# II SIMPÓSIO INTERNACIONAL

## GU - REVIEW 2018 - LACOG

23 E 24 | NOVEMBRO 2018 | HOTEL INTERCONTINENTAL | SÃO PAULO

II SIMPÓSIO INTERNACIONAL
GU - REVIEW 2018 - LACOG

# Existe papel para tratamento focal em doença de Risco Intermediário?

**GUSTAVO CARDOSO GUIMARÃES**

**DIRETOR GERAL DOS DEPARTAMENTOS DE CIRURGIA ONCOLÓGICA**

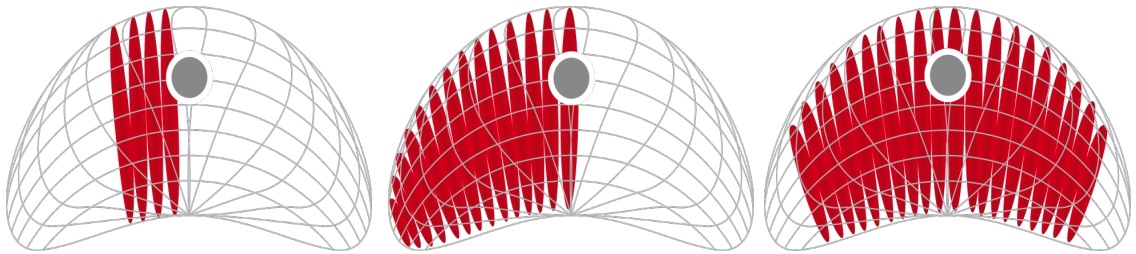
**BP A BENEFICENCIA PORTUGUESA DE SÃO PAULO**

# CONFLICT OF INTEREST DISCLOSURE

**I have no portential conflict of interest to report**

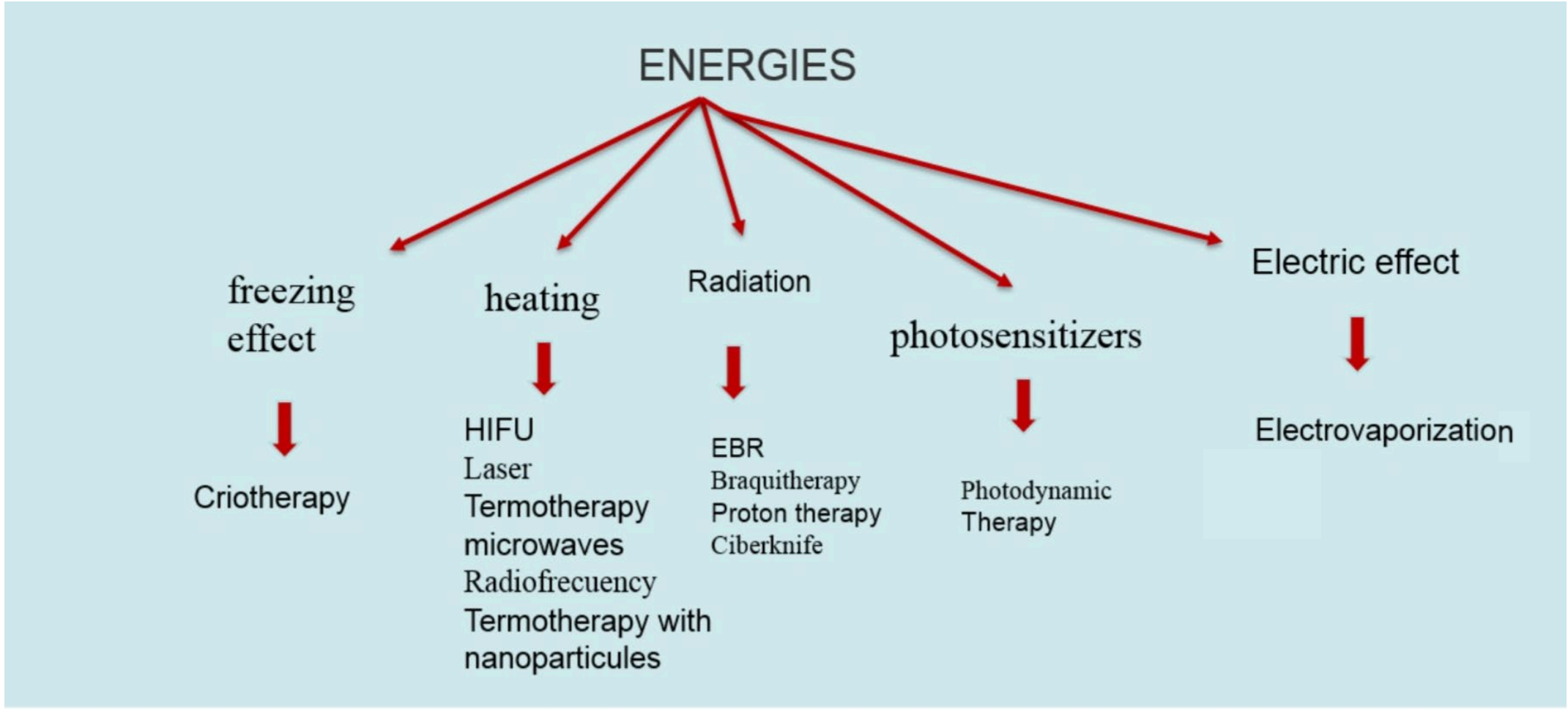
# Ablative Therapies

**FOCAL X TOTAL**

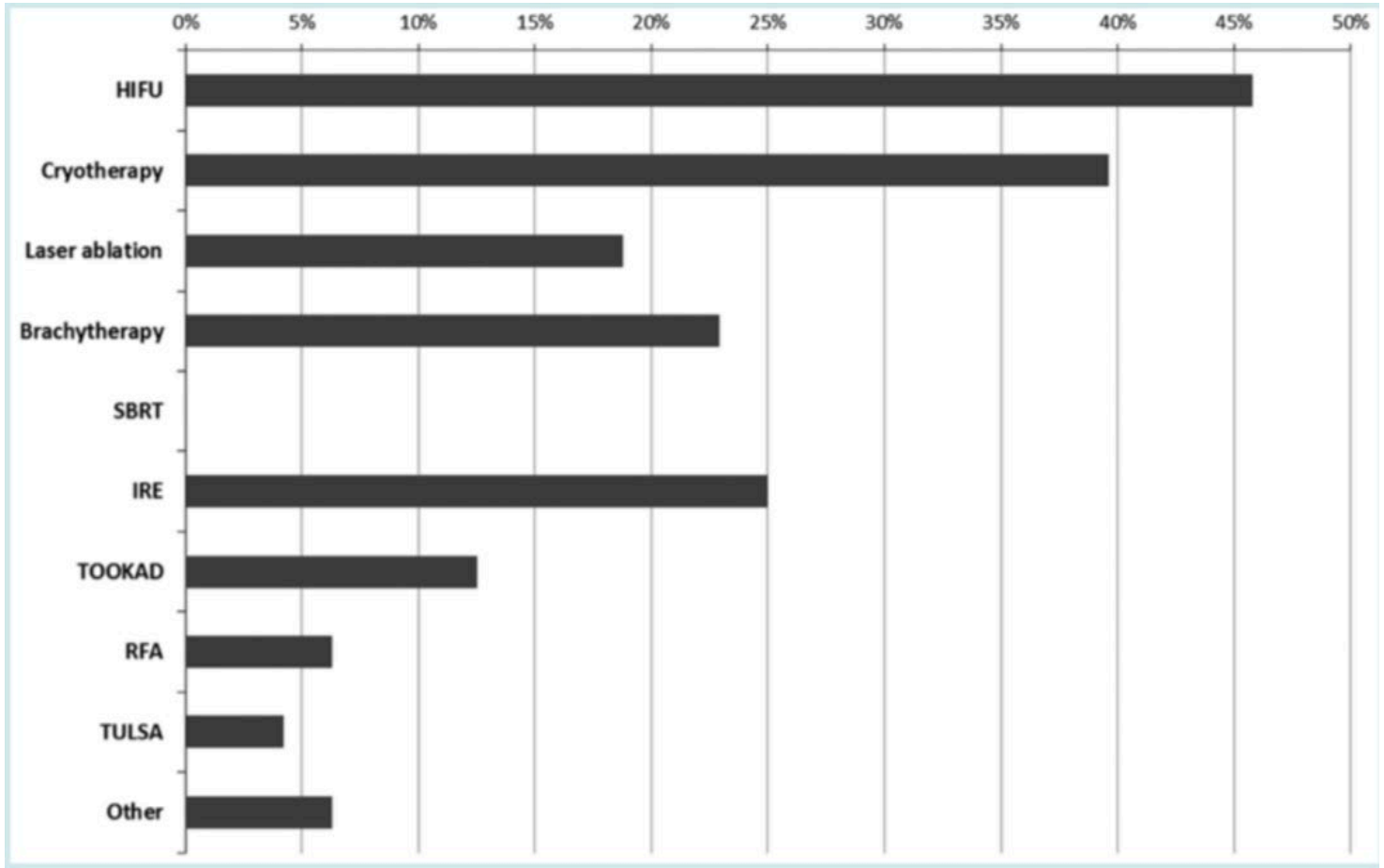


Zonal Hemiablation Nerve sparing

# Ablative Therapies



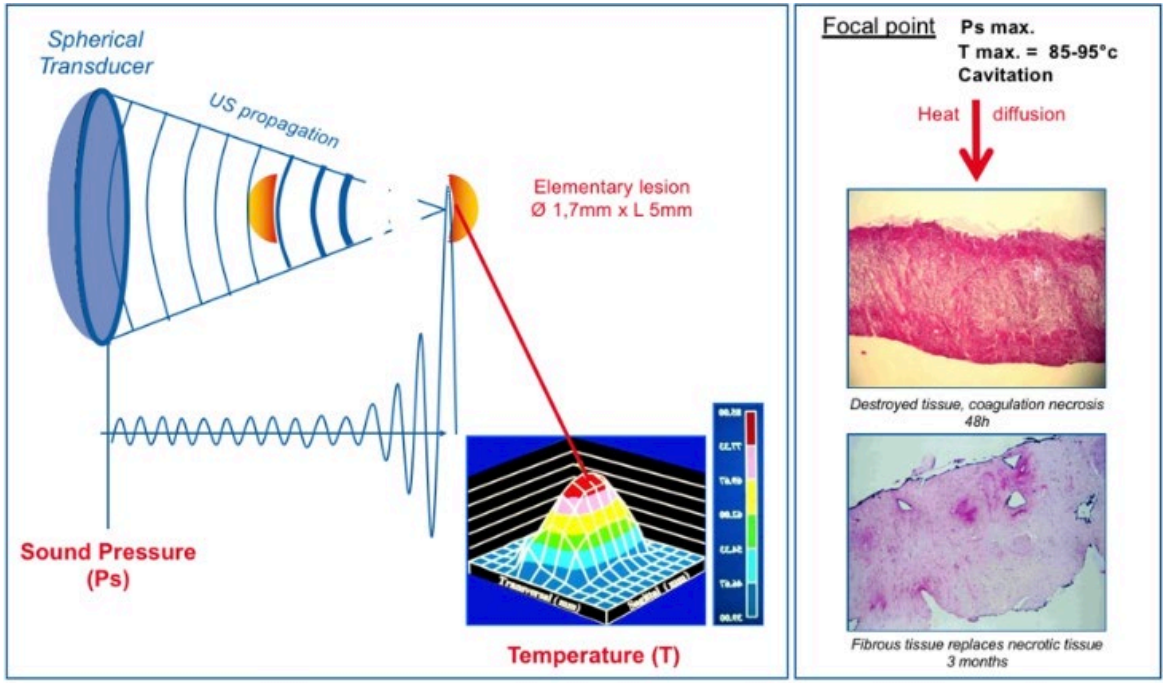
# Ablative Therapies




Tay JK. et al, Prostate Cancer and Prostatic Diseases (2017) 00, 1–6

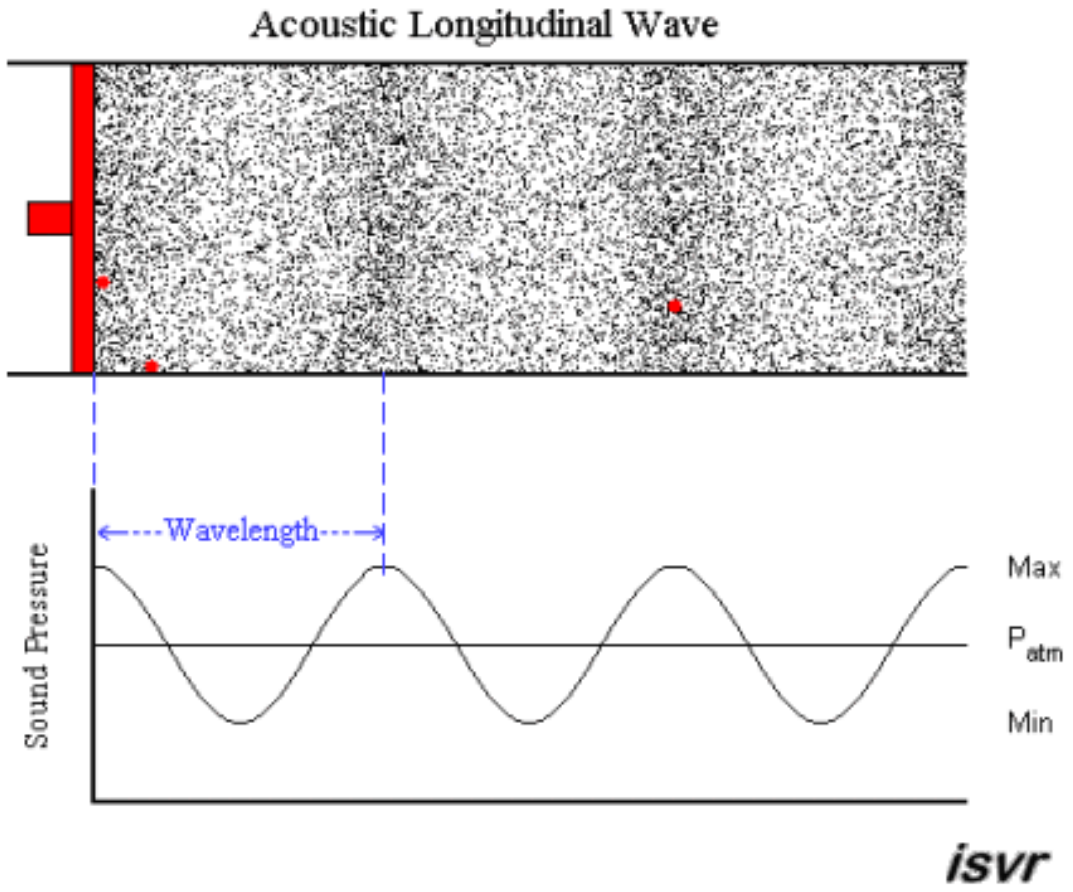
# HIFU - HIGH INTENSITY FOCUSED ULTRASOUND

**A noninvasive form of thermotherapy in which ultrasonic energy is used to generate heat for therapeutic purposes**




## ABLATIVE THERAPY

# Hyperthermia and Acustic Vacitation → tissue destruction



# FDA Approved HIFU for prostate tissue ablation in october 2015

AUA/ASTRO/SUO GUIDELINES 2017

Clinicians should inform patients that even HIFU is approved by the FDA for the destruction of prostate tissue, **it is not approved explicitly** for the treatment of prostate cancer (Expert Opinion).

**AUA 2017**

**PD56-10**
**UROLOGIST'S PRACTICE PATTERNS AND PREFERENCES REGARDING FOCAL THERAPY FOR PROSTATE CANCER**

*Amit L Jain*, Abhinav Sidana, Mahir Maruf, Brian Calio, Dordaneh Sugano, Bradford Wood, Peter Pinto, Bethesda, MD*

**J Urol 2017, vol197, Nº 4s.**

- **425 responses were received [AUA: 342, ES: 83]**
- **50.8% believed FT to be moderate to extremely beneficial in the treatment of Pca**
- **24.2% currently utilize FT in their practice**
- **Who were fellowship trained in urologic oncology were more likely to consider FT to be moderately to extremely beneficial (p<0.001)**
- **Surgeon's experience (>15 years) (p= 0.031) - the only independent predictor for utilizing FT**

**EAU 2018**

## 539: Is focal therapy for prostate cancer an attractive option? Results of an international survey from the young academic urologists (YAU) amongst 484 physicians

**By:** G. Marra, Turin (IT)

- **484 replies from 51 countries (88.4% were from European countries)**
- **78.0% agreed that FT will become a standard option after improvements in patient selection**
- **FT use was considered as an alternative to:**
  - **radical prostatectomy or radiotherapy - 33.0%**
  - **AS - 27.8%**
  - **Salvage treatment for radiation failure- 7.6%**

**The urological community considers FT an attractive option for PCa treatment with the majority stating they would recommend it to suitable patients**

**BUT, FOR WHO?, HOW?, WHEN?**

**HIFU CAN BE USED AS:**

**Whole gland, hemi and zonal ablation and true focal therapy**

- **PRIMARY TREATMENT**
- **SALVAGE TREATMENT**
- **PALLIATIVE AND ADJUVANT (Investigational)**

# PRIMARY TREATMENT

## Whole-Gland treatment

- **Ideal candidate:**

**Recommandations en Onco-Urologie 2010 : Cancer de la prostate**

L. Salomon, D. Azria[2], C. Bastide, P. Beuzeboc, L. Cormier, F. Cornud[1], D. Eiss, P. Eschwège[1], N. Gaschignard, C. Hennequin[2], V. Molinié, P. Mongiat Artus, J.-L. Moreau[1], Michel Péneau[1], M. Peyromaure, V. Ravery[1], X. Rebillard[1], P. Richaud, P. Rischmann[3], F. Rozet, F. Staerman[1], A. Villers[1], M. Soulié et les membres du CCAFU

Progrès en Urologie (2010), 20 Suppl. 4, S217-S252

- **Patients with contraindication for radical treatment – surgery/radiotherapy (Age, Concomitant diseases, ...) or refusal of surgery (any stage)**
- **Localized prostate cancer T1/T2**
- **PSA ≤ 20 and Gleason ≤ 7**

**LOW AND INTERMEDIATE RISK**

Platinum Priority – Prostate Cancer
*Editorial by XXX on pp. x–y of this issue*

# Whole-gland Ablation of Localized Prostate Cancer with High-intensity Focused Ultrasound: Oncologic Outcomes and Morbidity in 1002 Patients

*Sebastien Crouzet [a,b,*], Jean Yves Chapelon [b], Olivier Rouvière [c], Florence Mege-Lechevallier [d], Marc Colombel [a], Hélène Tonoli-Catez [a], Xavier Martin [a], Albert Gelet [a,b]*

[a] Hospices Civils de Lyon, Department of Urology and Transplantation Surgery, Edouard Herriot Hospital, Lyon, France; [b] Inserm, U1032, LabTau, Université de Lyon, Lyon, France; [c] Hospices Civils de Lyon, Radiology Department, Edouard Herriot Hospital, Lyon, France; [d] Hospices Civils de Lyon, Pathology Department, Edouard Herriot Hospital, Lyon, France

EUROPEAN UROLOGY 65 (2014) 907–914

**All patients were treated with Ablatherm HIFU devices (EDAP-TMS)**

**Prototype devices (1997–1999),**
**Ablatherm Maxis (1999–2005),**
**Ablatherm Integrated Imaging (since 2005)**

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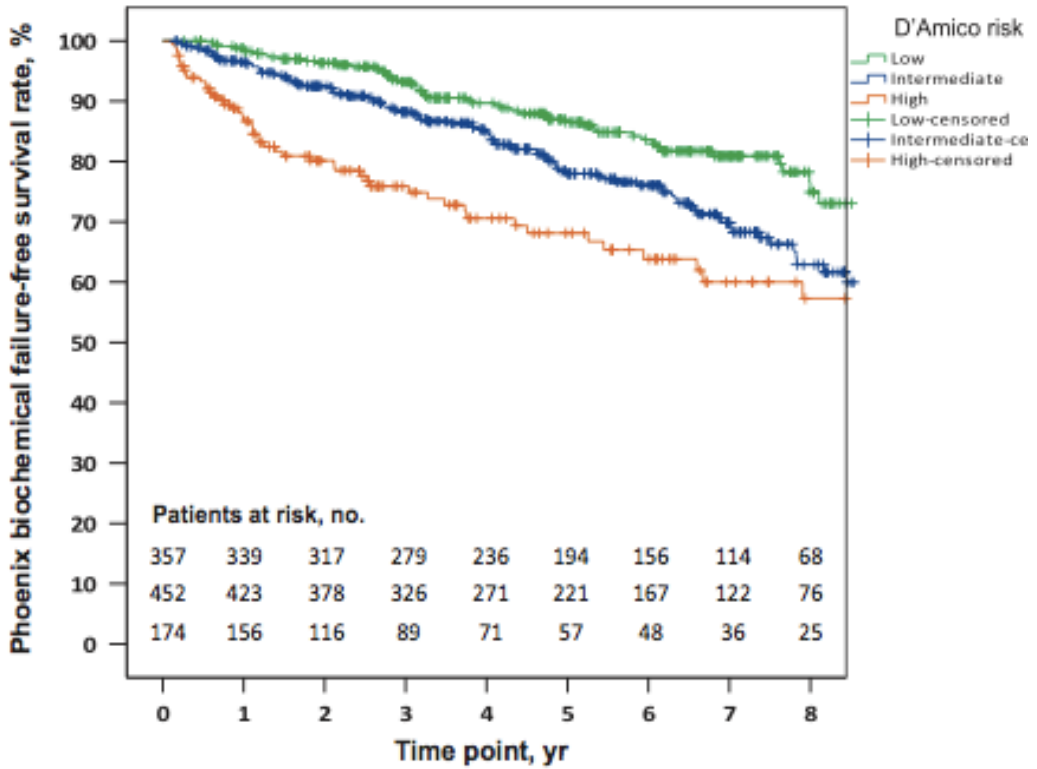
EUROPEAN UROLOGY 65 (2014) 907–914

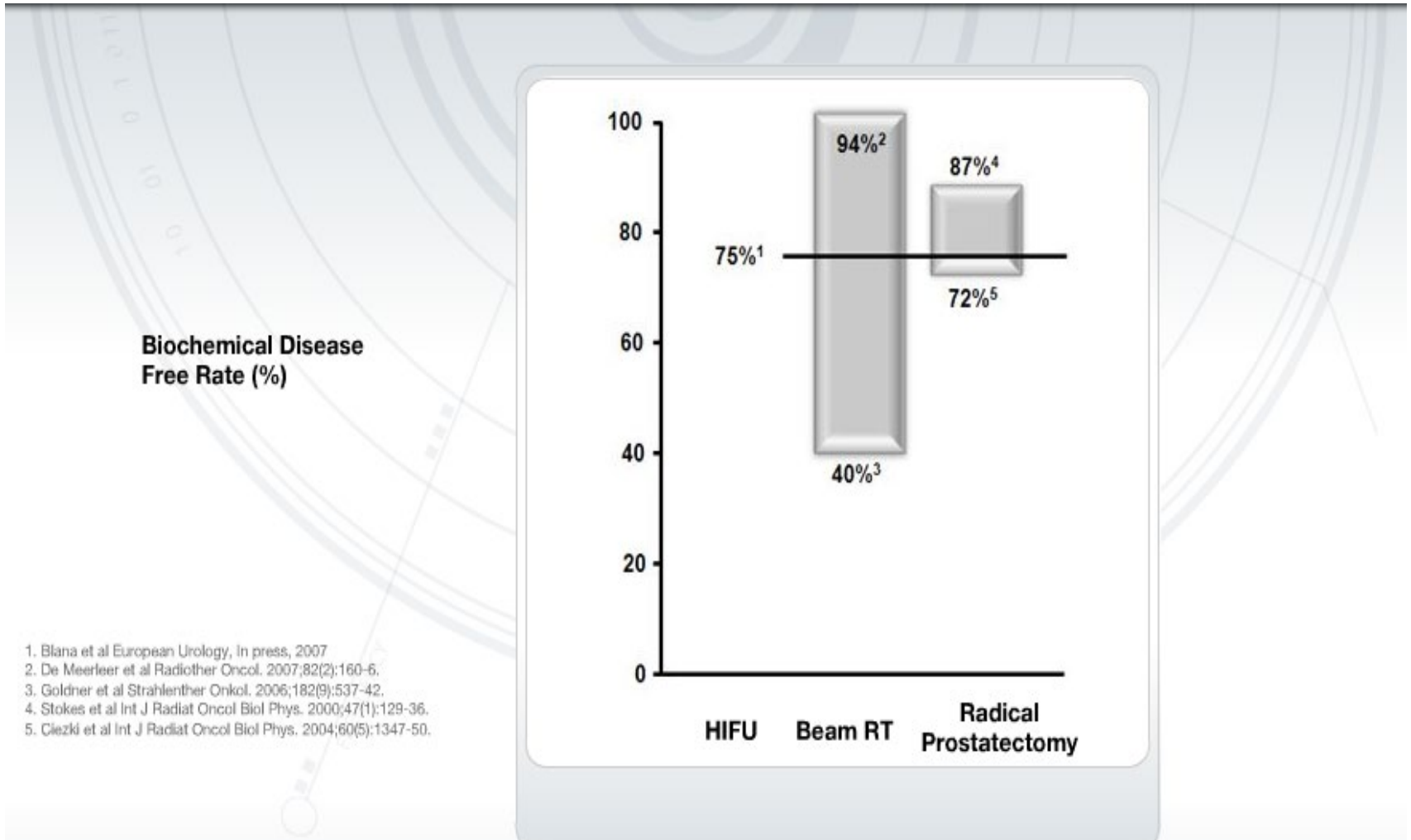



**5yr - 8-yr bFFS ( p < 0.001)**

| | |
|---|---|
| low-risk | 86 – 76% |
| Intermediate | 78 – 63% |
| high-risk | 68 – 57% |

**The overall 10 yr bFFS was 60%**

# Comparação HIFU - Sobrevida bioquímica
# **Risco Intermediário** publicado desde 2000




1. Blana et al European Urology, In press, 2007
2. De Meerleer et al Radiother Oncol. 2007;82(2):160-6.
3. Goldner et al Strahlenther Onkol. 2006;182(9):537-42.
4. Stokes et al Int J Radiat Oncol Biol Phys. 2000;47(1):129-36.
5. Ciezki et al Int J Radiat Oncol Biol Phys. 2004;60(5):1347-50.

Platinum Priority – Prostate Cancer
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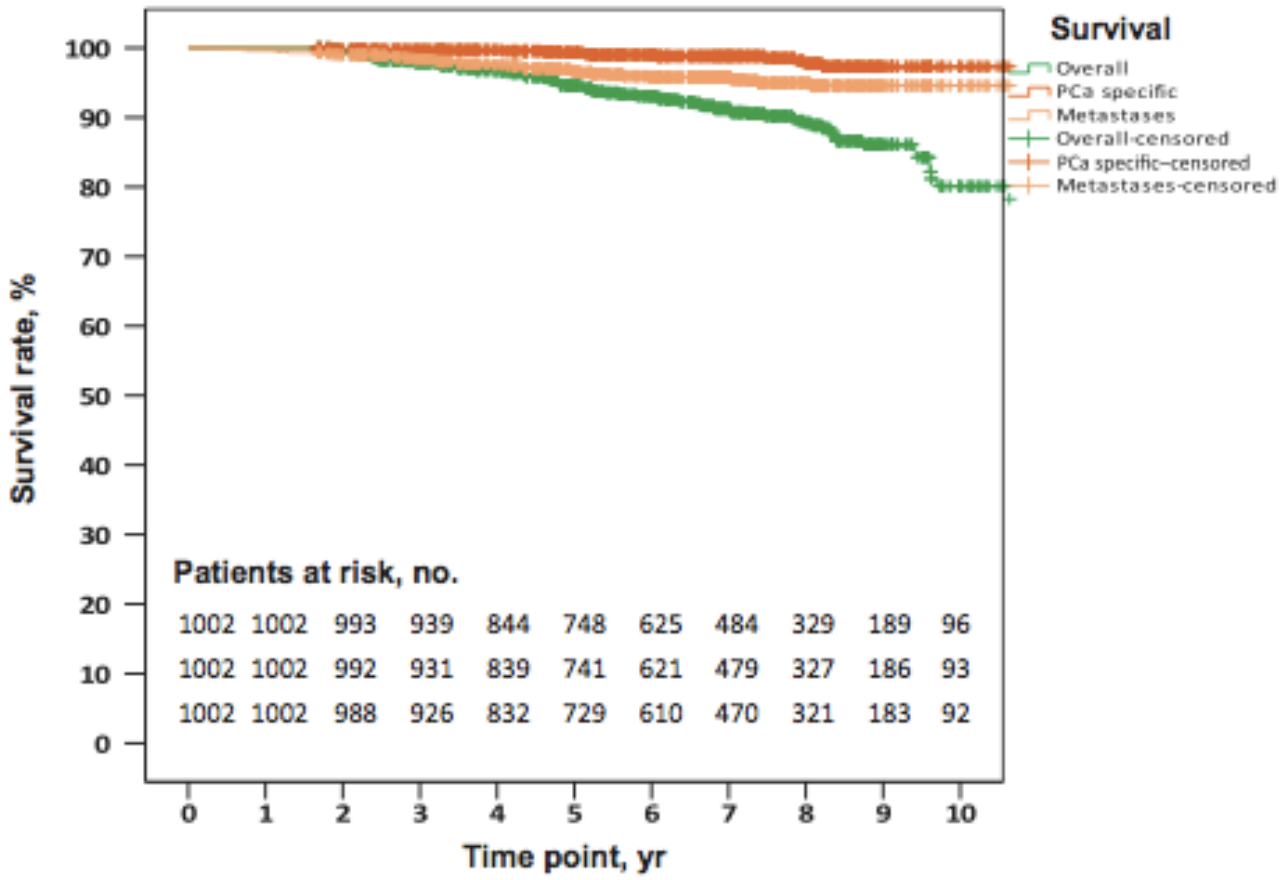
EUROPEAN UROLOGY 65 (2014) 907–914




**The 10-yr overall survival rate - 80%**

**PCa-specific survival rate - 97%**

**The 10-yr PCa metastasis–free survival - 94%**

Platinum Priority – Prostate Cancer
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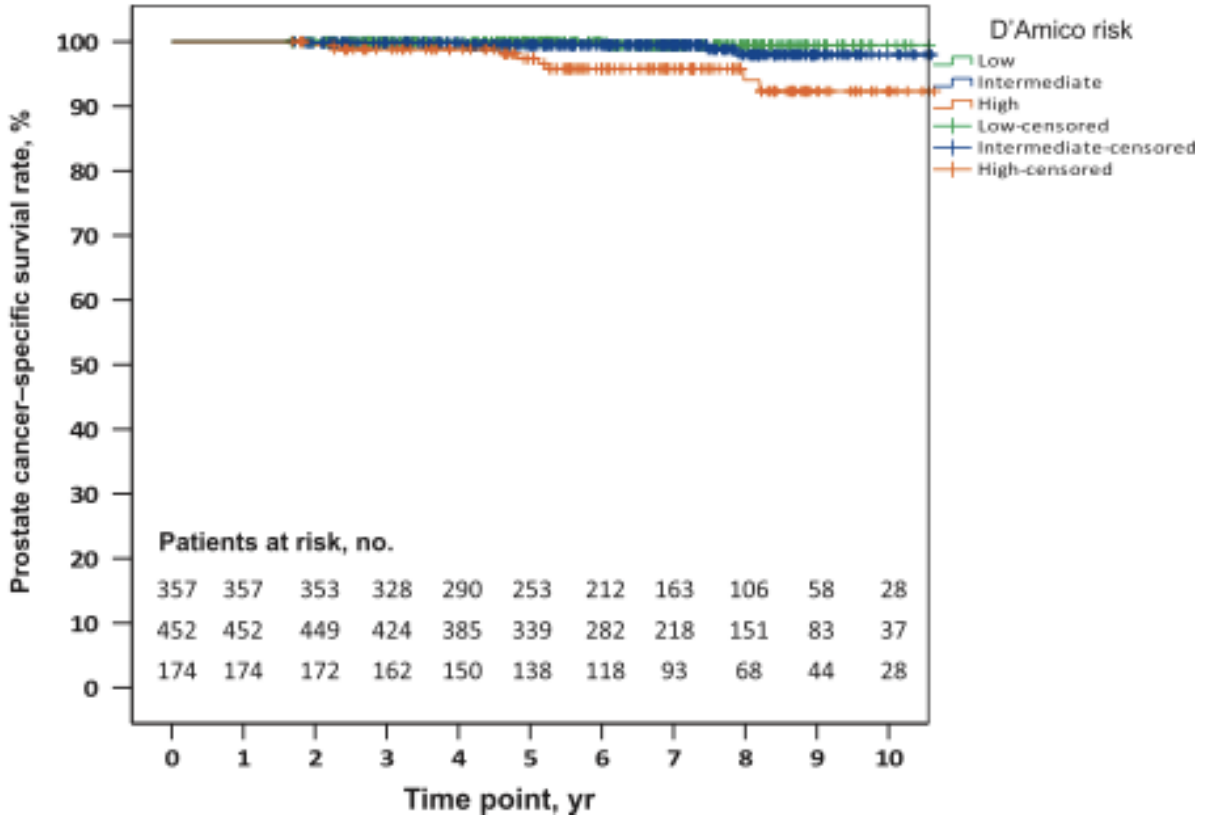
EUROPEAN UROLOGY 65 (2014) 907–914

## PCa-specific survival rate:

**low-risk - 99%**

**intermediate-risk - 98%**

**high- risk - 92%**



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EUROPEAN UROLOGY 65 (2014) 907–914

# HIFU

- **Potentially effective treatment of localized PCa,**
- **Has a low PCa-specific mortality rate**
- **and a high MFSR at 10 yr**
- **Has a acceptable morbidity**

# Hemi-ablation/Focal Ablation treatment

**Prostate cancer is multifocal in majority**

**No treat or treat everybody is not legitimate options**

**We have to make a paradigm shift !**

We must decide what to treat and what do no treat

Olivares R., EAU 2018

# HOW TO TREAT LOW VOLUME LOCALIZED PROSTATE CANCER

**ACTIVE SURVEILANCE**

tug of war

**RADICAL TREATMENT**

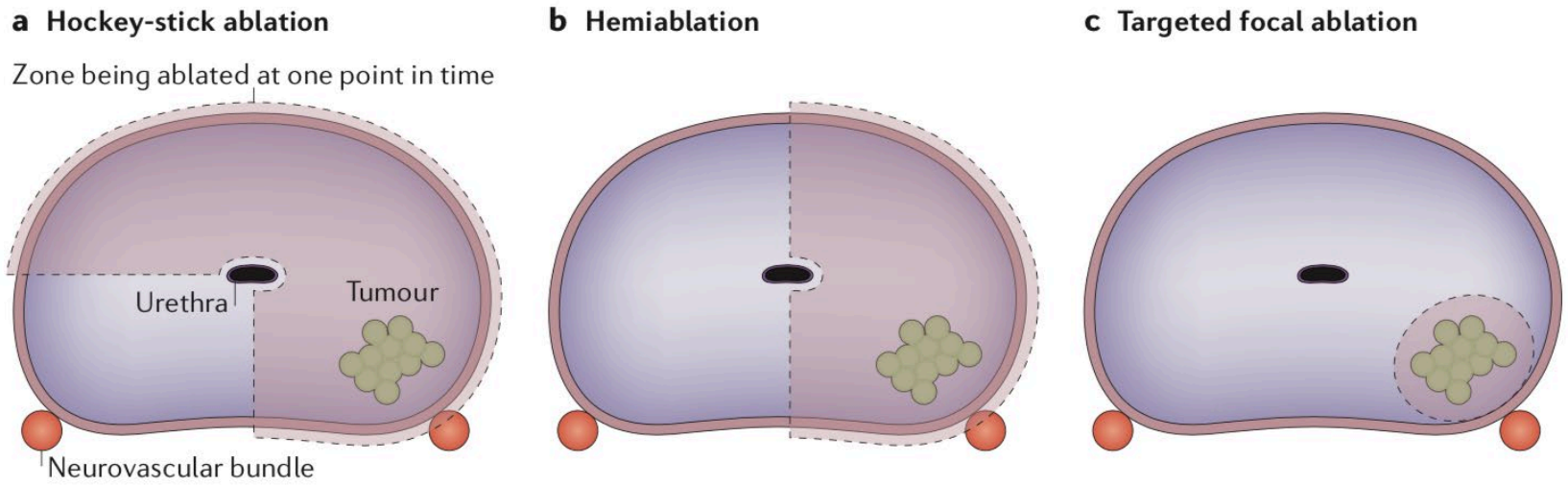
# HOW TO TREAT LOW VOLUME LOCALIZED PROSTATE CANCER

**ACTIVE SURVEILANCE**


**RADICAL TREATMENT**

# Focal Therapy

**Focal therapy is a treatment option that involves the focal ablation of prostate cancer with preservation of surrounding healthy tissue.**




Perera M. et al. Nat Rev Urol 13 (11), 641-653. 2016 Sep 27.

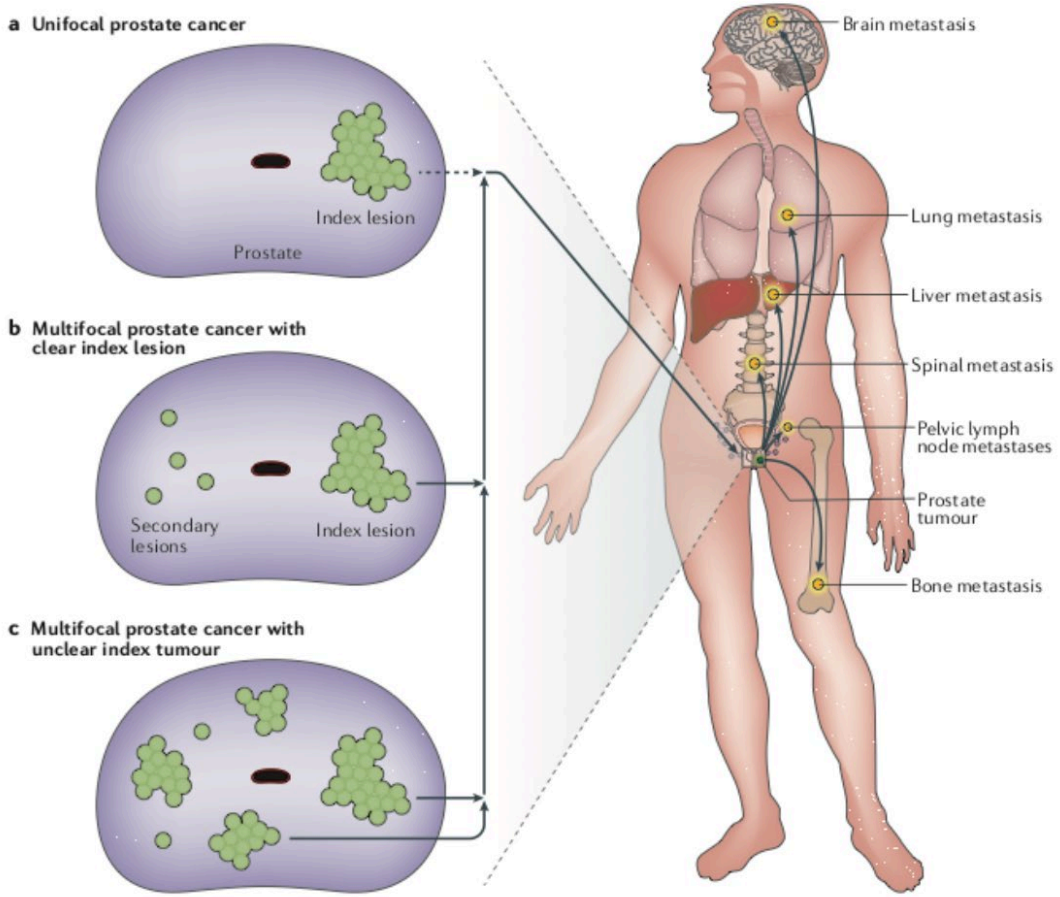



Figure 1 | **Metastatic properties of prostate cancer. a** | Unifocal prostate cancer. **b** | Multifocal prostate cancer with clear index lesion and one or more separate secondary tumour foci with smaller volumes (most common). **c** | Multifocal cancer with unclear index tumour.

# Focal Therapy

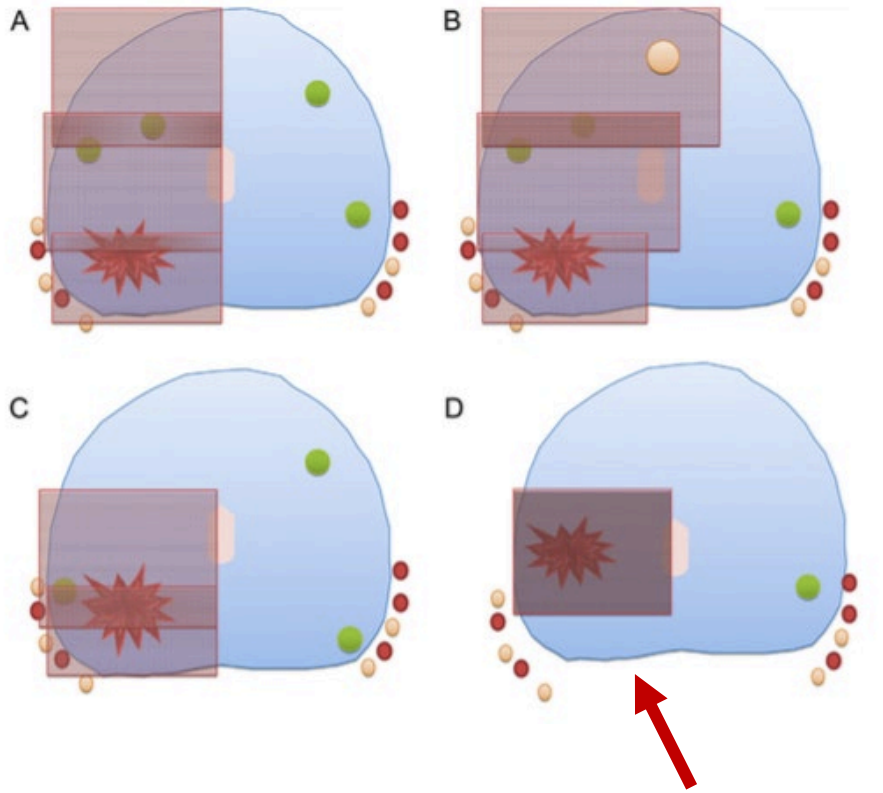
## Index lesion

Perera M. et al. Nat Rev Urol 13 (11), 641-653. 2016 Sep 27.

**This approach might result in reduced morbidity when compared with whole-gland therapies**

**It goals is:**

**Eradicate all significant cancer while preserve urinary and sexual function**




**Index lesion**

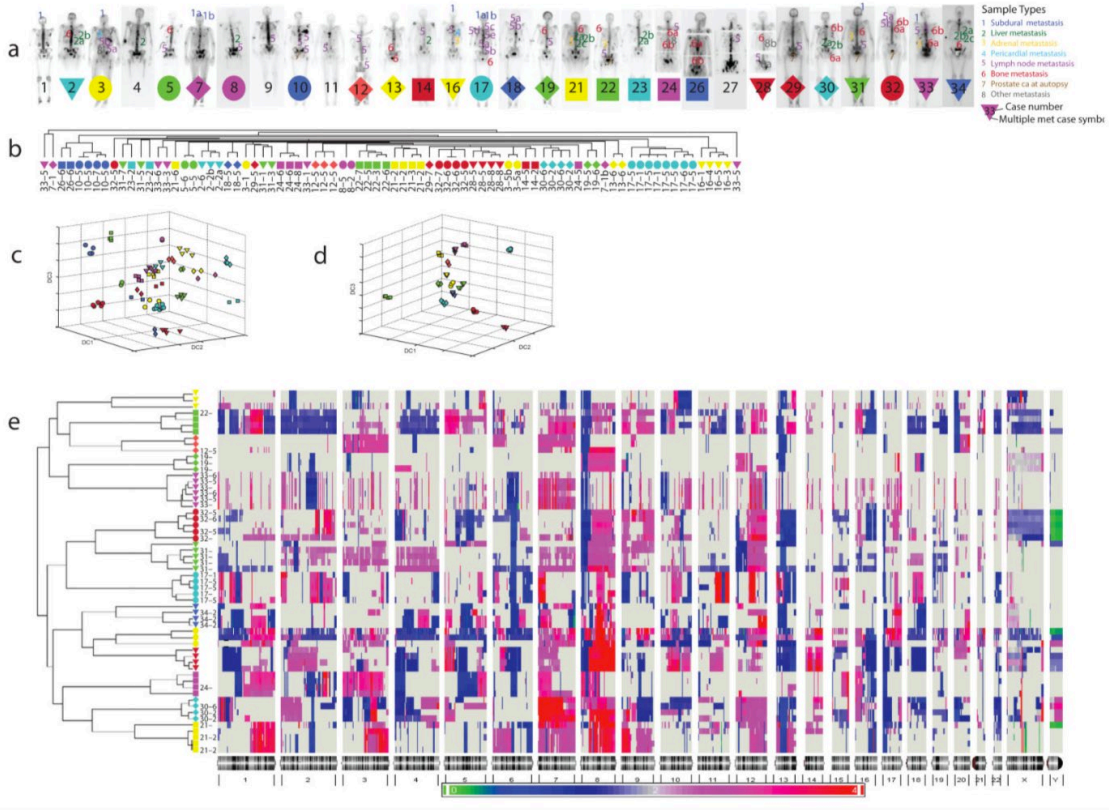
## Copy Number Analysis Indicates Monoclonal Origin of Lethal Metastatic Prostate Cancer

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

*Nat Med*. 2009 May ; 15(5): 559–565

**High-resolution genome-wide SNP and copy number survey.**

**SNP - single nucleotide polymorphisms**



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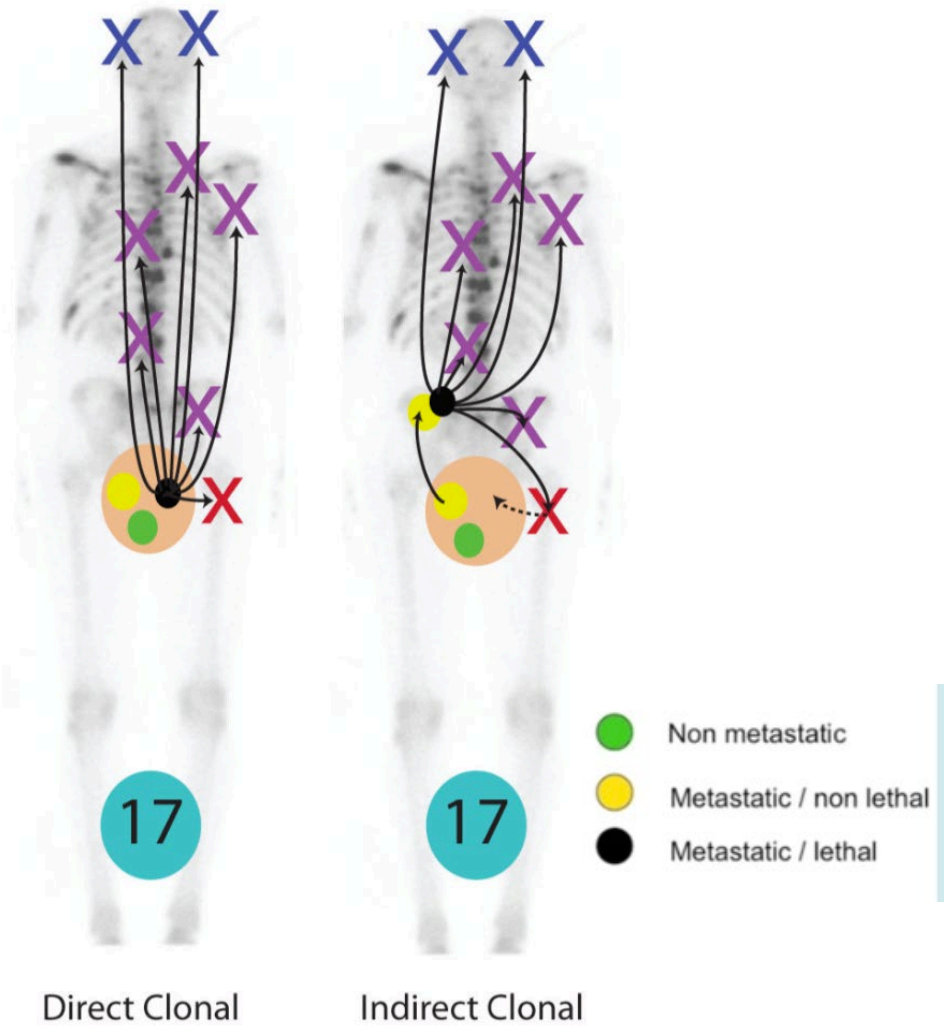
*Nat Med*. 2009 May ; 15(5): 559–565

**Metastatic prostate cancer have clonal origins in most if not all cases!!**



The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL IMPLICATIONS OF BASIC RESEARCH

# The Index Lesion and the Origin of Prostate Cancer

Hashim Uddin Ahmed, M.R.C.S., B.M., B.Ch.

**Ahmed HU, NEJM, 2009; 1704-6.**

**There is increasing evidence that the largest tumor focus within the prostate (called the index lesion) drives the natural history of prostate cancer.**

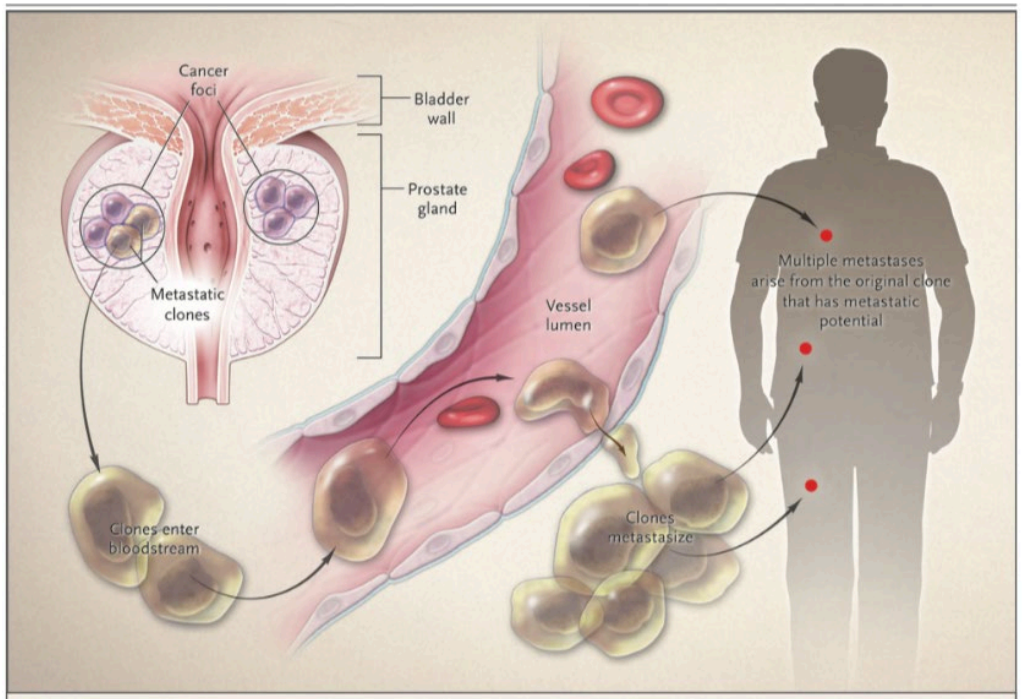



Figure 1. **Monoclonal Origin of Prostate-Cancer Metastases.**
A recent study by Liu and colleagues[3] has shown that metastases in prostate cancer have a common origin — that is, they originate from the same clone. If the single lesion harboring this metastatic clone could be accurately identified and then targeted, it seems likely that the side effects of treatment for prostate cancer would be reduced. The other lesions (depicted as purple cells in the prostate) would undergo surveillance.

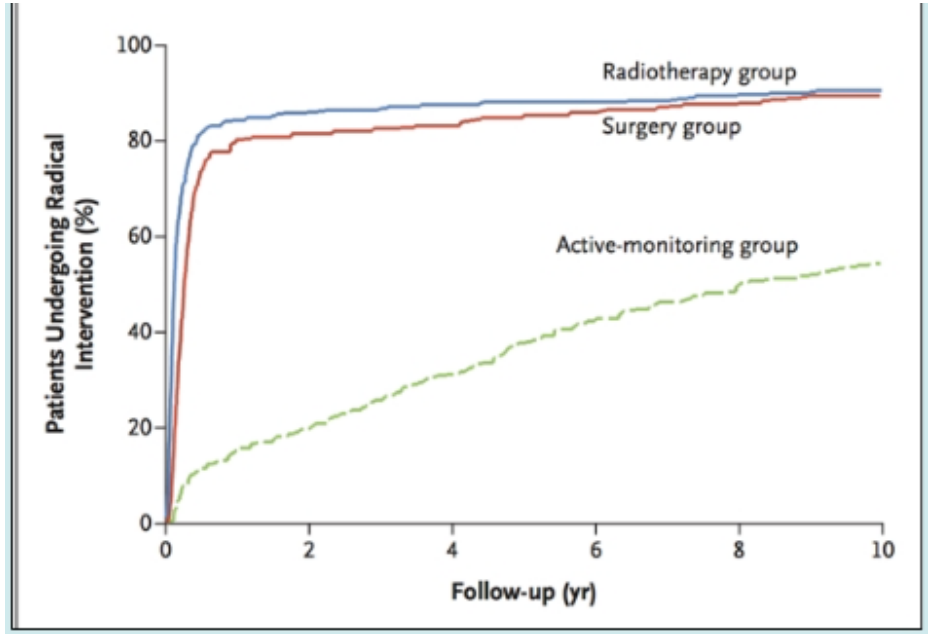
# ProtecT

- Low mortality rate (1%)
- Mortality (10y) – AS=Radiotherapy = RP

Active Surveillance arm

At 5y, 1/3 → Radical treatment

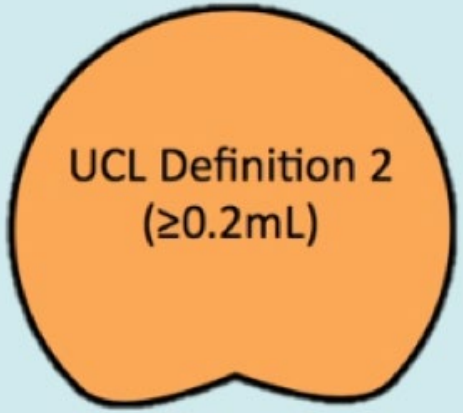
- 73% of RP pathology – **significant cancer**




Hamdy FC et al. New Eng J Med 2016;367

# Ideal Candidate for Focal Therapy

- Low – Intermediate risk prostate cancer
- Clinical Stage T1c—T2
- Up to Gleason 3+4
- PSA – up to 10 ng/ml
- MRI <= T2b




Gleason = ≥ 3+4
AND/ OR Max
Cancer length ≥
4mm

# In Ideal Candidate for Focal Therapy – How many they are?

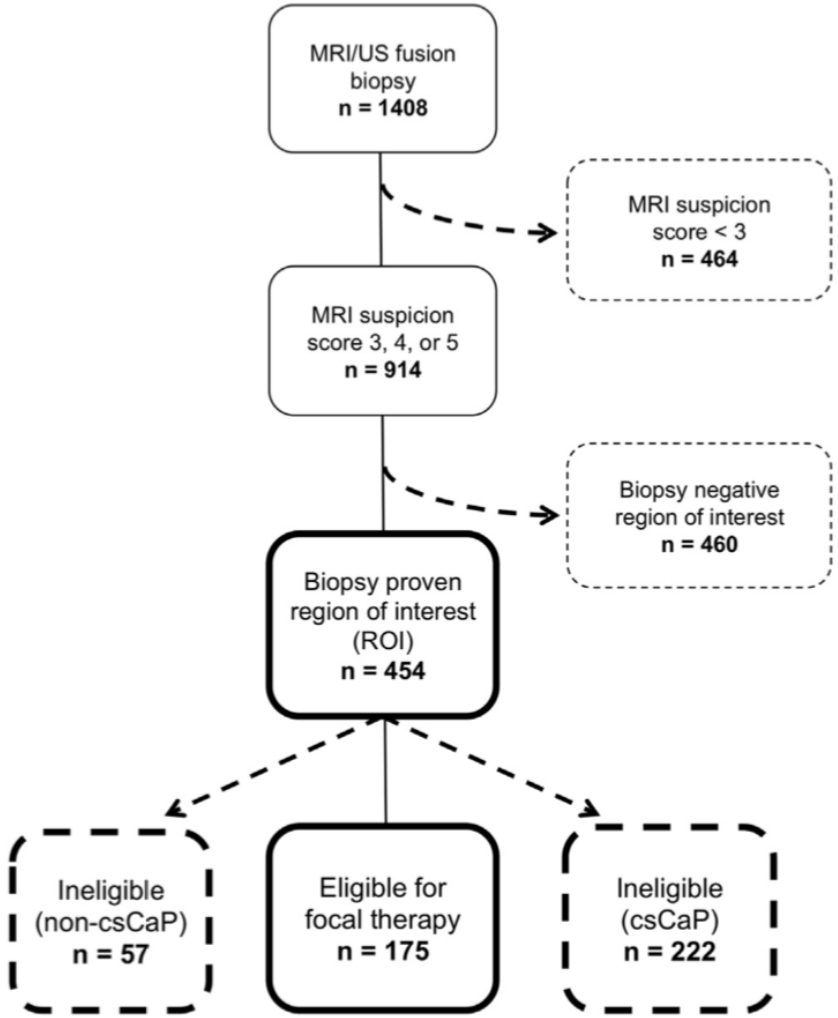
**Focal Therapy Eligibility Determined by Magnetic Resonance Imaging/Ultrasound Fusion Biopsy**

Nima Nassiri,* Edward Chang,* Patricia Lieu, Alan M. Priester, Daniel J. A. Margolis, Jiaoti Huang, Robert E. Reiter, Frederick J. Dorey, Leonard S. Marks and Shyam Natarajan†

**J Urol 2018; 199, 453-58**

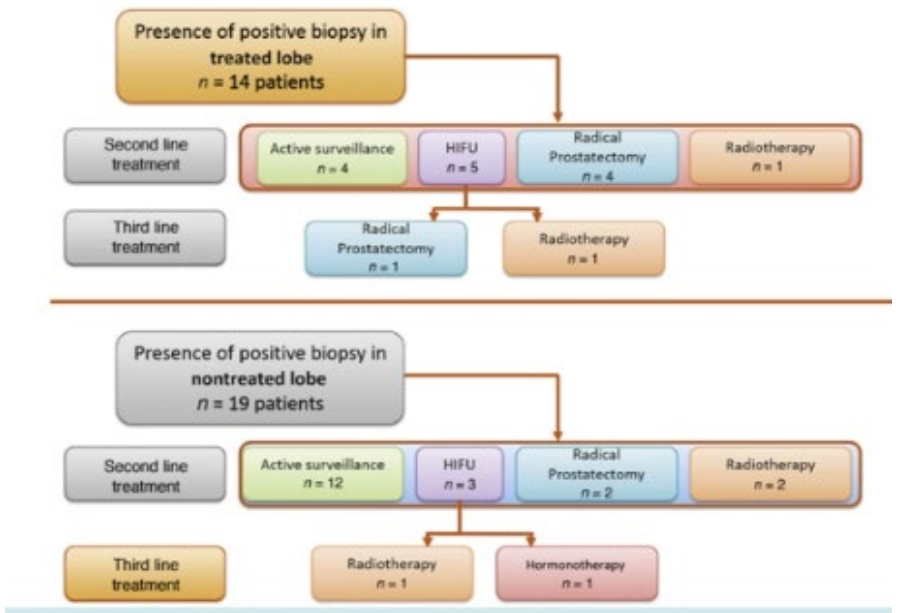
**454 –Biopsy proven of interest ROI**
**38,5% - Eligible for FT (175)**

Fusion biopsy (targeted and template biopsy)
80.0% sensitivity,
73.5% specificity
75.0% accuracy



# Focal High Intensity Focused Ultrasound of Unilateral Localized Prostate cancer: A Prospective Multicentric Hemiablation Study of 111 Patients

*Pascal Rischmann [a,*], Albert Gelet [b,c,d], Benjamin Riche [c,e], Arnauld Villers [f], Gilles Pasticier [g], Pierre Bondil [h], Jean-Luc Jung [i], Hubert Bugel [j], Jacques Petit [k], Harry Toledano [l], Stéphane Mallick [m], Olivier Rouvière [c,d,n], Muriel Rabilloud [c,e], Hélène Tonoli-Catez [b], Sebastien Crouzet [b,c,d]*




Rischmann P, Eur Urol 2017.

**All pts biopsy at 12 month**

**14 pts with failure (12.6%)**

**4 pts – Active surveillance**
**5 pts – Re- HIFU**
**4 pts – Radical prostatectomy**
**1 pts - Radiotherapy**

**336 pts from 2011 – 2017 (median FU 4 years)**

**56 pts salvage HIFU –**
**bFFS - 64,9%**

**271 pts Whole-glad**
**bFFS – 81,1%**

**9 pts Focal Ablation**
**bFFS -100%**

**Rectal Fistula – 0,6%**
**Bladder outlet obstruction - 13,1%**
**Urethral stenosis – 7,7%**
**Bladder obstrutction – 5,4%**

**D`Amico Risk Group**

| | |
|---|---|
| **Low Risk** | **32,4%** |
| **Intermediate Risk** | **31,8%** |
| **High Risk** | **35,9%** |

- **Failure after primary treatment (5 years):**

| | |
|---|---|
| **Low Risk** | **– 5,5%** |
| **Intermediate Risk** | **- 5,6%** |
| **High Risk** | **- 13,1%** |

# Focal Therapy in Primary Localised Prostate Cancer: The European Association of Urology Position in 2018

*Henk G. van der Poel[a,*], Roderick C.N. van den Bergh[a], Erik Briers[b], Philip Cornford[c], Alex Govorov[d], Ann M. Henry[e], Thomas B. Lam[f,g], Malcolm D. Mason[h], Olivier Rouvière[i], Maria De Santis[j,k], Peter-Paul M. Willemse[l], Hendrik van Poppel[m], Nicolas Mottet[n]*

van der Poel HG, et al. Focal Therapy in Primary Localised Prostate Cancer: The European Association of Urology Position in 2018. Eur Urol (2018)

- **Median follow up – 4 – 81 month**
- **Median rate of adverse events - 0 - 10,6%**
- **Pad free & leak free continence rate – 83,3% - 100%**
- **Potency rate – 81,5% - 100%**
- **Median rate significant disease at control biopsy – 0-13,4%**
- **Lack of clear results + difficulties in detecting all cancerous areas,**

**FT should be considered investigational**


OBRIGADO PELA ATENÇÃO!!
bp