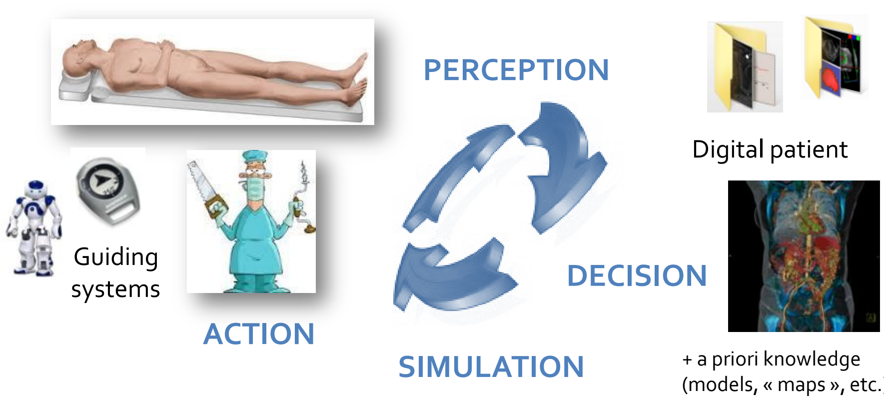
Imaging for Computer-Assisted Medical Intervention

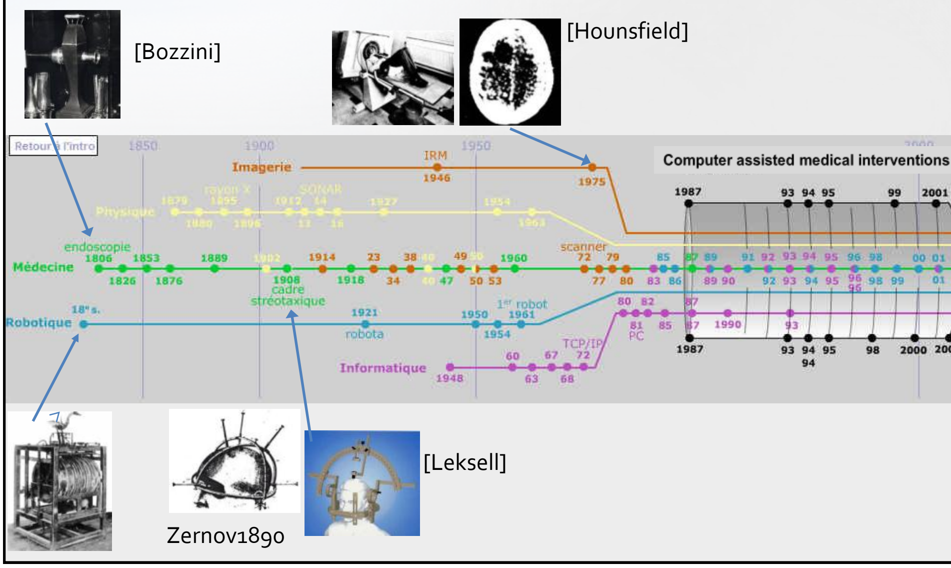
Jocelyne TROCCAZ, DR CNRS
Laboratoire TIMC-IMAG

What is CAMI ?

- Assistance to help the clinician to use multi-modality data in order to plan, to simulate and to accurately and safely execute minimally-invasive diagnostic or therapeutic procedures



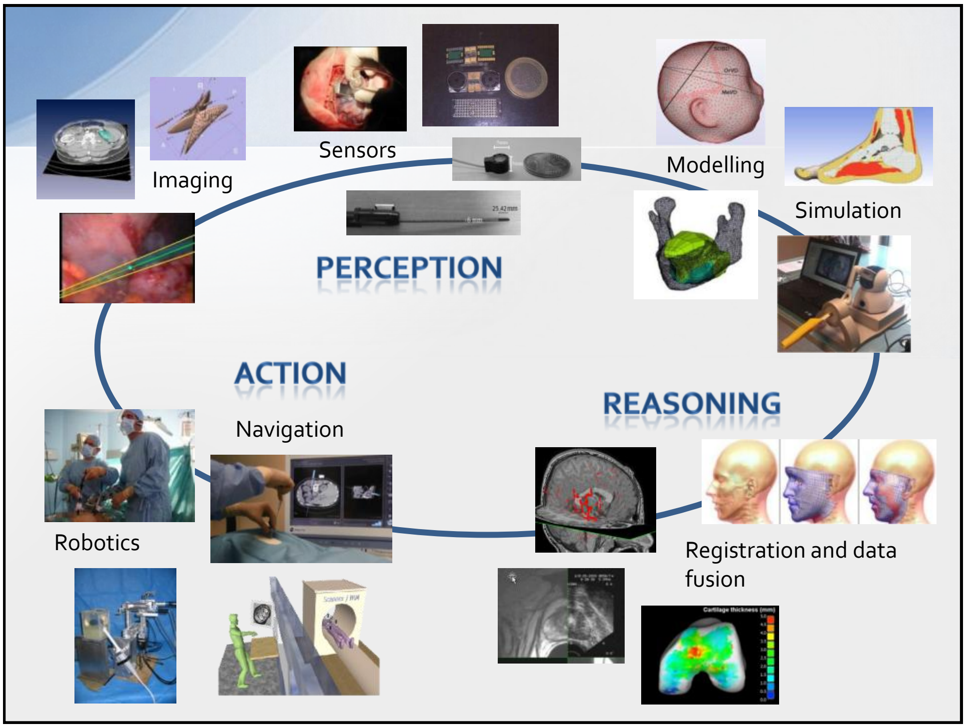
CAMI Historical perspective



Introduction to TIMC/GMCAO-CAMI team

- Created in 1985 –Team leaders : P. Cinquin (1985-96), J.Troccaz (1996-2013), Y.Payan
- First defended PhD in 1989 (S. Lavallée – robot for stereotactic neurosurgery)

- A few numbers
  - about 90 defended Ph.D. theses and 10 HDR (Computer science, Applied Maths, Biomed. eng.), also M.D. theses
  - About 45 people [11 permanent researchers (2 CNRS, 1 INSERM, 3 UJF, 3 UJF+Hospital+3 associated MDs]
  - ≈ 20 journal and 20 international conferences per year
  - More than 60 international patents, ≈ 10 startups created
  - Several 10^5 operated patients



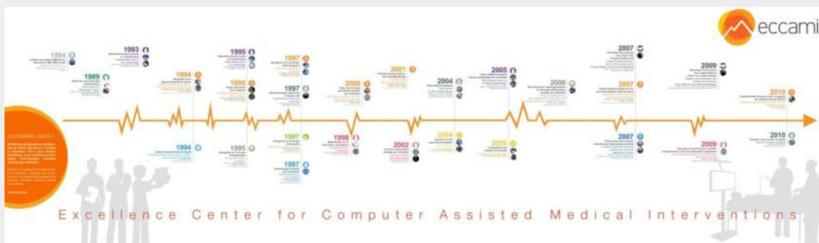
From workbench to bedside and back

- Imaging: sensors, sampling, 3D reconstruction, segmentation, registration
- Modelling: statistical, biomechanical
- Biomechanical simulation
- Medical robotics
- Human-Computer Interface for CAMI
- Biomed. eng.: surgical navigation
- Clinical evaluation

- CamiTK development and integration platform
  http://camitk.imag.fr/

CAMI Applications

- From rigid structures… (1985-1995)
  - Stereotactic neurosurgery, orthopedics-trauma, ENT, orthognatic surgery, dental implantology
  - Rigid targets ± mobile
  - Pre-op planning
  - Easy tracking
- … to soft tissue (1990- …)
  - Radiotherapy, cranio-facial surgery, cardiac, vascular, digestive surgery, urology, etc.
  - Mobile and deformable target
  - Need for modelling, updated planning



New issues

- Real-time acquisition, processing
- Real-time data fusion and plan update
- Real-time simulation
- More models and a priori information (biomechanics, statistics, clinical protocols)
- Tracking abilities
- Safety and reliability

Prostate cancer

- Most frequent cancer of men in the western developed countries
- In 2012 in France*: estimated 56841 new cases (1st in men), 8876 deaths (3rd in men after lung and colon-rectum)
- Europe (EU-28)**: 345000 news cases, 72000 deaths
- Estimated worldwide 2012**:
  - 1 112000 new cases
  - 307000 deaths

* Numbers from "Les cancers en France". Edition 2013
**Numbers from World Health Organization
http://globocan.iarc.fr/

Prostate cancer (continued)

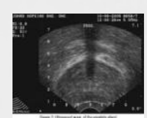
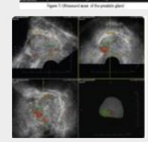
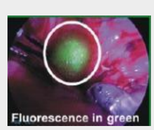
- Diagnosis:
  - Digital Rectal Examination (DRE)
  - Prostate Specific Antigen (PSA)
  - (MRI exam)
  - Histology of biopsy samples
- Treatments:
  - None / careful watching
  - Radical prostatectomy (open, laparoscopic): in France ≈30%
  - Radiotherapy (≈22%)
  - Adjuvant chemotherapy, hormonotherapy (≈23%)
  - Brachytherapy (≈5%)
  - Focal therapy (HiFU, cryotherapy, laser, etc.)

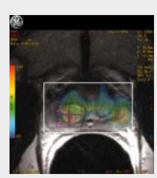
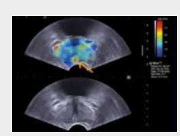
Clinical expectations

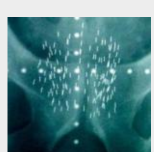
- Improve diagnosis
  - Increase sensitivity and specificity of exams
  - Improve localization of cancer
- Take better decisions
  - Avoid over-treatment
- Improve treatments
  - Less undesired effects (urinary or rectal incontinence, impotency)
  - Better control or cancer

Imaging the prostate

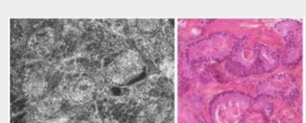
- Multi-parametric MRI
- US (multi-parametric)
- CT
- Fluoroscopy
- Endoscopy
- Fluorescence
- OCT
- Etc.

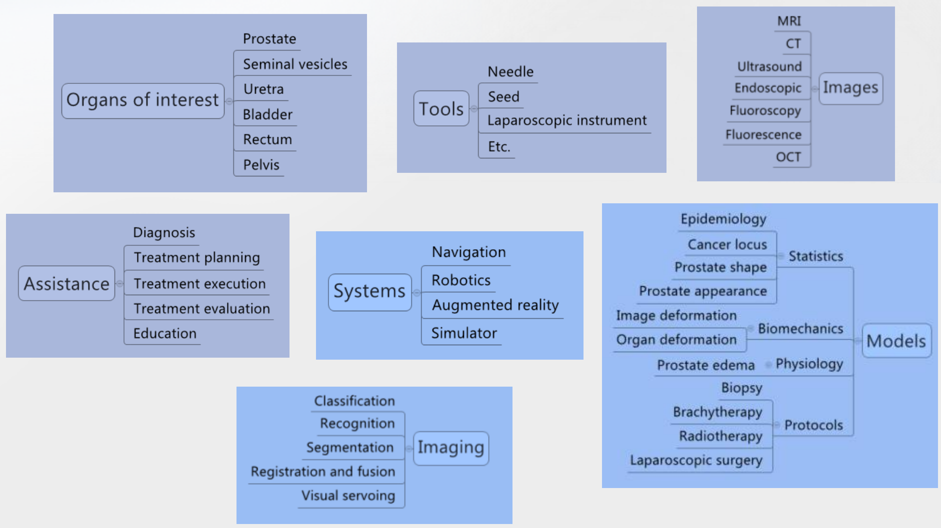





[Beuvon et al 2014]



The clinical /technical viewpoints

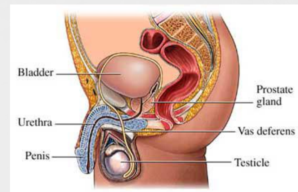


My choice of presentation: application-based

- Biopsy
  - Navigation
    - US/US fusion
    - US/MRI fusion
    - Atlas-based segmentation
  - Simulator
- Brachytherapy
  - Image processing
    - Seed detection
    - MRI/US fusion
    - Atlas-based segmentation
  - Robotics
    - US-based
    - Needle steering

UltraSound Guided Biopsy

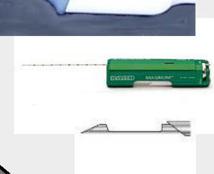
- Reference examination for cancer diagnosis
- Histopathological analysis of samples, grading
- Sensitivity 60 to 80% - specificity 95%
- False negative leads to repeated biopsies
- Most often: transrectal, US guided
- In France (resp. USA) 10^5 (resp. 10^6) biopsy series per year

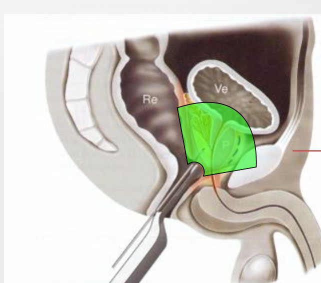


Transrectal biopsies

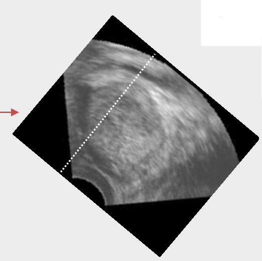
- 2D transrectal ultrasound (TRUS) control
- Needle guide on the probe

TRUS probe with needle guide





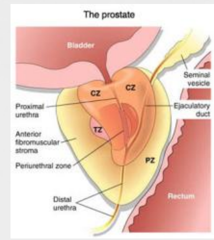
longitudinal cut

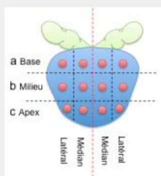


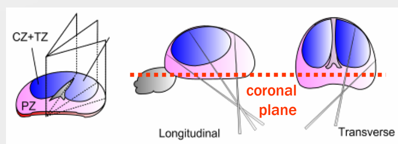
Corresponding 2D US image with needle trajectory

Biopsy targets

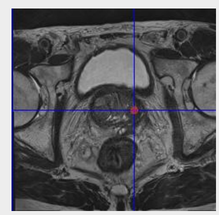
- 68% of cancer can be found in peripheral zone
- Prostate cancer is generally not visible in US images
  - ➢systematic targets (12-core protocol)







+ specific target(s) when visible

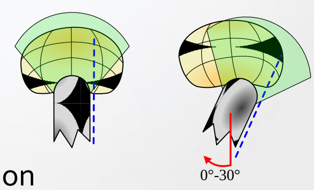

MRI

Computer-assisted prostate biopsy

- Difficulties of conventional protocol:
  - Guided by 2D images
  - Need for a mental 3D representation and transfer from a plan
  - Unknown prostate motion and deformation
- Objectives of computer-assistance:
  - To localize precisely biopsy samples in the gland
  - To guide a biopsy toward a precise location (e.g. from MRI)
- Approach based on 3D/3D non rigid image registration

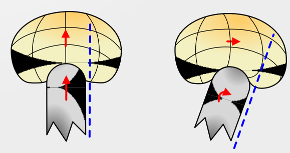
Tracking challenges

- Probe Motion



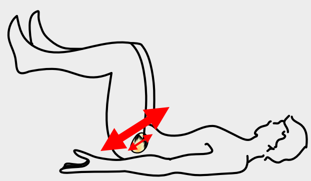
probe used to place needle!

- Prostate Motion



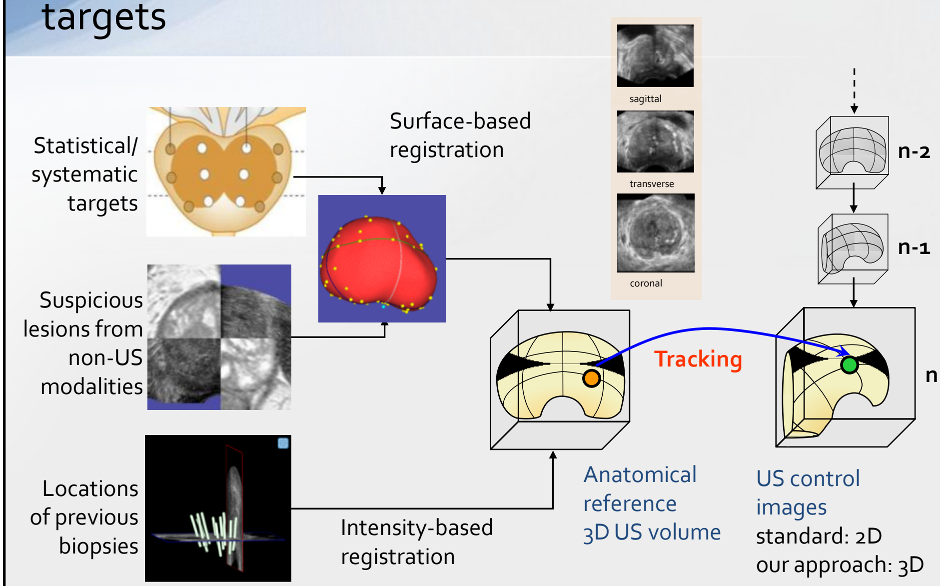
probe pressure required for image acquisition!
strong deformations near probe head

- Patient Motion

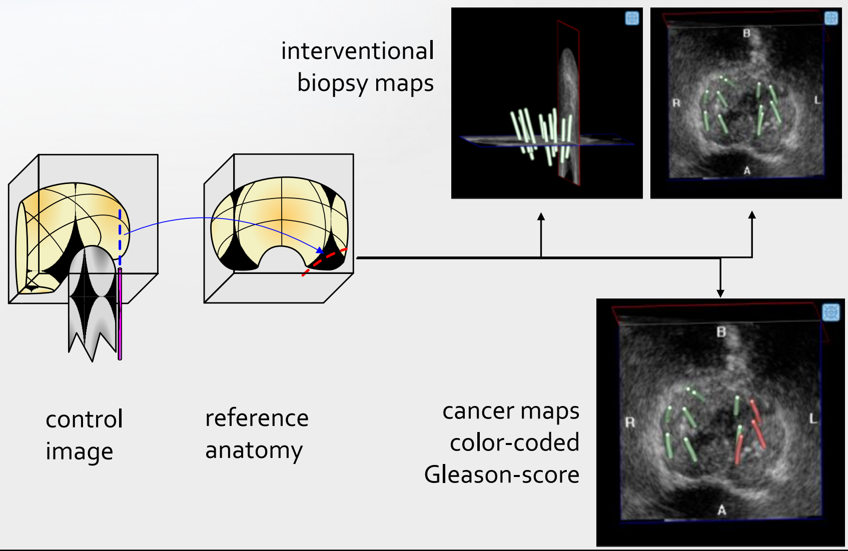


no total anesthesia → patient feels pain and moves!
cannot just track US beam in operational room coordinates

Prostate biopsy assistance: guidance to targets



Prostate biopsy assistance : 3D maps



3D/3D TRUS non rigid image registration

- Image-based registration (no organ segmentation)
- Construct a panorama reference volume (3 volumes registered and fused)
- Registration of intra-operative volumes
  - Rigid plus elastic registration
  - Image-based (CR and SSD), multi-resolution
  - Use of kinematic model of probe movement
  - Use a model of probe related deformations

A hierarchical approach

Probe kinematics based rigid presearch → Refinement of rigid estimate → Elastic registration

parametric systematic search

parametric local optimization

variational optimization

loss-containing multi-resolution techniques

Pearson correlation coefficient

SSD with local intensity shift

linear elasticity

endorectal probe kinematics

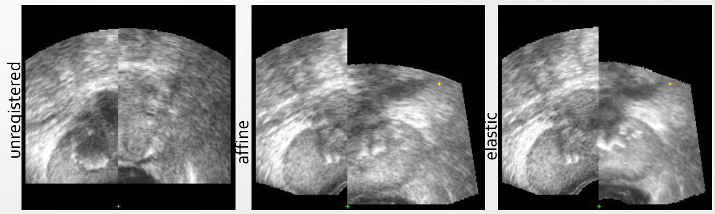
bio-mechanical probe insertion

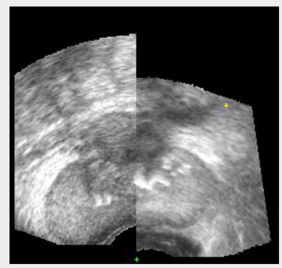
inverse consistency

More precisely

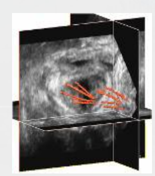
	Presearch	Rigid refinement I	Rigid refinement II	Elastic
Transformation space	Endorectal probe kinematics model	Translation and rotation	Translation and rotation	Linear elastic deformations
DOF	3	6	6	100-500k
Resolution level	Coarsest	Coarsest	Coarse to middle	Coarse to middle
Optimization technique	Global/ Systematic search	Local/ Powell-Brent	Local/ Powell-Brent	Variational/ Full multigrid

Example





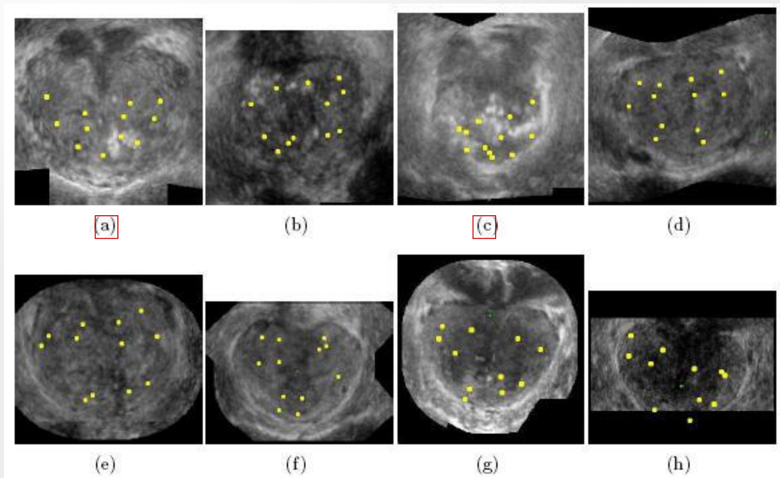
Registration evaluation



- 47 patients, 786 tracking volumes
  - 97.8% correctly registered (visual validation)
- 17 patients, 278 tracking volumes
  - Comparison to a gold standard computed using manually segmented point fiducials (calcifications mainly)

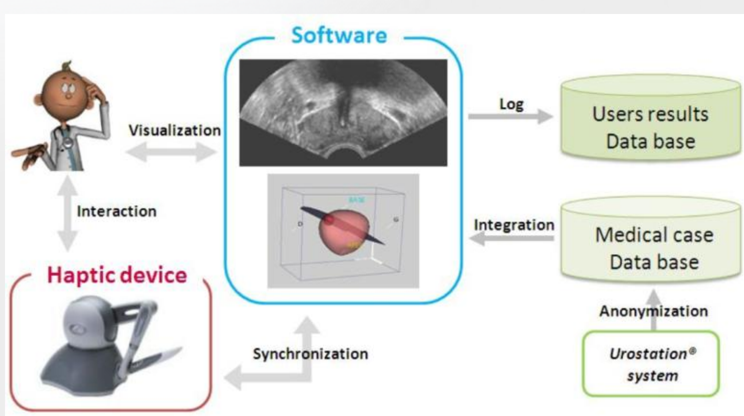
stage	mean distance	standard deviation	max distance	execution time
unreg.	13.76 mm	7.89 mm	51.61 mm	-
rigid	1.33 mm	0.85 mm	4.19 mm	2.1 s
elastic	0.83 mm	0.54 mm	4.14 mm	6.8 s

Recorded performances without assistance

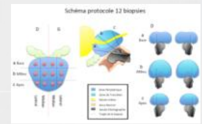


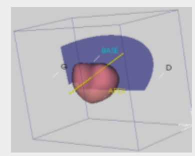
Biopsym

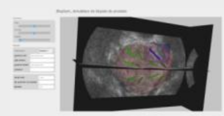
- Providing educational assistance based on acquired data



Biopsym originality







- Includes didactic material (collab with LES, Grenoble)
  - Specific exercises (US image understanding, 3D representation, ability to target a quadrant or a MRI target)
  - Related to relevant pieces of information
  - Two levels of guidance
- Quantitative evaluation of the trainee
  - Exercises proposed based on the trainee performances and weaknesses

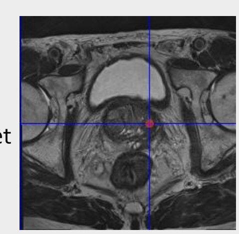
Seven types of exercises

- US image reading by asking the user to select the different anatomical structures 1 2 3
- Prostate volume measurement
- Estimation of the probability of positive biopsies based on clinical data
- Targeted biopsy 4

5 6 7

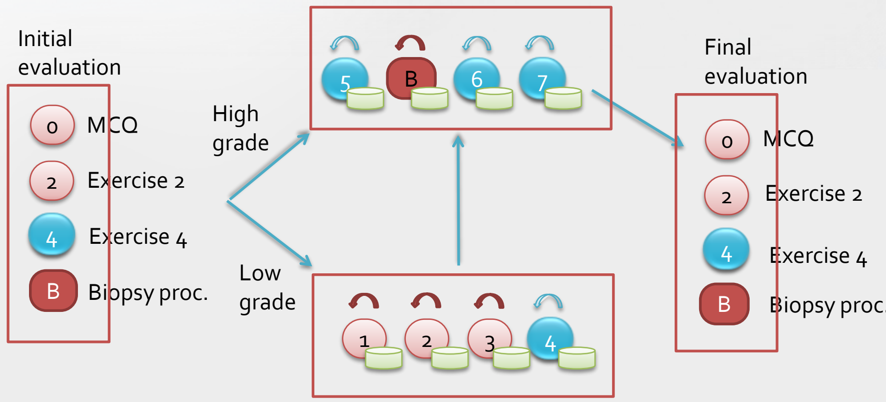
Volume measurement

MRI target

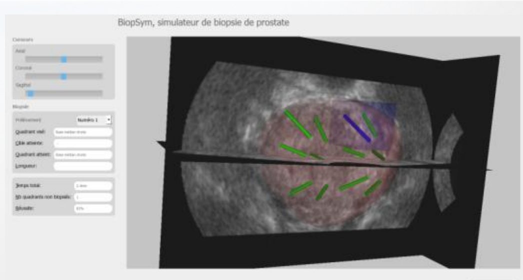


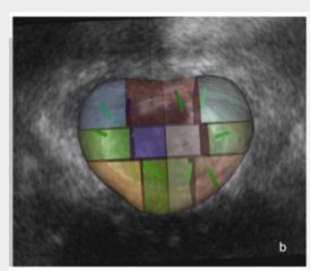
Learning path

- Choosing the most appropriate exercises depending on user results



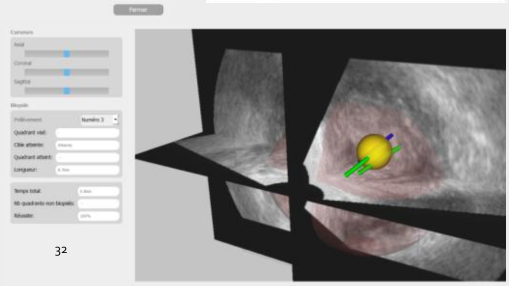
Performance assessment





A visual feedback about the real location of performed biopsy sessions allowed improvement of the biopsy distribution

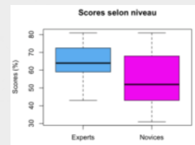
[P. Mozer et al., 2009]

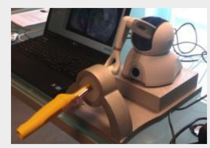


32

Biopsym evaluation

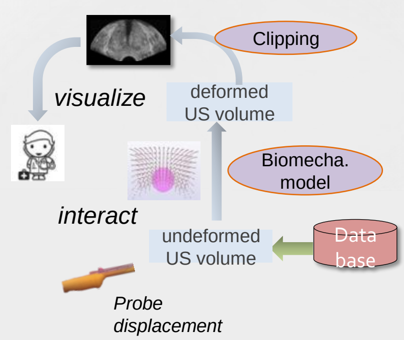
- First experimental evaluations with:
  - 8 non clinicians (PhD and master students): reliability, face validity (realism judged by non experts) > ok
  - 21 clinicians (14 medical students and 7 trained urologists): content validity (realism judged by experts), construct validity (scoring able to discriminate novice and expert)
- Modifications: score, probe mock-up, image real-time deformation
- Planned experiment: ability to transfer the acquired to skill to real patients

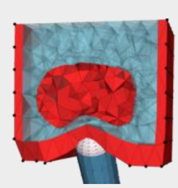




Prostate deformations

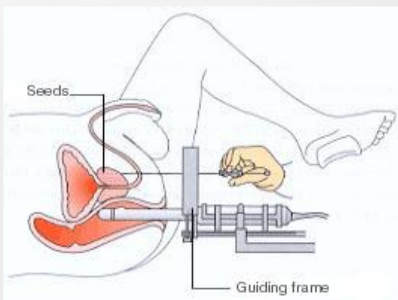
- 3D texture mapping and deformation (S. Selmi)
  - Simplified method
  - Shape memory model + control points + voxels
- Complex biomechanical model (J.Sarrazin)
  - Patient specific
  - More predictive
  - Interactive time
  - MEF, mass-spring, other?
  - Phantom study done
  - Data acquisition on patients

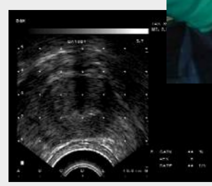




US-guided prostate brachytherapy

- Insert radioactive seeds into the prostate through the perineum

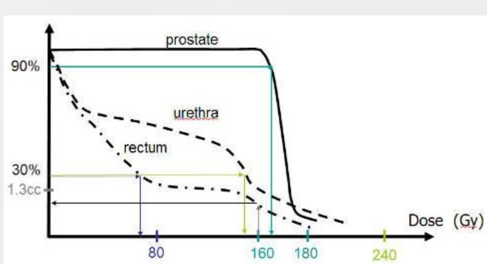




US guidance

Dose planning from US images

- Planned dose: for instance 160Gy
- Dose constraints
  - Prostate: 160Gy<D90<180Gy and V100>85%
  - Urethra: D30<240Gy
  - Rectum: less than 1.3cc>160 Gy and D90<80Gy



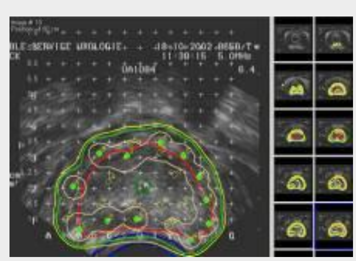
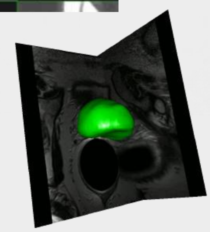
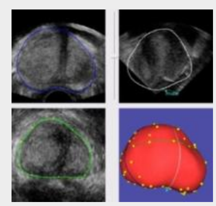


Image-guided brachy.

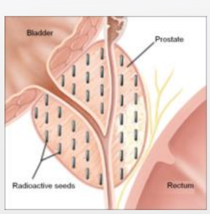
- MRI/US non rigid fusion
  - Surface based registration
  - Dosimetric evaluation (on 28 patients – PHRC Prostate-Echo)
    - Systematic underestimate of US volume w.r.t. MRI
    - Overestimate of the delivered dose
    - In average: volume -8,25% / D90 3% / V100 (160Gy) 3,91%
  - Development of semi-automated atlas-based segmentation (atlas built from 36 exams of patients)



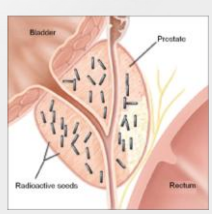


Post-implantation evaluation

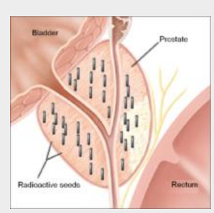
- Based on a CT exam performed one month after seed implantation
- No consideration of seed orientation



As planned



As implanted

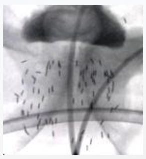


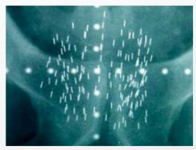
As considered in state of the art dose evaluation

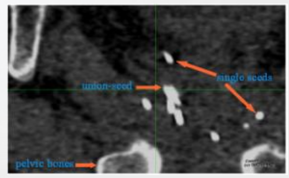
- Is it clinically important?

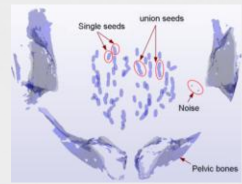
➢ Need for accurate seed localization and separation

INSERM Dorgipro Project (UJF, CHUG, LPSC)

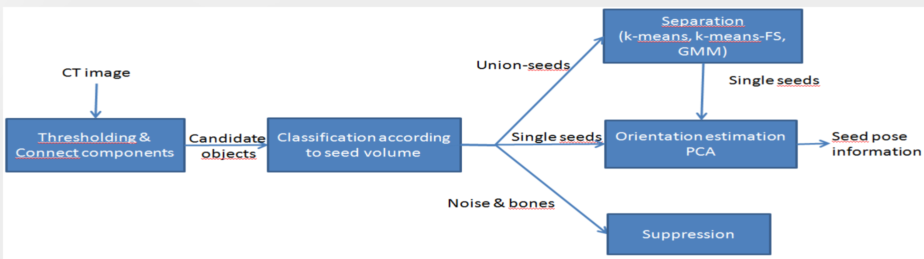






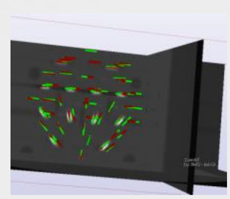


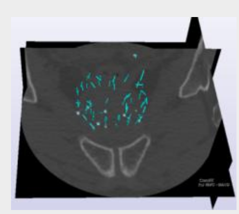
- Automatic detection and classification based on a priori information (seed volume, HU)



Method cont'ed

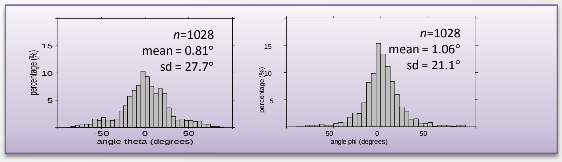
- Automatic separation of seeds
  - K-means
  - Modified k-means
  - Mixture of Gaussian
- Orientation given by PCA
- Implemented in CamiTK
- Evaluation on 2 phantoms and 14 patients (more than 1000 seeds)
  - Very good accuracy
  - Very fast
  - Very few false detections (1,8%)
- See N'Guyen 2015, IEEE TBME



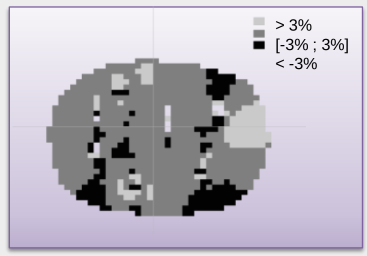


Impact on dose ?

- Mis-orientation of seeds

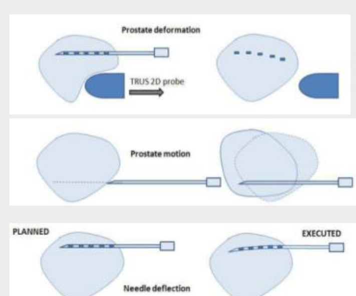


- Impact on dose
  - No difference on DVH
  - Local inhomogeneities (significant for about 25% of the volume)
- to be confirmed on a larger clinical study



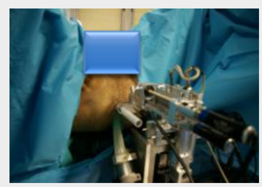
Sources of inaccuracy in seed positions

- The prostate moves and gets deformed due to:
  - Bladder or rectal filling
  - Patient leg position
  - Patient breathing
  - Ultrasound probe constraint
  - Needle penetration
  - Edema
- The needles may deflect

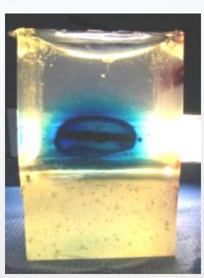


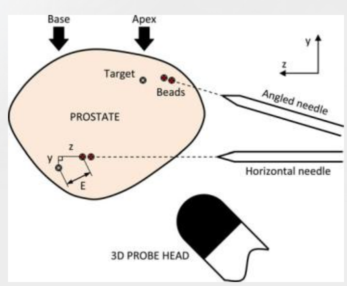
Prosper robot

- Objectives:
  - Seeds implanted as planned
  - Suppress pubic arch conflict
  - Make it more rapidly if possible
- Architecture
  - Needle pre-positioning (5dofs)
  - Needle insertion (2dofs)
  - Automatic disengagement system in case of collision with bone
- Our solution to prostate motion
  - Limiting US probe motion: 3D US
  - Rotate the needle
  - Prostate tracking using 3D/3D non rigid registration



Accuracy evaluation



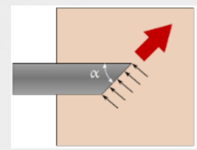


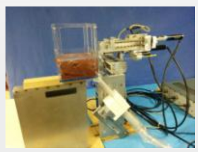
Location	# beads	Distance between target and inserted (mm) Euclidean	x	y	z	Depth correction (mm)
Apex	50	2.28 (0.73)	1.15 (0.77)	0.94 (0.66)	1.37 (0.79)	4.36 (1.73)
Horiz.	35	2.32 (0.64)			1.43 (0.80)	
Angled	15	2.19 (0.91)				
Base	40	3.86 (1.27)	2.40 (1.72)	1.52 (0.96)	1.91 (1.00)	6.94 (1.71)
Horiz.	32	3.92 (1.34)			1.98 (0.98)	
Angled	8	3.60 (0.99)				

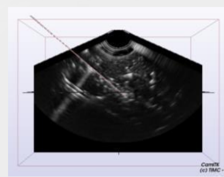
Values in parentheses represent standard deviations. The *x* and *y* axes are, respectively, the horizontal and vertical directions in the transverse plane, while z is in the horizontal cranio-caudal depth direction, as shown in Figure 13.

Work in progress

- Improvement of trajectory correction
  - Biomechanical model
  - Needle steering (collaboration with LIRMM – labex CAMI)



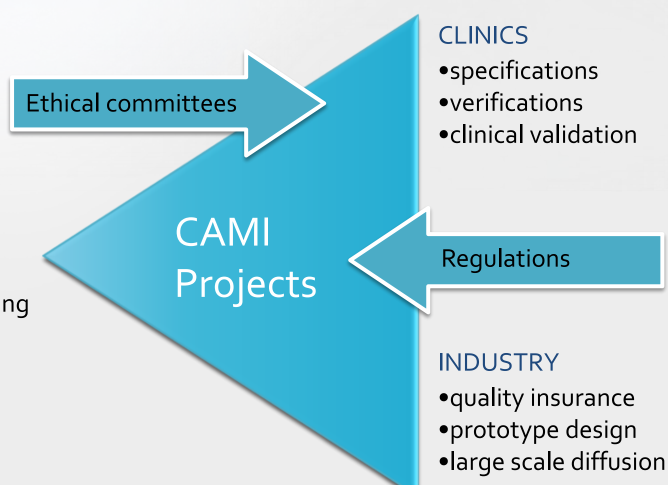




- Second version of prosper for use on patients (mid-end of 2015)

A pluri-disciplinary approach

SCIENCE
•modeling
•image processing
•robotics
•simulation
•etc.

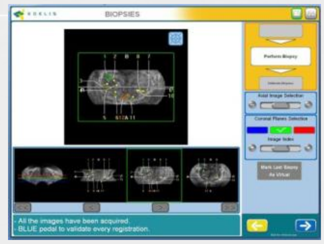


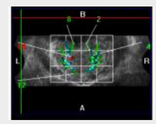
CLINICS
•specifications
•verifications
•clinical validation

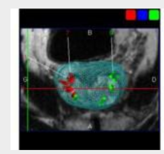
INDUSTRY
•quality insurance
•prototype design
•large scale diffusion

Industrial transfer of urology image processing tools

- Embedded in the Urostation® from Koelis (created 2007)
- Biopsy mapping in a product (EC, FDA approved)
- Early 2015: 30000 patients with 80 systems treated worldwide
- Integrates also
  - MRI/US image fusion
  - Semi-automatic image segmentation from statistical atlas







Conclusion

- Several application fields for CAMI with strong potential clinical impact
- Opportunity for new imaging modalities, image processing, models, robotic or navigation assistance, training assistance
- Still a lot to do, to evaluate and to transfer to clinical routine

Specific acknowledgements:

- Grenoble University Hospital (urology, radiation oncology and radiology and imaging departments) and La Pitié Salpétrière Hospital, Paris (urology department)
- TIMC colleagues and students
- Funding agencies (ANR, Ministry of Health, INSERM, Région Rhône-Alpes, ANRT)
- KOELIS

Related publications

- N'Guyen G, Fouard C, Meneu F, Giraud JY, Troccaz J. Automatic 3D seed location and orientation detection in CT images for prostate brachytherapy. Proceedings of the IEEE ISBI'2014 (International Symposium on Biomedical Imaging), Beijing, May 2014
- Selmi S, Promayon E, Sarrazin J, Troccaz J. 3D Interactive Ultrasound Image Deformation for Realistic Prostate Biopsy SimulationProceedings of the 6th International Symposium on Biomedical Simulation, Strasbourg, 16-17 October, Springer, LNCS vol 8789, Fernando Bello and Stéphane Cotin (Editors), pp122-130, 2014
- Fiard G, Selmi SY, Promayon E, Vadcard L, Descotes JL, Troccaz J. Initial validation of a virtual reality learning environment for prostate biopsies: realism matters! Accepté pour publication dans Journal of Endourology, online first 22oct2013
- Fiard G, Hohn N, Descotes JL, Rambeaud JJ, Troccaz J, Long JA. Targeted MRI-guided prostate biopsies for the detection of prostate cancer: Initial clinical experience with real-time 3-dimensional transrectal ultrasound guidance and magnetic resonance/transrectal ultrasound image fusion. Urology, 2013:81(6):1372-8, online March 1013
- Hungr N, Baumann M, Long JA, Troccaz J . A 3D Ultrasound Robotic Prostate Brachytherapy System with Prostate Motion Tracking. IEEE Transactions on Robotics, 2012, 28(6) : 1382-1397
- Long JA, Hungr N, Baumann M, Descotes JL, Bolla M, Giraud JY, Rambeaud JJ, Troccaz J. Development of a Novel Robot for transperineal needle-based interventions: Focal Therapy, Brachytherapy and Prostate Biopsies. Journal of Urology, 2012, 188:1369-1374, online 20 août 2012
- Hungr N, Long JA, Beix V, Troccaz J. A realistic deformable prostate phantom for multi-modal imaging and needle-insertion procedures. Medical Physics, 2012, 39(4)-2031-2041
- Baumann M, Mozer P, Daanen V, Troccaz J. Prostate Biopsy Tracking with Deformation Estimation. Medical Image Analysis, 2012, 16(3):562-576, Online first May 2011
- Martin S., Troccaz J., Daanen V.. Automated Segmentation of the Prostate in 3D MR Images Using a Probabilistic Atlas and a Spatially Constrained Deformable Model. Medical Physics, 2010, 37(4) :1579-1590
- P. Mozer, M. Baumann, G. Chevreau, A. Moreau-Gaudry, S. Bart, R. Renard-Penna, E. Comperat, P. Conort, M.-O. Bitker, E. Chartier-Kastler, F. Richard, J. Troccaz. Mapping of Transrectal Ultrasound Prostate Biopsies: Quality Control and Learning Curve Assessment by Image Processing. Journal of Ultrasound in Medicine, 2009, 28(4):455-460
- V. Daanen, J. Gastaldo, J.Y. Giraud, P. Fourneret, J.L. Descotes, M. Bolla, D. Collomb, J. Troccaz. MRI/TRUS data fusion for brachytherapy. The International Journal of Medical Robotics and Computer-Assisted Surgery, Vol2, No.3, pp256-261, September 2006

Thank you for your attention