

The SPARED **CRN** meeting

FDA, Washington 5/3/2018

To Develop and Regulate Modern PCa-Care:
a Secured, Integrated, Transversal Vision from Europe.

Pr Roland van Velthoven, MD, PhD

Dr Antoine Leroy, PhD – Koelis Founder&CEO

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- Introduction on SPARED CRN objectives and situation in Europe
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- WRAP-UP and PROPOSAL

Introduction on SPARED CRN objectives and situation in Europe

Coordinated Registry Network (CRN) Objectives and European Situation

- To improve and develop:
 - Patient information on Focal Treatment
 - Technical Innovation from Research and Industry
 - QoL and Economical data for Payers
- Through a **comprehensive collaborative database**, to **collect and monitor standardized data** from existing and emerging **non surgical treatments** of prostate cancer.



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the leading European professional organisation for medical oncology.

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ESMO / PRESS OFFICE / PRESS RELEASES / Press Statement ESMO Welcomes Final Version of European Data Protection Regulation

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Press Statement: ESMO Welcomes Final Version of European Data Protection Regulation

Date: 14 Apr 2016

Topic: **Bioethics, legal and economic issues**

- **Inclusion of one-time consent “crucial” for future of cancer research**
- **Regulation will aim to harmonise public health research across all 28 EU member states**

Lugano, Switzerland -- ESMO – the leading European professional organisation for medical oncology – has today welcomed the European Parliament’s adoption of the EU General Data Protection Regulation, which it describes as being “crucial” for the future of cancer research.

Coordinated Registry Network (CRN)

GDPR: in the urological field: where do we stand ??

GDPR

Period



Events



Sessions



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ESU
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EU Articles



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Guidelines



Hands-on
Training



Live Surgery



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ePosters



UROsource
The EAU learning library for urologists

Back to UROsource

Filters

Type of Content

Period

Events

0 results for 'GDPR'

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FAQ

In Europe:

EAU guidelines 2018 not in favor of mpMRI before first Bx nor Focal Therapy

In spite of multiple proofs of value for :

MRI and MRI-guided prostate biopsy (eg PROMIS, Precision)
Focal Energy Ablation (eg HIFU hemiablation)

HIFI ΔRI ΔTION THERΔPY FOCΔI « ONE »

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journal homepage: www.europeanurology.com



European Association of Urology



Platinum Priority – Position Paper

Editorial by XXX on pp. x–y of this issue

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

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Alex Govorov^d, Ann M. Henry^e, Thomas B. Lam^{f,g}, Malcolm D. Mason^h, Olivier Rouvièreⁱ,
Maria De Santis^{j,k}, Peter-Paul M. Willemse^l, Hendrik van Poppel^m, Nicolas Mottetⁿ**

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HIFU ABLATION THERAPY FOCAL « ONE »



Platinum Priority – Position Paper
Editorial by XXX on pp. x–y of this issue

Focal Therapy in Primary Localised Prostate Cancer:

- **Patient summary:** Focal therapy of prostate cancer is the targeted destruction of cancer within a specific part of the prostate gland, sparing the rest of the prostate and nearby tissue.
- This procedure could potentially reduce side effects when compared with established standard treatments, such as surgery or radiotherapy, which treat the entire prostate.
- Studies show that for most men with low-risk cancer, active surveillance is the preferred treatment option.
- **However, the available data regarding all forms of focal therapy are still poor and inconclusive. Consequently, due to both the lack of clear results associated with focal therapy and the difficulties in detecting all cancerous areas of the prostate, focal therapy should be considered an investigational modality only.**

**→ OUR VISION of a Secured, Integrated,
Transversal REGISTRY**

Data Protection Context for CRN: GDPR and
HIPAA

Coordinated Registry Network (CRN)

data protection context

EU - GDPR

- any information that can be **used to directly or indirectly identify EU citizens** such as
 - race, religion,
 - political affiliations,
 - sexual preferences,
 - biometric
 - genetic data,
 - any other information relating to their **health (=PHI)**

US - HIPAA

- Scope limited to dealing with **protected health information (PHI)**.
- PHI includes any information that can be used to **identify a patient**,
 - name, address, DOB,
 - bank/credit card details,
 - social security number, photos
 - and insurance information.

Coordinated Registry Network (CRN)

GDPR in Healthcare

- Creating a uniform set of rules governing how personal data can be used in today's digital age, the Regulation will aim to harmonise the different frameworks governing health research across the EU's 28 Member States.
- In particular, the Regulation includes provision for a **'one-time consent'** from patients allowing their data and tissues to be used for future research, which will also ensure the viability of bio-banking.

Coordinated Registry Network (CRN)

GDPR in Healthcare

- The new Regulation also ensures that researchers have access to **high-quality, population-wide data**, which by definition must include the entire population, and therefore **cannot be subject to patient consent**.
- This exemption from consent is important because it allows **disease-based registries** to continue to exist and benefits not only cancer research but medical research in general.
- In the case of cancer, this data is **collected and stored in cancer registries**, which are used by governments to formulate new cancer control policies and update national cancer plans and **ultimately improve patient outcomes**.

Coordinated Registry Network (CRN)

GDPR in Healthcare

- Scientific steering committee
- Data Protection Officer (DPO)
- Explicit Consent
 - The definition of consent is stricter – requiring that consent be “freely given, specific, informed and unambiguous,”
- Right to access, correct, erasure
- Secure sensitive data

Coordinated Registry Network (CRN)

GDPR: Sensitive Data (How to protect?)

- Each greater level of de-identification provides more protection and further reduces risk to individuals
- GDPR-Through-the-De-Identification-Lens-describes four levels of identifiability,
 - (1) Identified,
 - (2) Identifiable,
 - (3) Article 11 De-Identified, and
 - (4) Anonymous / Aggregated

Coordinated Registry Network (CRN)

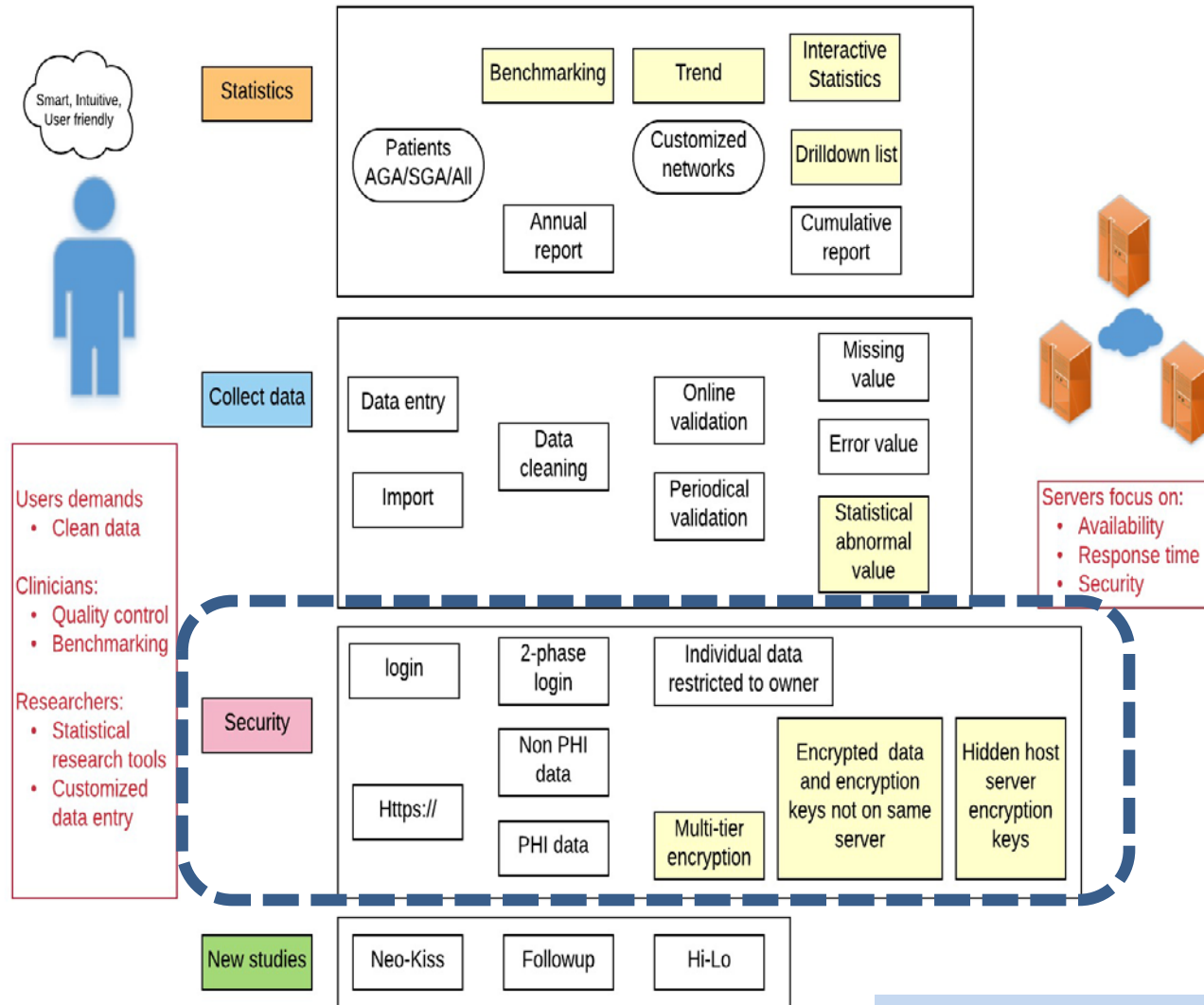
GDPR: Sensitive Data (How to protect?)

- **Protected Health Information (PHI data)**
 - Phi data are separated from medical data in other server and de-identified.
 - Phi data are encrypted
 - Patient key dependent encryption (Each patient has its own encryption)
- **GDPR Sensitive Non PHI data**
 - Non PHI data are stored in medical data.
 - Every medical data are **pseudonymized**
 - **Every medical data are encrypted and key encryption is item dependent**

Sample implementation of an International Secured Registry

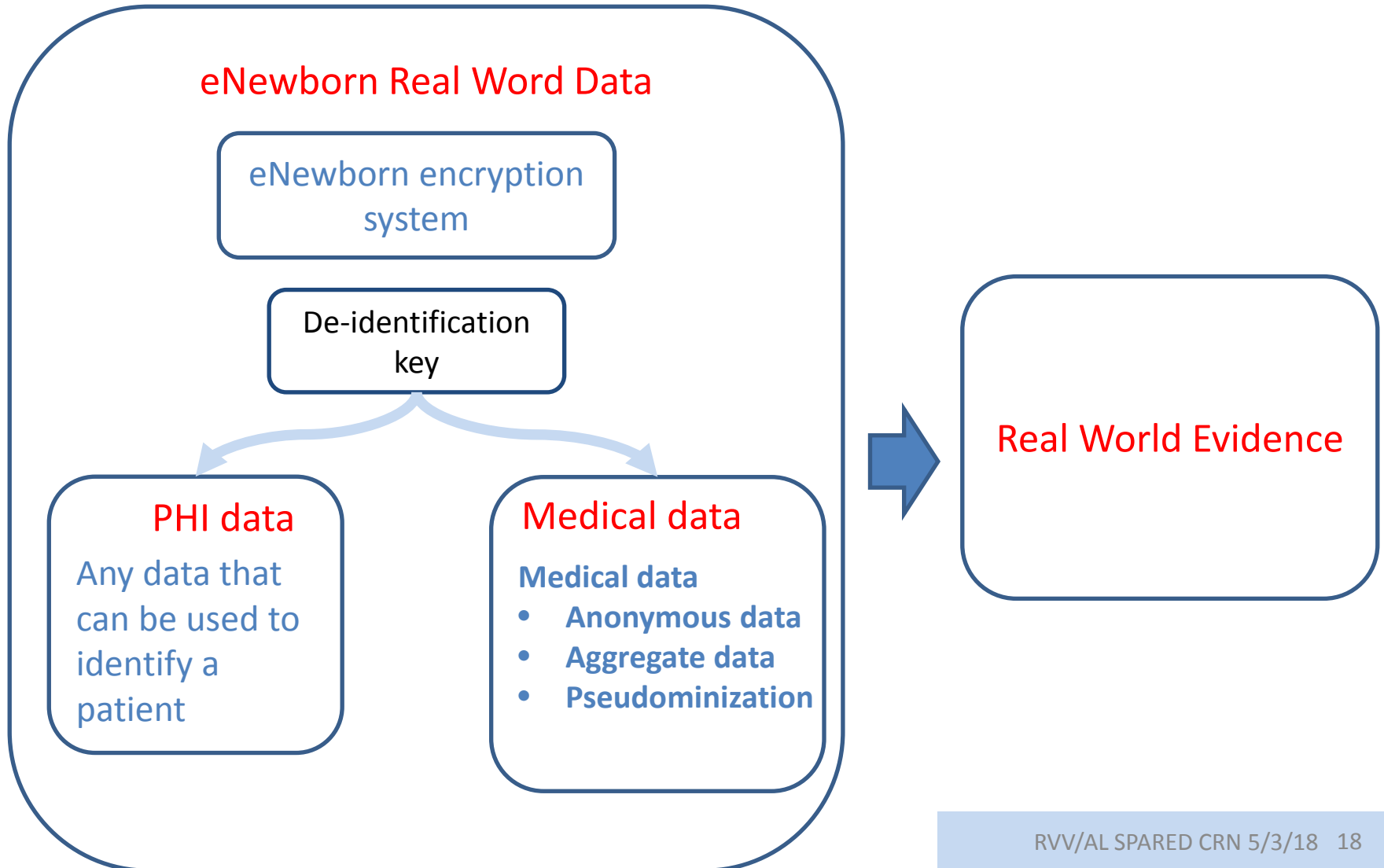
GDPR: Sensitive Data (How to protect?)

eNewborn Functionalities



GDPR: Sensitive Data (How to protect?)

eNewborn GDPR Compliance



Coordinated Registry Network (CRN)

GDPR: Sensitive Data (How to process?)

- **Protected Health Information (PHI data):**
 - Phi data are not processed for statistical analysis.
 - Phi data can be decrypted by the owner / hospital / physician who has the privilege to access.
 - Each access is traced.
- **GDPR Sensitive Non PHI data**
 - Medical data can be de-crypted by the owner / hospital /physician with adequate privilege.
 - Medical data can be processed by statistical analysis.
 - When in aggregate form, medical data can be decrypted by users having statistical privilege or by statistical process.
 - Each access is traced.

Registry Items and need for standardization: 2 sample studies

Author's Accepted Manuscript

Quality indicators for global benchmarking of localised prostate cancer management

Fanny Sampurno , Jia Zheng , Lydia Di Stefano , Jeremy L. Millar , Claire Foster , Ferran Fuedea , Celestia Higano , Hartwig Hulan , Stephen Mark , Caroline Moore , Alison Richardson , Frank Sullivan , Neil S. Wenger , Daniela Wittmann , Sue Evans

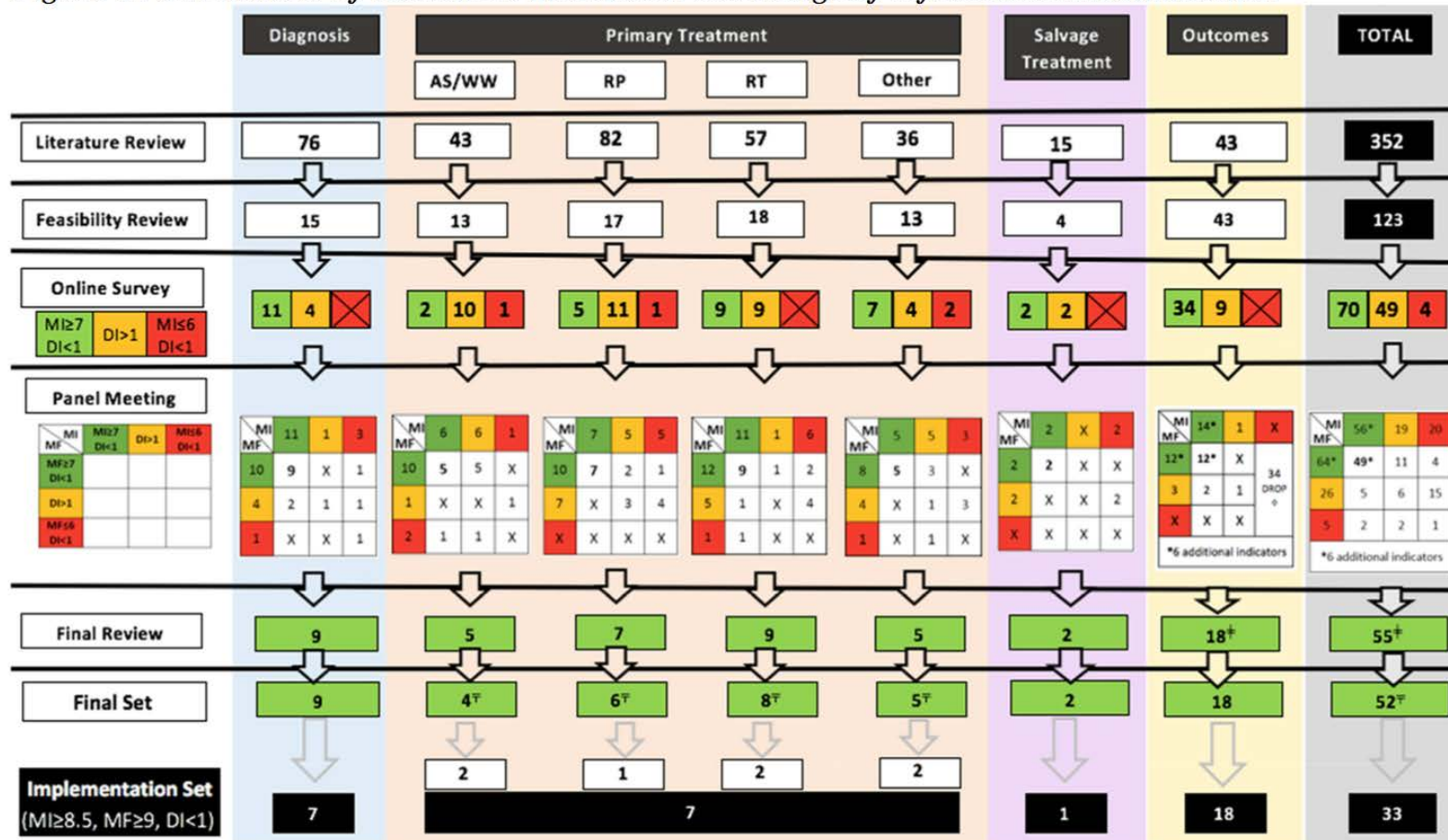


PII: S0022-5347(18)39377-7
DOI: [10.1016/j.juro.2018.02.071](https://doi.org/10.1016/j.juro.2018.02.071)
Reference: JURO 15289

To appear in: *The Journal of Urology*
Accepted Date: 15 February 2018

Please cite this article as: Sampurno F, Zheng J, Di Stefano L, Millar JL, Foster C, Fuedea F, Higano C, Hulan H, Mark S, Moore C, Richardson A, Sullivan F, Wenger NS, Wittmann D, Evans S, Quality indicators for global benchmarking of localised prostate cancer management, *The Journal of Urology*® (2018), doi: [10.1016/j.juro.2018.02.071](https://doi.org/10.1016/j.juro.2018.02.071).

Figure 1: The number of indicators involved in each stage of refinement and elimination



MI: Median importance

MF: Median feasibility

DI: Disagreement index

AS/WW: Active surveillance/ watchful waiting

RP: Radical prostatectomy

RT: Radiotherapy

*6 indicators added (QI 22-27, Table 4)
during the panel meeting.

◇ 34 indicators were removed during the
panel meeting.

Author's Accepted Manuscript

Quality indicators for global benchmarking of localised prostate cancer management

Fanny Sampurno , Jia Zheng , Lydia Di Stefano , Jeremy L. Millar , Claire Foster , Ferran Fuedea , Celestia Higano , Hartwig Hulan , Stephen Mark , Caroline Moore , Alison Richardson , Frank Sullivan , Neil S. Wenger , Daniela Wittmann , Sue Evans



CONCLUSIONS

- This study defined a set of 33 indicators conceived on the basis of existing international evidence-based clinical guidelines and endorsed by an international multidisciplinary expert panel.
- The indicators encompass the diagnosis, treatment and outcome aspects of Pca management.
- This set will be used to benchmark performance internationally in order to improve consistency and quality of care for men with PCa on a global basis.

Outcomes of Focal Therapies for Prostate Cancer

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. **⚠** [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT03492424

[Recruitment Status](#) ⓘ : Recruiting

[First Posted](#) ⓘ : April 10, 2018

[Last Update Posted](#) ⓘ : April 10, 2018

See [Contacts and Locations](#)

Sponsor:

Weill Medical College of Cornell University

Descriptive Information	
Brief Title	Outcomes of Focal Therapies for Prostate Cancer
Official Title	Outcomes of Focal Therapies for Prostate Cancer
Brief Summary	The purpose of this study is collect observational data regarding patterns of care and outcomes of focal therapies for prostate cancer, including but not limited to: high-intensity focused ultrasound (HIFU), cryotherapy, focal laser ablation, irreversible electroporation, photodynamic therapy, and brachytherapy.
Detailed Description	Through the use of a prospective registry, the investigators will collect information on patient characteristics including age, co-morbidities, imaging and biopsy information, and prior treatments. Information on treatment details will also be captured, including treatment time, anesthesia delivered, and length of stay, when applicable. Oncologic outcomes including PSA, post-treatment biopsy and imaging data, need for re-treatment, and survival outcomes will also be captured. Safety outcomes will be captured using the Clavien-Dindo classification scale, and additional specific GU complications will be recorded, which include urinary retention, urethral stricture, recto-urethral fistula, osteomyelitis, and urinary tract infection. Finally, the investigators will capture functional outcomes using health related quality of life questionnaires including the EPIC questionnaire, IIEF-5, MSHQ-EjD, and IPSS.
Study Type	Observational [Patient Registry]
Study Design	Observational Model: Other Time Perspective: Prospective
Target Follow-Up Duration	12 Months
Biospecimen	<i>Not Provided</i>
Sampling Method	Non-Probability Sample
Study Population	Participants are generally healthy men diagnosed with prostate cancer, undergoing focal therapy for treatment of prostate cancer.

Recruitment Information	
Recruitment Status	Recruiting
Estimated Enrollment (submitted: April 6, 2018)	200
Original Estimated Enrollment	<i>Same as current</i>
Estimated Study Completion Date	March 1, 2020
Estimated Primary Completion Date	March 1, 2020 (Final data collection date for primary outcome measure)
Eligibility Criteria	<p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • >18 years of age • Undergoing focal therapy for primary or salvage treatment of prostate cancer, or • Have received prior focal therapy <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • Clinically-evident metastatic disease • Unable to fill out an English-language questionnaire
Sex/Gender	Sexes Eligible for Study: Male
Ages	18 Years and older (Adult, Senior)
Accepts Healthy Volunteers	No

transrectal Koelis fusion biopsy from 2010 to 2017.

list of study items

Clinical	mp-MRI	Biopsy strategy	Pathology of targeted biopsies	Pathology of randomized biopsies
Center	MRI date	Biopsy device	<i>Pca on target 1</i>	Pca on random biopsies
Surname	Number of targets	#Target cores taken	<i>Primary Gleason score of target 1</i>	Primary Gleason score of random biopsies
Name	Target 1 Localisation of target 1	Number Random cores taken	Secondary Gleason score of target 1	Secondary Gleason score of random biopsies
Dossier number		Number Total cores taken	#positive cores of target 1	#positive cores of random biopsies
Birthdate	mm PIRADS1		Max core length of Pca on target 1	Max core length of Pca on random biopsies
Biopsy date	ADC1	Pathology	Pca on target 2	
Age	Target 2 Localisation of target 2	Pca finding on biopsy	Primary Gleason score of target 2	
DRE		Localisation of Pca	Secondary Gleason score of target 2	
Vol (cc)	mm PIRADS2 ADC2		#positive cores of target 2 Max core length of Pca on target 2	

Accrual: 2.115 patients retrospectively enrolled from 15 institutions in 4 European countries,

Global HIFU in Pca: patient's data set

Item	Value	Cell format
Patient data		
Confidential identifiant	Text	Auto
Patient initials		
Inclusion date	DD/MM/YYYY	Date
Date of birth	DD/MM/YYYY	Date
Age at the biopsy exam date	Number	integer
Prostate cancer diagnostic date	DD/MM/YYYY	Date
PSA date	DD/MM/YYYY	Date
PSA value	Number	Integer
Free PSA rate before biopsy exam		
DRE result	Soft/ suspect-left/ suspect-right/suspect bilateral	
Cancer grade from DRE	T1/T2a/T2b/T2c/T3a/T3b/T4	
Indication	Early detection/ active monitoring/ suspicion of cancer exceeded	

1995 up to now:

Accrual: about 30000 patients enrolled

Lack of comprehensive prospective registry

April 2015 gov.fr / AFU Driven study:
Global hifu vs RP

HIFU focal treatment for unilateral prostate cancer: a comprehensive study of pooled data

Materials

- The National Library of Medicine Database was searched for articles published between January 2007 and April 2017.
- A wide search was performed including the combination of following words: “HIFU”, “prostate”, “cancer”, “focal”.
- Overall, 167 articles were reviewed. Of these, **7 articles** were identified and eligible for the pooled analysis.
- Data on HIFU hemiablation or focal prostate ablation oncologic and functional results were pooled from these 7 studies that **included 366 men with unilateral PCa.**

HIFU focal treatment for unilateral prostate cancer: a comprehensive study of pooled data

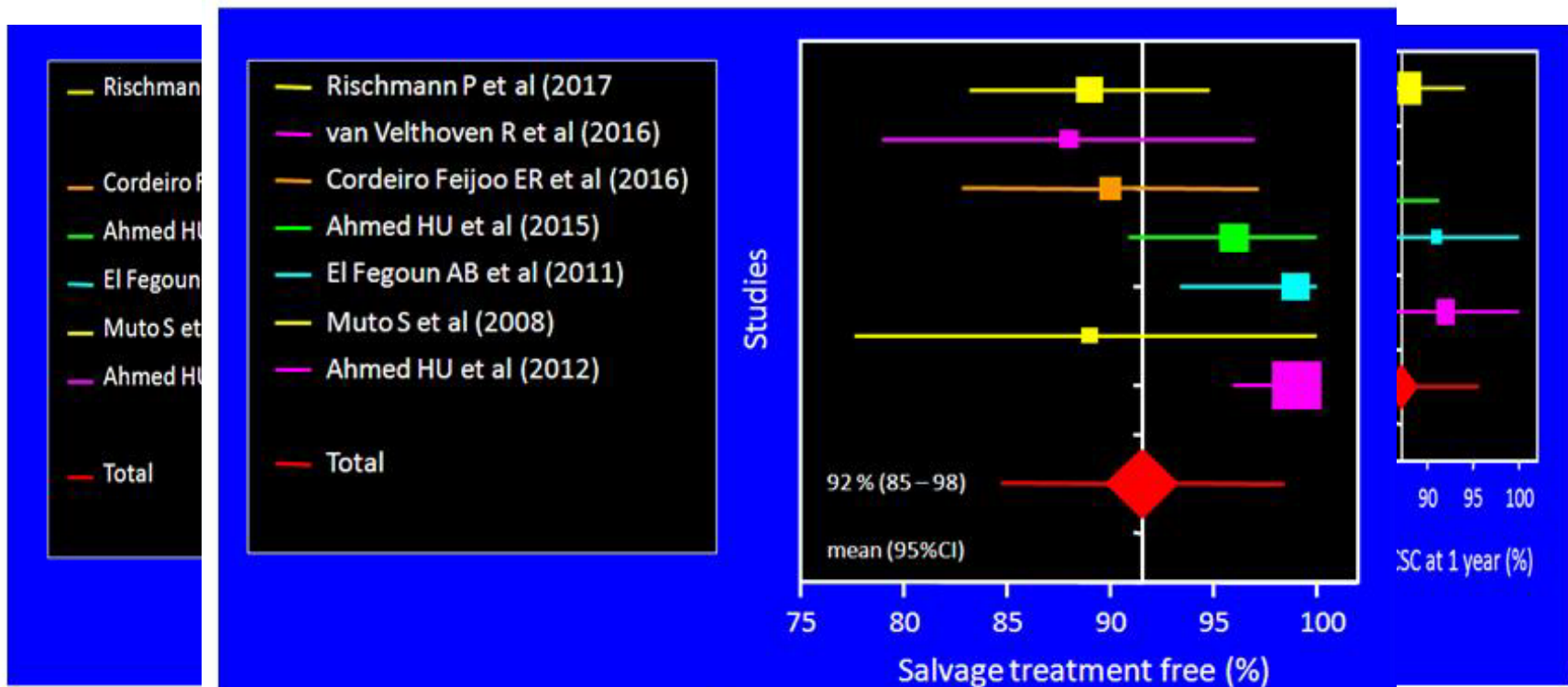
General characteristics of selected studies

Author	Year	Design	N patients	Age	PSA	Biopsy	Max Gleason for inclusion
Muto	2008	retrospective	29	72	5.4	Not specified	10 (5+5)
El Fegoun	2011	retrospective	12	70	7.3	random	7 (3+4)
Ahmed	2012	prospective	41	63	6.6	template biopsy	7 (4+3)
Ahmed	2015	prospective	56	64	7.4	template biopsy	7 (4+3)
van Velthoven	2016	prospective	50	73	6.6	Target and systematic	7 (4+3)
Feijoo	2016	prospective	67	70	6.1	random	7 (3+4)
Rischmann	2017	prospective	111	65	6.2	random and target	7 (3+4)

Simone Albisinni, Christian Melot, Ksenija Limani, Alexandre Peltier, Pascal Rischmann and Roland van Velthoven

HIFU focal treatment for unilateral prostate cancer: a comprehensive study of pooled data

Oncological outcomes



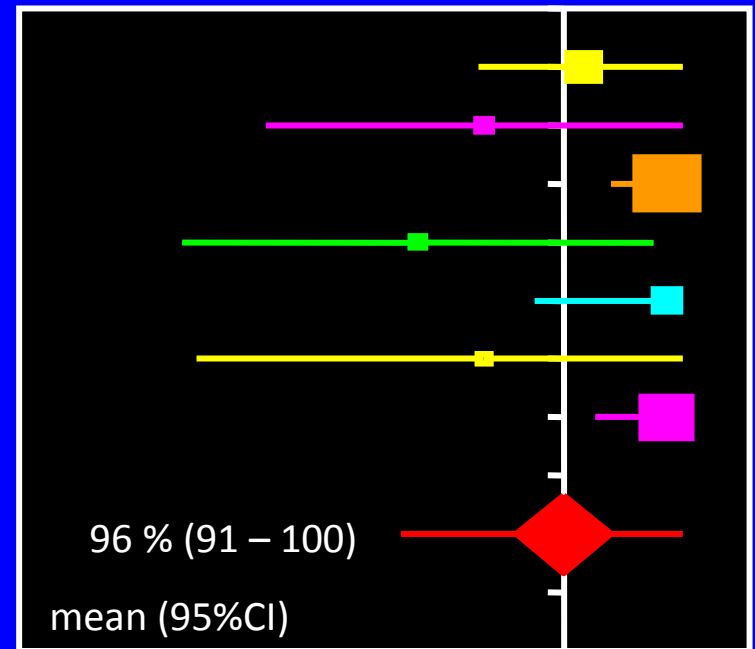
Simone Albisinni, Christian Melot, Ksenija Limani, Alexandre Peltier, Pascal Rischmann and Roland van Velthoven

HIFU focal treatment for unilateral prostate cancer: a comprehensive study of pooled data

Functional results

- Rischmann P et al (2017)
- van Velthoven R et al (2016)
- Cordeiro Feijoo ER et al (2016)
- Ahmed HU et al (2015)
- El Fegoun AB et al (2011)
- Muto S et al (2008)
- Ahmed HU et al (2012)
- Total

Studies



80 85 90 95 100
Urinary continence at 12 months (%)

Technology update and personal view of modern PCA-Care & registry

COMPREHENSIVE PATIENT PATHWAY



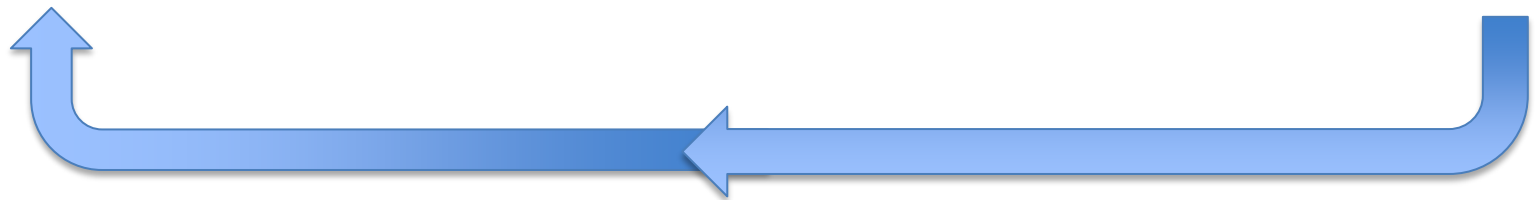
Pathology (Gleason, Epstein)
Biomarkers (Epigenetics)

Multiparametric
(MRI - PET) image fusion
Smart biopsy planning
Live 3D viewing
Targeted biopsies
3D Cartography

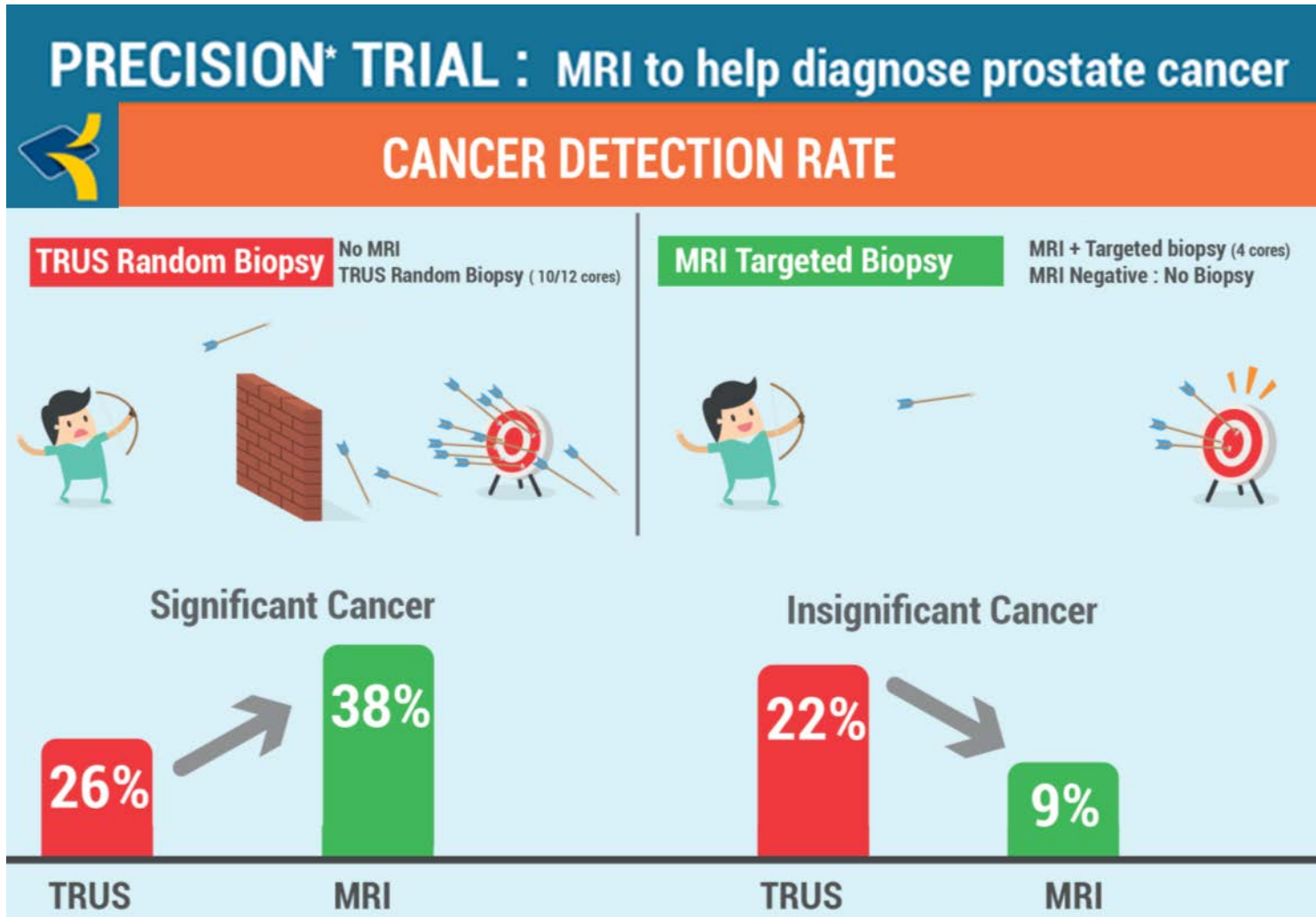
Confident patient selection
Multi-disciplinary decision

Accurate guidance
Confident and precise intervention
Cost-efficient & time-efficient
Targeted treatment.

Recall capability
Streamlined Workflow
Surveillance Active
Quality control
Data Management
Registre



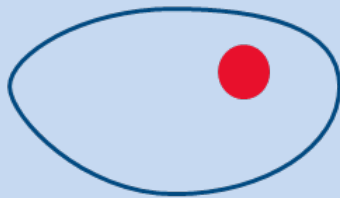
Fusion Targeted Biopsy: Precision Diagnosis proven by world RCT*



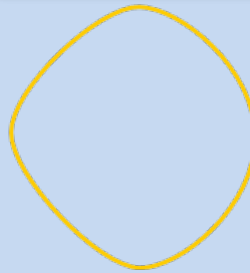
PRCS NP στυδισ Δρ ασισισ Βανατηαν ετ αλ UC Μονδον NP εω νγλανδ JM'2, □□



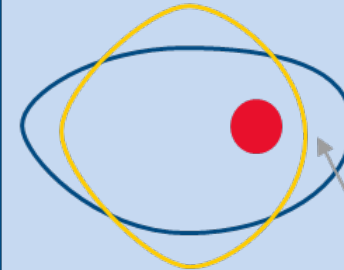
MRI image showing lesion-to-biopsy



Ultrasound image



Fusion image



Precision error from rigid fusion mislocates biopsy target

Non elastic fusion image

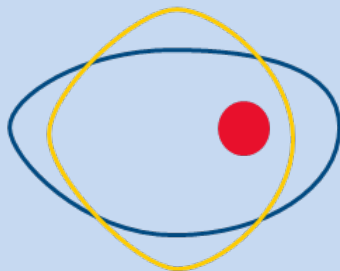
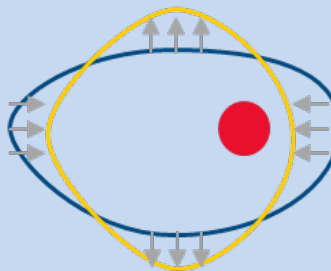
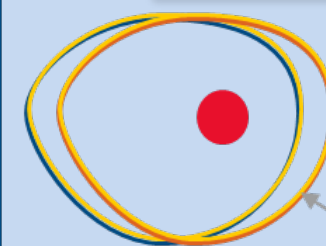


Image treatment



Elastic fusion image

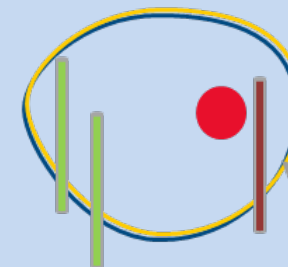


Fusion biopsy starts with precise target location BUT Prostate motion during biopsy rapidly leads to high Precision error

- The Organ Based Tracking® is a patented real-time imaging algorithm that permits the automatic recalculation of the prostate position and shape during biopsy intervention.
- OBT® enables to grow an exclusively accurate cartography of biopsy cores and MRI lesions over time. OBT® also enables an exclusively accurate "Second Look® fusion" to enable targeted re-biopsy and treatment protocols.
- Consequence to OBT®, elastic fusion MRI/US image is updated everytime the patient moves. It repositions the MRI images instantly on the ultrasound image that has moved with the patient therefore achieving the highest level of targeting precision amongst all available devices on the market

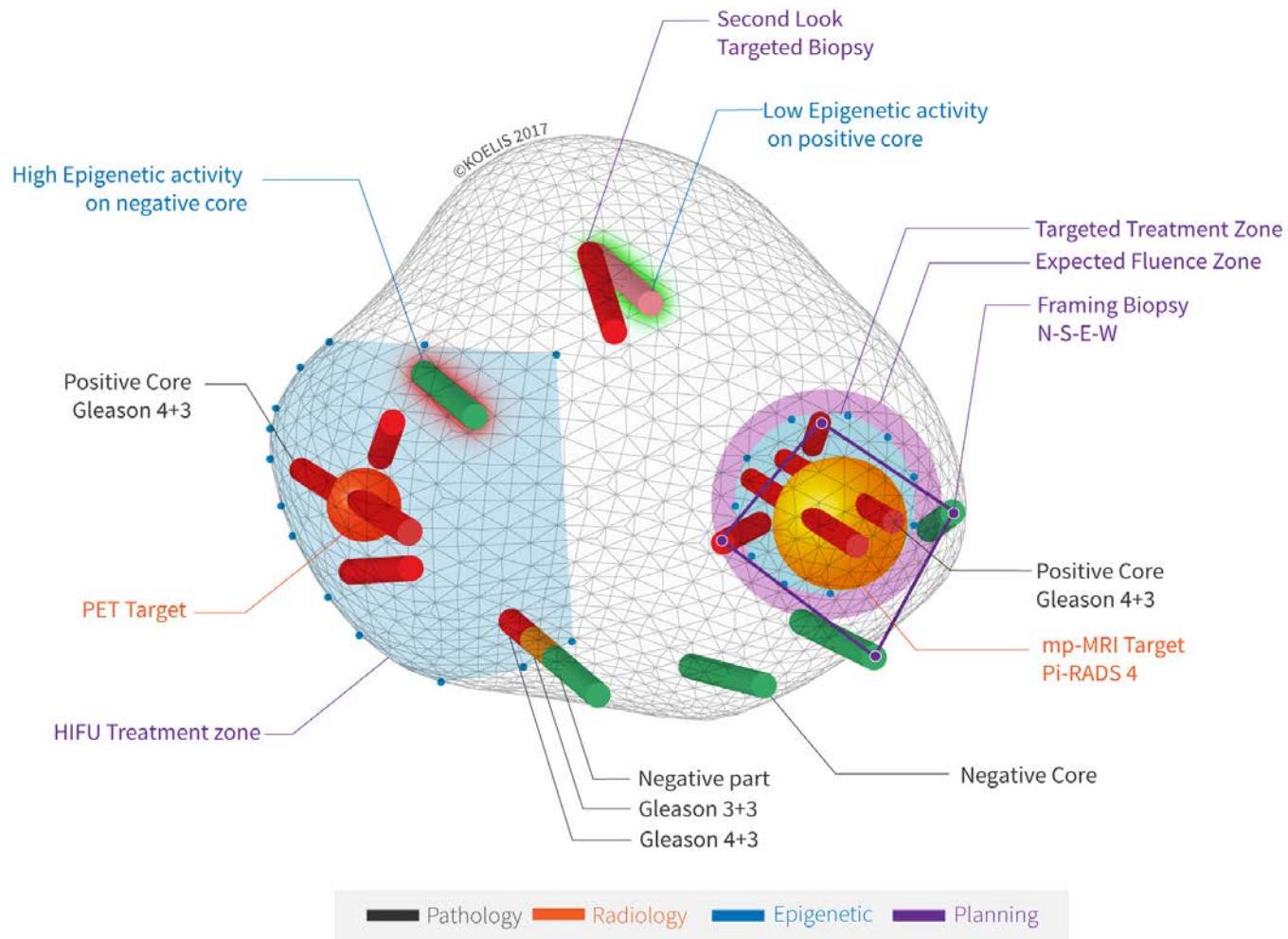


Motion compensation

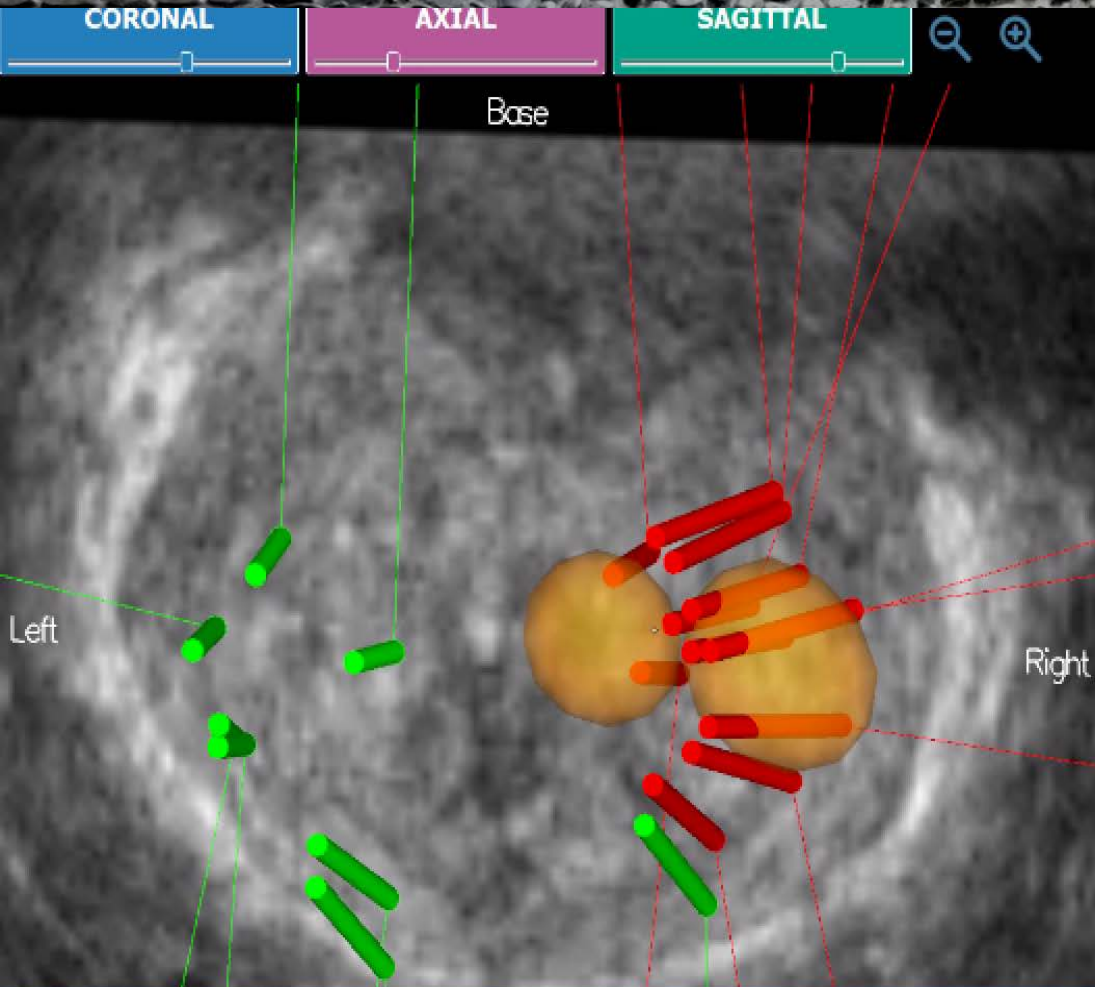


Target and Cores location error shows an unmatched accuracy over biopsy time thanks to the motion compensation algorithm

Optimal quality control



MRI/PET fusion + TRUS guided biopsy



HISTOLOGICAL DATA

Positive biopsy cores 11/19 | Maximum Gleason score
 Cancerous tissue length (mm) 126/183 | Cancer grade

Biopsy No.	Biopsy length	Tumor length	Gleason score	PCI	PNI	ASAP	PIN
1	10	7	3+4	■	■	■	■
2	16	6	3+4	■	■	■	■
3	15	13	3+3	■	■	■	■
4	12	10	3+4	■	■	■	■
5	17	15	3+4	■	■	■	■
6	24	21	3+4	■	■	■	■
7	17	16	3+3	■	■	■	■
8	15	8	3+3	■	■	■	■
9	18	10	3+3	■	■	■	■
10	20	6	3+4	■	■	■	■
11	0	-	-	■	■	■	■
12	19	14	3+4	■	■	■	■
13	0	-	-	■	■	■	■
14	0	-	-	■	■	■	■
15	0	-	-	■	■	■	■
16	0	-	-	■	■	■	■
17	0	-	-	■	■	■	■
18	0	-	-	■	■	■	■
19	0	-	-	■	■	■	■

PATIENT DATA TRACEABILITY AND QUALITY MANAGEMENT

3D VIEW

TARGETS

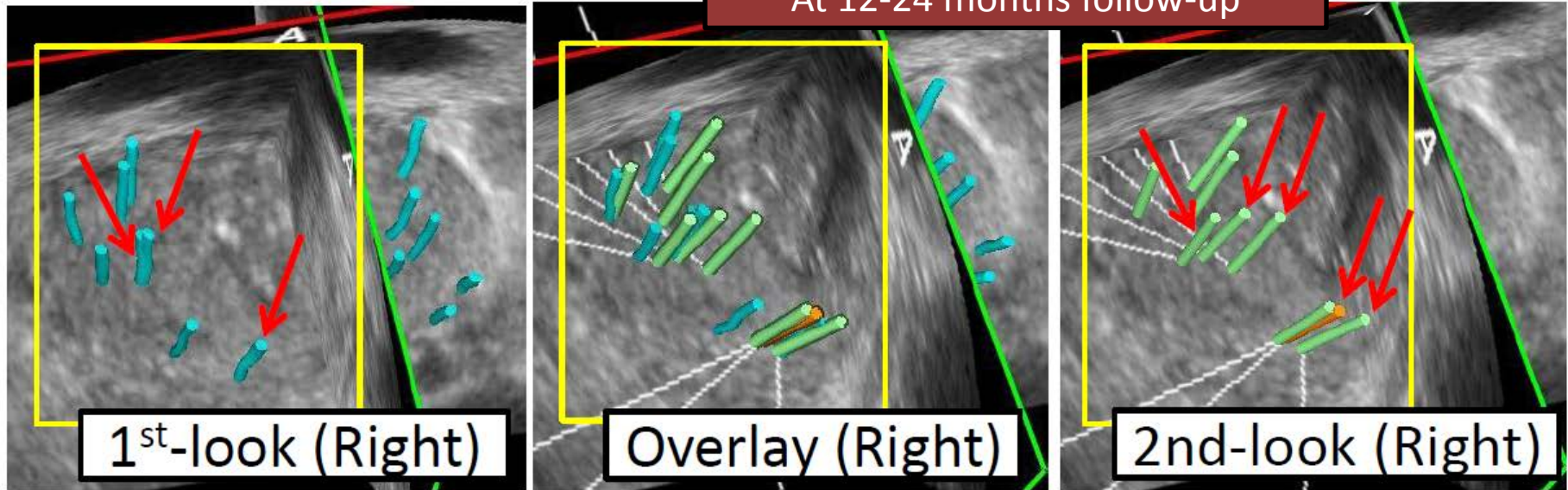
MRI

RVV/AL SPINED CRN 5/3/18

“Re-visiting-TBx”

from the positive trajectories on AS
(“Documented trajectory is the target”)

At 12-24 months follow-up

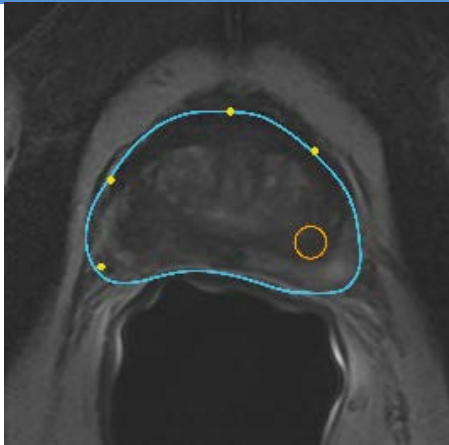


1st look biopsy, 3 cores
(shown as a **red arrow**)
positive for Gleason 3+3,
in the right lobe only

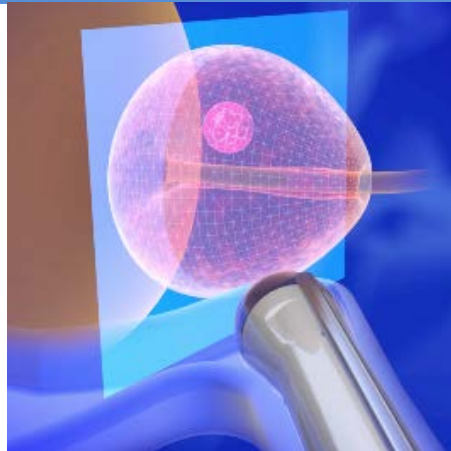
2nd look biopsy : 5 cores
positive for Gleason 3+3, in
right-mid (n=3) and
right-apex (n=2).

3D REAL TIME TARGETING and MAPPING

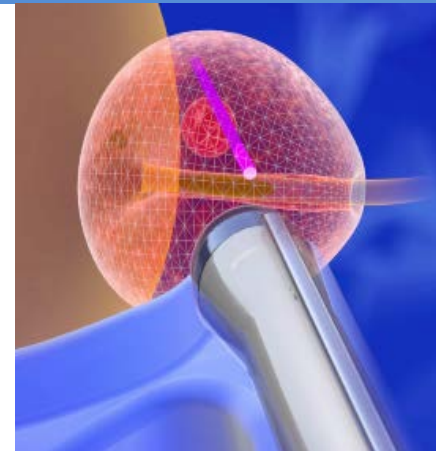
40



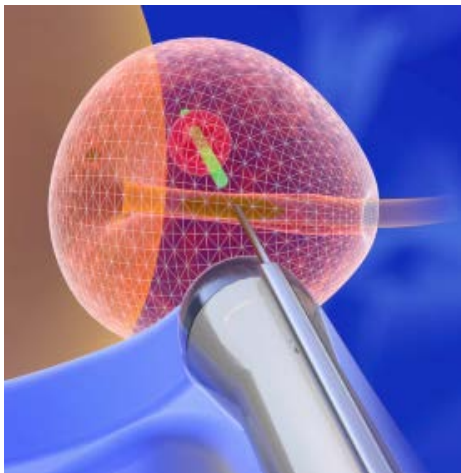
1. Radiologist defines areas of interest on the prostate MRI



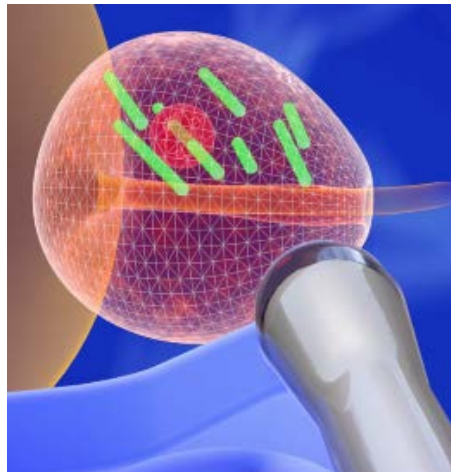
2. MRI and 3D Ultrasound Image Fusion



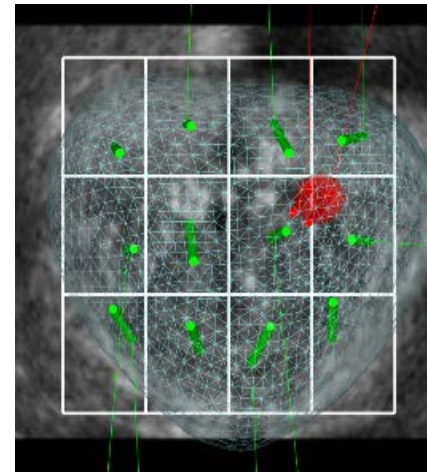
3. Virtual Biopsy



4. Real Biopsy



5. Samples at the surrounding area



6. 3D Cartography

A method to SEE, TARGET, REGISTER and RECALL biopsy cores' position

WRAP-UP and PROPOSAL

The SPARED **CRN** meeting

FDA, Washington 5/3/2018

To Develop and Regulate Modern PCa-Care:
a Secured, Integrated, Transversal **PROPOSAL** from Europe.

The **READBRED** Network:
Registry for Energy Ablative Devices, Big Real-world E-Data

Pr Roland van Velthoven, MD, PhD
Dr Antoine Leroy, PhD – Koelis Founder&CEO

The SPARED CRN meeting

FDA, Washington 5/3/2018

FIELD: - localized prostate cancer (IPCa)

ACTORS: - health providers, organisations,
- industry: medical devices
- « 3rd party » stakeholders

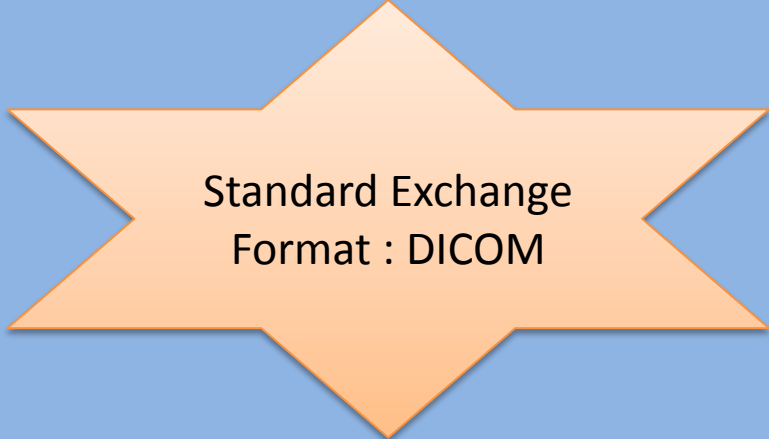
METHOD: PROSPECTIVE REGISTRY
- complying with IPHAA, GDPR regulations
- web based encrypted database
- real time access to data entry,
 local data management, individual benchmarking
- data quality control (CRA)

The SPARED **CRN** meeting

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METHOD: **PROSPECTIVE REGISTRY ITEMS**

- Preclinical data
- Clinical data
- Diagnosis data
- First intention treatment
- Second intention treatment
- Salvage treatment
- Outcomes
- Quality of life
- Quality Control



Standard Exchange
Format : DICOM