Slide 1

HIFU – Focal One :
where do we stand ?

Daniel Benamran
Service d'Urologie
Hôpitaux Universitaires de Genève

HUG Hôpitaux Universitaires Genève

BAU2018
Dolce – La Hulpe/Terhulpen 6 & 7 DECEMBER 2018

Slide 2

Disclosures

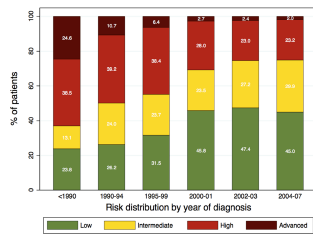• Astellas, MSD, Sanofi, Janssen, EDAP-TMS, IBSA

• The views expressed within this presentation are the personal opinions of the author.

Slide 3

Why ?

• Prostate cancer landscape has changed

• More screening
 -> more detection
     + stage-shift

Slide 4

1990 Patient lived < 10 years with Prostate Cancer

Treatment strategy: **efficacy at all price**
- Single treatment approach
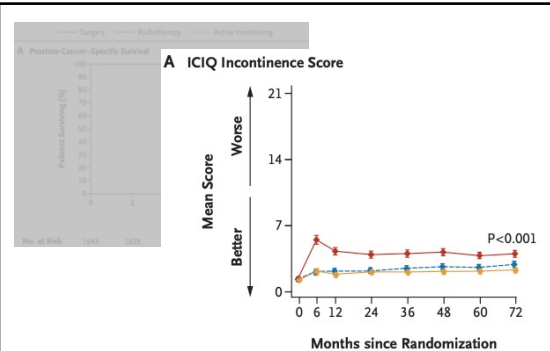- Aggressive Radical Surgery
- Radical Radiotherapy

Patient age 60   70   80
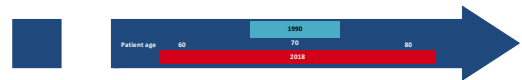
2018 Patient lives > 20 years with Prostate Cancer

Treatment strategy: **disease control with QoL preservation**
- Active surveillance
- Step-by-step approach
- Focal Therapy

Slide 5

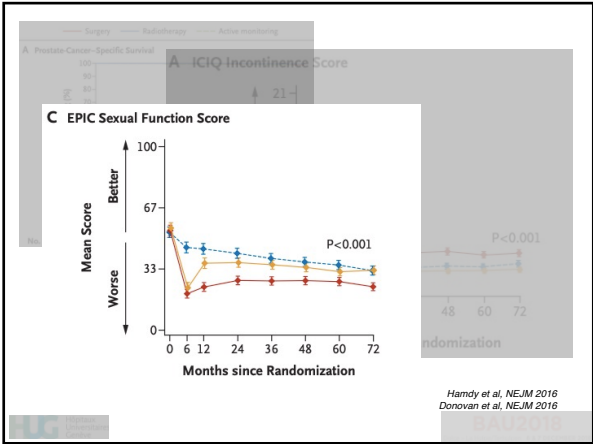A Prostate-Cancer–Specific Survival

Surgery Radiotherapy Active monitoring
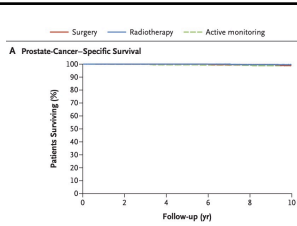
No. at Risk 1643 1628 1605 1575 1286 746

Hamdy et al, NEJM 2016

Slide 6

A ICIQ Incontinence Score

P<0.001

Hamdy et al, NEJM 2016
Donovan et al, NEJM 2016

Slide 1

C EPIC Sexual Function Score

P<0.001

P<0.001

Months since Randomization

Hamdy et al, NEJM 2016
Donovan et al, NEJM 2016

Slide 2: Rationale

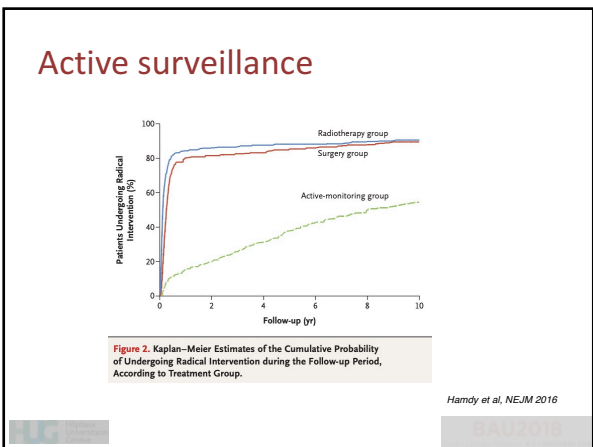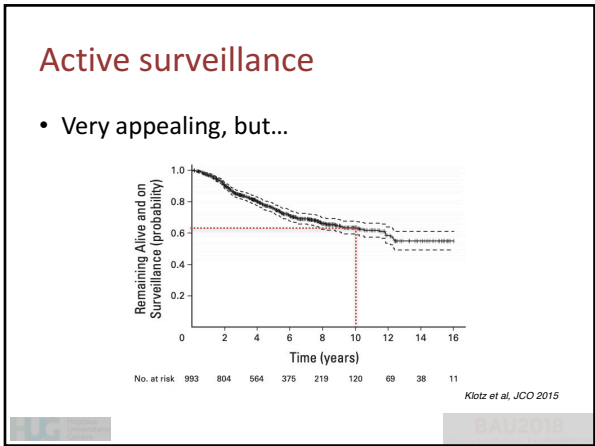# Rationale

- Patients ask for less radical treatment
- Patients are not willing to be cured at all cost

-> One treatment cannot fit all patients !

-> **Alternatives to radical treatments are needed**

Slide 3

To improve is to change;
to be perfect is to change often.

-Winston Churchill

»Alireza Yavari

Slide 4: Active surveillance

Active surveillance

- Very appealing, but…

No. at risk 993   804   564   375   219   120   69   38   11

Klotz et al, JCO 2015

Slide 5: Active surveillance

Active surveillance

Figure 2. Kaplan–Meier Estimates of the Cumulative Probability of Undergoing Radical Intervention during the Follow-up Period, According to Treatment Group.

Hamdy et al, NEJM 2016
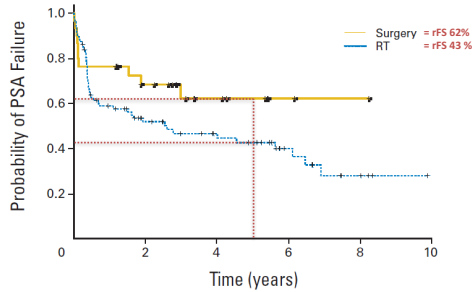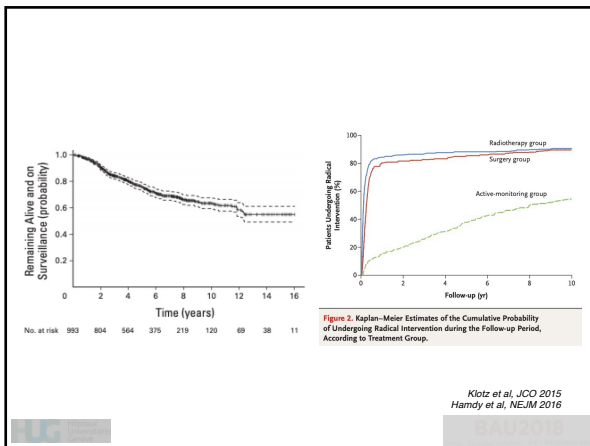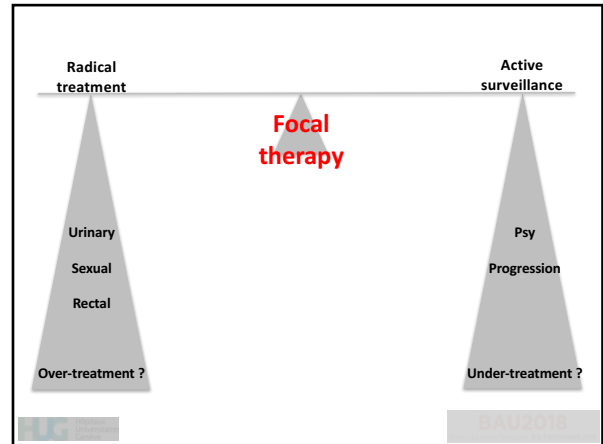
Slide 6: Active surveillance

Active surveillance

- Cancer upgrading
- Psychological burden (« Why do nothing ? »)
- Physical burden
- Economical burden
- Missing the right treatment opportunity ?
- Worst oncological long-term outcomes ?

Zeliad et al, Cancer 2006
Dale et al, Cancer, 2005
Pickles et al, BJU Int, 2009
Latini et al, J Urol, 2007
Klotz et al, Urol Oncol, 2006

Worst outcomes ?

Klotz et al, Journal of Clinical Oncology, 2010

Radical treatment — **Focal therapy** — Active surveillance

Urinary
Sexual
Rectal

Over-treatment ?

Psy
Progression

Under-treatment ?

Figure 2. Kaplan–Meier Estimates of the Cumulative Probability of Undergoing Radical Intervention during the Follow-up Period, According to Treatment Group.

Klotz et al, JCO 2015
Hamdy et al, NEJM 2016

The goals

- Treat the cancer that needs to be treated (*index lesion*)
  - -> Less over-treatment
  - -> Less treatment-induced toxicity/morbidity

  -> Not for a patient who perfectly fits active surveillance criteria

- Reduce the conversion to total treatment observed in active surveillance

- Allow salvage treatment in case of failure

The prerequisite

- Accurate diagnosis
  - including mapping of the cancer in the prostate

- Effective treatment tool
  - allowing to conform to anatomy/cancer localization
  - allowing to control the planned treatment
    - to avoid under-treatment
    - to avoid complications

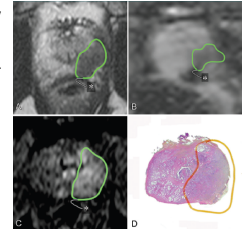
Prostate cancer diagnosis and the urologist...
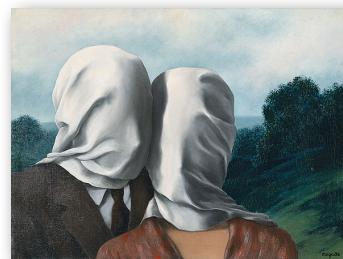
The lovers
René MAGRITTE
Belgium, 1898-1967
National Gallery of Australia

Accurate diagnosis

- mpMRI is the cornerstone of the diagnosis

- Biopsies with at least targeted biospies on all the suspicious lesions on mpMRI
  - targeted/template transrectal or transperineal

- Mapping of the tumor is mandatory

---

mpMRI

- mpMRI has an excellent NPV for significant foci :
  - Sen 90%, Spec 88%, NPV 95% for foci >0.5cc

- However, mpMRI underestimates tumor volume :
  - T2w underestimate histologic volume (-45% to +2%)
  - security margins (9mm)

Villers et al, J Urol 2006
Puech et al, Urology 2010
Mazaheri et al, Radiology 2009
Le Nobin et al, BJU Int 2014

Negative predictive value of MRI

Validation of the European Society of Urogenital Radiology Scoring System for Prostate Cancer Diagnosis on Multiparametric Magnetic Resonance Imaging in a Cohort of Repeat Biopsy Patients.
Portalez et al. Eur Urol.. 2012 62(6):986-96.

Table 5 – Receiver operating characteristics of the European Society of Urogenital Radiology sum of scores and the Likert scale in a training set and a validation set randomly drawn from the total cohort of 1524 cores*

	Training set, n = 1018		Validation set, n = 506	
Positive cores, no. (%)	132 (12.9)		68 (13.4)	
Random systematic cores, no. (%)	750 (73.7)		375 (74.1)	
Targeted cores, no. (%)	268 (26.3)		131 (25.9)	
	ESUR score	Likert Scale	ESUR score	Likert scale
AUC of the ROC curve	0.855 ± 0.019	0.845 ± 0.019	0.873 ± 0.022	0.848 ± 0.024
Youden-selected threshold	≥9	≥3	–	–
Sensitivity, % (95% CI)	67.4 (58.7–75.3)	75.0 (66.7–82.1)	69.1 (56.7–79.8)	73.5 (61.4–83.5)
Specificity, % (95% CI)	92.3 (90.3–94.0)	79.9 (77.1–82.5)	92.2 (89.2–94.5)	81.5 (77.5–85.0)
Positive predictive value, % (95% CI)	92.7 (89.0–94.0)	33.7 (30.7–41.7)	58.0 (45.3–68.7)	38.1 (33.8–47.7)
Negative predictive value, % (95% CI)	95.0 (93.3–96.3)	95.5 (93.7–96.9)	95.1 (92.4–96.8)	95.2 (92.4–97.0)
Overall accuracy, % (95% CI)	89.1 (87.0–90.9)	79.3 (76.6–81.7)	89.1 (86.0–91.6)	80.4 (76.6–83.7)

ESUR = European Society of Urogenital Radiology; AUC = area under the curve; ROC = receiver operating characteristics; CI = confidence interval.
* The predictive characteristics of multiparametric magnetic resonance imaging are presented for ESUR sum of scores ≥9 and Likert scale ≥3 thresholds, as determined by the Youden J statistics.
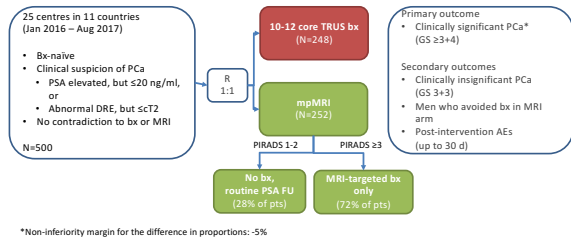
NPV ESUR PiRADS <9: 95%

THE LANCET

Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study.
Ahmed HU et al. PROMIS study group. Lancet. 2017 Feb 25;389(10071):815-822.

- Multicentre, paired-cohort, confirmatory study to test diagnostic accuracy of MP-MRI and TRUS-biopsy against template prostate mapping biopsy [TPM-biopsy].
- Clinically significant PCa: Gleason score ≥4 + 3 or a maximum cancer core length 6 mm or longer.
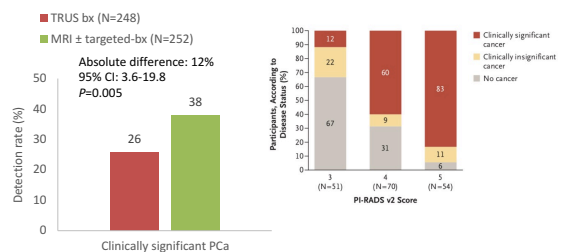
Diagnostic accuracy

Test attribute	TRUS guided	MP-MRI	Odds ratio (95 %CI)	P
Sensibility	48%	93%	0,06 (0,02-0,12)	<0,0001
Specificity	96%	41%	0,02 (0,003-0,05)	<0,0001
Positive Predictive Value	90%	51%	8,2 (4,7-14,3)	<0,0001
Negative Predictive Value	74%	89%	0,34 (0,21-0,55)	<0,0001

Multi-centre, non-inferiority RCT (PRECISION)

25 centres in 11 countries (Jan 2016 – Aug 2017)

- Bx-naïve
- Clinical suspicion of PCa
  - PSA elevated, but ≤20 ng/ml, or
  - Abnormal DRE, but ≤cT2
- No contradiction to bx or MRI

N=500

R 1:1

10-12 core TRUS bx (N=248)

mpMRI (N=252)

PIRADS 1-2 → No bx, routine PSA FU (28% of pts)

PIRADS ≥3 → MRI-targeted bx only (72% of pts)

Primary outcome
- Clinically significant PCa* (GS ≥3+4)

Secondary outcomes
- Clinically insignificant PCa (GS 3+3)
- Men who avoided bx in MRI arm
- Post-intervention AEs (up to 30 d)

*Non-inferiority margin for the difference in proportions: -5%

Kasivisvanathan et al. NEJM 2018

Primary endpoint

- TRUS bx (N=248)
- MRI ± targeted-bx (N=252)

Absolute difference: 12%
95% CI: 3.6-19.8
P=0.005

Detection rate (%)

26 — 38 (Clinically significant PCa)

Participants According to Disease Status (%)

- Clinically significant cancer
- Clinically insignificant cancer
- No cancer

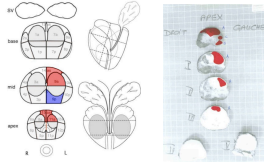| PI-RADS v2 Score	3 (N=51)	4 (N=70)	5 (N=54)
Clinically significant cancer	12	60	83
Clinically insignificant cancer	22	9	6
No cancer	67	31	11

Non-inferiority demonstrated
Superiority suggested, but not in trial design

Kasivisvanathan et al. NEJM 2018

Slide 1: Targeted biopsies allow precise mapping

All foci considered :
- Detection of 39/40 (97 %) significant foci

Considering only index lesions :
- Detection of 24/25 (96 %) of index lesions

Considering Gleason score (GS) :
- Maximal GS in biopsies matches maximal definitive GS for 84 % of the patients (21/25)
- 2 patients understaged (one high-risk falsely staged intermediate-risk)
- 2 patients overstaged (two intermediate-risk falsely staged high-risk)

Benamran et al, Prog Urol 2015

Demographics :

n	25
Age	66 (62-73)
PSA (ng/ml)	8.6 (6.4-13.5)
Prostate volume (cm³)	57 (39-76)
Tumor volume (cm³)	3.8 (2.2-7.4)
Tumor vs prostate volume ratio (%)	7 (5-10)
All foci (n)	62 (2.48 / specimen)
Significant foci (n)	40 (65 %)

Values are median + IQR

Slide 2
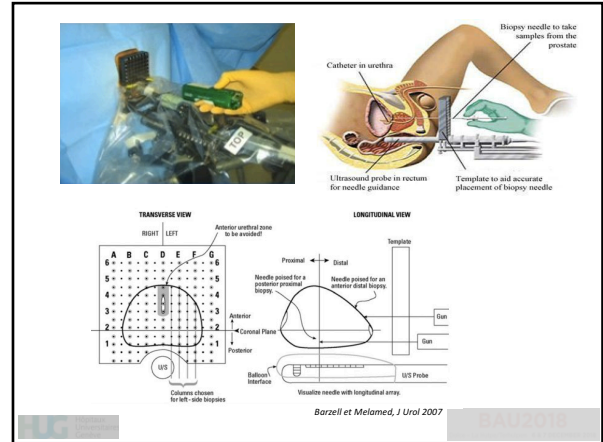
Barzell et Melamed, J Urol 2007

Slide 3: Pitfall

Failure of diagnosis

=

Worst outcomes

≠ **Failure of treatment**

Slide 4

New and Established Technology in Focal Ablation of the Prostate: A Systematic Review.
Valerio M. et al. Eur Urol. 2017 Jan;71(1):17-34.

37 trials - 3230 patients

HIFU (13), Cryotherapy (11), Laser induced interstitial thermotherapy, Vascular Photodynamic Therapy (3), Brachytherapy (2), Electroporation (4), Radiofrequency ablation (2)
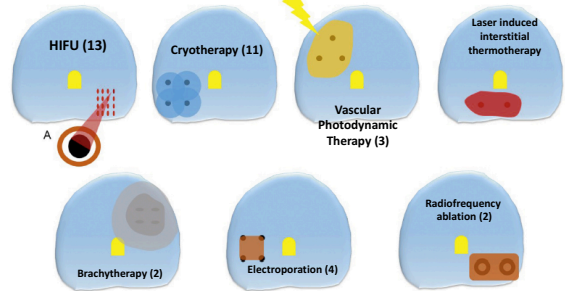
(n studies)

Slide 5: Effective treatment tool : HIFU
A very 'simple' technology

Diagnostics
- parallel beam
- **very low energy** (0.02 Watts)
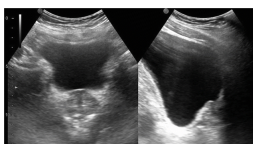
Therapeutics (HIFU)
- focalized beam
- **very high energy** (200 Watts)
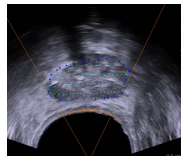
Slide 6: A very 'old' technology

Prototype n° 1 : 1993-1995
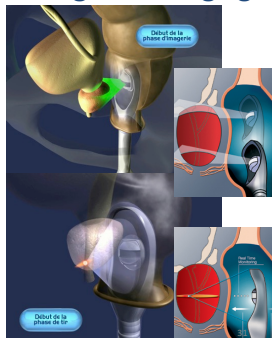
Prototype n° 2 1995 - 1999

Ablatherm Maxis 2000 - 2005

Courtesy of Dr A. Gelet

2000 – 2005 Ablatherm® Maxis

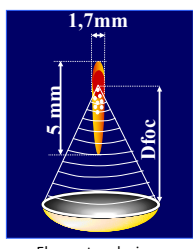**From 2006 Integrated Imaging**

Imaging position
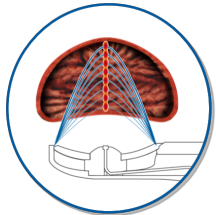HIFU position

Ablatherm II 2006 -2013

Focal-One 2014 …
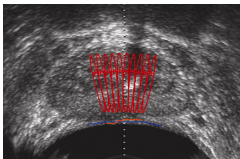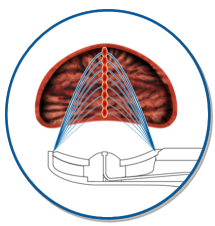
What does the Focal One do ?
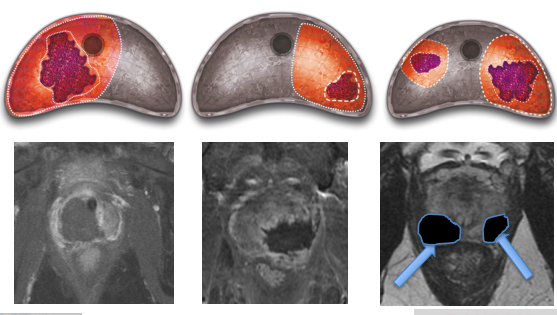

1,7mm
5 mm
Dfoc

Elementary lesion

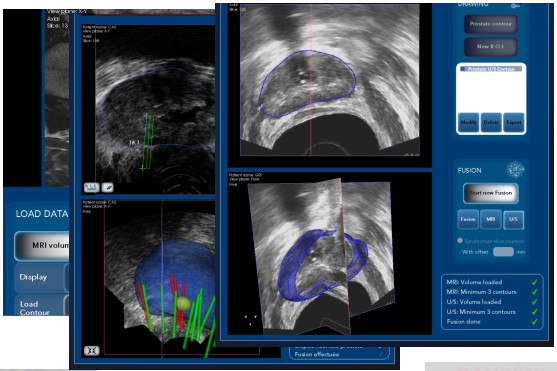With the Focal One : « dynamic focusing » (8 different focal points)
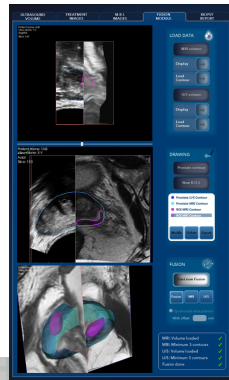
How is it different from the old devices ?
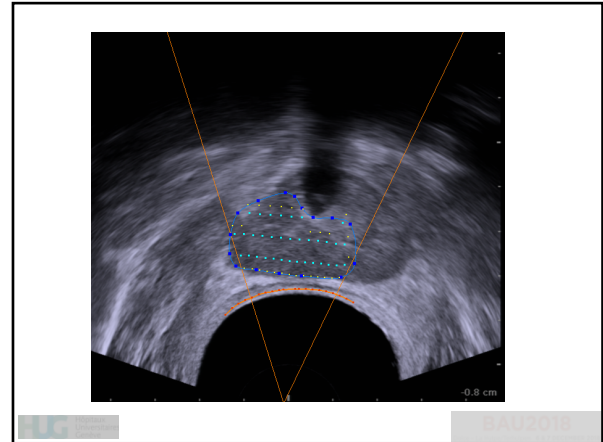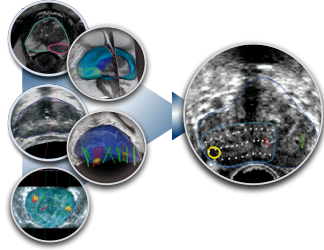

Allows conformational treatment

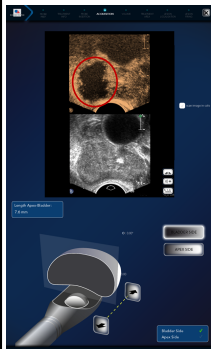
Precise planning of the treatment

MRI / Biopsy / Ultrasound elastic fusion

- Automatic registration of 3D contours of prostate (3D translations and rotations)
- Elastic transformation
- Transformation applied to MRI targets and biopsy trajectories to be visualized in the ultrasound
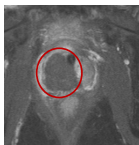

-0.8 cm

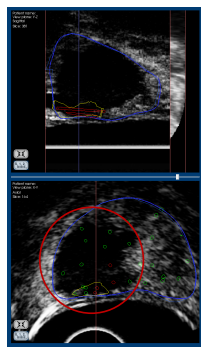## Validation of treatment and retreatment if needed

Use of standard Contrast-Enhanced Ultrasound Technology (Sonovue™)

Allows to confirm de-vascularized area

Allows to re-treat areas not completely treated

Clinical results

Padeliporfin vascular-targeted photodynamic therapy versus active surveillance in men with low-risk prostate cancer (CLIN1001 PCM301): an open-label, phase 3, randomised controlled trial

Abdel-Rahmène Azzouzi, Sébastien Vincendeau, Eric Barret, Antony Cicco, François Kleinclauss, Henk G van der Poel, Christian G Stief, Jens Rassweiler, Georg Salomon, Eduardo Solsona, Antonio Alcaraz, Teuvo T Tammela, Derek J Rosario, Francisco Gomez-Veiga, Göran Ahlgren, Fawzi Benzaghou, Bertrand Gaillac, Billy Amzal, Frans M J Debruyne, Gaelle Fromont, Christian Gratzke, Mark Emberton, on behalf of the PCM301 Study Group
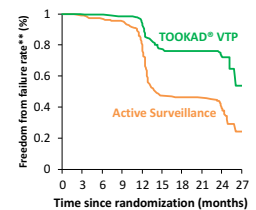
Lancet Oncol. 2017 Feb;18(2):181-191.

Padeliporfin vascular-targeted photodynamic therapy versus active surveillance in men with low-risk prostate cancer (CLIN1001 PCM301): an open-label, phase 3, randomised controlled trial

Co-Primary endpoints	TOOKAD® VTP vs. Active Surveillance
Absence of any positive biopsy at 24 mos*	RR=3.62# 95%-CI=[2.50-5.26]
Failure on composite primary endpoint**	HR=0.34 95%-CI=[0.24-0.46]

Overall p-value for the co-primary analysis: p<0.001

After 3 consecutive biopsies, very significant difference in presence of GS≥7 or other tumour burden criteria in the TOOKAD® VTP arm at M24

In either the treated or contralateral lobe.

** Patients moving outside of the inclusion criteria: GS≥7, or > 3 positive cores, or MCCL>5mm, or PSA>10ng/mL in 3 consecutive measures, or T3 stage or above, or metastasis, or PCa death

#Presence of cancer in 51% of VTP patients is due to unilateral treatment with limited capability to retreat progressing patients within the trial (discovery at 24 months, study criteria Gleason<7, others)

Azzouzi et al. Lancet Oncol. 2017 Feb;18(2):181-191.

Slide 1

Padeliporfin vascular-targeted photodynamic therapy versus active surveillance in men with low-risk prostate cancer (CLIN1001 PCM301): an open-label, phase 3, randomised controlled trial

	Vascular-targeted photodynamic therapy (n=206)	Active surveillance (n=207)	Hazard ratio (95% CI)	p value
Progression	58 (28%)	120 (58%)	0·34 (0·24–0·46)†	<0·0001‡
Criteria for progression§				
>3 positive cores	23 (11%)	58 (28%)	NC	<0·0001¶
Gleason pattern ≥4	49 (24%)	91 (44%)	NC	<0·0001¶
Cancer core length >5 mm	25 (12%)	51 (25%)	NC	0·001¶
PSA >10 ng/mL in three consecutive measures	3 (1%)	14 (7%)	NC	0·007¶
Any T3 prostate cancer	0	4 (2%)	NC	NA
Metastasis	0	0	NC	NA
Prostate cancer-related death	0	0	NC	NA
Negative biopsy result at month 24	101 (49%)	28 (14%)	3·67 (2·53–5·33)||	<0·0001¶

Data are n (%), unless otherwise stated. NA=not applicable. NC=not calculated. PSA=prostate-specific antigen. *The Hochberg procedure was used to adjust for multiplicity of the two co-primary endpoints. †Adjusted hazard ratio. Cox proportional hazards model with treatment as fixed effect and baseline age, number of positive cores, prostate volume, and disease status (unilateral/bilateral) as covariates. ‡From the log-rank test of equality of survival curves across treatment groups Cox proportional hazards model with treatment as fixed effect and baseline age, number of positive cores, prostate volume, and disease status (unilateral/bilateral) as covariates. §A participant might have met more than one criterion for progression. ¶From Pearson's χ² test for observed success. ||Adjusted risk ratio. Logistic regression model with treatment as fixed effect and baseline age, number of positive cores, prostate volume, and disease status (unilateral/bilateral) as covariates.

Table 2: Co-primary efficacy endpoints

Azzouzi et al. Lancet Oncol. 2017 Feb;18(2):181-191.

Slide 2

Long term clinical results

Slide 3

Long term clinical results

Ganzer et al. 2013

538 patients
14 years of follow-up

Thüroff et al. 2013

702 patients
15 years of follow-up

Crouzet et al. 2013

1002 patients
17 years of follow-up

	10 Year Cancer Specific Survival	10 Year Metastasis Free Survival
Low	99-100%	99-100%
Intermediate	96-98%	94-95%
High	92%	86%

Slide 4

Clinical results focal therapy

Slide 5

Clinical results focal therapy

Feijoo et al. 2015

71 patients
12 months follow-up

- 15% Bx+ in the treated lobe
- 25% Bx+ in the whole gland
- **100% fully continent**
- 3% urinary retention (TURP)

van Velthoven et al. 2015

50 patients
40 months follow-up

- 100% 5-year cancer specific survival
- **94% continence preservation**
- 80% erectile function preservation

Rischmann et al. 2016

111 patients
10 centers
30 months follow-up

- 95% absence of CSC in the treated lobe
- 80% 2 yrs. Radical Treatment Free Survival
- **97% continence preservation**
- 78·4% erectile function preservation

Ganzer et al. 2018

51 patients
17 months follow-up

- 92% absence of CSC in the treated lobe
- **100% continence preservation**
- 21/30 erectile function preservation

Slide 6

Longer follow-up ?

A Multicentre Study of 5-year Outcomes Following Focal Therapy in Treating Clinically Significant Nonmetastatic Prostate Cancer

Stephanie Guillaumier, Max Peters, Manit Arya, Naveed Afzal, Susan Charman, Tim Dudderidge, Feargus Hosking-Jervis, Richard G. Hindley, Henry Lewi, Neil McCartan, Caroline M. Moore, Raj Nigam, Chris Ogden, Raj Persad, Karishma Shah, Jan van der Meulen, Jaspal Virdi, Mathias Winkler, Mark Emberton, Hashim U. Ahmed

Guillaumier et al, Eur Urol 2018

- 625 patients (only 13% low risk)

- Median follow-up 56 months

@5yr :
- failure-free survival 88%
- metastasis-free survival 98%
- CSS 100 %
- OS 99 %

- Incontinence : 2 %

Geneva experience

- No age limit
- PSA < 15
- T1-T2
- mpMRI concordance with the biopsies

SIPC | SWISS INTERNATIONAL PROSTATE CENTER

With at least 12 months f-u

- 50 patients treated between 2014 and 2016
- Intermediate risk : 78 %
- 12 patients underwent concomitant TURP/ICP
- 26 % immediate re-treatment after SonoVue

SIPC | SWISS INTERNATIONAL PROSTATE CENTER

Results

- 10 de novo erectile dysfunction (20 %)
- 1 de novo stress incontinence (2 %)
- 6 de novo LUTS (12 %)

- 40/50 no positive biopsy at 12 months
- In the treated area : 46/50 no positive biopsy (92 % success)
  - 2 clinically significant cancer (4 %) -> *failure of treatment ?*
- Outside the treated area :
  - 2 clinically significant cancer (4 %) -> *failure of diagnosis ?*

SIPC | SWISS INTERNATIONAL PROSTATE CENTER

What else ?

Salvage HIFU

Gelet et al. Urology 2004

Murat et al. European Urology 2008

Berge et al. Scan J of Urol and Nephrol 2010

Berge et al. Int. J of Urology 2011

Crouzet et al. Radiotherapy & Oncology 2012

Salvage HIFU

BJUI

Salvage high-intensity focused ultrasound (HIFU) for locally recurrent prostate cancer after failed radiation therapy: Multi-institutional analysis of 418 patients

- **418 patients**
- 7 yr OS rate : 72 %
- 7 yr **CSS** rate: **82 %**
- 7 yr **metastasis free** rate: **81 %**

Over the time, specific post-radiation parameters decreased toxicity :

Incontinence : 32 % -> 19 %

BOO / Stricture : 30 % -> 15 %

Fistula : 9 % -> 0.6 %

Salvage Focal-HIFU

Hemi salvage high-intensity focused ultrasound (HIFU) in unilateral radiorecurrent prostate cancer: a prospective two-centre study

Eduard Baco, Albert Gelet*†, Sébastien Crouzet*†, Erik Rud‡, Olivier Rouvière†‡, Hélène Tonoli-Catez*, Viktor Berge, Jean-Yves Chapelon† and Heidi B. Eggesbø‡

- **42 patients treated in 2 institutions**

- **median f/u 16 months**

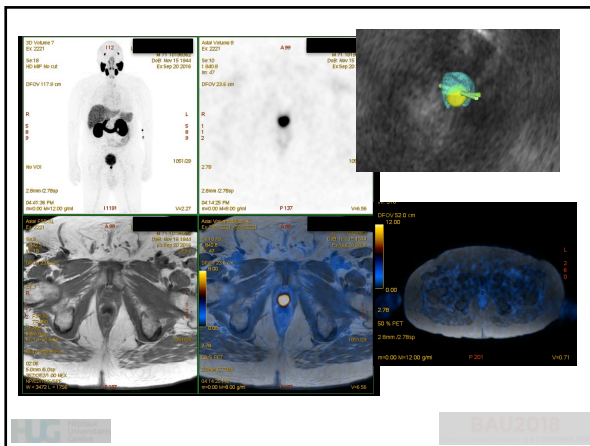*Incontinence : 8 %*

No fistula

---

73 yo, very active

GS 4+9 in 2001 ; RP without lymphadenectomy

Salvage lymphadenectomy in 2005

Salvage radiotherapy in 2006

PSA recurrence in 2013

Adressed in December 2016 : PSA 5.6

Take home messages

- Prostate cancer heterogeneity needs different treatment approaches.

- We have the tools to accurately diagnose our patients (but these are not 100 %)

- We have the tools to selectively treat our patients (but these are not 100%)

- Focal therapy with HIFU provides cancer control and QoL preservation.

- HIFU treatment offers an option for radio-recurrent prostate cancer

- Good patient selection and diagnosis = most important part of success.

" This procedure is cancer-sparing surgery "

Quote in the 1980s about nerve-sparing prostatectomy

" … total prostatectomy remains the optimal treatment for patients with clinically localized carcinoma of the prostate "

Gibbons et al, J Urol 1984

Acknowledgments

Service d'Urologie des HUG

Dr Stefano Regusci, Geneva
Dr Albert Gelet, Lyon
Pr Bertrand Tombal, Binche

HUG Hôpitaux Universitaires Genève

Slide 1

" **Progress is impossible without change**, and those who cannot change their minds cannot change anything "

George Bernard Shaw

"**All truth passes through three stages**. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident."

Arthur Schopenhauer

Thank you !

HUG Hôpitaux Universitaires Genève

BAU2018
Dolce – La Hulpe/Terhulpen 6 & 7 DECEMBER 2018

Slide 3 — Role of index lesion

ORIGINAL ARTICLE

Histological characteristics of the index lesion in whole-mount radical prostatectomy specimens: implications for focal therapy

M Karavitakis[1,2], M Winkler[3], P Abel[1,3], N Livni[4], I Beckley[3] and HU Ahmed[5]

[1]Department of Surgery, Imperial College, London, UK; [2]Department of Urology, 'St Panteleimon' General Hospital of Nikaia, Piraeus, Greece; [3]Department of Urology, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London, UK; [4]Department of Histopathology, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London, UK and [5]Department of Urology, University College London, London, UK

It has been suggested that in multifocal prostate cancer (PCa), focal therapy to the largest (index) lesion is sufficient, because secondary non-index lesions are unlikely to contribute to disease progression. In this study, the role of PCa focality in selecting men for focal therapy was evaluated. A histopathological analysis of the index and non-index lesions of 100 consecutive radical prostatectomy specimens was carried out. Cases that would have been suitable for focal ablation were also evaluated. Tumours were more often multifocal (78%) and bilateral (86%). In total, 270 tumour foci were identified. In multifocal disease, tumour volume, Gleason score and pathological stage were almost invariably defined by the index lesion of the specimen; among the 170 satellite foci, 148 (87%) were <0.5 cm³ and 169 (99.4%) had Gleason score ⩽6. Using the defined criteria, 91% of men in this series would have been considered suitable for focal ablation of the index lesion. Histological features of poor prognosis in the prostate are associated with the index lesion. There is a high proportion of patients who may be suitable for focal therapy, and clinical trials of index lesion ablation should be considered as part of this therapeutic strategy.
Prostate Cancer and Prostatic Diseases (2011) **14,** 46–52; doi:10.1038/pcan.2010.16; published online 25 May 2010

Karavitakis et al, Prostate Caner Prostatic Dis 2011

Slide 4 — Role of index lesion

ORIGINAL ARTICLE
Histological characteristics of the index lesion in whole-mount

Table 4 Histological characteristics of the individual tumour foci

Tumour type	Total	Gleason ⩾7		Gleason ⩽6		Volume ⩾0.5 cm³		ECE		SVI	
		N	%	N	%	N	%	N	%	N	%
Unifocal	22	7	31.8	15	68.2	18	81.8	5	22.7	7	31.9
Index lesions	78	24	30.7	54	69.3	66	84.6	13	16.6	5	6.4
Secondary lesions	170	1	0.6	169	99.4	22	12.9	2	1.1	0	0
Total	270	32		238		106		20		12	

Abbreviations: ECE, extracapsular extension; SVI, seminal vesicle invasion.

Karavitakis et al, Prostate Caner Prostatic Dis 2011

Slide 5 — What about satellite lesion ?

Human
PATHOLOGY
www.elsevier.com/locate/humpath

ELSEVIER

Original contribution

The relationship of *TMPRSS2-ERG* gene fusion between primary and metastatic prostate cancers☆

Charles C. Guo MD, Yan Wang PhD, Li Xiao MD, Patricia Troncoso MD, Bogdan A. Czerniak MD, PhD*

Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030-4009, USA
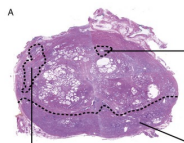
" The concordance of the ERG gene rearrangement status between the index primary tumor focus and metastasis suggests that metastasis most likely arises from the index tumor focus in multifocal prostate cancer. "
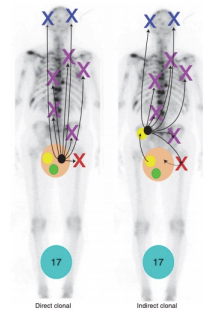
Guo et al, Hum Pathol 2012

Slide 6 — What about satellite lesion ?

nature medicine

Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer

Wennuan Liu[1,8], 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], Jianfeng Xu[1], William B Isaacs[6,7], Tapio Visakorpi[2] & G Steven Bova[6–8]

"…despite common genomic heterogeneity in primary cancers, most metastatic cancers arise from a single precursor cancer cell"

Direct clonal   Indirect clonal

Liu et al, Nat Med 2009

What about true GS 6 ?

Predicting 15-Year Prostate Cancer Specific Mortality After Radical Prostatectomy

Scott E. Eggener,* Peter T. Scardino, Patrick C. Walsh, Misop Han, Alan W. Partin,
Bruce J. Trock, Zhaoyong Feng, David P. Wood,† James A. Eastham,
Ofer Yossepowitch, Danny M. Rabah, Michael W. Kattan, Changhong Yu,
Eric A. Klein and Andrew J. Stephenson‡
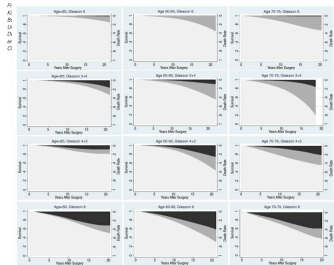
" only 3 of 9,557 patients with organ confined, pathological Gleason score 6 cancer died of prostate cancer "

After review of the 3 cases :
all had higher grade disease !

Eggener et al, J Urol 2011

What about true GS 6 ?

Do Adenocarcinomas of the Prostate With Gleason Score (GS)≤6 Have the Potential to Metastasize to Lymph Nodes?

Hillary M. Ross, Oleksandr N. Kryvenko,† Janet E. Cowan,‡ Jeffry P. Simko,‡§ Thomas M. Wheeler,‖ and Jonathan I. Epstein, MD*¶‡*

Abstract: Although rare, there are cases within reported series of men with Gleason score (GS)≤6 on radical prostatectomies that show pelvic lymph node (LN) metastases. However, there are no studies on whether pelvic LN metastases occur in tumors with GS≤6 using the International Society of Urological Pathology (ISUP) updated GS system. We performed a search of the pattern 4 or 5, as better defined by the current ISUP updated grading system, is required for metastatic disease.

Key Words: Gleason score, radical prostatectomy, lymph node metastases

(*Am J Surg Pathol* 2012;36:1346–1352)

14'123 case of true GS 6 on whole-mount pathology

22 lymph nodes positive – on review : all had higher grade

Ross et al, Am J Surg Pathol 2012