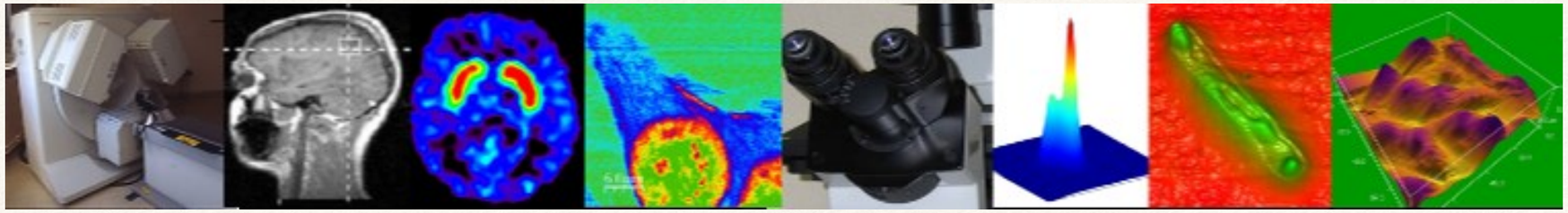


Preclinical MRI Imaging of liver colorectal metastases

Workshop: 3D model and applications in Oncology

Toulouse, 26/06/2014

Institut de Recherche en Cancérologie de Montpellier (IRCM)
&
Laboratoire Charles Coulomb (L2C)

FERRER Cyril

Colorectal Cancer (CRC)

- Incidence:
  - 3rd most common cancer worldwide
  - 4th most common cause of death
  - In France in 2012, Second in women and men
  - Prevision in France: 45 000 new cases every year in 2020
  - 50 % of CRC metastases in liver

INSTITUT NATIONAL DU CANCER

(Source : National institue of Cancer, GLOBOCAN 2012, IARC)

Risk Factors

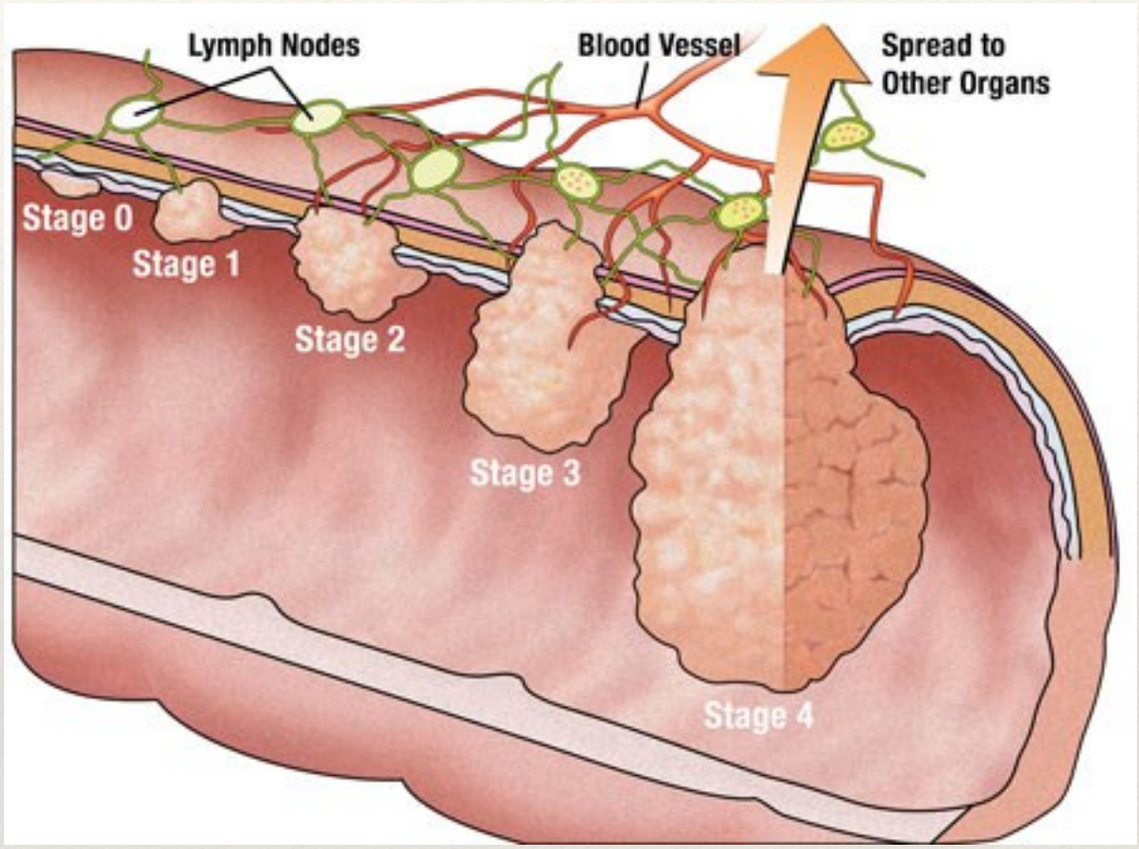
- Familial and heredital (Adenomatous Polyposis, Hereditary nonpolyposis Colon cancer…)
- Age: 90% colon cancer patients are diagnosed after the age of 50.
- Diet, physical inactivity, smoking & alcohol consumption
- Inflammatory Bowel Disease (IBD)
- Obesity type 2 diabetes

INSTITUT NATIONAL DU CANCER

(Source : National institue of Cancer, GLOBOCAN 2012, IARC)

Colorectal Cancer

- Treatment :
  - Depends on the stage:
    - 0 and I: Surgery
    - II and III: Surgery, if needed: radiotherapy, chemotherapy
    - IV: Mainly chemotherapy
- Five-year survival rate: 56%
- 90% if early detection (American Cancer Society)



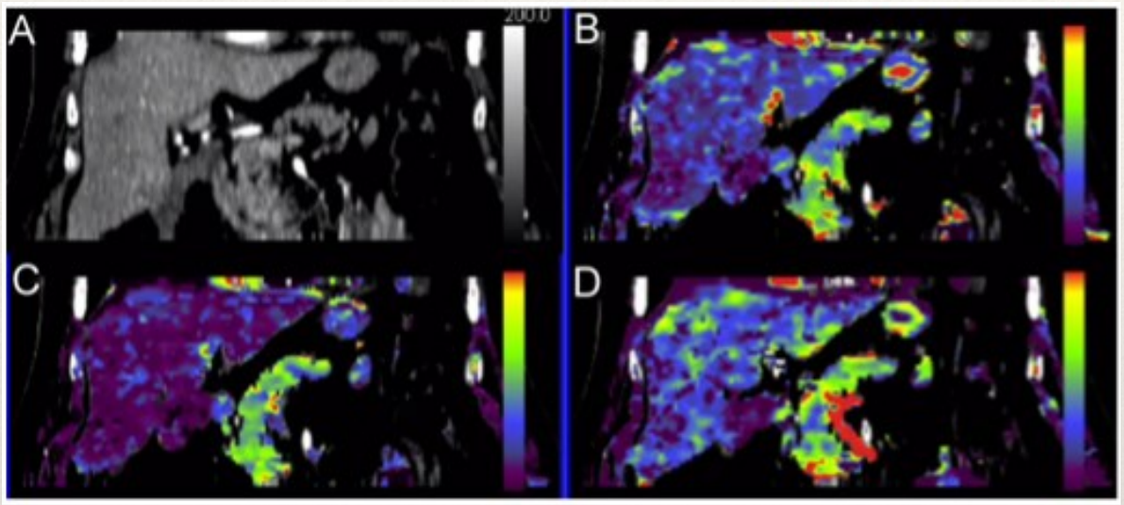
INSTITUT NATIONAL DU CANCER

How to improve this survival rate?

- Pre-clinical imaging allow us to try to improve:
  - Earlier detection
  - Functional acquisition
- But also :
  - Evaluate new treatments
  - Evaluate combination of therapies (time, dose):
    - chemotherapy (FUFOL, FOLFOX, XELOX, FOLFIRI)
    - anti-angiogenic drugs (Avastin anti-VEGF, Erbitux anti-EGFR)

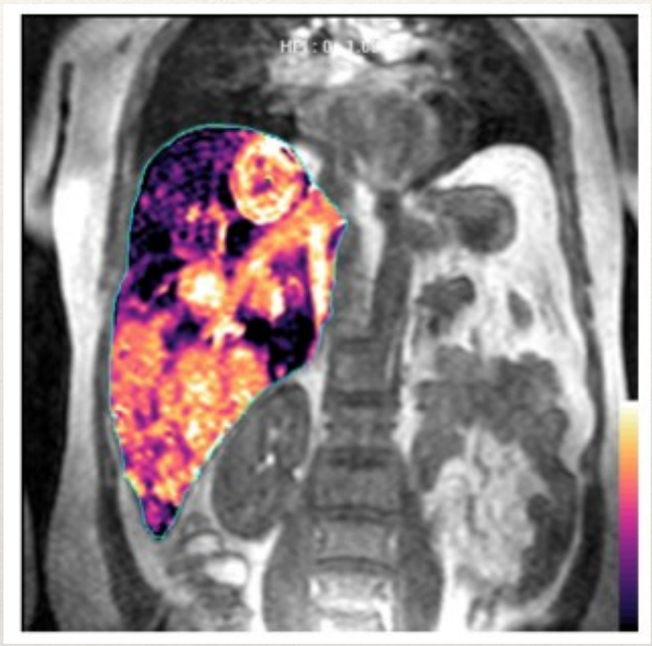
Clinical Detection

- Dynamic Contrast Enhanced CT:



Volumetric helical dynamic contrast enhanced CT of upper abdomen enabling multiplanar assessment of the liver. Images in the coronal plane are shown: anatomical (A), blood flow (B), blood volume (C), and extraction fraction (D).

- Dynamic Contrast Enhanced MRI:

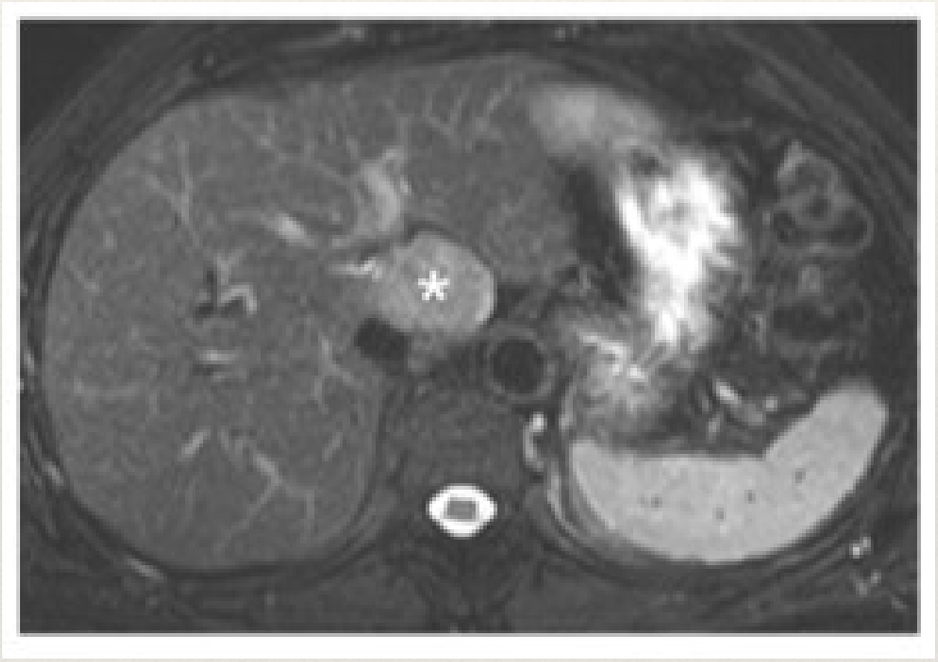


hepatic perfusion index (HPI) map through the liver

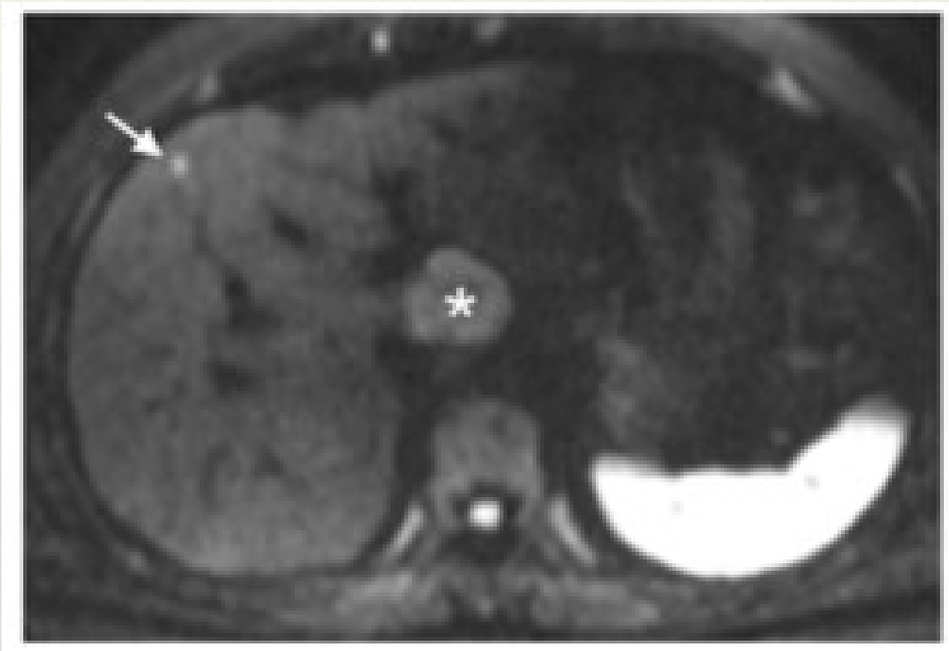
Functional Imaging of the Liver Vicky Goh, MD, FRCR, Sofia Gourtsoyianni, PhD, and Dow-Mu Koh, MD, FRCR Semin Ultrasound CT MRI 34:54-65 C 2013

Clinical Detection

- Diffusion Weighted MRI:



fat-suppressed T2-weighted



diffusion-weighted image b=750 s/mm²

Functional Imaging of the Liver Vicky Goh, MD, FRCR, Sofia Gourtsoyianni, PhD, and Dow-Mu Koh, MD, FRCR Semin Ultrasound CT MRI 34:54-65 C 2013

Aim of the study

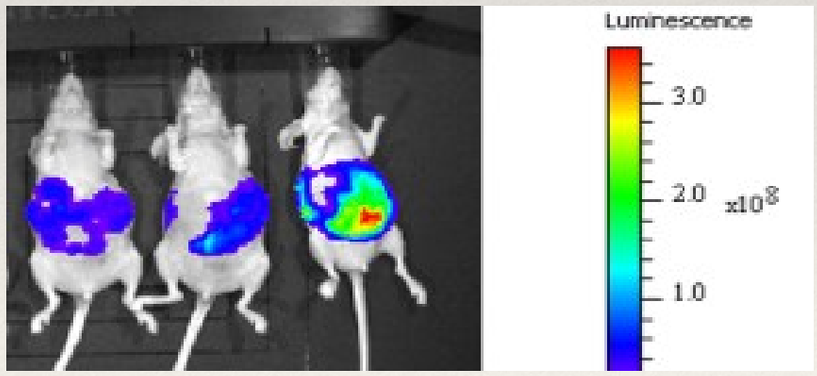
- BioNanoNMRI academic preclinical imaging platform
- 9,4T Agilent MRI
- Aim: Detect and follow-up liver colorectal cancer metastases, on order to evaluate new therapies or combinaisons

IPAM
IMAGERIE DU PETIT ANIMAL DE MONTPELLIER
Institut de Recherche en Cancérologie
I R C Montpellier
BioNanoNMRI
LABORATOIRE CHARLES COULOMB MONTPELLIER

Methods

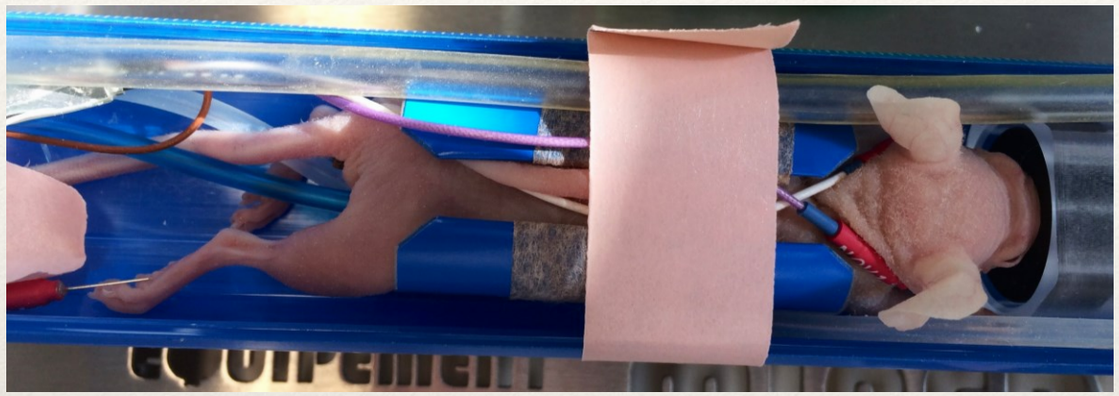
- Pre-clinical model:
  - Primary tumor model is too aggressive to follow-up metastases
  - Secondary tumor model is more interesting:
    - Intrasplenic injection of human colorectal cancer cell line (SW-620-luc) cells followed by splenectomy
- Bioluminescence is currently the reference:
  - Fast, high sensitivity, not invasive
  - False positive, low resolution, non quantitative, need cell expressing luciferase

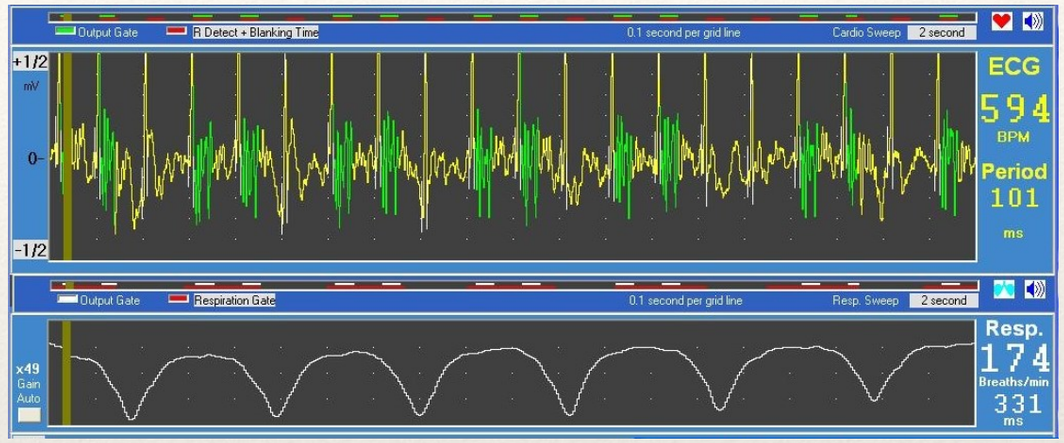
Surgery and injection of SW 620 cell



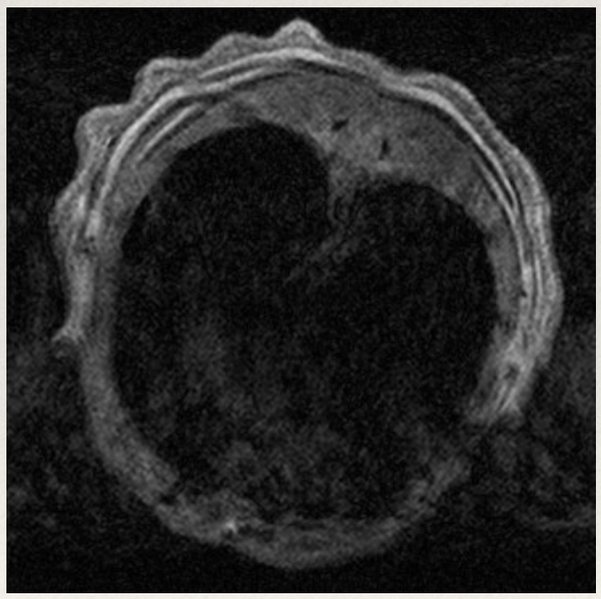
Observation with bioluminescence

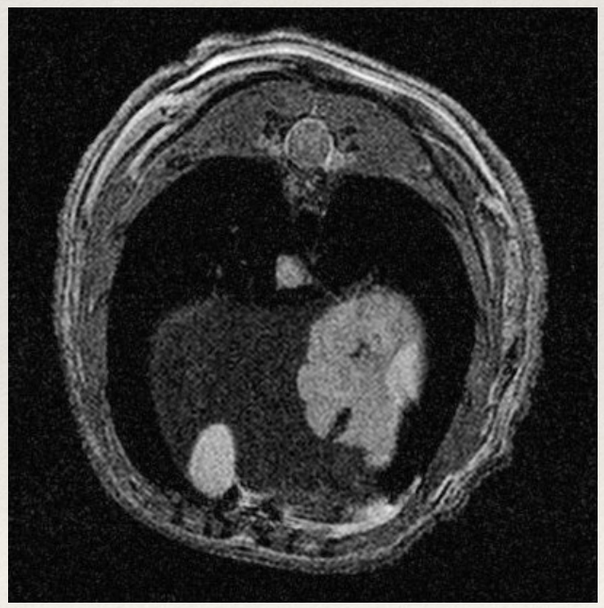
Gating is mandatory





Without Gating





Respiration and Cardiac Gating

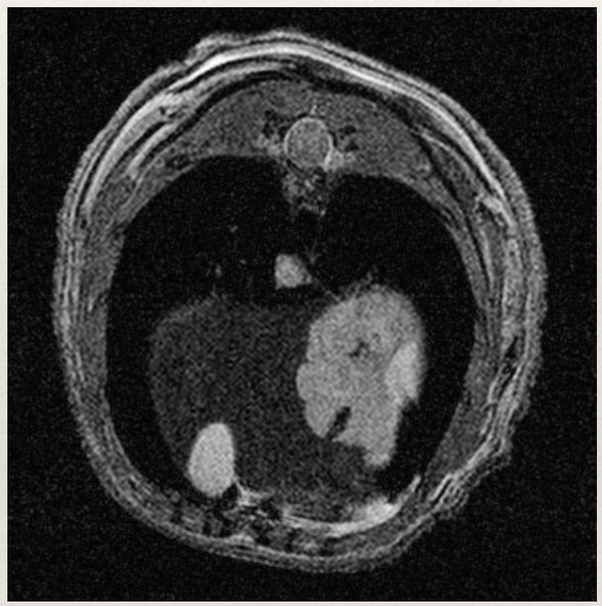
Spin Echo Multiple Slice Acquisition TR=3s
TE=18ms

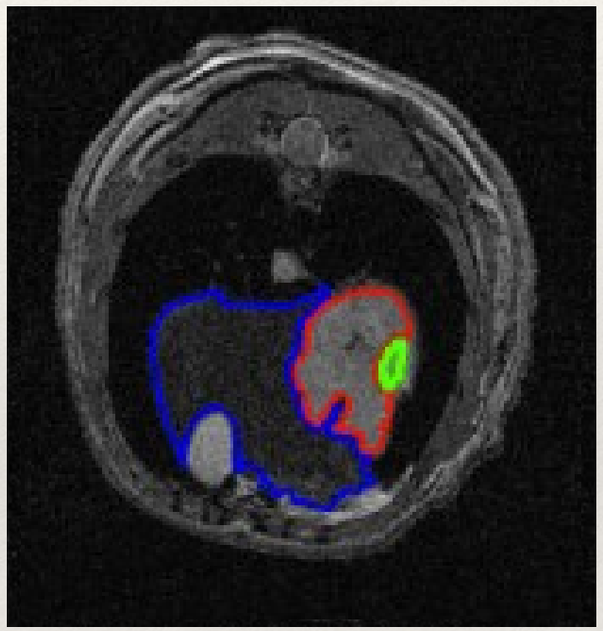
Tissue Characterization

- After relaxation times measurement, we optimized a gated T2 weighted pulse sequence to allow accurate segmentation :

At 9,4T:

Healthy liver:
T1 = 577ms
T2=20,92ms
Metastases:
T1=920ms
T2=38ms



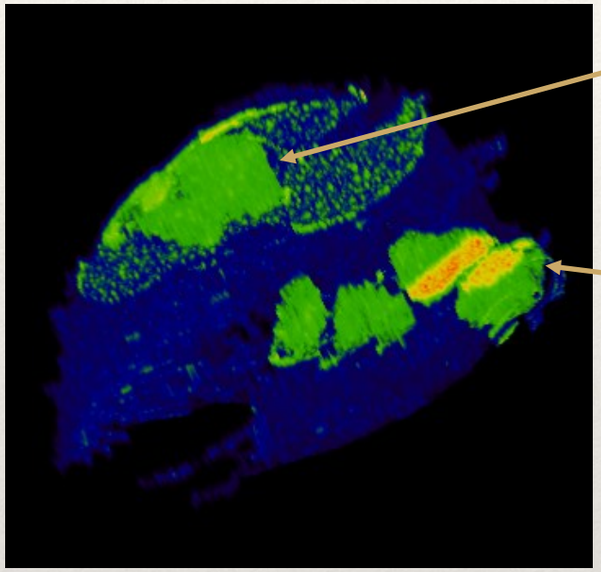


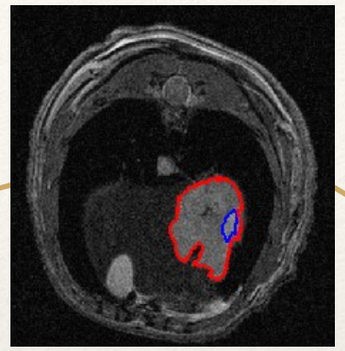
Spin Echo:

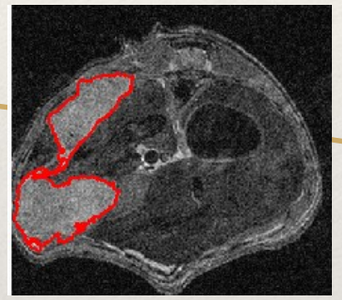
TR=3s
TE=18ms
Thickness=0.5m
m
Full liver ≈
45 slices in 40min

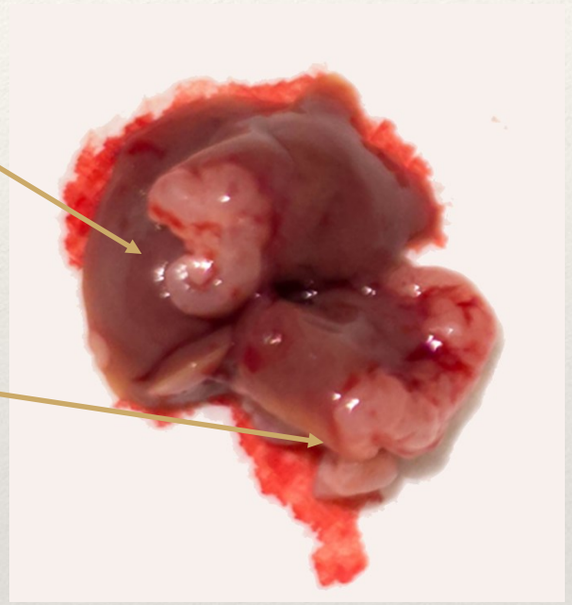
- Reveals an heterogeneity in the tumor tissue
- Needs to be correlated with histological study to understand the origin of this difference

Tumor Volume Measurements









Computed 3D

Total Tumor Volume:

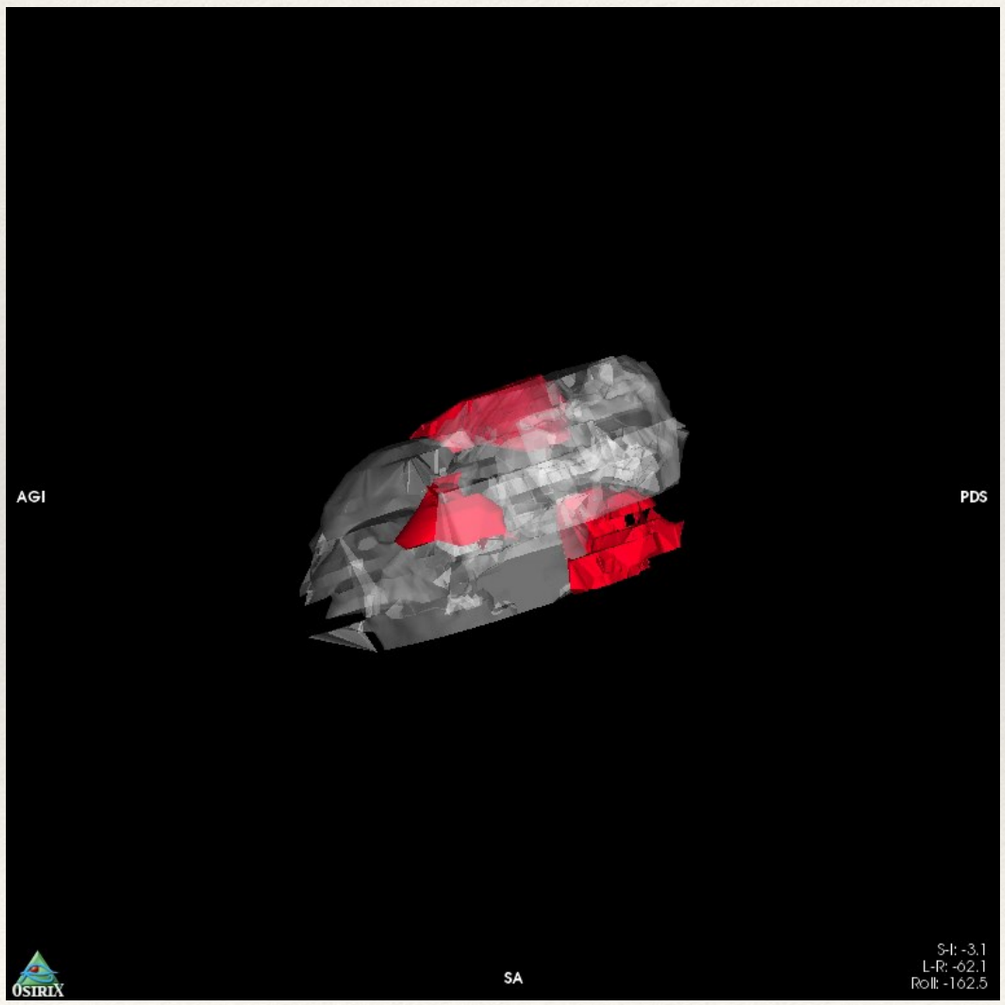
week 3: 132 mm^3 +/- 15 mm^3

week 4: 625 mm^3 +/- 60 mm^3

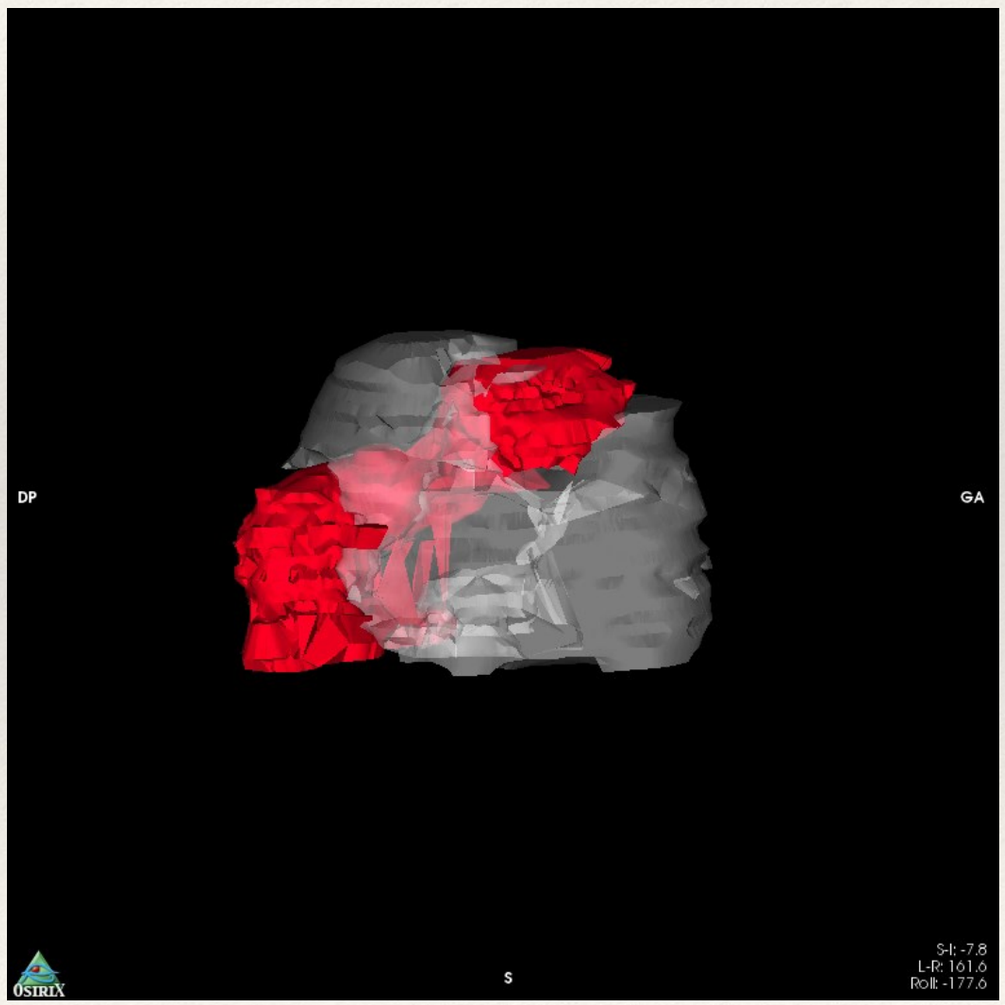
Measured with Myrian©

Tumor Volume Measurements

Week 3: 132mm^3:

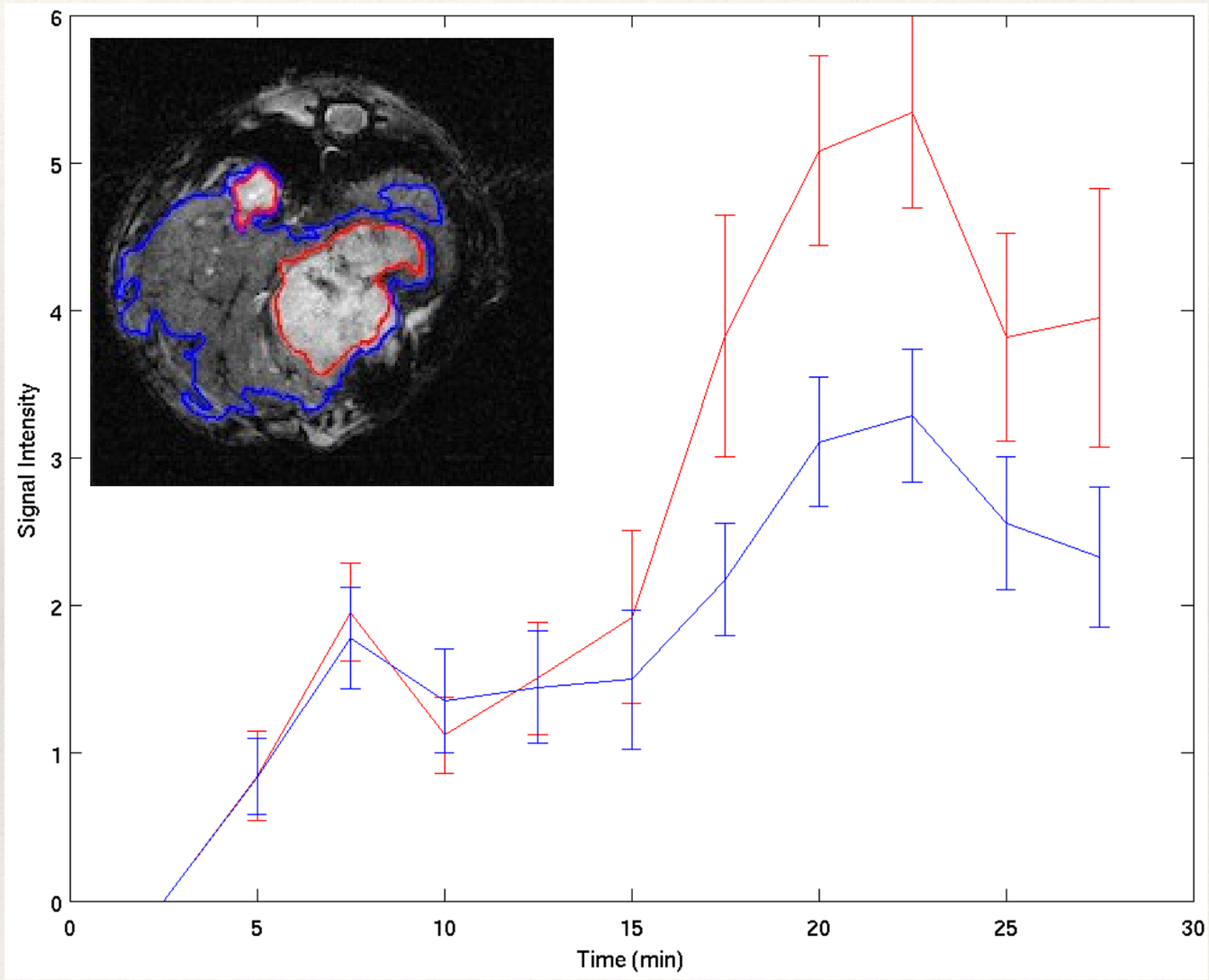


Week 4: 625mm^3:



Functional Acquisition

- Preliminary experiment:
- IP Injection of gadolinium-based contrast agent (Dotarem), and (Inversion with Flash Detection)
  - Measurable signal variation with contrast agent

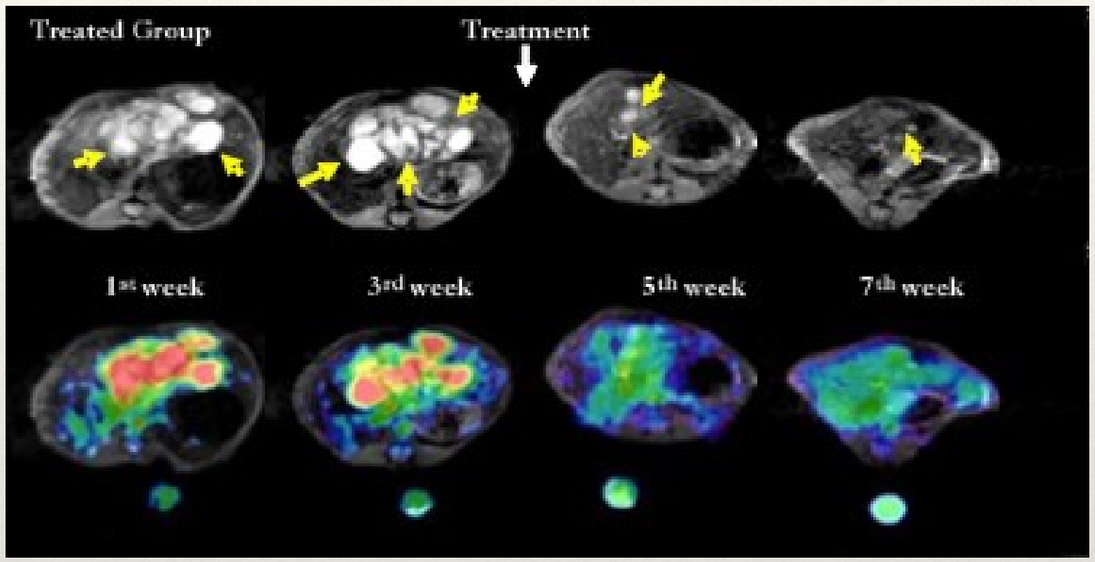


Conclusion

- ✓ Validation of a pre-clinical model of colorectal liver metastases
- ✓ MRI anatomical detection and follow-up of metastases
- ✓ MRI functional detection of metastases growing
- ✓ Optimization of a complete acquisition and characterization chain on an innovative model

Possible development

- Perspective on Imaging:
  - Diffusion MRI
  - Sodium MRI, (UTE)
    - Faster sequences to get rid off gating (propeller, …)
- High througput screening
- Evaluation of tumor micro-environment before and after targeted therapies (anti-VEGF…)



^{1}H and Na MRI of the treated mouse with liver tumor

Monitoring of Liver Tumor Response to Treatment by Na MRI S. K. Hekmatyar et al. Imaging Science Division, Radiology, Indiana University, Indianapolis, Indiana, United States, Pfizer, Inc, Ann Arbor, Michigan, United States, 2007

Thanks for your attention

Collaborators:

Muriel Busson IRCM
Maguy Del Rio IRCM
André Pèlegrin IRCM
Christophe Goze-Bac BioNanoNMRI L2C
Michel Zanca BioNanoNMRI CHU