Exploration of Melanoma Metastases in Mice Brains Using Endogenous Contrast Photoacoustic Imaging

Jonathan Lavaud[1,2], Maxime Henry[1,2], Jean-Luc Coll[1,2], Véronique Josserand[1,2]

[1]UGA/INSERM U1209 CNRS UMR 5309
Institute for Advanced Biosciences, Team Coll
Grenoble, France
[2]Optimal Small animal platform, Grenoble, France

Supervisor : Dr. Véronique Josserand

Melanoma in brain

- Melanoma is the most aggressive form of skin cancer. (*Hall 1999, Jemal 2011*)
- One of the most common and devastating complications of melanoma is the development of metastases to the central nervous system (CNS). *(Sawaya 2001)*
- In patients with brain metastases, the median survival for these patients is ~4 months from diagnosis, and >50% of melanoma- related deaths are caused by brain metastases. *(Lotze 2001)*
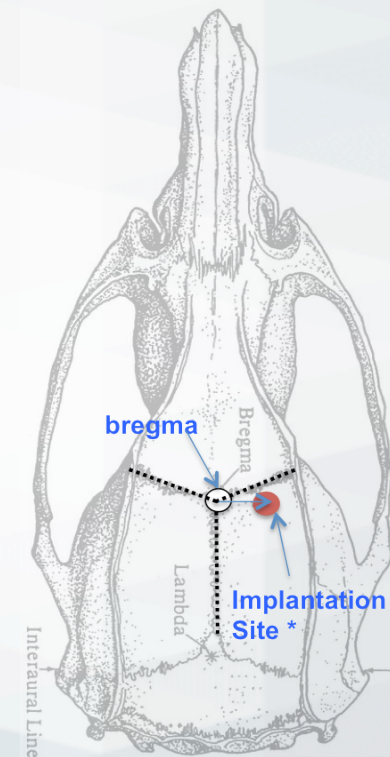
Implantation in the left hemisphere (Striatum)

- **Use of the melanin contrast for B16F10**

Imaging sequences :

- **B16F10** : Multispectral Photoacoustique (Oxy-hemo and melanin)

Goal : see if PA allow the visualisation of tumor in the entiere skull (skin, bone, brain) without contrast agents.
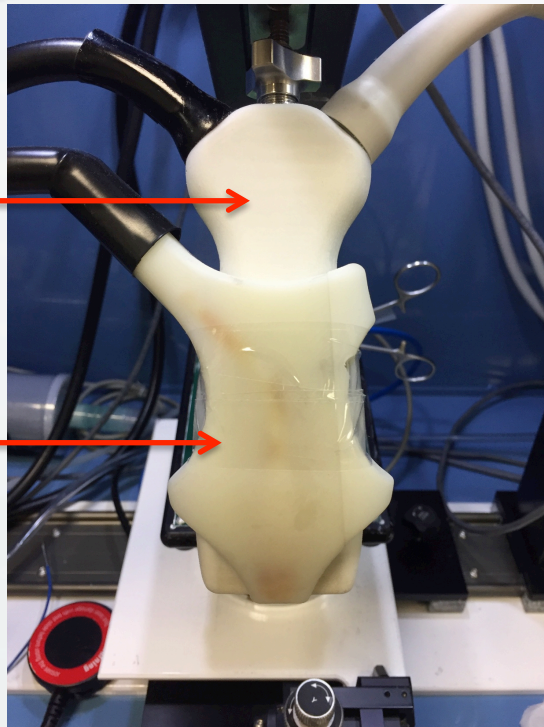
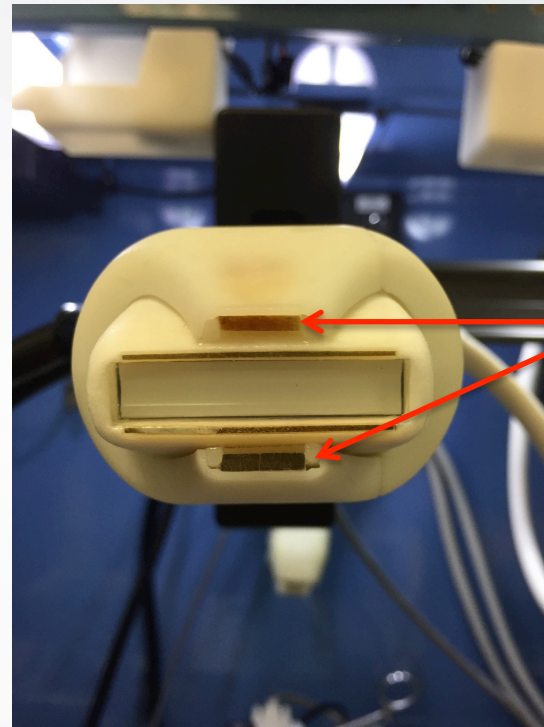***3mm depth**

Photoacoustic imaging
Brain imaging illumination setup
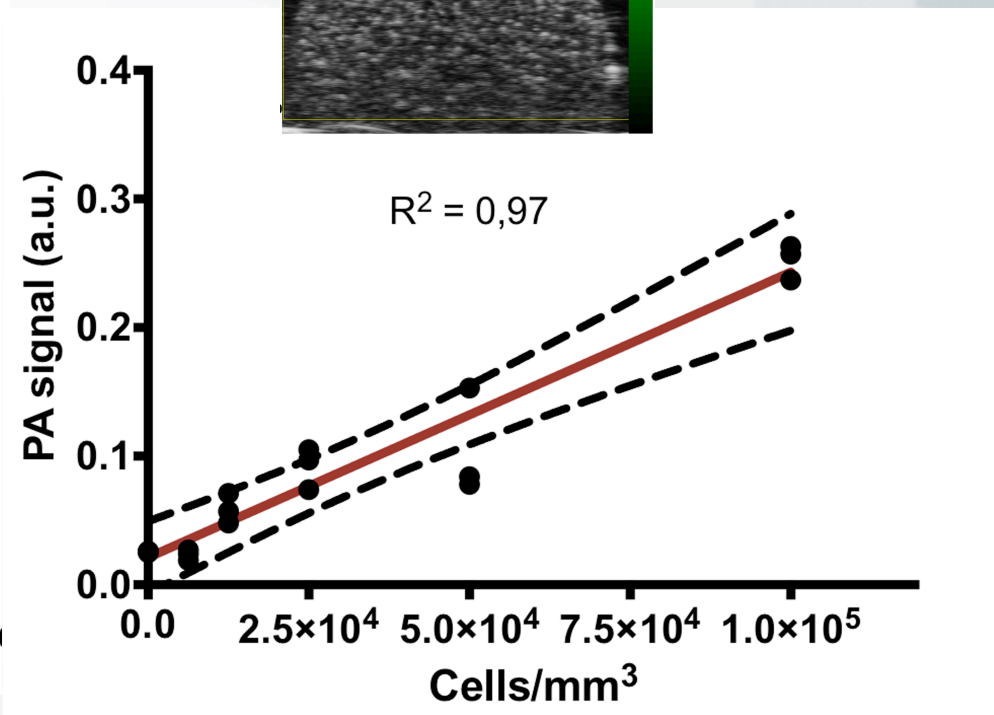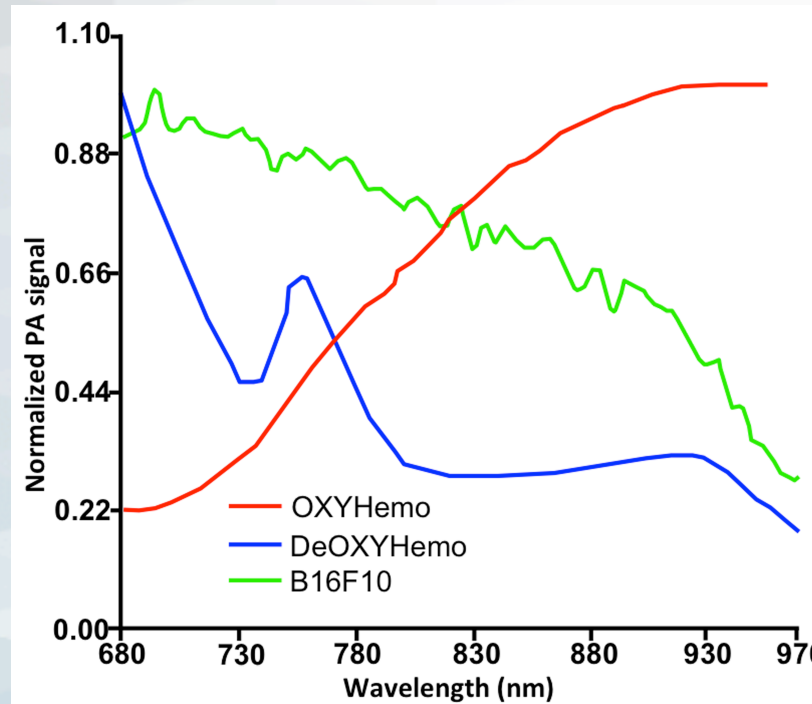

15MHz US transducer

Illumination jacket

Optical fibers

- **Vevo LAZR (2100)**
- **Lower frequency transducer : 15MHz, 200µm resolution : high sensitivity (PA)**
- **Illumination jacket : focus light on a smaller area**

B16F10 cells can be detected via the production of melanin using PAI

**Tissue mimicking phantom characterization :**

- Tunnel filed with different numbers of cells

→ **B16F10 Melanoma cells displayed a specific photoacoustic spectrum**

→ **that can be clearly separated from those of oxy- and deoxyhemoglobin**

→ **photoacoustic signal linearly correlated to the cell concentration**

→ **Detection limit : 625 cells**

Lavaud, J….and Josserand, V. (2017). *Int. J Pharm*.

In vivo experiments
Color dopler, Oxy-Hemo & Spectral unmixing 3D
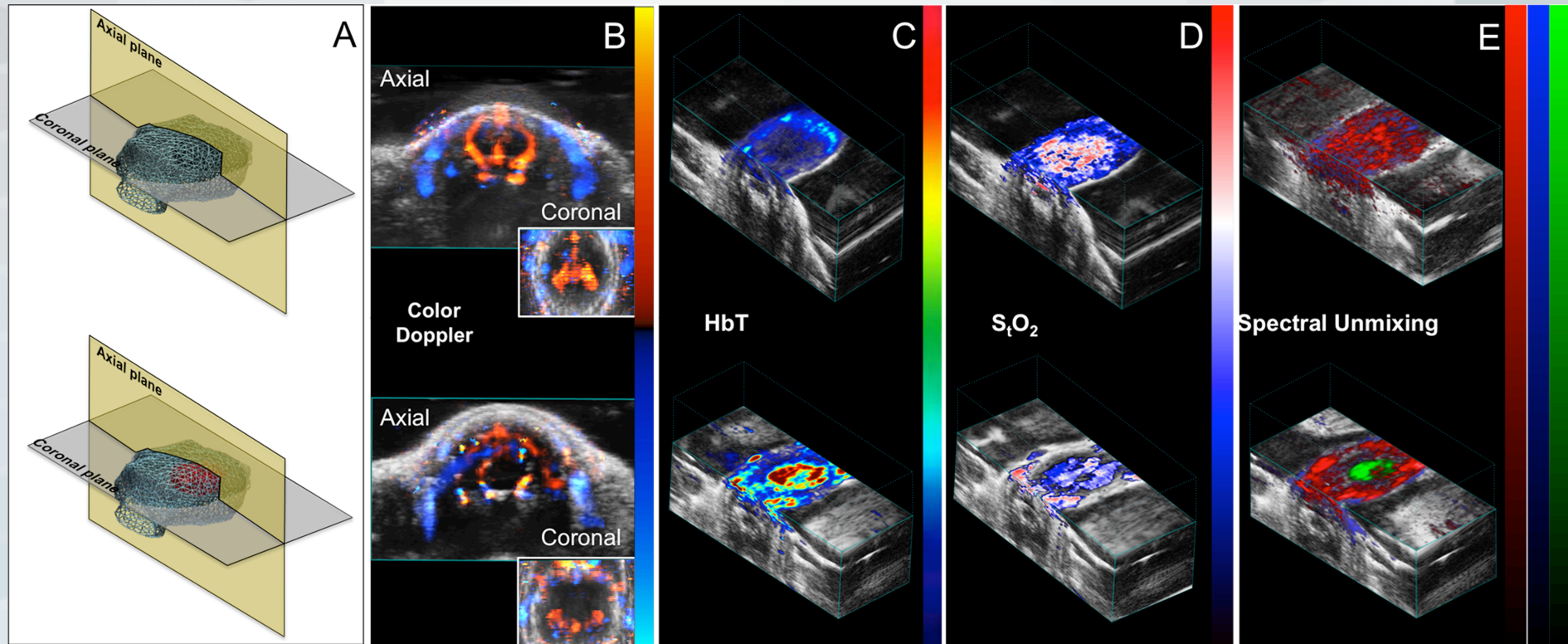
➔ **3D color Doppler allow access to brain vascularization in vivo**

➔ **Disorder of the cerebral vascularization in the tumor bearing animals**

➔ **High concentration of hemoglobin in the tumor area. Furthermore**

➔ **Oxygenation of the tumor is poor**
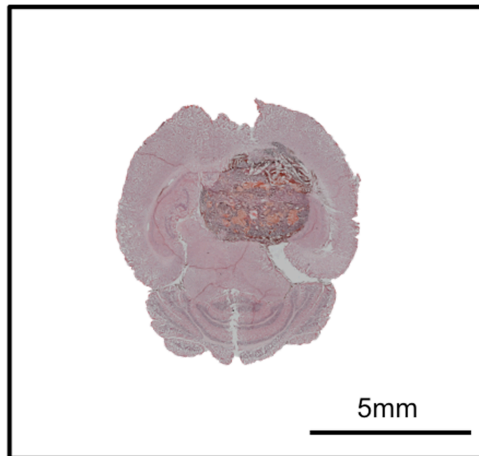
➔ **Clear spectral signature of B16F10 cells in the tumor region**

Lavaud, J....and Josserand, V. (2017). *Int. J Pharm*.
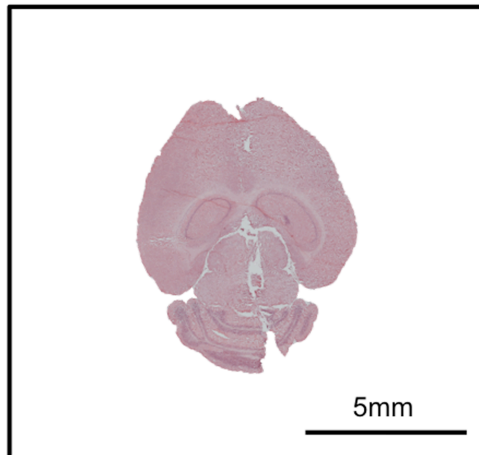
Ex vivo validation
Ex vivo spetroscopic PA & brain coloration
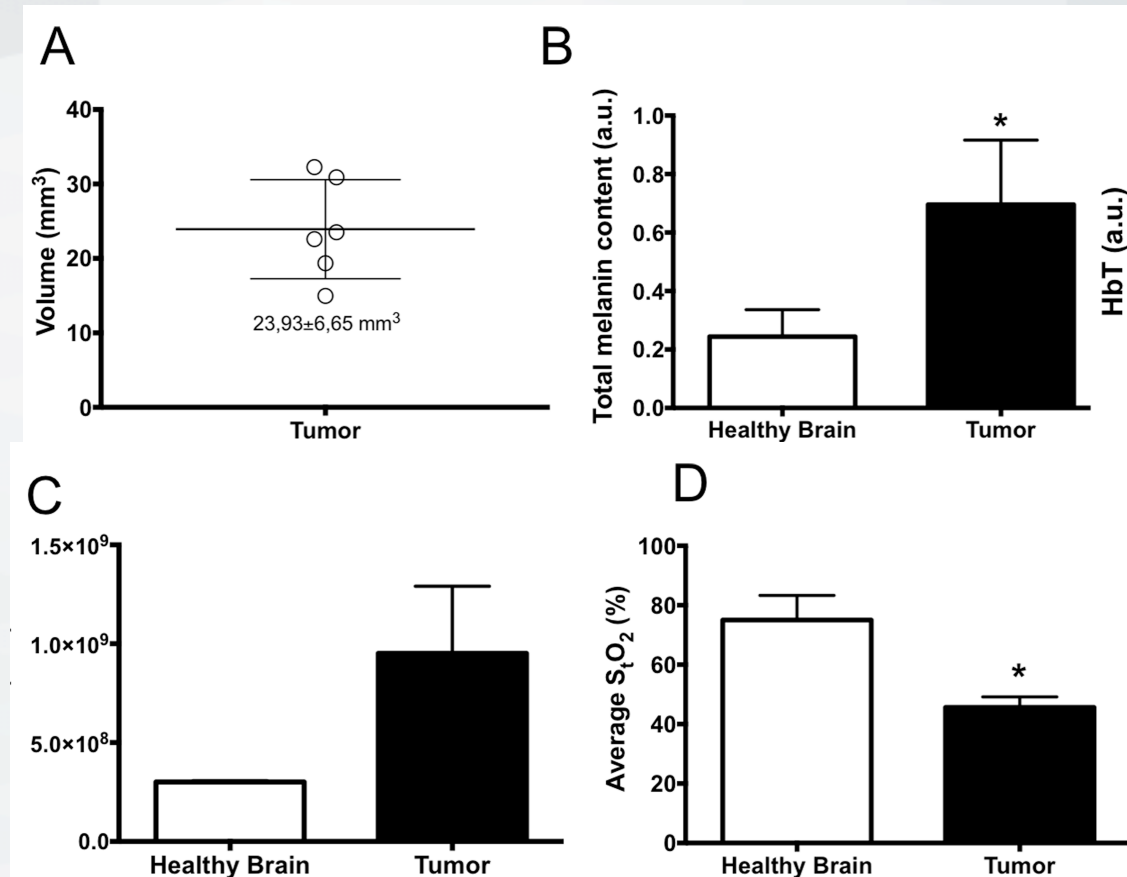

A *ex vivo* PA

B Histology

5mm

5mm
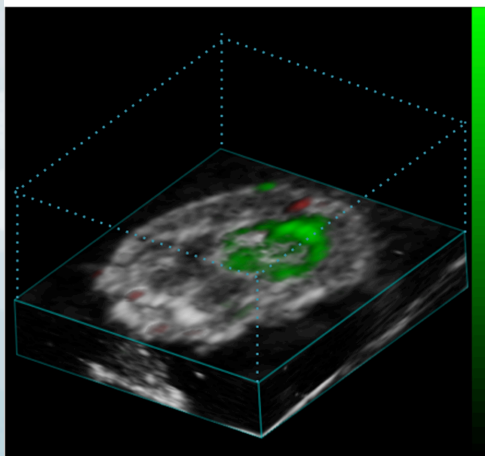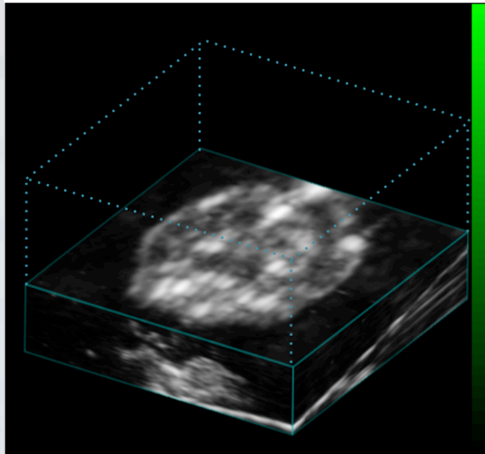
→ **High PA signal coming from melanin secreted by tumors**

→ **HE coloration cross-validation : presence of melanoma tumor cells on the right part of of the brain.**

**Lavaud, J**….and Josserand, V. (2017). *Int. J Pharm*.

In vivo experiments
B-mode, Oxy-Hemo & Spectral unmixing 3D

➜HbT and StO2 measurements in healthy brains were very reproducible (4 and 11% COV)

➜HbT appeared to be 0.70 to 6.31 times higher in tumor bearing brains

➜Tumors were hypoxic : mean StO2 39% lower

➜Spectroscopic PAI clearly revealed thepresence of melanin, PA signal 3 times higher

In vivo experiments
Oxy-Hemo 3D regio-selective analysis
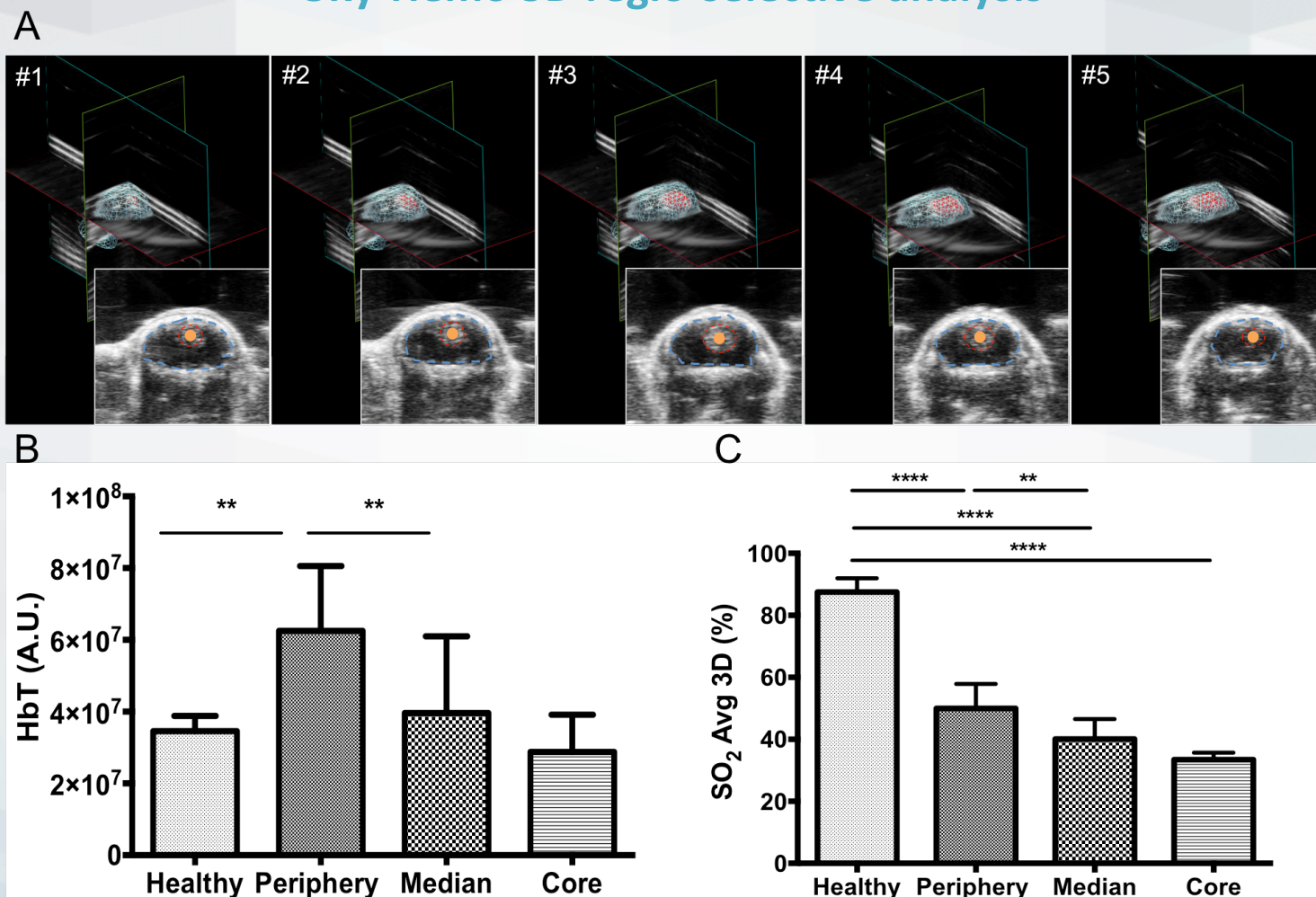
➔ **High vascularization on the periphery of tumors**
➔ **Progressive decrease when heading to the core**
➔ **Tumor less : oxygen gradient, from the periphery to the core of tumors**

**Lavaud, J**….and Josserand, V. (2017). *Int. J Pharm*.

Take Home Messages

PAI (Vevo LAZR) :

- **Sensitivity** of Optical imaging and **Resolution** of US imaging
- **Multi-wavelengths studies** (680 to 970nm)
- Access to **Anatomical**, **Functionnal** and **Molecular** imaging within the same acqusition
- Detection of a small amount of B16F10 cells (phantom) : **625** cells

Brain imaging:

- Access to main brain vascularization (Color doppler)
- Light delivery in depth :
  - ✓ Hemoglobin content & tissues oxygene saturation
  - ✓ *In vivo* detection of melanoma via melanin production
- Biological informations about tumor heterogeneity
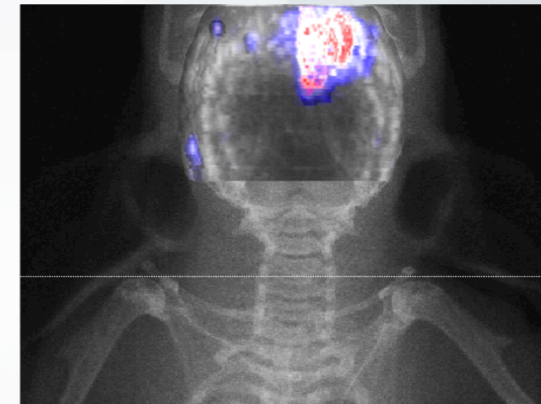
THANKS !

UGA/INSERM U1209
Team Coll

Jean Luc Coll
Amandine Hurbin
Annie Molla
Véronique Frachet
Benoit Busser
Lucie Sancey
Xavier Leguevel
Maxime Henry
Morgane Couvet

Laetitia Falcon
Pascal Perron
Thibault Jacquet
JungYoon Choi
Estelle Porret
Pauline Gilson
Tao Jia
Tristan Legast
Tristan Leclainche

Optimal Grenoble

Véronique Josserand
Julien Vollaire
Mélanie Guidetti

FUJIFILM
VISUALSONICS

Philippe Trochet

IAB
EPIGENETICS
CHRONIC DISEASES
CANCER

cnrs

Inserm

Secteur Santé
UNIVERSITÉ
Grenoble
Alpes

FINYS
French Imaging Network of Young Scientists