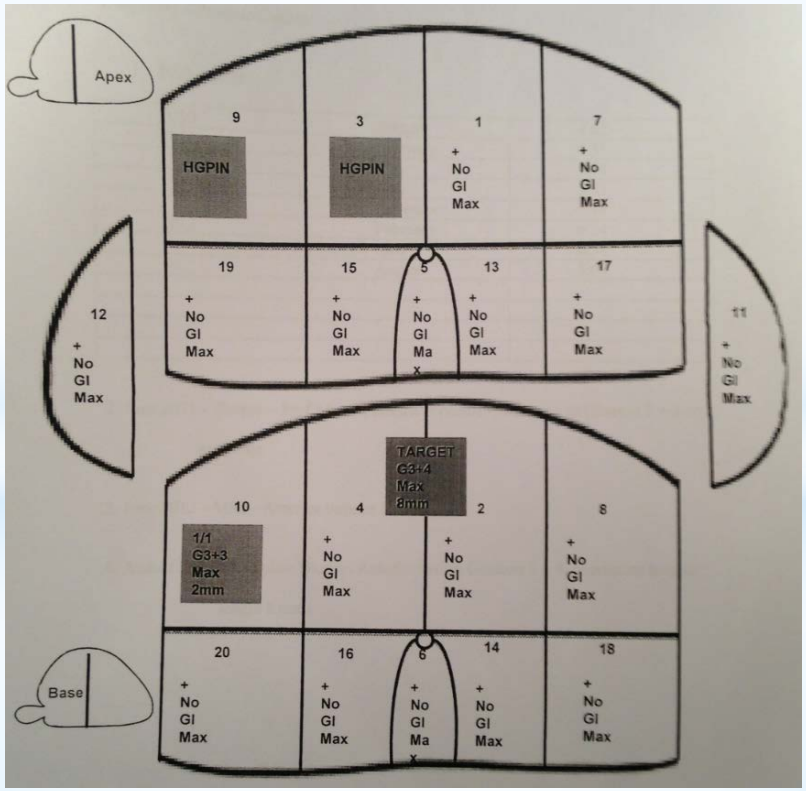
Post treatment follow up

Salvage treatments

* Challenges of Focal Cryotherapy

Male, 59
PSA – 5.09

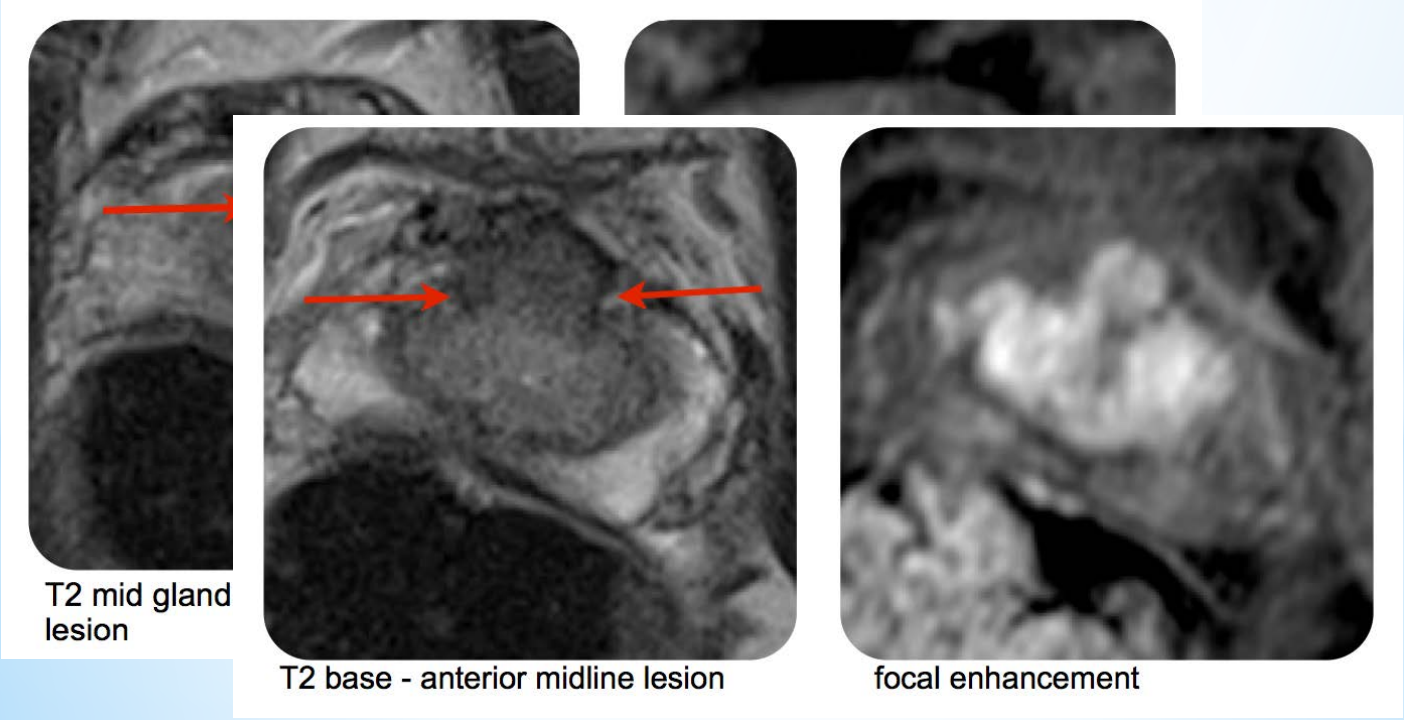
MRI – T2, DW, DCE – 1.3 cc anterior gland tumor at the mid gland between 10 and 2 o'clock



* Challenges of Focal Cryotherapy

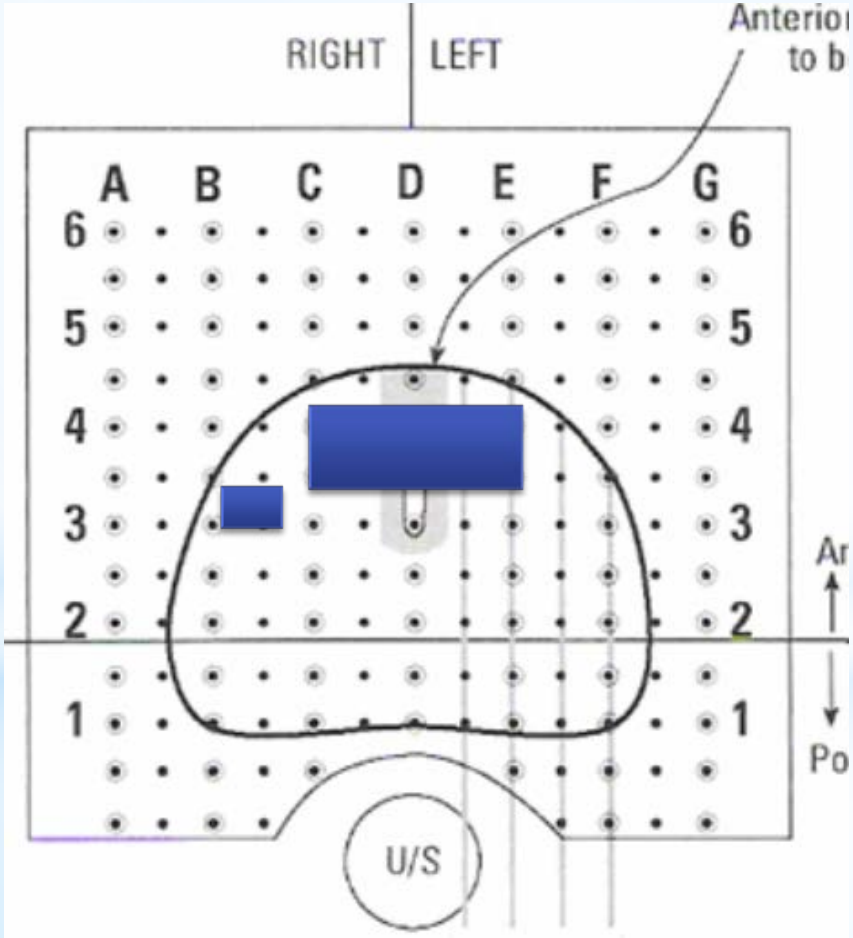
12. Oct. 2012 – Electroporation to anterior lesion

PSA (Jan2013) 3.25
PSA (Mar2013) 5.02
PSA (May2013) 6.47



* Challenges of Focal Cryotherapy

Template mapping biopsy:14 of 64 cores



* Conclusions

1. Both Active Surveillance and Focal PCA Therapy will play major roles avoiding radical therapy

2. Focal PCA therapy is certainly promising as an alternative to AS (young low risk pts)

3. Focal PCA therapy may be considered as salvage for AS Pts

4. Focal PCA therapy may be considered for intermediate risk pts