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

PERCEPTION

DECISION

A priori knowledge (models, « maps », etc.)

Digital patient

Guiding systems

ACTION

SIMULATION
CAMI Historical perspective

Introduction to TIMC/GMCAO-CAMI team

- 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 (1\textsuperscript{st} in men), 8876 deaths (3\textsuperscript{rd} in men after lung and colon-rectum)
- Europe (EU-28)**: 345000 new cases, 72000 deaths
- Estimated worldwide 2012**:
  - 1112000 new cases
  - 307000 deaths

**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 \( \approx 30\% \)
  - Radiotherapy (\( \approx 22\% \))
  - Adjuvant chemotherapy, hormonotherapy (\( \approx 23\% \))
  - Brachytherapy (\( \approx 5\% \))
  - 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

- 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

My choice of presentation: application-based
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
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

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!
  - Probe pressure required for image acquisition!
  - Strong deformations near probe head

- **Prostate Motion**
  - 0°-30°
  - 180°

- **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

- Statistical/systematic targets
- Suspicious lesions from non-US modalities
- Locations of previous biopsies

Surface-based registration

Sagittal
Transverse
Coronal

Tracking

Anatomical reference 3D US volume

Intensity-based registration

US control images standard: 2D
Our approach: 3D
Prostate biopsy assistance: 3D maps

- Interventional biopsy maps
- Control image
- Reference anatomy
- Cancer maps: color-coded Gleason-score

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
- Parametric systematic search
- Refinement of rigid estimate
- Parametric local optimization
- Elastic registration
- Variational optimization
- Loss-containing multi-resolution techniques
  - Pearson correlation coefficient
  - SSD with local intensity shift
  - Linear elasticity
  - Bio-mechanical probe insertion
  - Inverse consistency
- Endorectal probe kinematics

More precisely

- Transformation space
- DOF
- Resolution level
- Optimization technique
- Presearch
- Endorectal probe kinematics model
- Translation and rotation
- Translation and rotation
- Linear elastic deformations
- Global/ Systematic search
- Local/ Powell-Brent
- Local/ Powell-Brent
- Variational/ Full multigrid
Example

![Example images](image1)

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)

<table>
<thead>
<tr>
<th>stage</th>
<th>mean distance</th>
<th>standard deviation</th>
<th>max distance</th>
<th>execution time</th>
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<tr>
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<td>13.76 mm</td>
<td>7.89 mm</td>
<td>51.61 mm</td>
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<td>rigid</td>
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<td>0.85 mm</td>
<td>4.19 mm</td>
<td>2.1 s</td>
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<tr>
<td>elastic</td>
<td>0.83 mm</td>
<td>0.54 mm</td>
<td>4.14 mm</td>
<td>6.8 s</td>
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</tbody>
</table>
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
- Prostate volume measurement
- Estimation of the probability of positive biopsies based on clinical data
- Targeted biopsy
Learning path

- Choosing the most appropriate exercises depending on user results

Initial evaluation
- MCQ
- Exercise 2
- Exercise 4
- Biopsy proc.

High grade

Final evaluation
- MCQ
- Exercise 2
- Exercise 4
- Biopsy proc.

Low grade

Performance assessment

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

[P. Mozer et al., 2009]
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

Dose planning from US images

- Planned dose: for instance 160Gy
- Dose constraints
  - Prostate: $160\text{Gy} < D_{90} < 180\text{Gy}$ and $V_{100} > 85\%$
  - Urethra: $D_{30} < 240\text{Gy}$
  - Rectum: less than $1.3\text{cc} > 160\text{Gy}$ and $D_{90} < 80\text{Gy}$
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’d

- 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

![Histograms showing distribution of angles](image)

- 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

![Diagram showing prostate deformation and needle deflection](image)
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

<table>
<thead>
<tr>
<th>Location</th>
<th># beads</th>
<th>Distance between target and inserted (mm)</th>
<th>Depth correction (mm)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Euclidean</td>
<td>x</td>
</tr>
<tr>
<td>Apex</td>
<td>50</td>
<td>2.28 (0.73)</td>
<td>1.15 (0.77)</td>
</tr>
<tr>
<td>Horiz.</td>
<td>35</td>
<td>2.32 (0.64)</td>
<td></td>
</tr>
<tr>
<td>Angled</td>
<td>15</td>
<td>2.19 (0.91)</td>
<td></td>
</tr>
<tr>
<td>Base</td>
<td>40</td>
<td>3.86 (1.27)</td>
<td>2.40 (1.72)</td>
</tr>
<tr>
<td>Horiz.</td>
<td>32</td>
<td>3.92 (1.34)</td>
<td></td>
</tr>
<tr>
<td>Angled</td>
<td>8</td>
<td>3.60 (0.99)</td>
<td></td>
</tr>
</tbody>
</table>

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 crano-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.

- CAMI Projects

- CLINICS
  - specifications
  - verifications
  - clinical validation

- Ethical committees

- Regulations

- 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

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- KOELIS
Related publications


Thank you for your attention.