Hybrid imaging
and
coupling between modalities

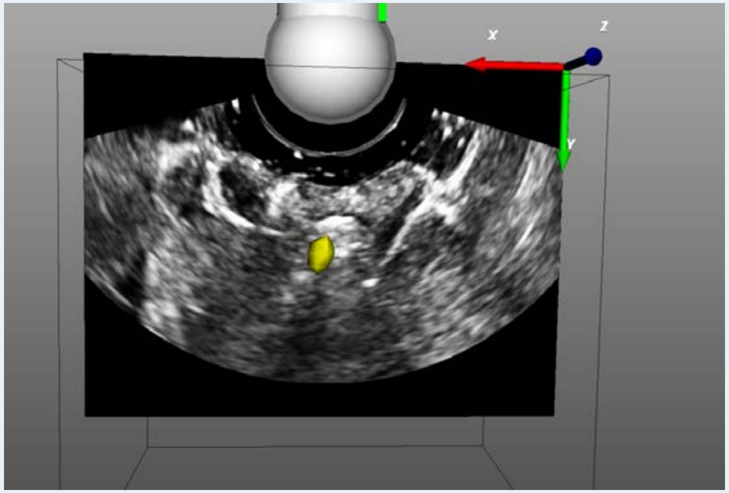
Teams: 1, 2, 3, 4, 5

Hybrid imaging and coupling between modalities

- **Background: single modality imaging**
  - Limited in resolution and scale
  - Limited in information (anatomic, functional, metabolic, …)

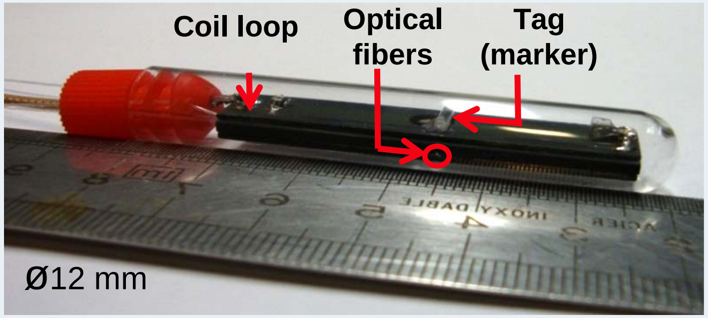
- **Challenges: multiphysics**
  - New emerging hybrid imaging requires
    - Simulation, modeling adapted to hybrid
    - Specific instrumentation
    - Processing of heterogeneous information

Hybrid imaging and coupling between modalities



- **1) Combine anatomic and functional/parametric information**
  - US+ optics, photoacoustic, US+MR elastography

  Presented by Philippe Delachartre, team3



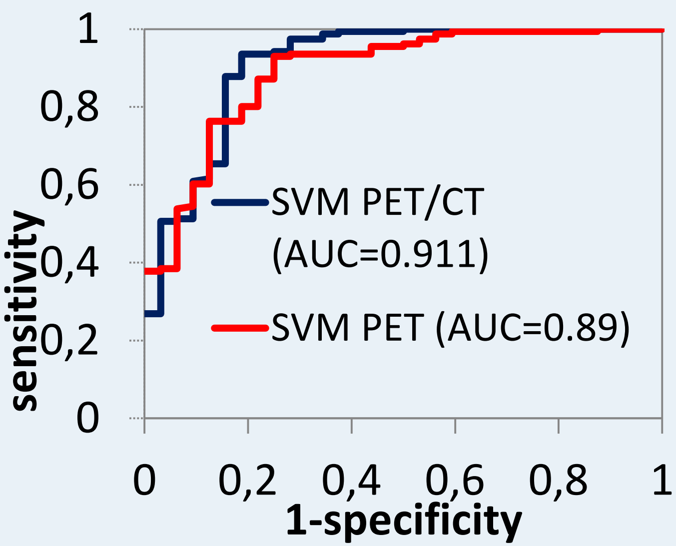
- **2) Develop new instrumentation**
  - MR+optics

  Presented by Olivier Beuf, team 5

Hybrid imaging and coupling between modalities

- **3) Process multimodality data**
  - Computed Aided Diagnosis

Presented by Denis Friboulet, team 2

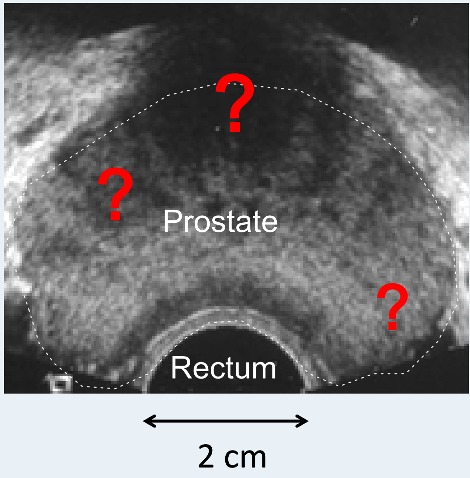


1) US/optics for cancer prostate diagnosis

Speaker: Philippe Delachartre – Team 3

US/optics

- **Current limits in prostate cancer detection**
  - Risk to not detect a premature tumor
  - Secondary effects due to multiple biopsies (10-12 biopsies)
  - Limited contrast for tumor detection with US

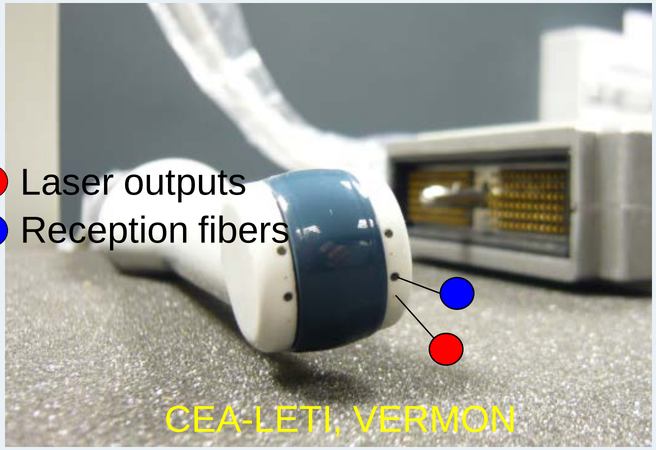


- **Proposed approach**
  - Anatomy → transrectal US imaging
  - Mark the tumoral cells by means of a fluorescent tracer to localize the premature tumors→ Fluorescence time-resolved optical imaging
  - Bimodal Image Registration

COOPERATIVE PROJECT WITH CEA LETI Grenoble:
3 Year Bioengineering grant ANR TecSan PROSTAFLUO

US/optics -results

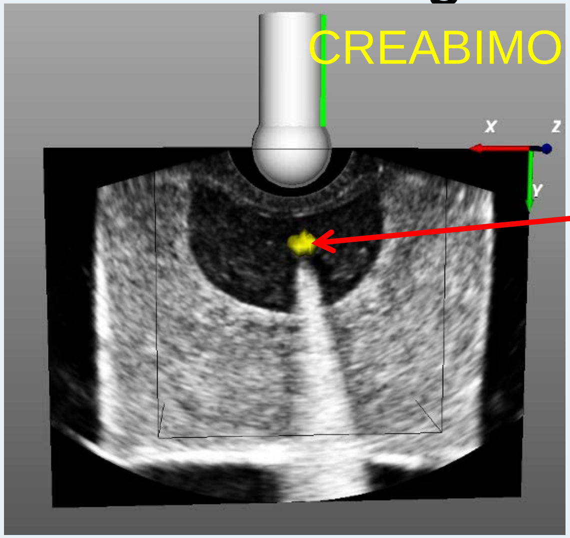
- **Design of an hybrid probe**



Phantom design

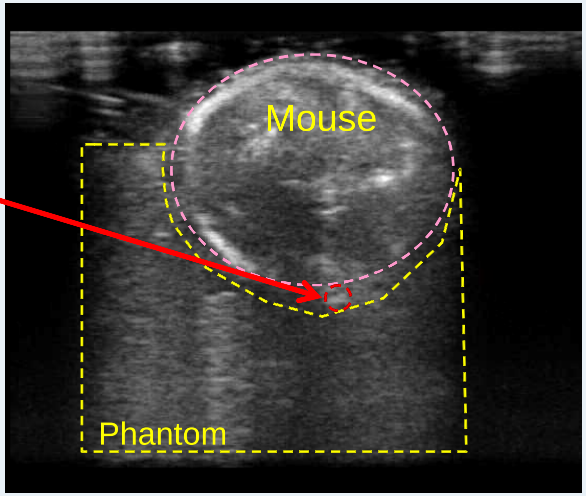
Tuning US scattering, Optical scattering and absorption

- **Software for co-registration**



Inclusion localized by the two imaging modalities

Pre-clinical result



J. Biomed. Opt., 2009, 2011

Patent on bimodality phantoms, 2009

US/Optics : towards photoacoustic imaging

- **Context**

Optical imaging

- (+) Contrast
- (−) Resolution > ~ 1 mm
- (−) Investigation Depth < ~ 5 cm
- (+) Functional imaging

US imaging

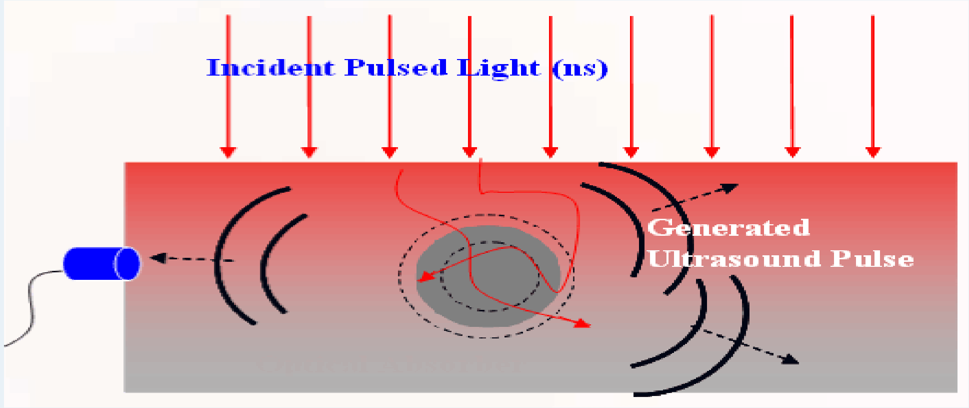
- (−) Contrast
- (+) Resolution > ~ 100 µm
- (+) Investigation Depth ~ 10 cm
- (−) No functional imaging

Photoacoustic Imaging

- (+) Contrast (optical absorption)
- (+) US resolution
- (+) Investigation Depth (several cm)
- (+) Functional imaging linked to optical absorption
- (+) Non invasive, non ionizing, real-time (several images per second)

US/Optics : towards photoacoustic imaging

- **Photoacoustics for biological and medical issues**
  - Optical contrast at US resolution
  - Tissue characterization and differentiation:
    - Functional imaging: endogenous (hemoglobin) and exogenous (contrast agents) **optical absorption** of biological tissues
    - Spectroscopic imaging: optical properties vary with light wavelength
    - Sensing biochemical changes in tissue: vasculature, blood oxygenation, angiogenesis …
- **Principle**
  - Tissue is irradiated with a short laser pulse
  - Optical energy is absorbed by tissue and converted into thermal energy
  - Optical absorption → thermal expansion → acoustic pressure transients
  - Acoustic signals are recorded to form the photoacoustic image



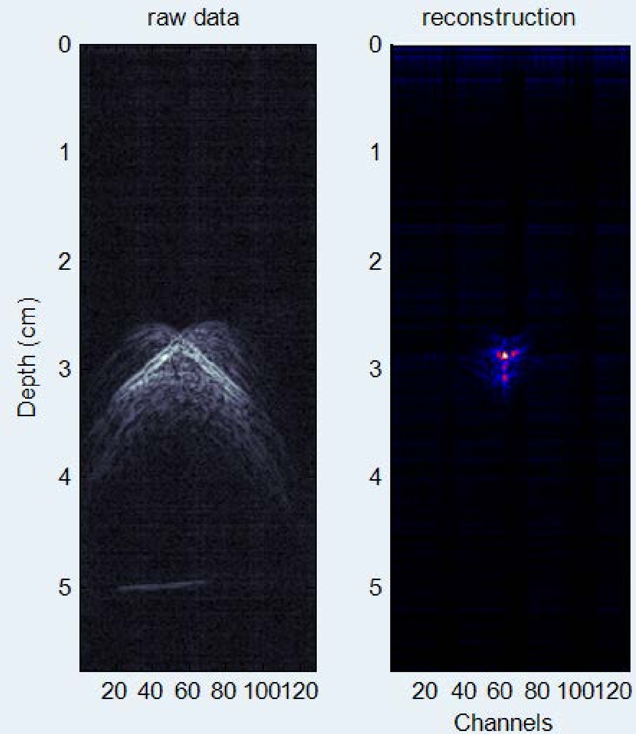
US/optics - Photoacoustic imaging

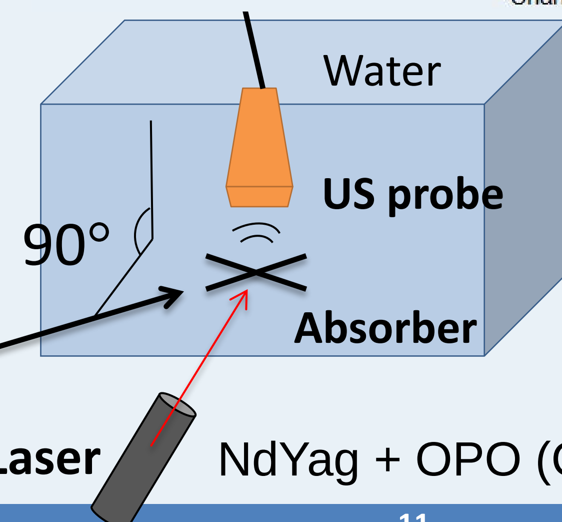
- **Perspectives : photoacoustic for prostate cancer diagnosis**
  - Sensing tissues for cancer diagnosis
  - Multiphysic approach
  - Aim: 2D and 3D real time imaging of tissue perfusion at different wavelengths
- **Proposed approach:**
  - Modeling, simulation and reconstruction algorithms US/Optics (transverse project – teams 3, 4, 5)
  - Multispectral reconstruction
  - Evaluation with home-made phantoms and in vivo experiments
- **Work in progress**
  - Collaboration with CEA LETI Grenoble, PhD thesis Labex Primes on going
  - European Grant FP7 ITN Oiltebia (2013-2017) - partners: IBMI München, Polimi Milano, Ruhr Univ., Philips, Vermon…
  - Development of CMUT (lead free) arrays with Industrial partnership Vermon, France (Grant ANR BBMUT (team 3), FP7 ITN Oiltebia)

US/Optics - Photoacoustic imaging

- **Set-up and preliminary result**

Sonix DAQ ⟶ Photoacoustic image





Phantom

Ultrasonix scanner

NdYag + OPO (CEA)

US and MR Elastography

US and MR elastography

- Scientific and medical interest: accessing the mechanical properties to better differentiate between benign and malignant lesions **in vivo**

- Bottleneck: taking into account non linear effects of biological tissues in vivo.

for an improved contrast between benign and malignant tissues

Breast Tissue Type	Tissue Elastic Modulus (kPa)					
	5% precompression			20% precompression		
	Loading frequency (Hz)			Loading frequency (Hz)		
	0.1	1.0	4.0	0.1	1.0	4.0
Normal fat (n = 8)	18 ± 7	19 ± 7	22 ± 12	20 ± 8	20 ± 6	24 ± 6
Normal glandular tissue (n = 31)	28 ± 14	33 ± 11	35 ± 14	48 ± 15	57 ± 19	66 ± 17
Fibrous tissue (n = 18)	96 ± 34	107 ± 31	116 ± 28	218 ± 87	232 ± 60	244 ± 85
Ductal carcinoma *in situ* (n = 23)	22 ± 8	25 ± 4	26 ± 5	291 ± 67	301 ± 58	307 ± 78
Invasive and infiltrating ductal carcinoma (n = 32)	106 32	93 ± 33	112 ± 43	558 ± 180	490 ± 112	460 ± 178

Krouskop et al. 1998

✓ Differences in values with the nature of the tissues

✓ Role of precompression

benign

malignant

US and MR elastography

- Elastography
  - Different imaging modalities (Ultrasound, MRI)
  - Quasi-static (information on tissue strain under compression)
  - dynamic stress (information on the shear modulus)

- Proposed approach

  → towards a combination of the two methods

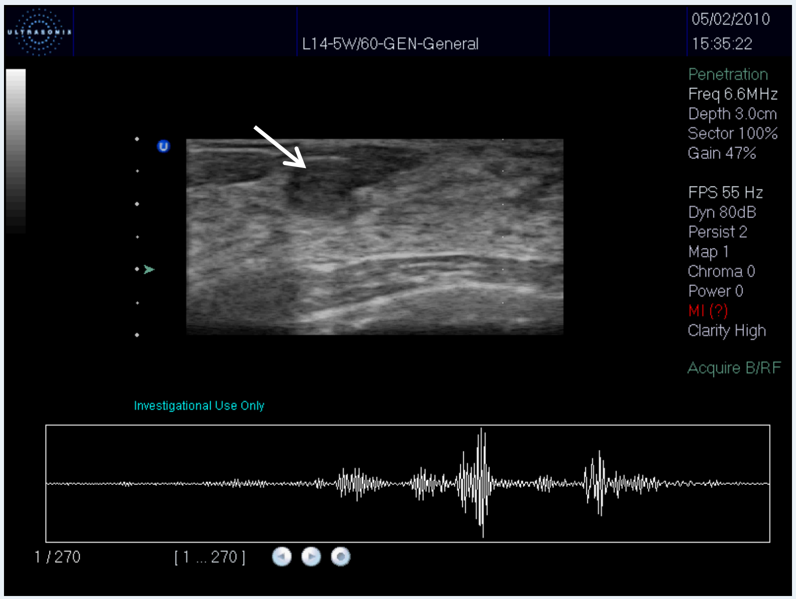
  - Quasi static ultrasound elastography (pre-compression)
  - MR elastography (shear modulus)
  - Shear modulus - Precompression curve: optimized in-vivo contrast between benign and malignant lesions

Ophir *et al.* Elastography: a quantitative method for imaging the elasticity of biological tissues. *Ultrason Imaging* 13:111–34, 1991.
Muthupillai *et al.* Magnetic resonance elastography by direct visualization of propagating acoustic strain waves, *Science* 269, 1854–57, 1995.
Catheline et al. Diffraction field of a low frequency vibrator in soft tissues using transient elastography, *IEEE UFFC*, 46, 1013-1019, 1999.
Parker *et al.* Imaging the elastic properties of tissue: the 20 year perspective, Phys. Med. Biol. 56, 2011.

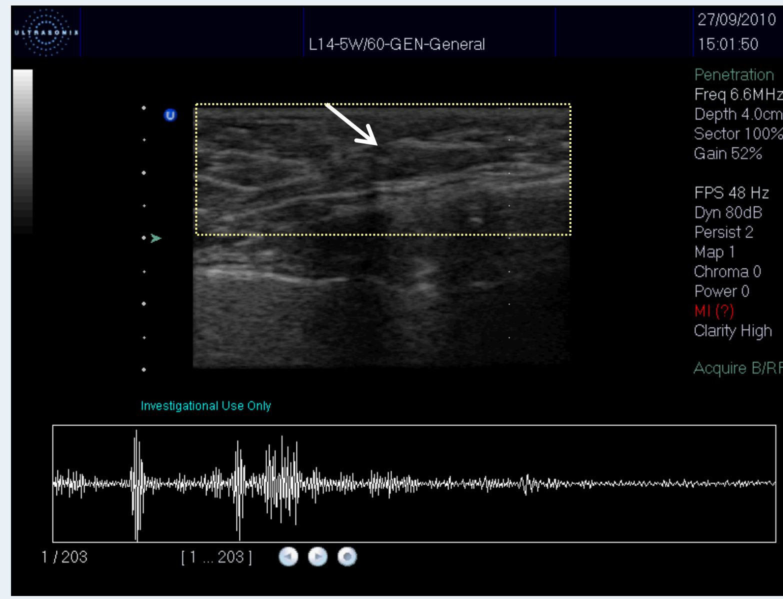
Ultrasound elastography

- Strain locally estimated using constrained optimization and local regularization
- Several medical applications investigated among which thyroid and breast lesion examination (Basarab et al. 2009,2011; Deprez et al 2011; Brusseau et al 2013)

Fibroadenoma

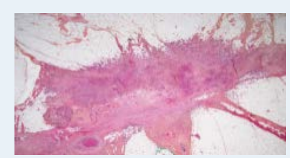


Carcinoma



Cancer tend to appear larger in elastograms than in sonograms

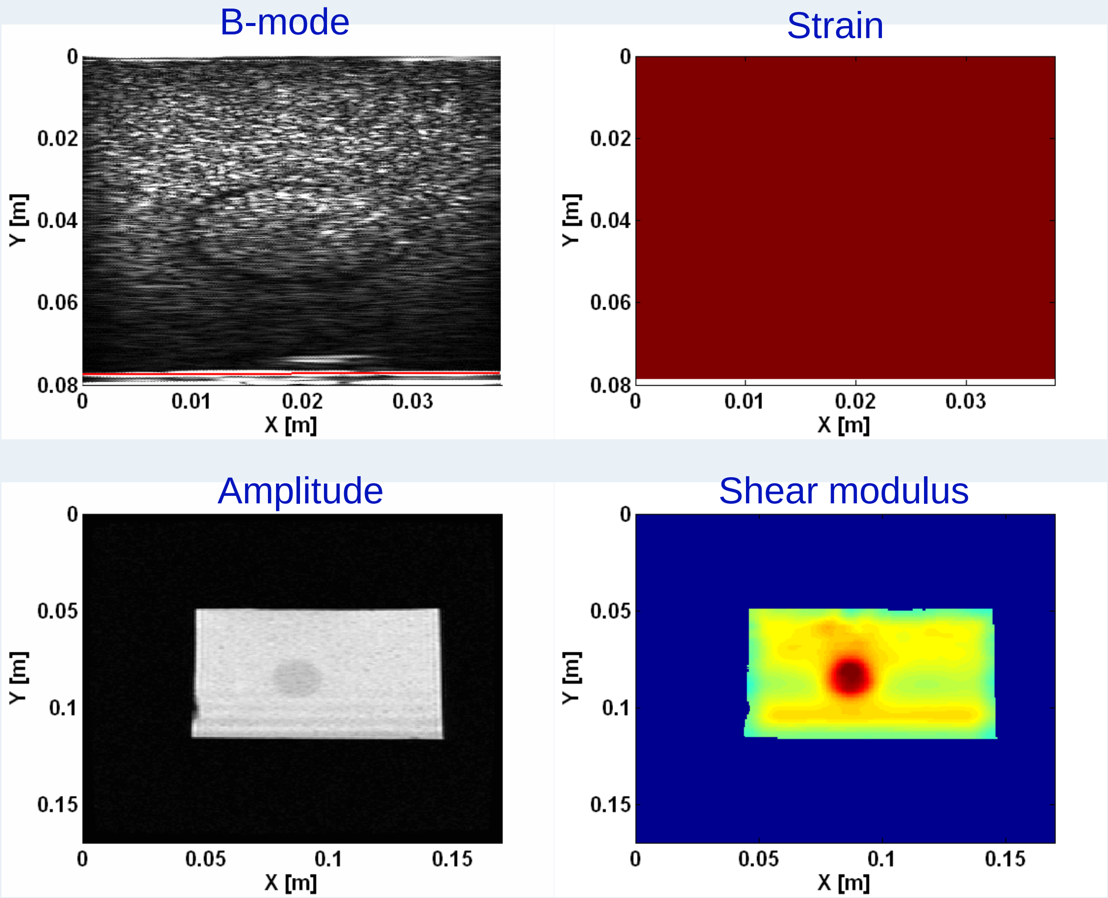
Strain/B-mode area ratio = 2.59±1.36 for cancers
1.04±0.26 for fibroadenomas



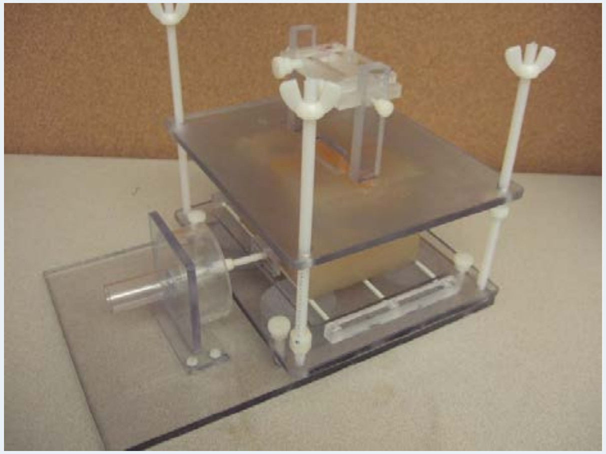
Further analysis with histogical sections

US/MRE: Combining local information

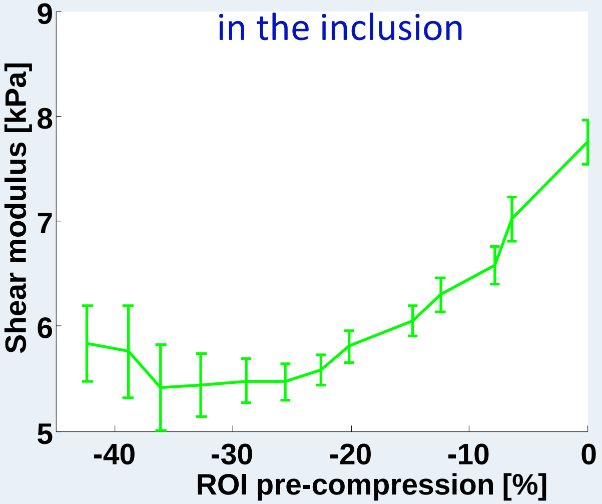
- Currently : sequential acquisition of US and MR data
- Necessity of maintaining deformation during acquisition



Collaboration with the Mayo Clinic



Shear modulus – pre-compression curve in the inclusion



Blanchard et al, ISMRM 2012

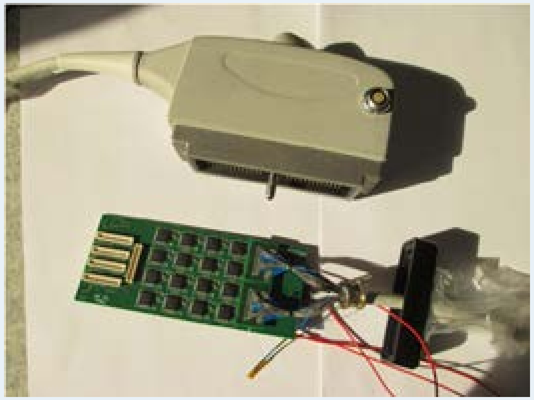
US/MRE: perspectives

- **Combining MR and US elastography:**

  - instrumentation:

    + new probe to measure 3D displacements

    + need of developing an US probe compatible with MR



  - future works:

    + wave polarization effect analysis for tissues under compression

    + Working at different frequency ranges (100 Hz – 10 kHz)

    + additional mechanical parameters: viscosity imaging

2) MR-optics coupling

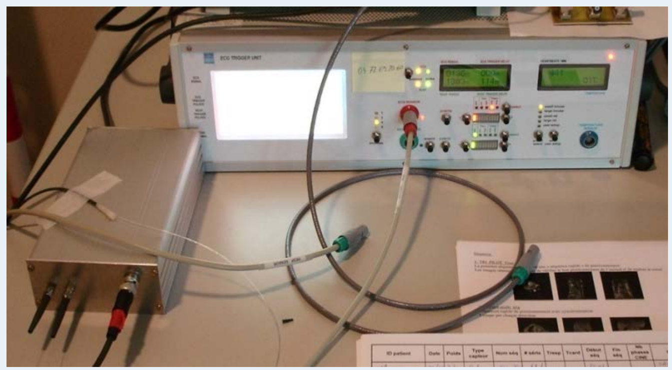
Speaker: Olivier Beuf – Team 5

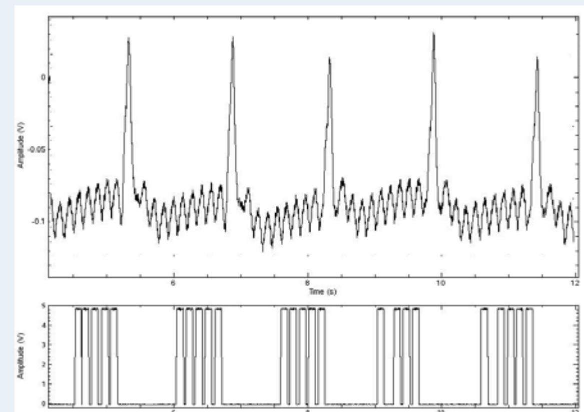
An optical fiber-based gating device for prospective mouse cardiac MRI

Goal: To obtain a reproducible gating in any conditions: animal size, sequence, strength of magnetic field, RF coils. Not based on possible corrupted ECG signal.

Literature: Carbon leads (Choquet 2011) followed by electo-optic conversion, inductive pick-up coil (Fischbein 2001), stethoscope in esophagus (Brau 2002).

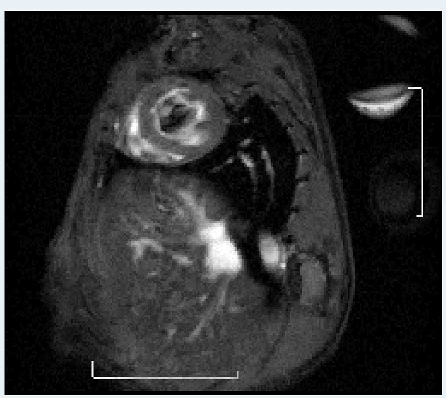
820 nm LED

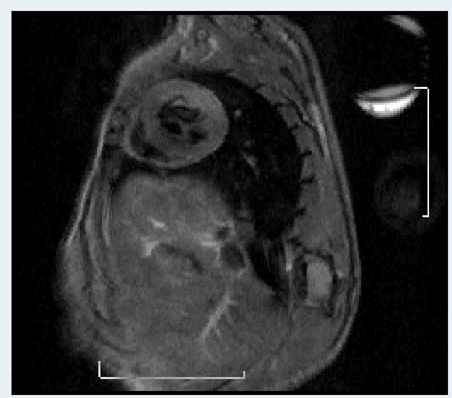




4,7T

CINE FLASH



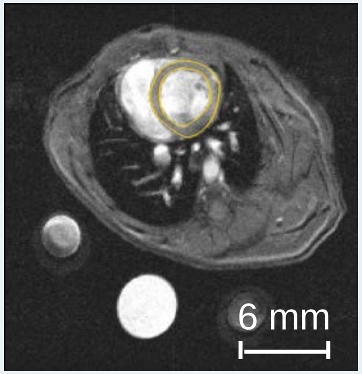


CINE FLASH
Dark Blood

[R. Sablong et al., IEEE TBME, 2013]

An optical fiber-based gating device for prospective mouse cardiac MRI

n=10



4,7T horizontal

	Respiratory period (s)	Cardiac period (ms)	Scan time (s)	SNR	CNR
Optical	1.8±0.2	149±14	432±90	21.1 ± 3.8	20.8 ± 2.1
ECG	1.8±0.2	147±16	384±102	20.4 ± 4.8	22.3 ± 2.8
Pressure	1.9±0.2	146±13	414±78	20.1 ± 2.6	22.8 ± 3.1

[R. Sablong et al. IEEE TBME, 2013]

CRMBM UMR 6612

11,7T vertical

Gating device independent of:
- field strength
- sequence (RF and gradient switching)
- RF coils (volume or surface)
- animal model of heart failure.

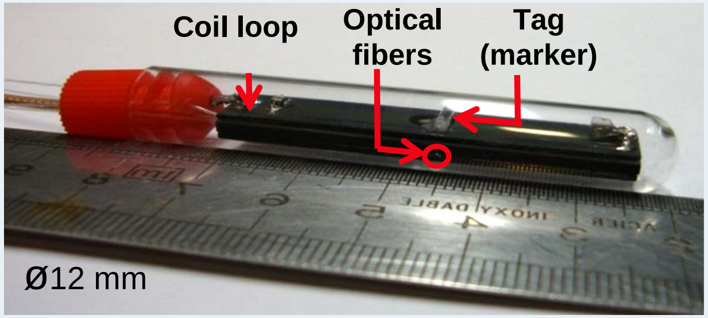
Perspectives: Dual channels and wavelengths device.

Bi-modal NMR-optics endoluminal probe for digestive wall assessment

Context : In France, colorectal cancer is the third most frequent cancer and the second cause of mortality (Inca). Survival at 5 years is 56 % (all stages) and increasing to 94 % with early detection. Today, the reference method is still the colonoscopy associated with tissue biopsy.

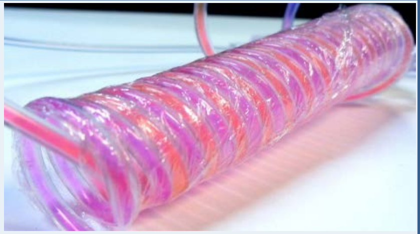
Ultimate Goal is to develop a probe allowing: **[Sonmez et al. JMR 2012]**

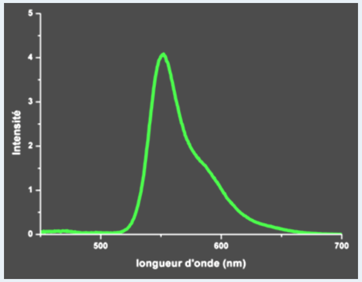
- Tissular characterization (metabolism) by fluorescence spectroscopy (endogenous contrast)
- HR-MRI for lesion staging (TNM classification) and morphological knowledge



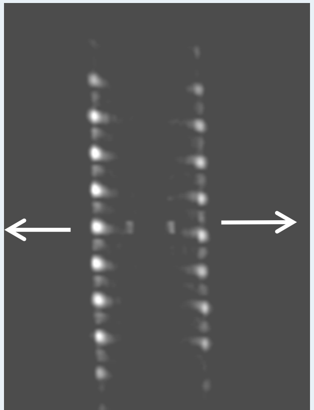
Two-channels NMR-optical probe + optical bench

1,5T et 3T

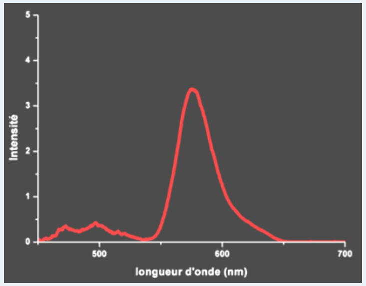




Eosine (0,2 g/L)
+ Gd (~2,2 mmol/L)



MRI Turbo-FLASH
(1 image/sec)

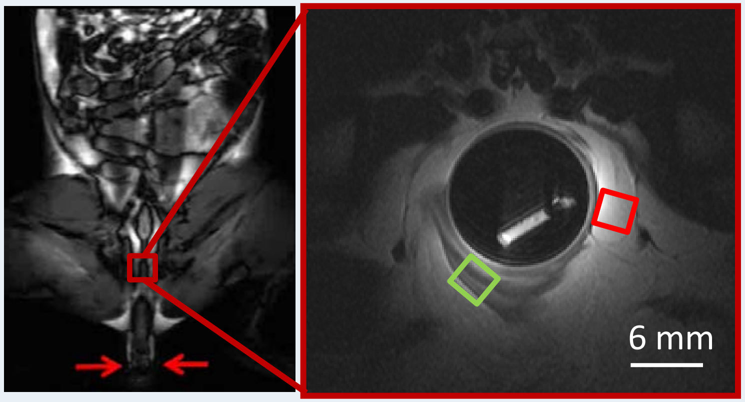


Rhodamine (0,01 g/L)

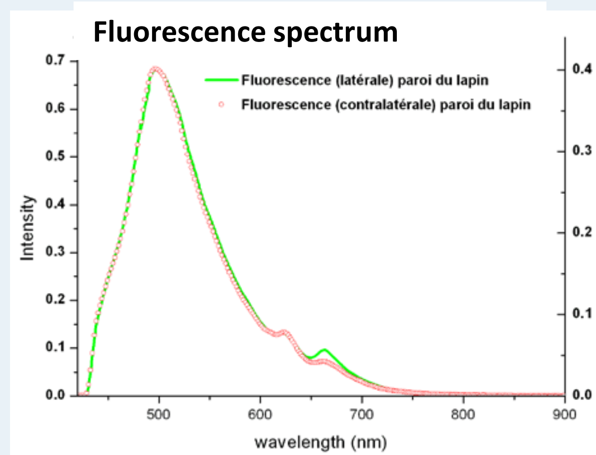
Bi-modal NMR-optics endoluminal probe for digestive wall assessment

[Ramgolam et al. JBO 2011]

In vivo



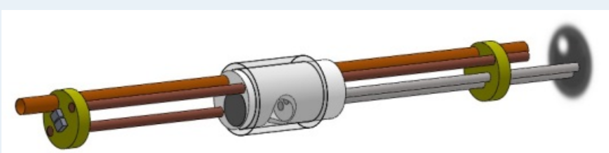
Rabbit



Strengths: Compatible techniques and simultaneous acquisition.

Perspectives

Large animals and humans



Prototype with 6 mm outer diameter
(guidewire and memory shape materials)

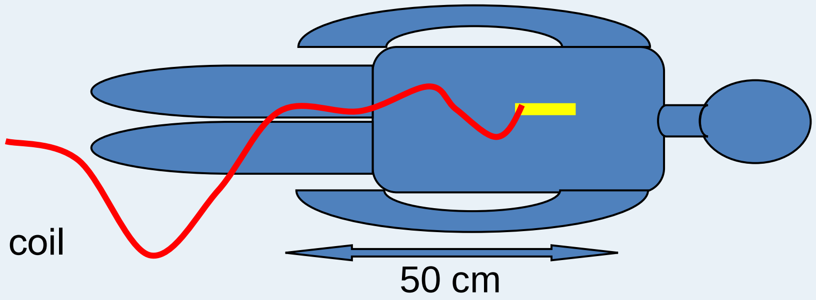
Bottleneck: Safety issues!

Mouse models of colon and rectum adenocarcinoma

Endogeneous tissular contrast spectro-photometry

PRIMES UNIVERSITE DE LYON

Safe MR endoluminal coil



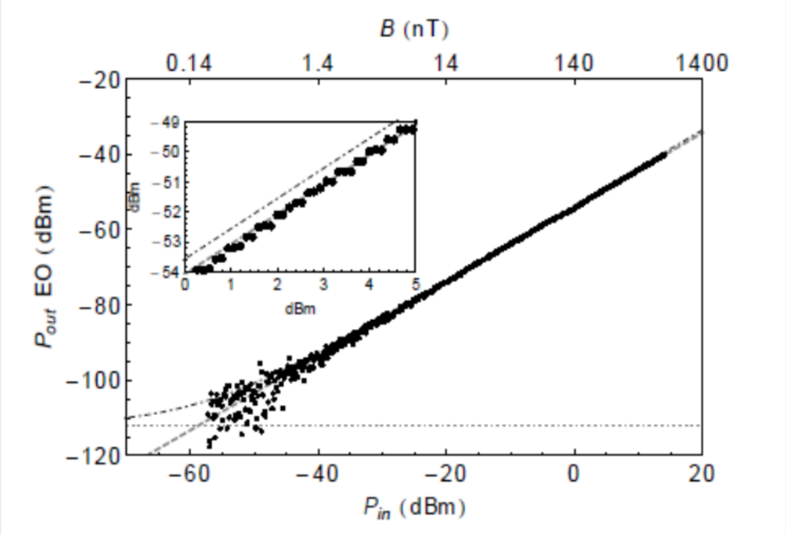
Strong local concentrations (close to the coil and along the cable) of E field and SAR leading local heating.

[Detti et al. MRM 2011]

ADR and project from Rhône-Alpes région, DGA project

Coil without electrical connection:

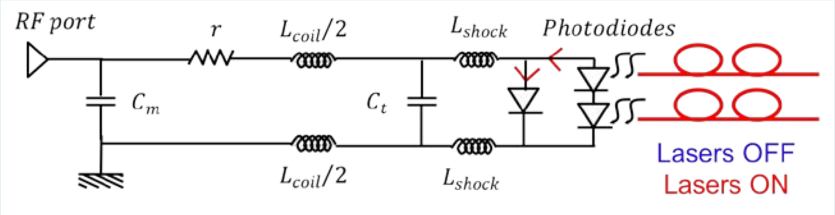
- Direct RF magnetic field conversion by electro-optic effect (Pockels occurring in a LiTaO3 crystal)

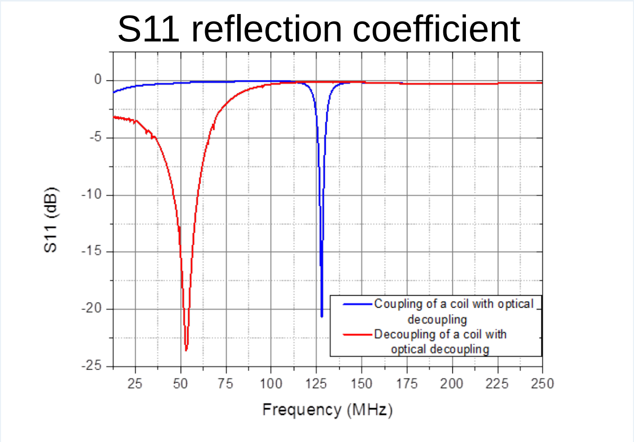


$B1_{min}$ ≈ 160 pT / 50dB dynamic

[Aydé et al. IEEE sensors 2013]

- Active optical decoupling





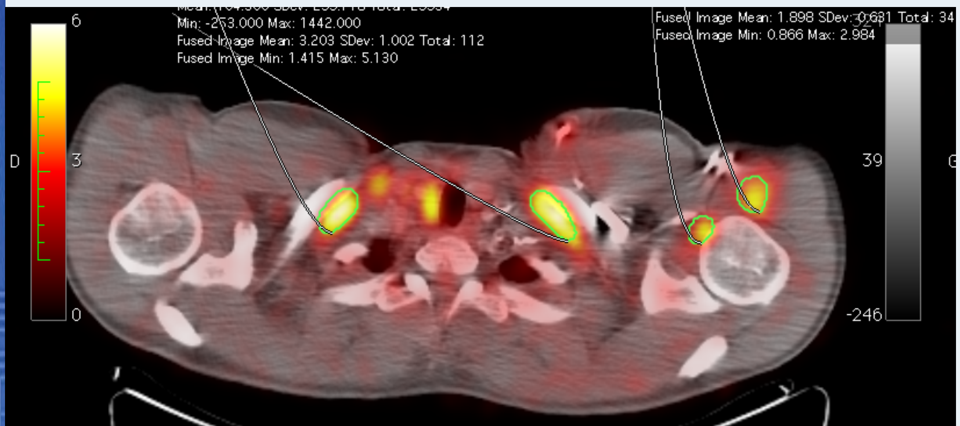
3) Learning from multi-modality data to assist the medical diagnostic

Speaker: Denis Friboulet – Team 2

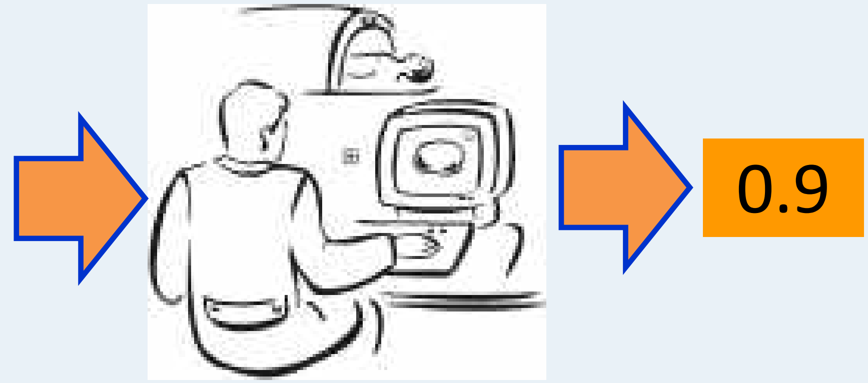
Learning from multi-modality data to assist the medical diagnostic

- **Objective**: Develop computer aided diagnostic systems (CAD) based on the learning from discriminative features extracted from different imaging modalities : MRI, PET, MEG, US..
- **Two main clinical applications** : cancer and epilepsy imaging
- **Current focus**:
  - Supervised learning (SVM),
  - Evaluate the gain of multi-modality imaging,
  - From a local ROI approach to patient specific probability maps

Lymphoma staging based on PET/CT imaging



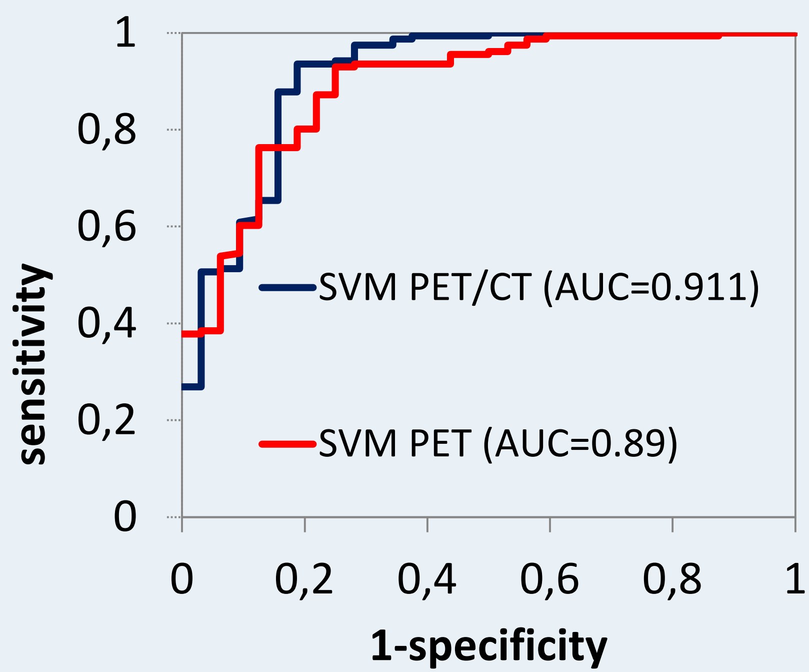
Suspected ROIs are outlined



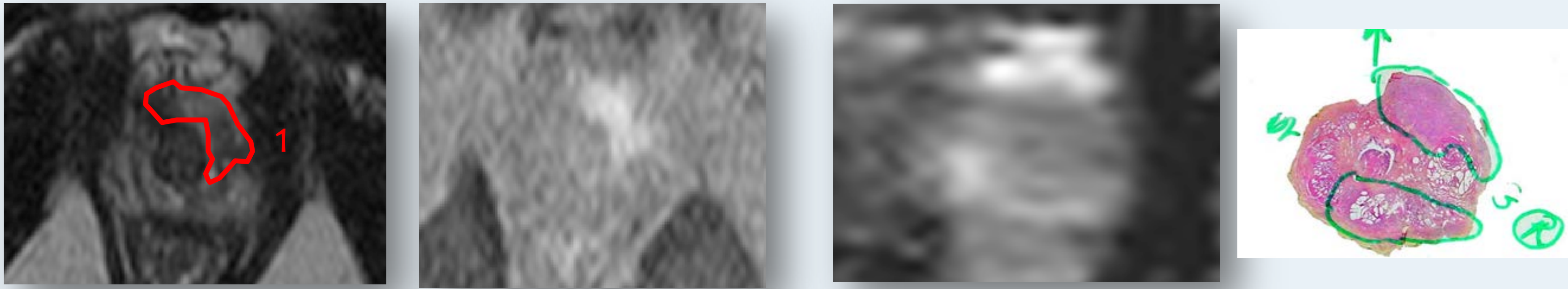
The CAD system returns a malignancy score

- CAD system based on the **SVM classifier** and **>100 features extracted from the PET and CT images**
- Best classification performance achieved with a series of 12 selected PET and CT features : **AUC=0.91** for the discrimination of **cancer lesions vs inflammatory processes**

[Lartizien IEEE JBHI 13]

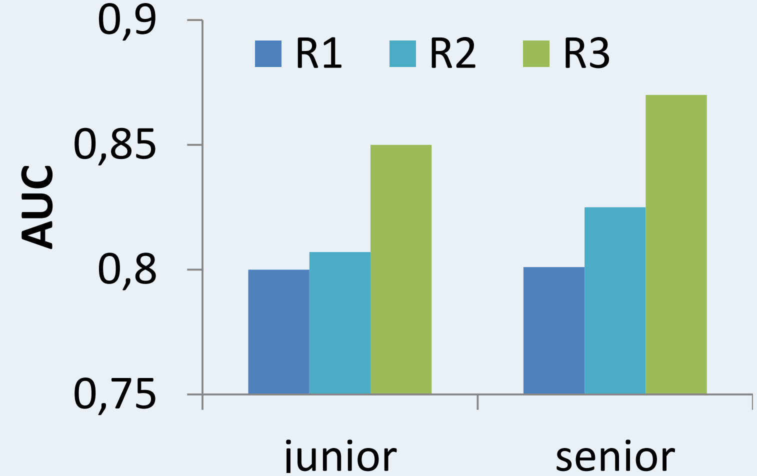


Multi-parametric MR prostate imaging



From left to right, T2-w MR, DCE and ADC transverse slice together with the corresponding digitized histology slice.

- CAD system based on the **SVM classifier** and >140 features extracted from the 3 MR sequences
- Performances in discriminating suspicious but benign targets from cancer targets : **area under the ROC curve (AUC) =0.82** **[Niaf PMB 12]**

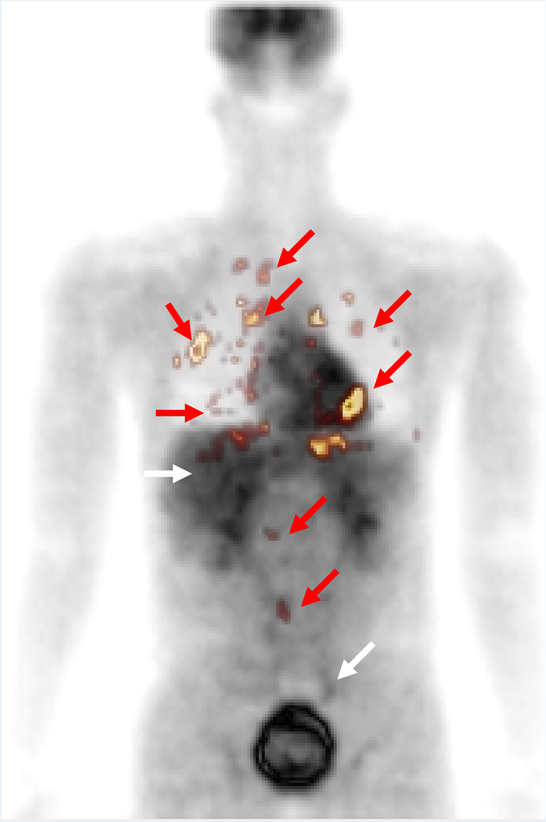


Average performance of junior and senior readers without (R1 and R2) and with (R3) the assistance of the CAD system. **[Niaf Radiology, submitted]**

INCa PAIR project 'CARTOGRAPHIX'

PERSPECTIVES :From a local analysis (ROI) to the extraction of 3D probability maps

- **Main bottleneck**: the individual voxel-based analysis generates high rates of false positives
- **Hypothesis**: Increased specificity is expected from the fusion of complementary discriminant features from hybrid imaging



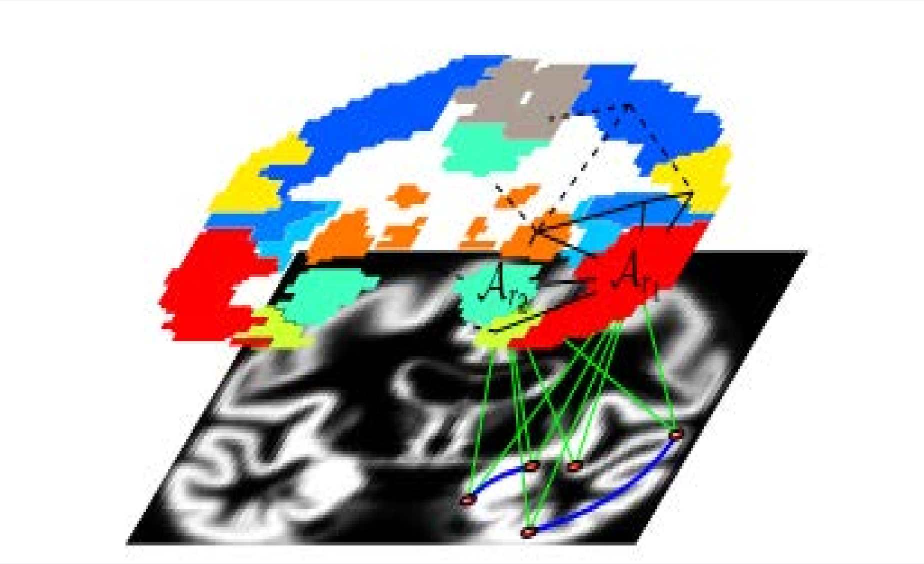
MIP rendering of a whole-body PET image with lesions shown by the arrows superimposed on the binary map obtained with a SVM classifier.

[Lartizien IEEE TNS 12]

Challenges and questions

How to integrate the different features:

- ✓ concatenation in a unique feature vector (heterogeneous format (image, mesh..) or spatial resolution
- ✓ Perform a separate classification for each modality and merge the outputs (majority voting etc..)
- ✓ **Integrate anatomical or functional priors derived from one modality**
- ✓ …



Example: the brain connectivity is encoded by a graph. The node connectivity (blue) depends on the probability of each node to belong to a specific anatomical region (green) and on the relationship between the different regions (black line)

from R. Cuingnet’s PhD thesis

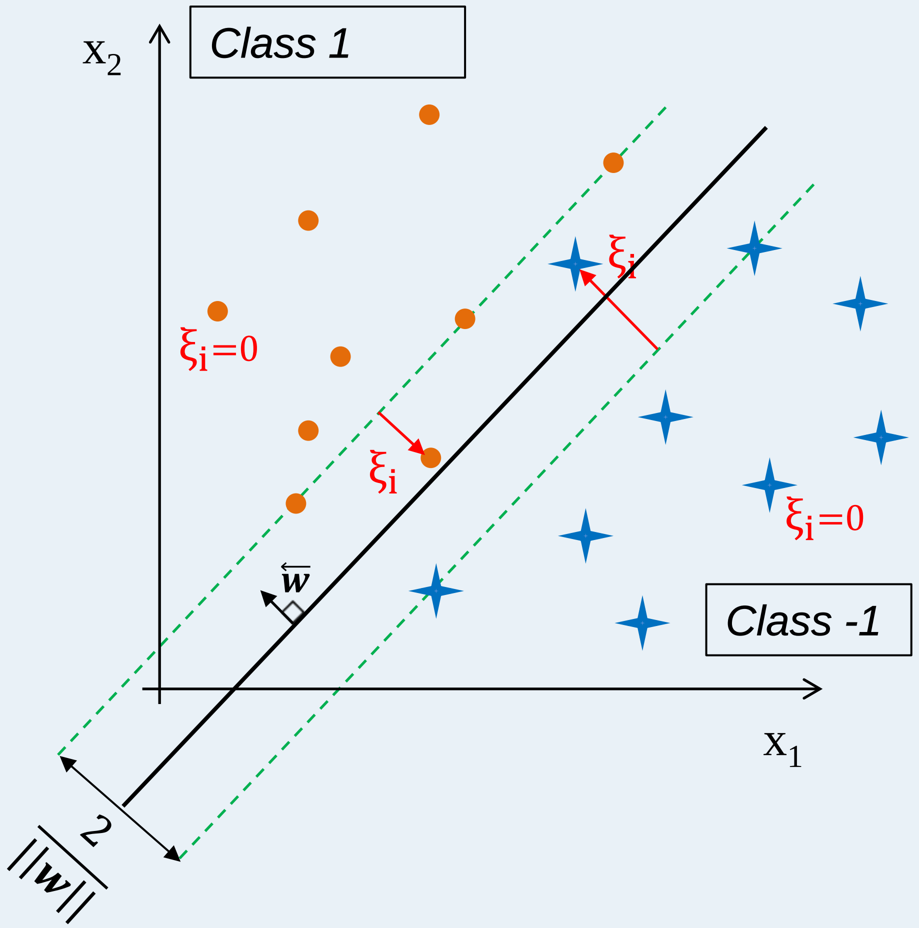
Theoretical context

The SVM framework enables to model different types of proximity between voxels

- In the linear case, the discriminant function is of the form $f(\mathbf{x}) = \boldsymbol{w}.\mathbf{x} + b$

- An extra penalization term (red) can be added to the regular SVM optimization problem (black) to model spatial or anatomical priors:

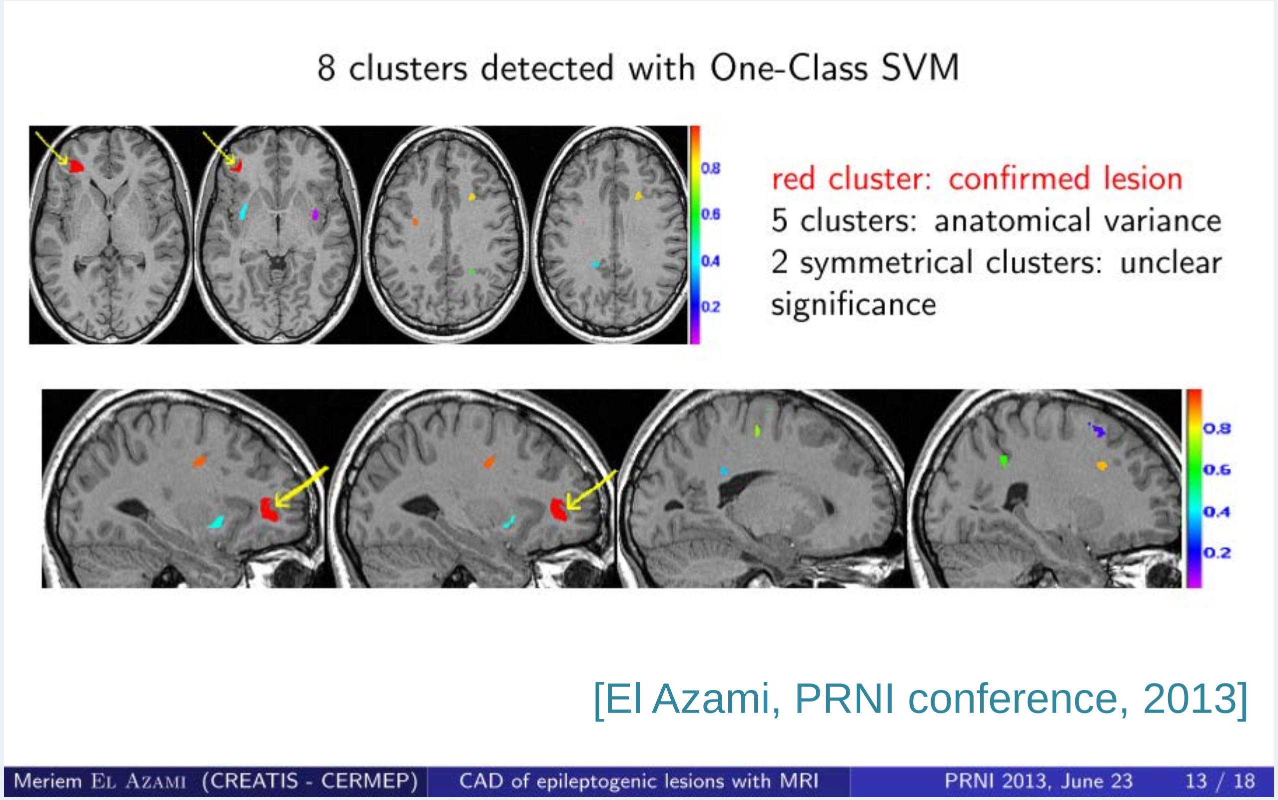
$$\underset{\boldsymbol{w},b,\xi}{\operatorname{argmin}} \quad \frac{1}{2}\|\boldsymbol{w}\|^2 + C\sum_{i=1}^{n}\xi_i + \lambda\, L(\boldsymbol{w})$$



e.g $L(\boldsymbol{w}) = \frac{1}{8l}\sum_i^l \sum_j^8 \|\boldsymbol{f}(\mathbf{P}_i) - \boldsymbol{f}(\mathbf{P}_{ij})\|^2$
where $\mathbf{P}_{ij}$ is the j^{th} spatial neighbor of $\mathbf{P}_i$

Perspectives

- Collaboration with the machine learning community :
  - ➢ LITIS Lab (Rouen) and OCA Lagrange Lab (Nice) → ANR project proposal
- PhD thesis funded by the LABEX PRIMES starting fall 2013 :
  - ➢ Detection and characterization of epileptogenic lesions based on MR, PET and MEG. Collaboration with CERMEP and CRNL.



[El Azami, PRNI conference, 2013]

Challenge and questions

- **Photoacoustic**
  - Which US probe design for real time photoacoustic for premature tumor in prostate cancer?
  - Which beamforming strategies 2D, 3D, and which technology Capacitive micromachined ultrasonic transducers (CMUT)?
  - Other medical problems to be addressed?

- **US/MR elastography**
  - Will the combination of information significantly improve diagnosis?
  - Complementary information but imaging protocol difficult to conduct on humans. Which strategies to be adopted?

Challenge and questions

- **Coupling between modalities**
  - **Coupling between modalities**
    - How to combine simultaneous multi-modal information?
    - Why not more than bimodality?
  - **Hybrid imaging:**
    - A useful research tool (method validations) but what about diagnosis?
    - Technically challenging

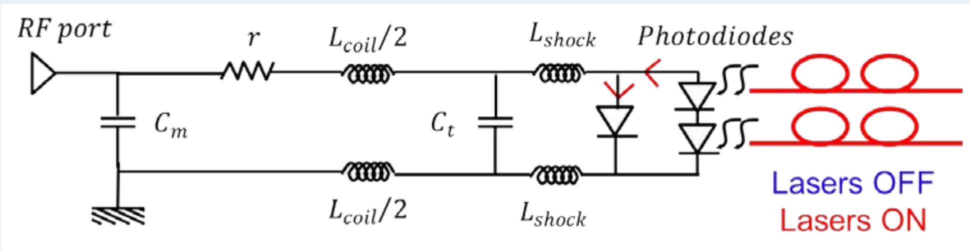
- **CAD based on multiple modalities**
  - **Beyond local ROI-based analysis:**
    - Extraction of patient specific, 3D probability maps
  - **Integrate anatomical/functional priors at the learning step within the SVM framework:**
    - Graph-based encoding of connectivity,
    - Enhanced SVM optimization: introduction of spatial constraint terms
  - **Will this significantly improve specificity? Alternative to this strategy based on nonsupervised strategies (unmixing...)?**

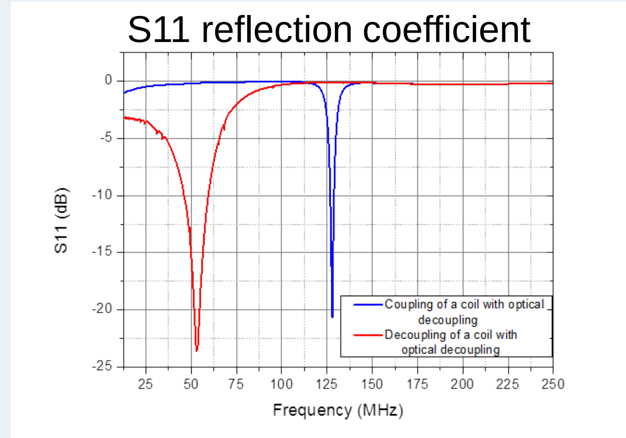
Extra slides

Safe MR endoluminal coil

Coil without electrical connection:

- Active optical decoupling

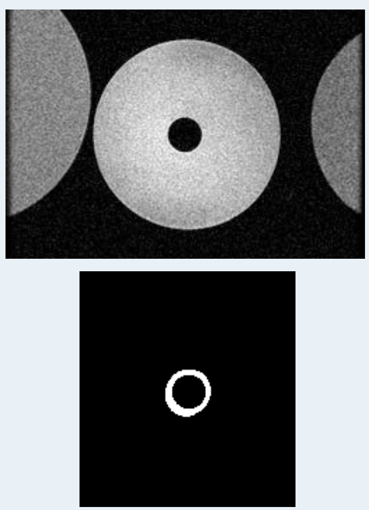




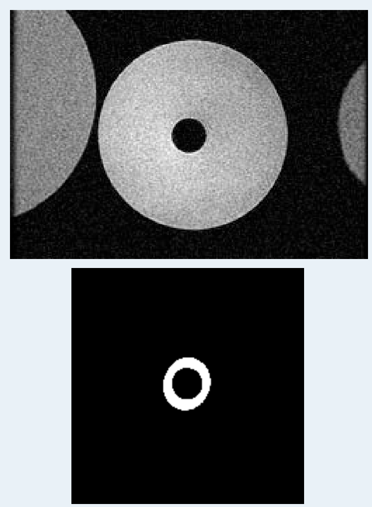
During RF transmission, two optical fibers illuminate the photodiodes thus providing the DC current for PIN diodes

Coil connected but decoupled

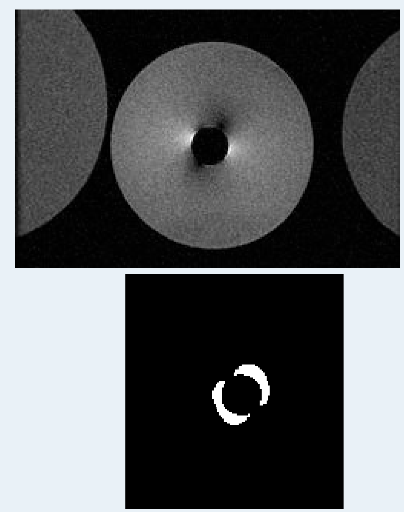
Coil actively decoupled



Electrical DC bias

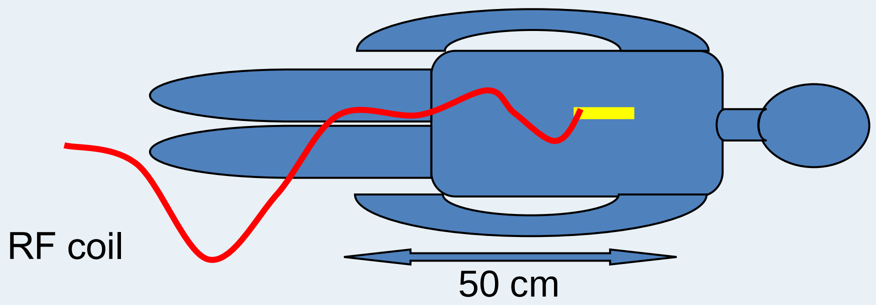


Optical DC bias



Circuit failure

Safe MR endoluminal coil



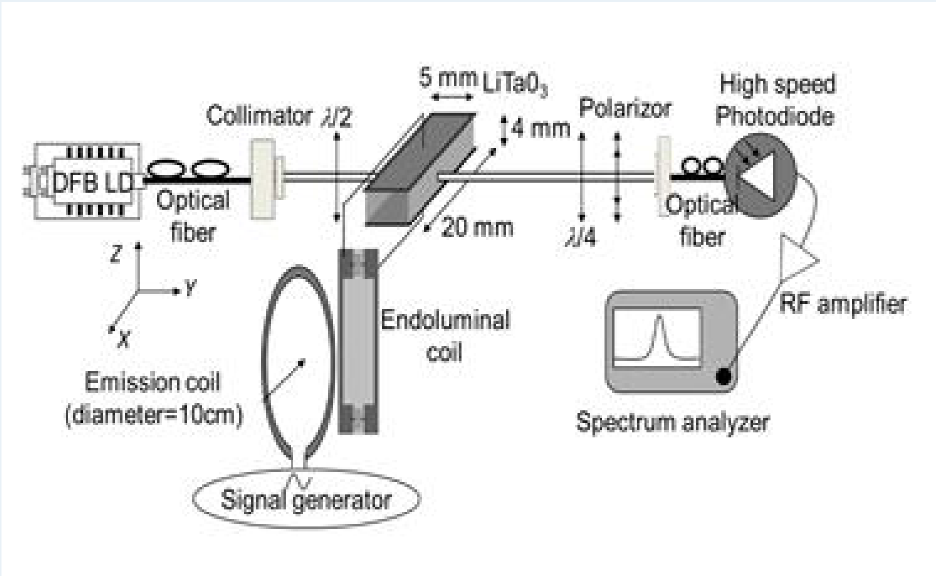
Strong local concentrations (close to coil and along the cable)

- E field
- SAR (local heating)

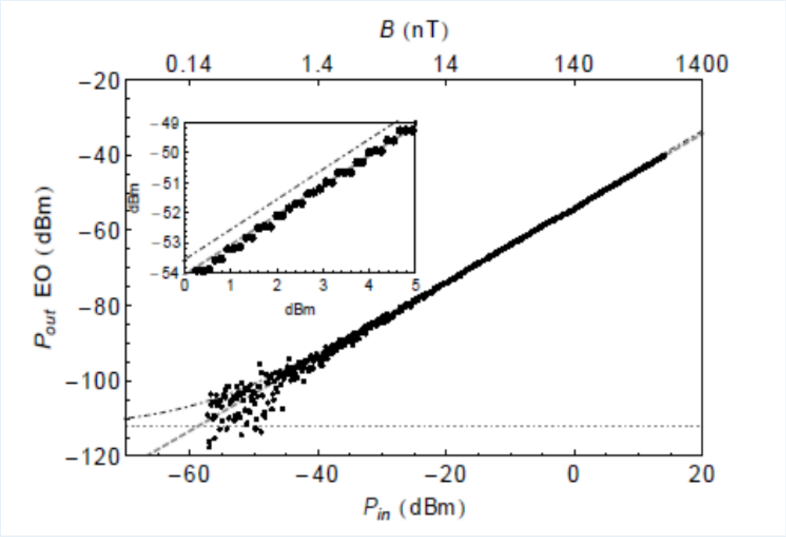
[Detti et al. 2011]

Coil without electrical connexion:

- Direct RF magnetic field conversion by electro-optic effect



Electro-optic effect (Pockels) occurring in a LiTaO3 crystal



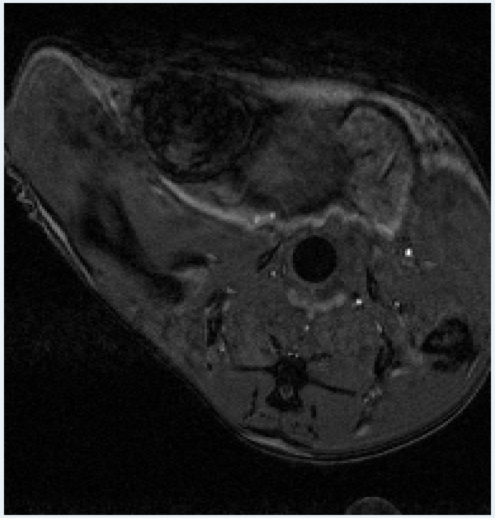
$B1_{min}$ ≈ 160 pT / 50dB dynamic

[Aydé et al. IEEE sensors 2013]

MRI of mouse rectal wall

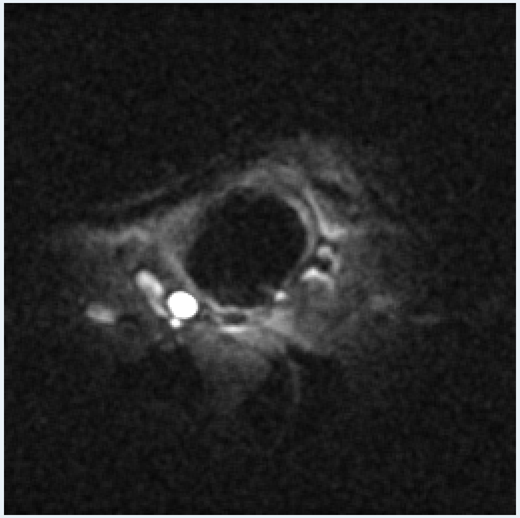
Friday 20th of September

Volume coil



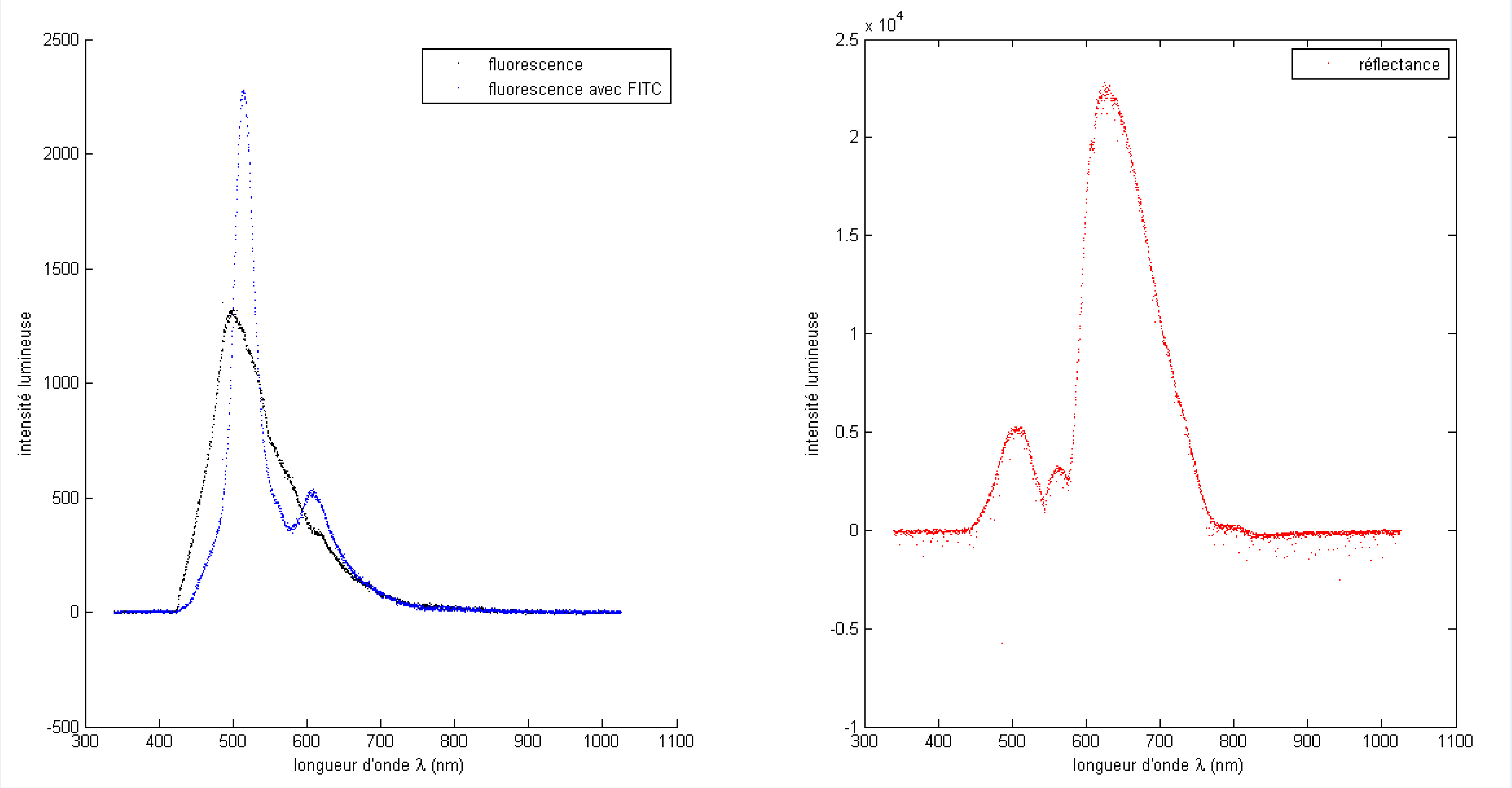
Voxel size = 78 x 78 x 260µm^3
Acquisition time = 11min31s

Endorectal coil



Voxel size = 39 x 38 x 195µm^3
Acquisition time = 14min11s

Optical spectroscopy



Hybrid imaging and coupling between modalities

- **OTHER TOPIC**
- **Combine image and therapy for image guided therapy**
  - Example: US + RX in pelvic radiotherapy