

# Utilisation d'une sonde miniaturisée de détection de la fluorescence dans la chirurgie des métastases hépatiques: étude clinique préliminaire

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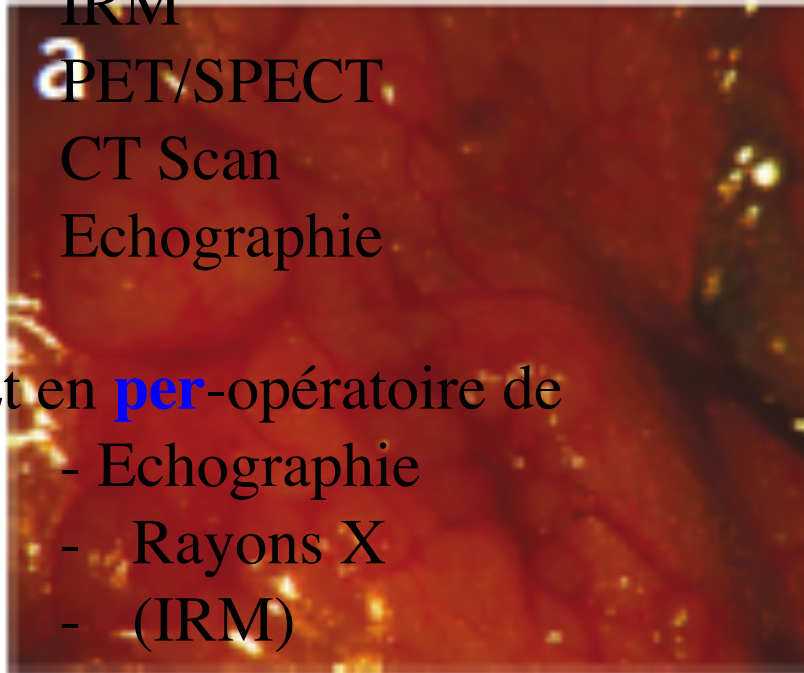
# Intérêt de l'imagerie per-opératoire

Le chirurgien dispose d'une visualisation **pré**-opératoire en :

- IRM
- PET/SPECT
- CT Scan
- Echographie

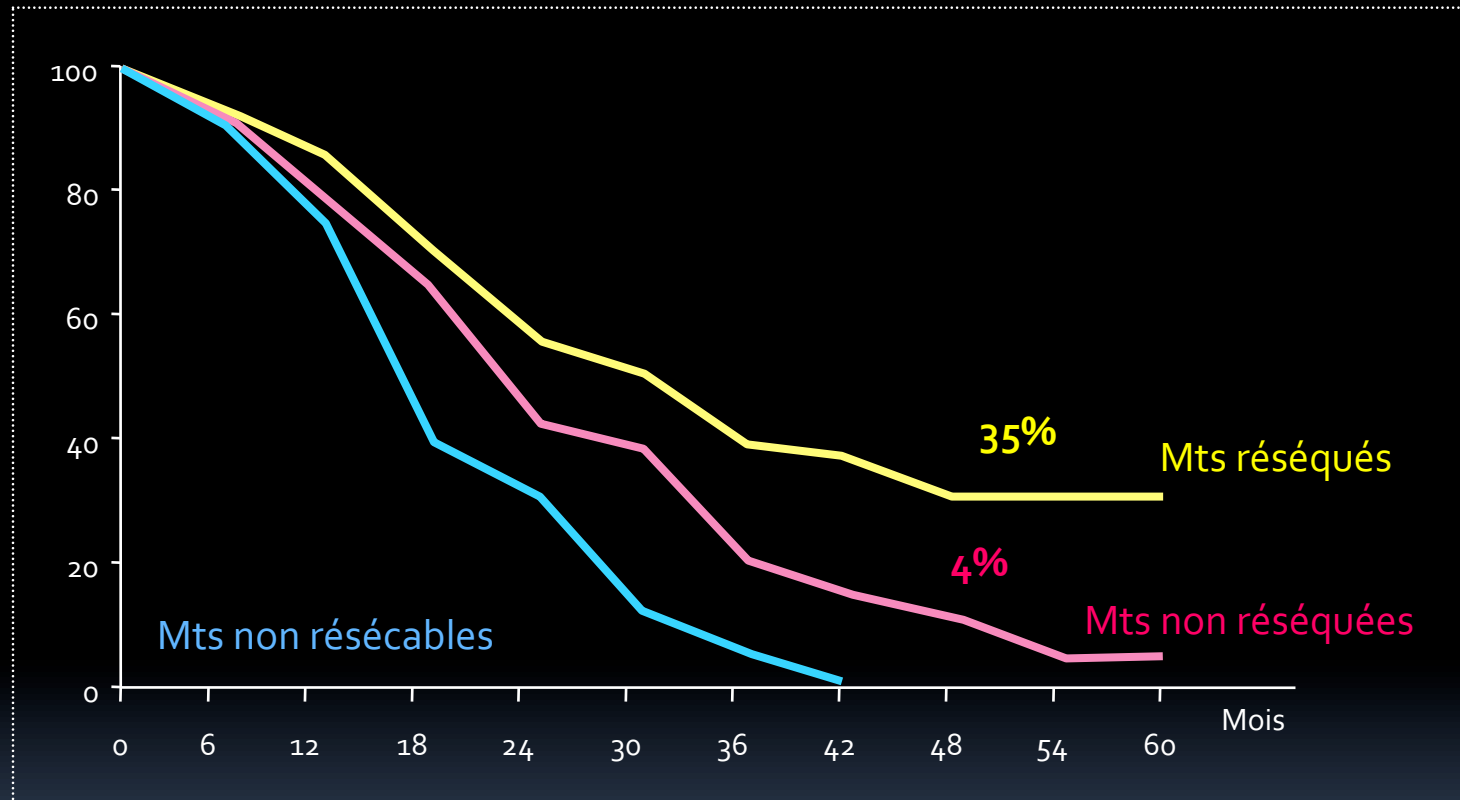
Et en **per**-opératoire de

- Echographie
- Rayons X
- (IRM)



Van Dam et al. Nature Medicine, 2011

# LA RÉSECTION EST LE SEUL TRAITEMENT CURATIF\*



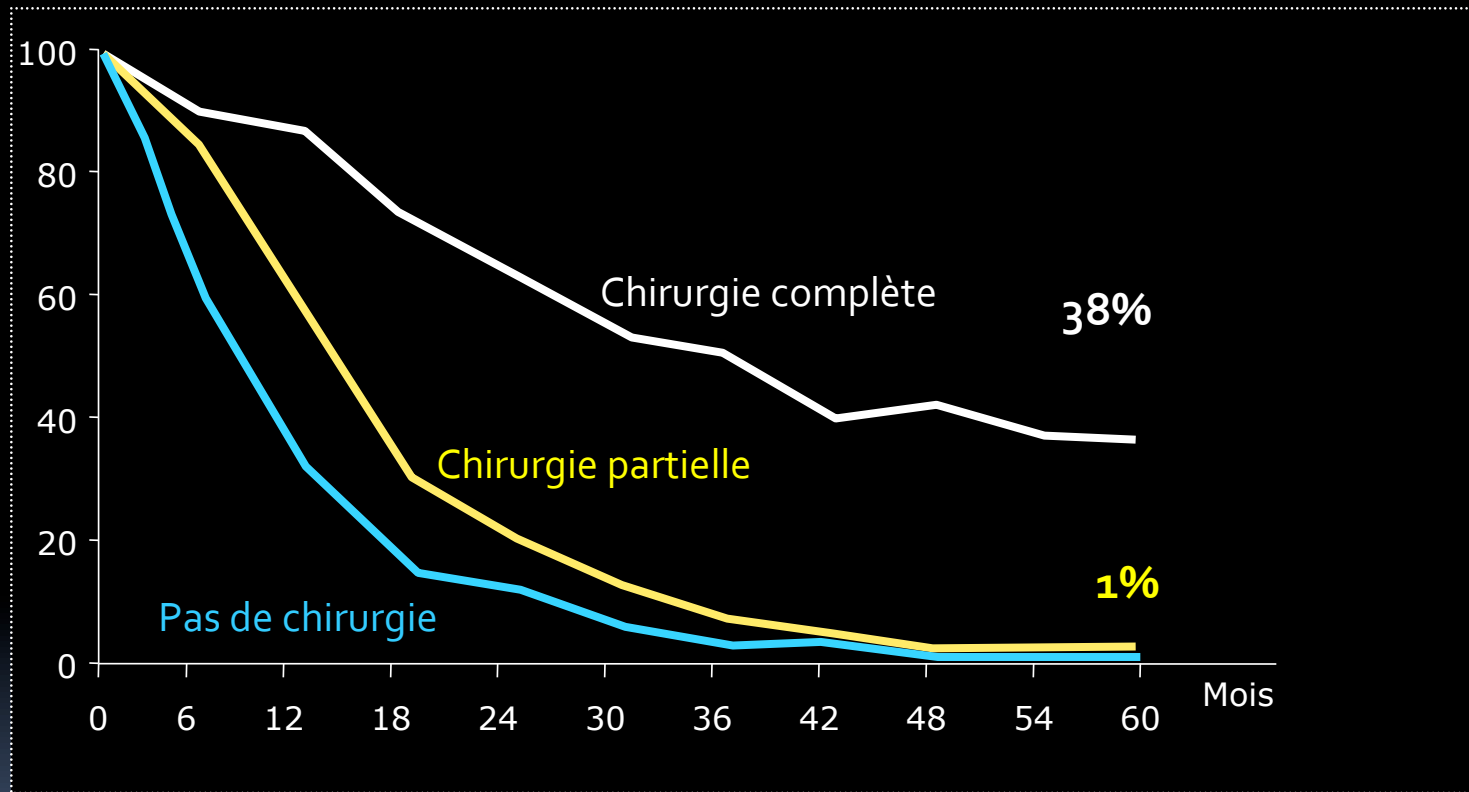
**Même si il existe quelques survies a long terme avec la seule chimio!**

NCCTG, 30 trials 74-93, 3514 patients, 36 survivants (1%) à plus de 5 ans\*\*

\*Wagner JS. Ann Surg 1984;199:502-8

\*\*Hobday TJ, ASCO 2002, Abstract #693

# LA RÉSECTION PARTIELLE EST SANS INTÉRÊT ONCOLOGIQUE\*



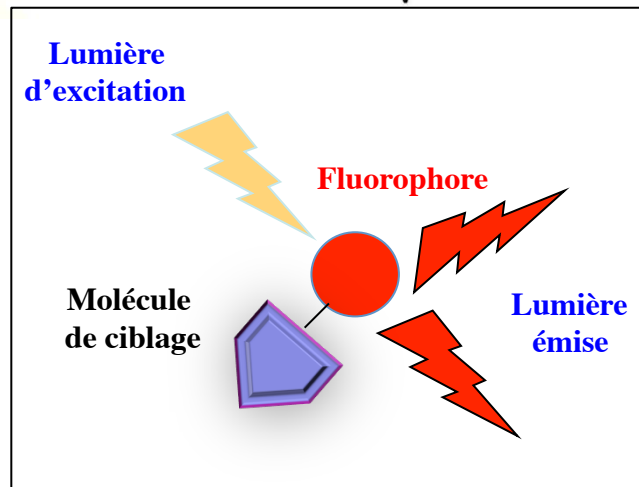
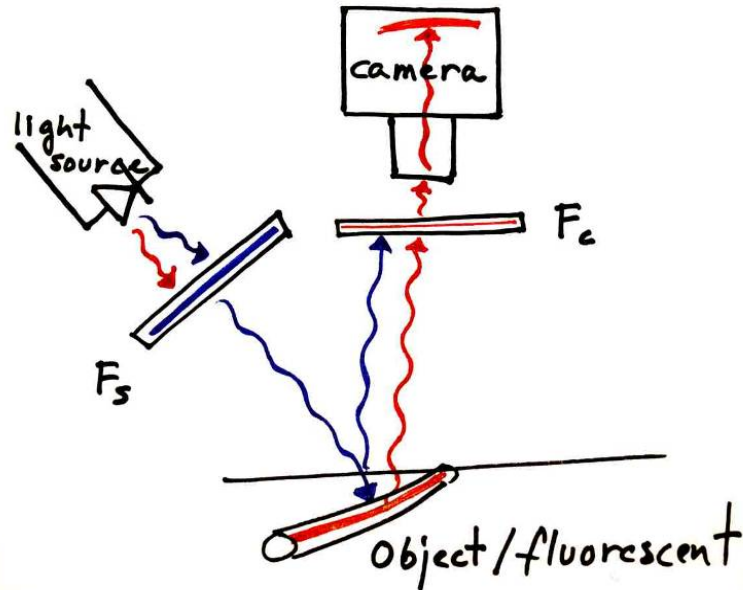
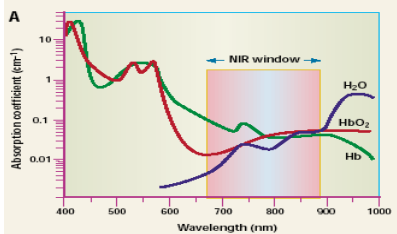
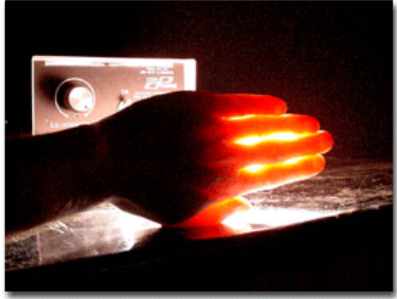
\*Scheele J. World J Surg 1995;19:59-71

# Intérêt de l'Imagerie optique pour le chirurgien????



**Verrou:** voir dans le proche infra-rouge même si la lampe scialytique est allumée (>150 000 Lux de lumière blanche)

# Comment ça marche...



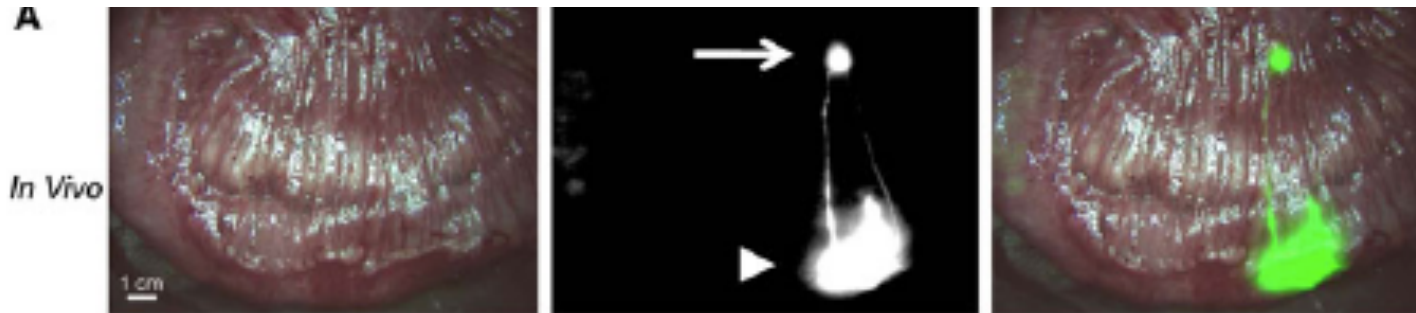
# Intérêt de l'Imagerie optique pour le chirurgien????

- Ganglion sentinelle
- Détection de petites tumeurs
- Marges saines
- Chirurgie vasculaire
- ....



# DETECTION DU GANGLION SENTINEL

## Clinical Translation of Ex Vivo Sentinel Lymph Node Mapping for Colorectal Cancer Using Invisible Near-Infrared Fluorescence Light

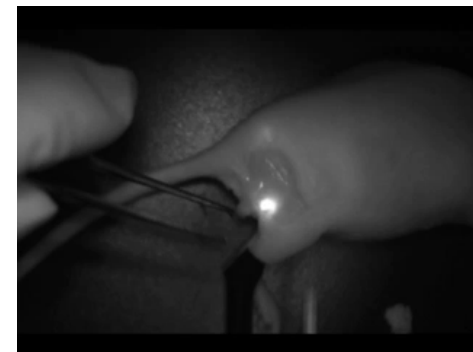


Hutteman *et al.*

Ann Surg Oncol  
DOI 10.1245/s10434-010-1426-0



Le chirurgien ne voit pas l'écran



Le chirurgien voit l'écran....



TABLE II. Clinical Trials Using ICG as a Near-Infrared Fluorescent Lymphatic Tracer for SLN Procedures

| Refs.                           | No. patients | Tumour stage                        | Imaging system   | Dose of ICG                          | Site of injection                                  | Other used SLN tracer | IR (%)            | FNR       | Avg. no. SLNs    |
|---------------------------------|--------------|-------------------------------------|------------------|--------------------------------------|--|-----------------------|-------------------|-----------|------------------|
| <b>Breast cancer</b>            |              |                                     |                  |                                      |  |                       |                   |           |                  |
| Kitai et al. [13]               | 18           | T1-2, cN0                           | PDE              | 5.0 ml, 6.4 mM                       | Subareolar   | None                  | 94                | NA        | 2.8              |
| Ogasawara et al. [19]           | 37           | Tis-T4                              | PDE              | 5.0 ml, 6.4 mM                       | s.c. subareolar and peritumoural                   | BD or BD + RT         | NA                | NA        | NA               |
| Sevick-Muraca et al. [16]       | 24           | <3 cm, cN0                          | FDPM imager      | 0.1-3.0 ml, 0.31-100 µg <sup>a</sup> | s.c. periareolar and/or i.e. and deep peritumoural | RT                    | 87.5 <sup>b</sup> | NA        | 1.7 <sup>b</sup> |
| Tagaya et al. [18]              | 25           | <3 cm                               | PDE              | 1.0 ml, 6.4 mM                       | s.c. periareolar                                   | BD                    | 100               | NA        | 5.4              |
| Troyan et al. [3]               | 6            | T1                                  | FLARE            | 1.6 ml, 0.01 mM ICG:HSA              | Deep and s.c. peritumoural                         | RT                    | 100               | NA        | 1.5              |
| Murawa et al. [12]              | 30           | <3 cm, cN0                          | IC-view          | 1.0-3.0 ml, 6.4 mM                   | i.e. periareolar                                   | None or RT            | 97                | 2/21      | 1.75             |
| Hirche et al. [14]              | 43           | <3 cm, cN0                          | IC-view          | 11 mg <sup>a</sup>                   | Subareolar   | BD                    | 97.7              | 1/18      | 2.0              |
| Hojo et al. [15]                | 141          | Tis-T2, cN0                         | PDE              | 2.0 ml <sup>a</sup>                  | i.e. peritumoural and subareolar                   | BD or RT              | 99.3              | NA        | 3.8              |
| Tagaya et al. [20]              | 150          | <3 cm, cN0                          | PDE              | 0.75 ml, 3.2 mM                      | s.c. periareolar                                   | BD                    | 98.7              | NA        | 3.7              |
| Tagaya et al. [21]              | 50           | <2 cm, cN0                          | PDE              | 1.0 ml, 1.6 mM                       | s.c. periareolar                                   | BD                    | 100               | NA        | 3.7              |
| Mieog et al. [17]               | 24           | Tis-T2, cN0                         | Mini-FLARE       | 1.6 ml, 0.05-1 mM                    | i.e. periareolar or s.c. peritumoural              | BD + RT               | 100               | NA        | 1.45             |
| <b>Skin cancer</b>              |              |                                     |                  |                                      |  |                       |                   |           |                  |
| Fujiwara et al. [22]            | 10           | MM, SCC, T1-4, cN0-3                | PDE              | 0.6-0.8 ml, 6.4 mM                   | Peritumoural                                       | None or BD            | 100               | NA        | NA               |
| Tanaka et al. [24]              | 6            | MM, EPD, SCC                        | PDE              | 1.0 ml, 6.4-10.2 mM                  | Peritumoural                                       | RT                    | 100               | NA        | NA               |
| Tsujino et al. [25]             | 2            | EPD, SCC                            | PDE              | 1.0 ml, 6.4 mM                       | Intra- or peritumoural                             | RT                    | 100               | NA        | NA               |
| Mizukami et al. [23]            | 24           | MM, EPD, SCC, EPC                   | PDE              | 0.6-2.0 ml, 6.4 mM                   | Peritumoural                                       | None                  | 95.8              | NA        | NA               |
| <b>Gastro-intestinal cancer</b> |              |                                     |                  |                                      |  |                       |                   |           |                  |
| Kusano et al. [26]              | 22, 26       | Gastric T1-3, colorectal T1-3       | PDE              | 2.0 ml, 6.4 mM                       | s.s. intraoperative                                | None                  | 90.9, 88.5        | 6/10, 4/6 | 3.6, 2.6         |
| Miyashiro et al. [27]           | 3            | Gastric T1                          | PDE              | 2.0-4.0 ml <sup>a</sup>              | Intra- or 1 day preoperative                       | None                  | 100               | NA        | 3.0              |
| Tajima et al. [28]              | 56           | Gastric pT1-3                       | PDE              | 2.0 ml, 6.4 mM                       | s.m. 1-3 days preoperative or s.s. intraoperative  | None                  | 96.4              | 6/17      | 7.2              |
| Noura et al. [7]                | 25           | Rectal T1-3                         | PDE              | 1.0 ml, 6.4 mM                       | s.m. before laparotomy                             | None                  | 92                | 0/3       | 2.1              |
| Tajima et al. [29]              | 77           | Gastric T1-3                        | PDE              | 2.0 ml, 6.4 mM                       | s.m. 1-3 days preoperative or s.s. intraoperative  | None                  | 94.8              | 4/17      | 7.5              |
| <b>Other cancer</b>             |              |                                     |                  |                                      |  |                       |                   |           |                  |
| Crane et al. [4]                | 10           | Stage IA1, IB1, IIA cervical cancer | Munich prototype | 1.0 ml, 0.64 mM                      | Intraoperative in four quadrants of the cervix     | BD                    | 60 in vivo        | 0/1       | 1.5              |
| Crane et al. [8]                | 10           | Stage T1/2 vulvar cancer            | Munich prototype | 1.0 ml, 0.64 mM                      | Peritumoural                                       | BD + RT               | 100               | NA        | 2.6              |
| Bredell [9]                     | 8            | Oropharyngeal cancer                | PDE              | 1.0 ml, 12.9 mM                      | Peritumoural                                       | None                  | 100               | NA        | 3.0              |
| Yamashita et al. [10]           | 31           | Stage I non-small-cell lung cancer  | NS               | 2.0 ml, 6.4 mM                       | Peritumoural                                       | None                  | 80.7              | NA        | 1.3              |
| Hirche et al. [11]              | 12           | Anal squamous-cell cancer, cN0      | IC-View          | 5.0 ml, 6.4 mM                       | Peritumoural subdermal                             | BD + RT               | 83.3              | NA        | 1.6              |

IR, identification rate; FNR, false-negative rate; NA, not available; s.c., subcutaneous; BD, blue dye; RT, radiotracer; i.e., intracutaneous; ICG:HSA, indocyanine green adsorbed to human serum albumin; MM, malignant melanoma; SCC, squamous cell carcinoma; EPD, extramammary Paget's disease; EPC, eccrine porocarcinoma; s.s., subserosal; s.m., submucosal; NS, not specified.

<sup>a</sup>Concentration not available.

<sup>b</sup>Only in those patients receiving >10 µg ICG (N = 7).

# Intérêt de l'Imagerie optique pour le chirurgien????

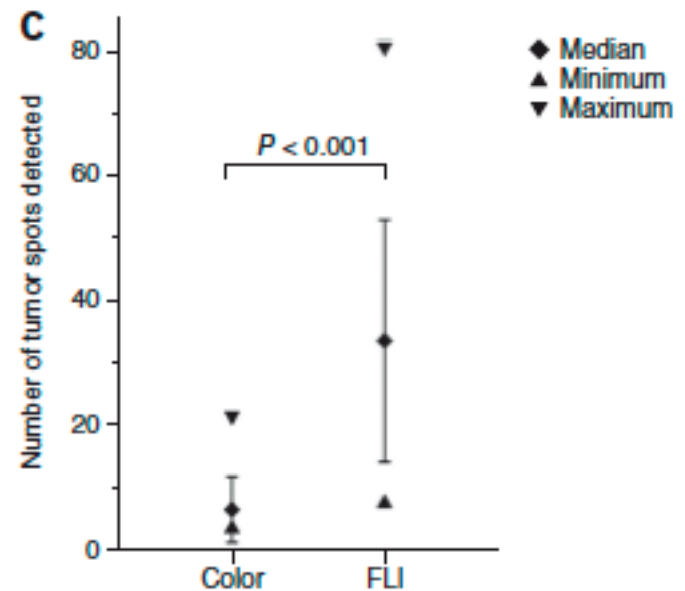
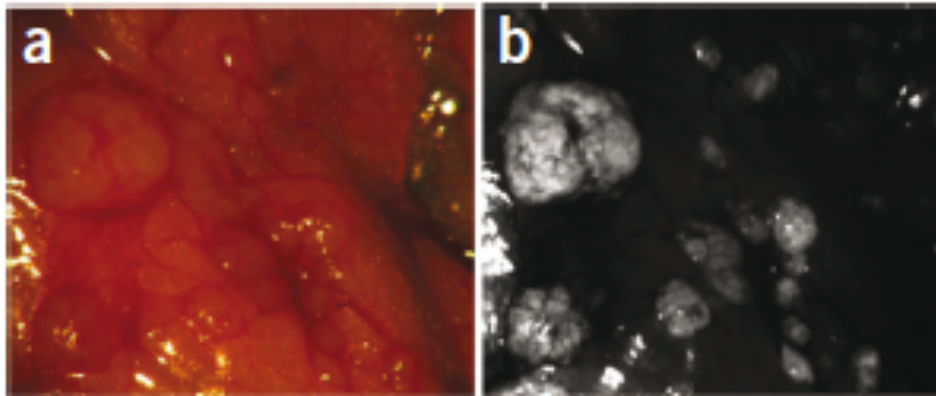
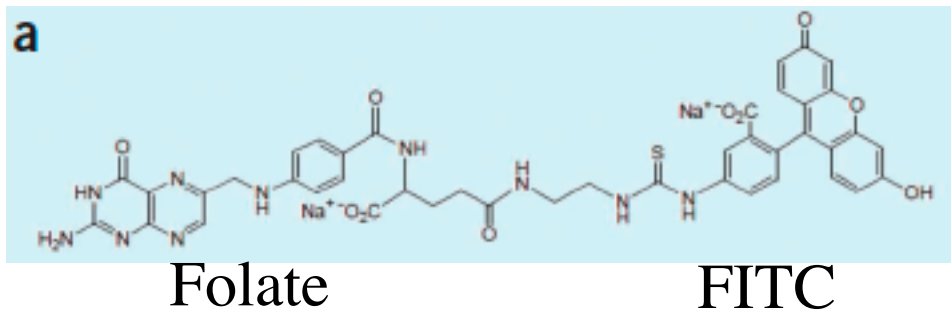
- Ganglion sentinelle
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- Marges saines
- Chirurgie vasculaire
- ....



# Intraoperative tumor-specific fluorescence imaging in ovarian cancer by folate receptor- $\alpha$ targeting: first in-human results

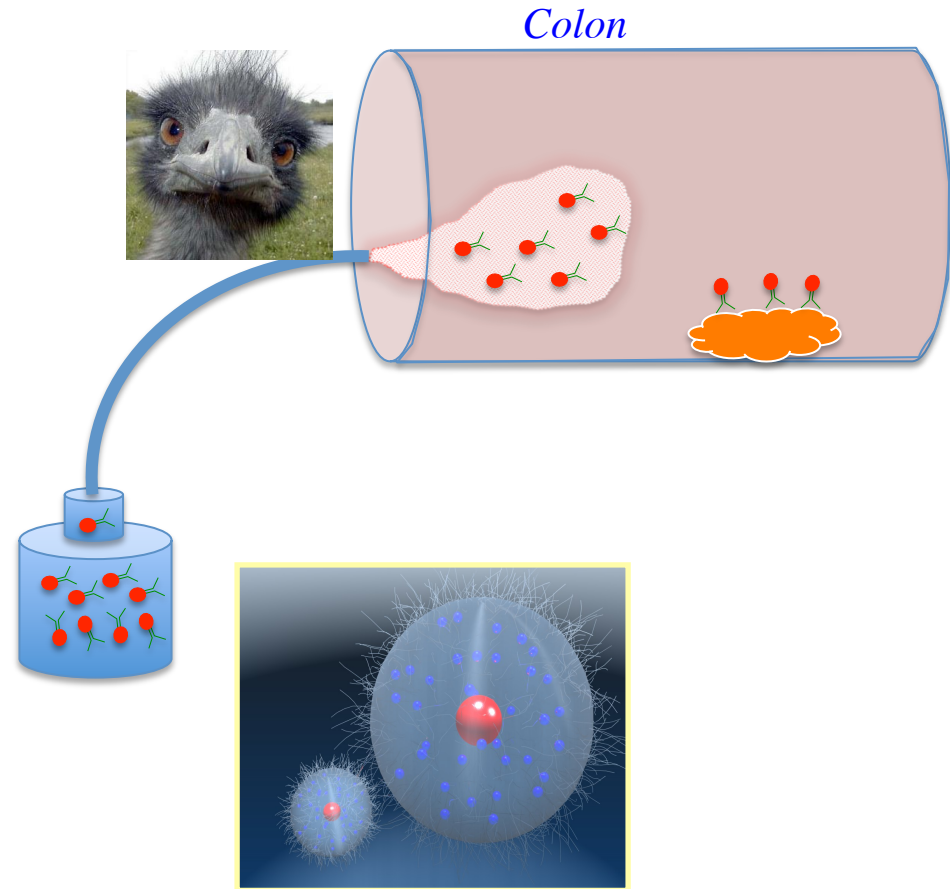
Gooitzen M van Dam<sup>1</sup>, George Themelis<sup>2</sup>, Lucia M A Crane<sup>1</sup>, Niels J Harlaar<sup>1,2</sup>, Rick G Pleijhuis<sup>1</sup>, Wendy Kelder<sup>1</sup>, Athanasios Sarantopoulos<sup>2</sup>, Johannes S de Jong<sup>1</sup>, Henriette J G Arts<sup>3</sup>, Ate G J van der Zee<sup>3</sup>, Joost Bart<sup>4</sup>, Philip S Low<sup>5</sup> & Vasilis Ntziachristos<sup>2</sup>

NATURE MEDICINE VOLUME 17 | NUMBER 10 | OCTOBER 2011



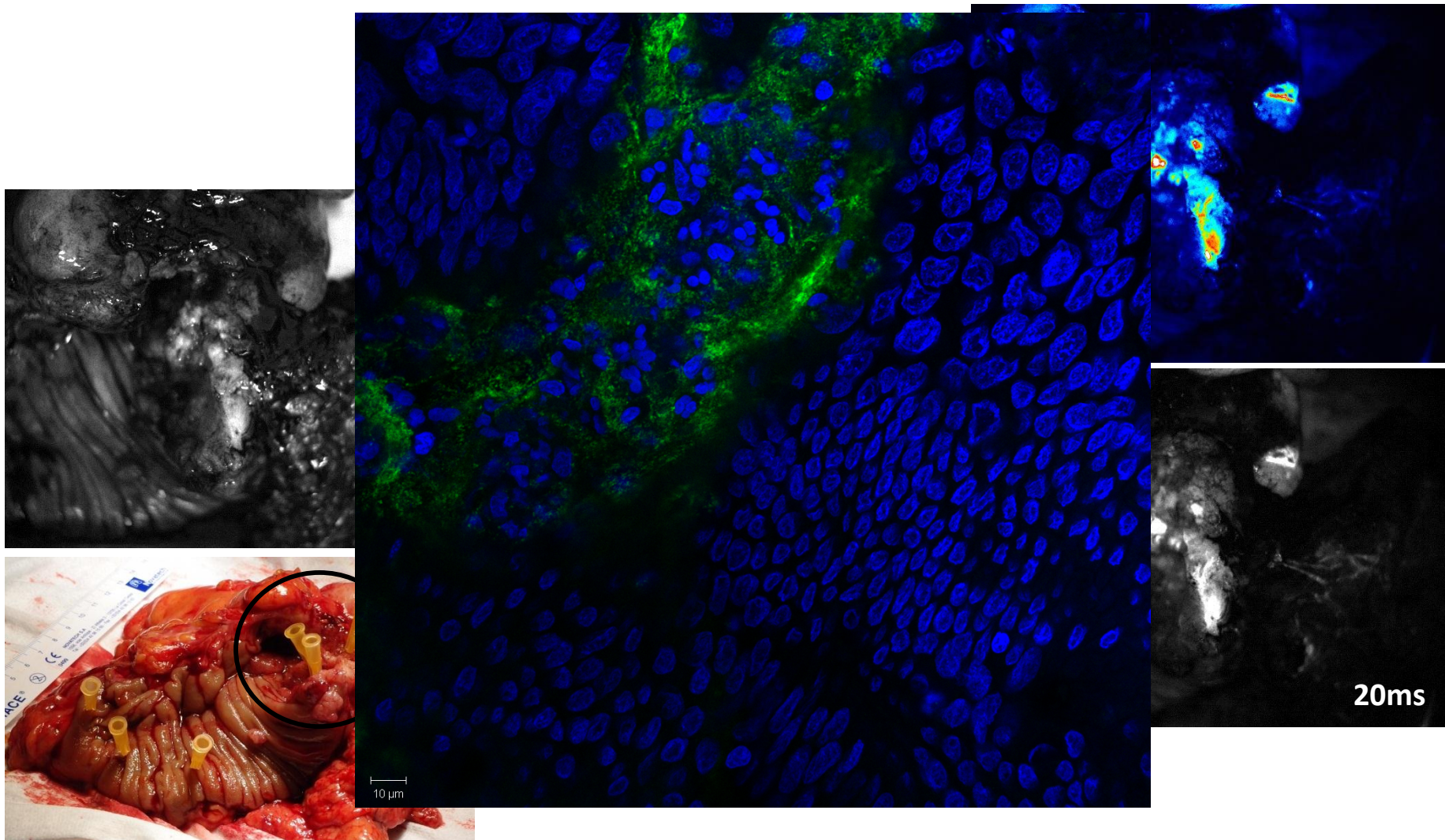
# Chirurgie du cancer du colon chez l'homme

- Dr Gabriele BARABINO
- *Université Jean Monnet – CHU Saint Etienne*
- *Laboratoire LINA EA 4624 (Saint Etienne)*
- *Equipe 5 Institut Albert Bonniot INSERM 823*



F. Lux, O. Tillement, LPCML, Lyon

# Chirurgie du colon guidée par l'optique



# Intérêt de l'Imagerie optique pour le chirurgien????

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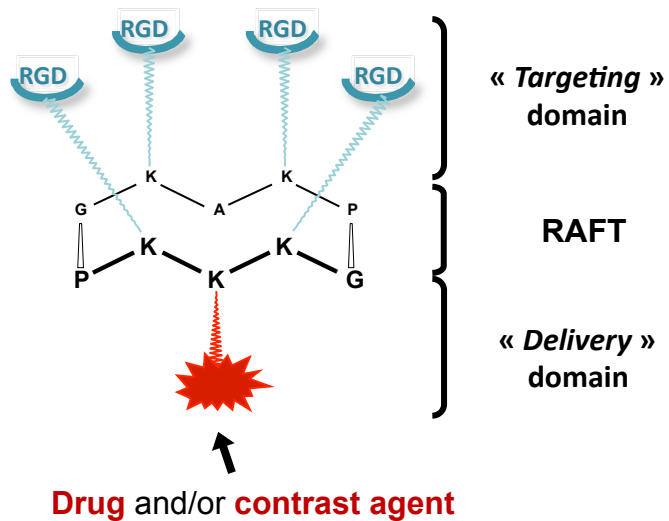


# Chirurgie du fibrosarcome chez le chat: Marges saines

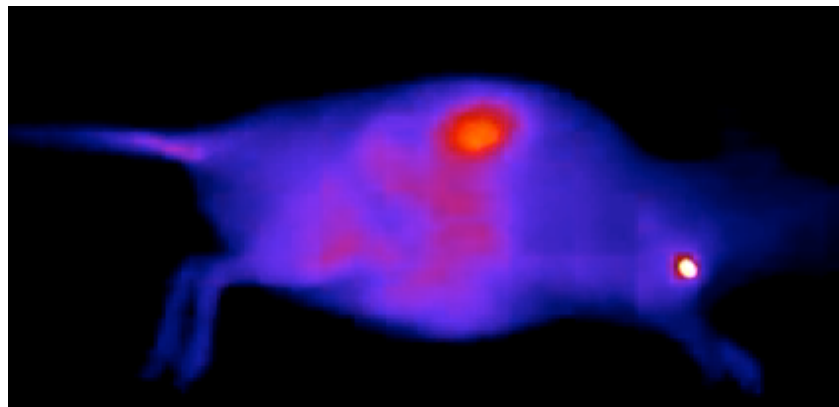
- Christiane Wenk



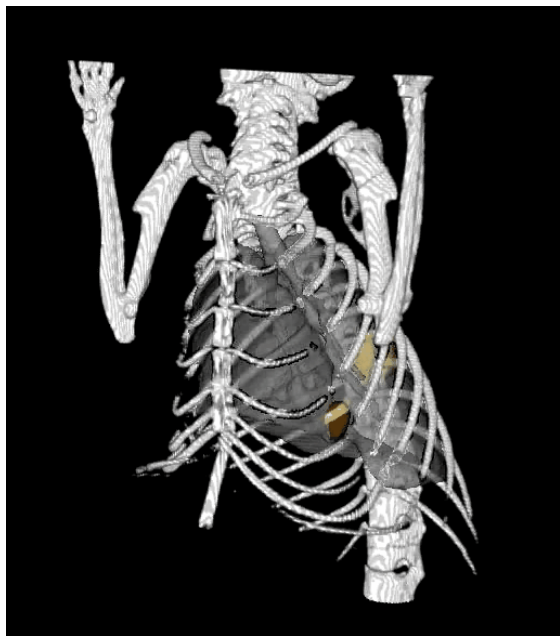
# Ciblage des tumeurs



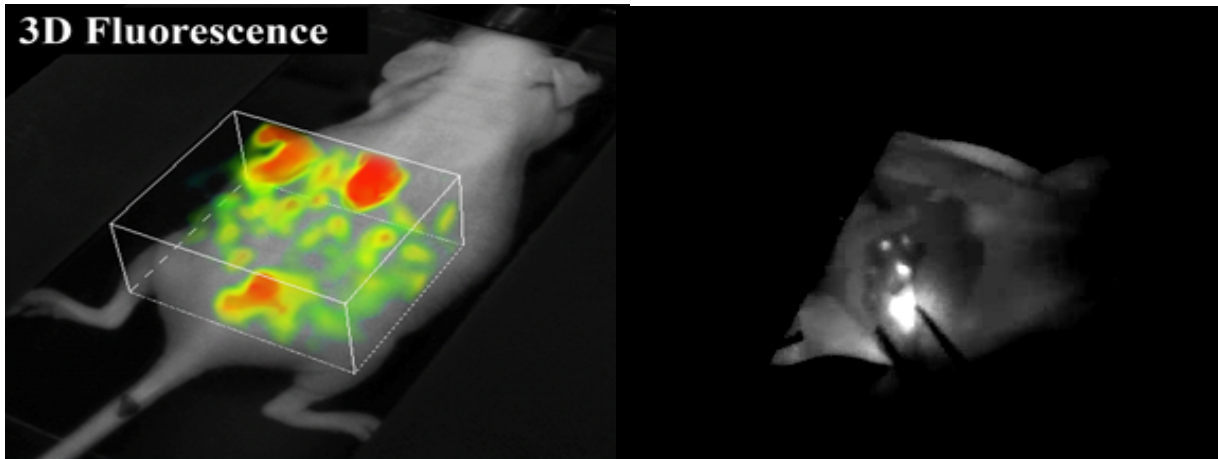
Tumeurs sous cutanées



Tumeurs orthotopiques du poumon

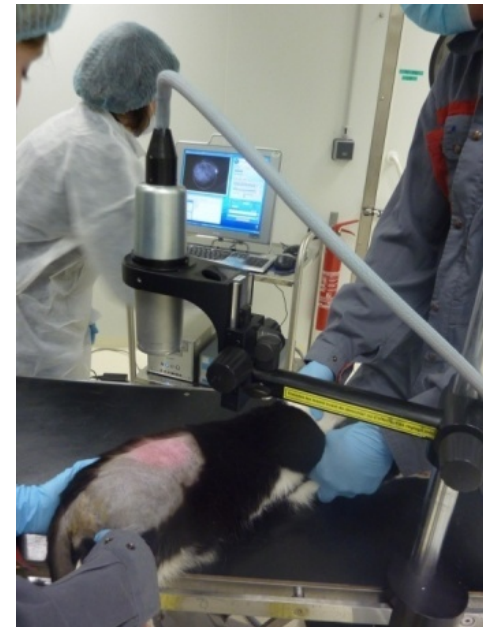
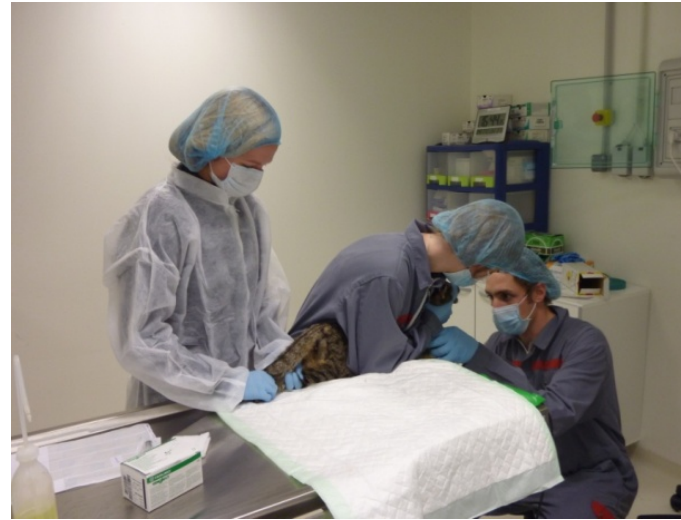


Métastases ovariennes





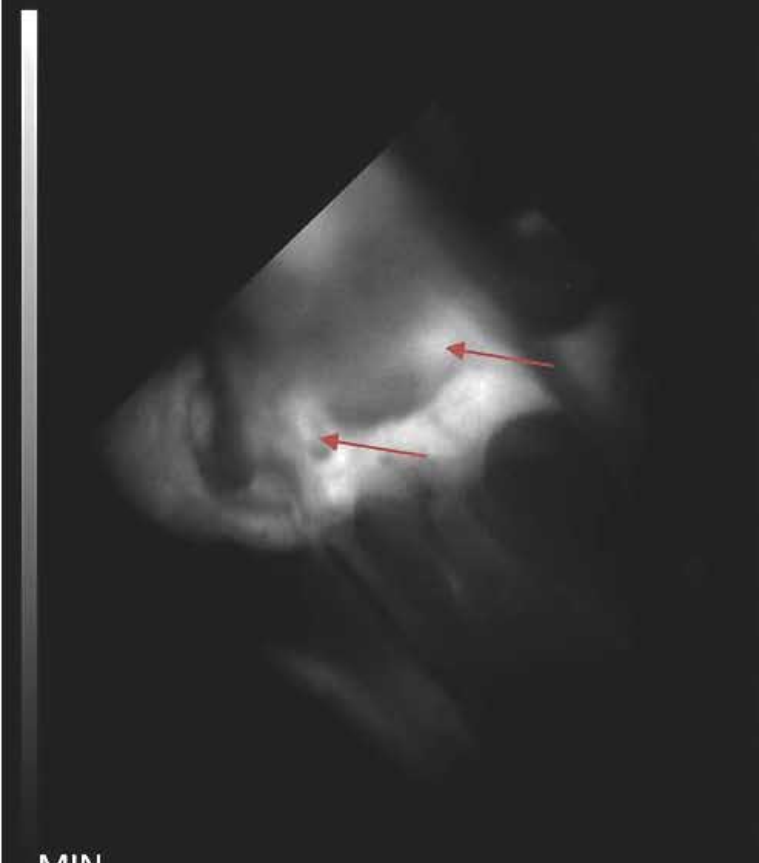
# Chirurgie chez le chat



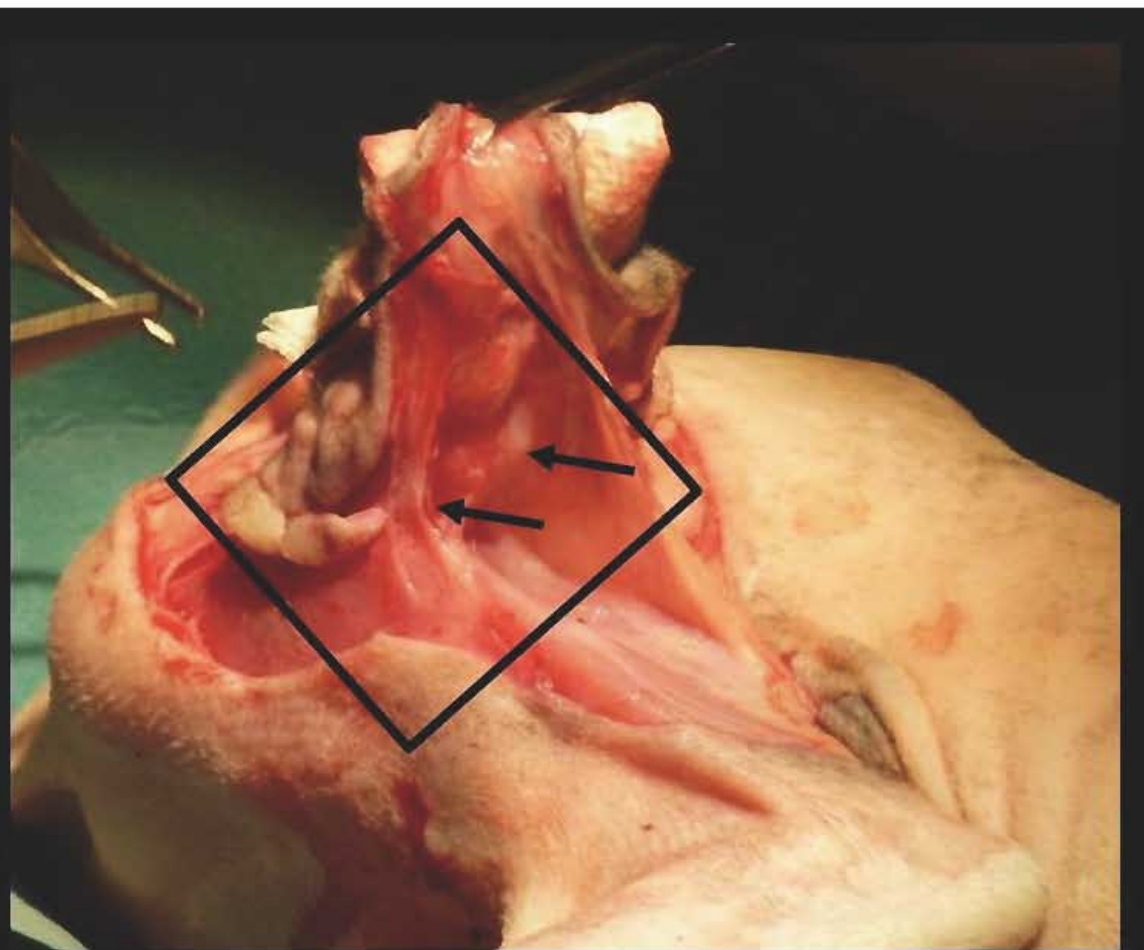
- Collaboration:
- Vet AgroSup – Lyon
  - CLB Lyon

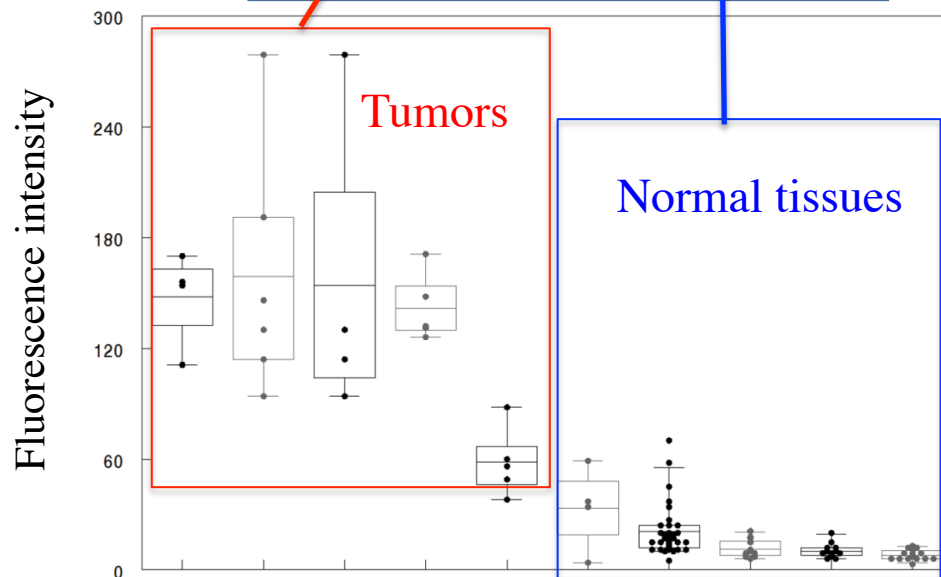
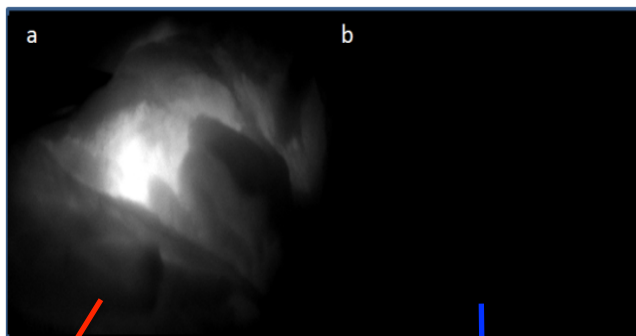
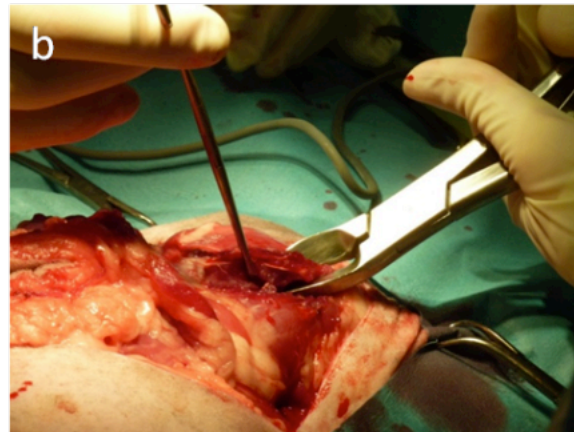


MAX



MIN





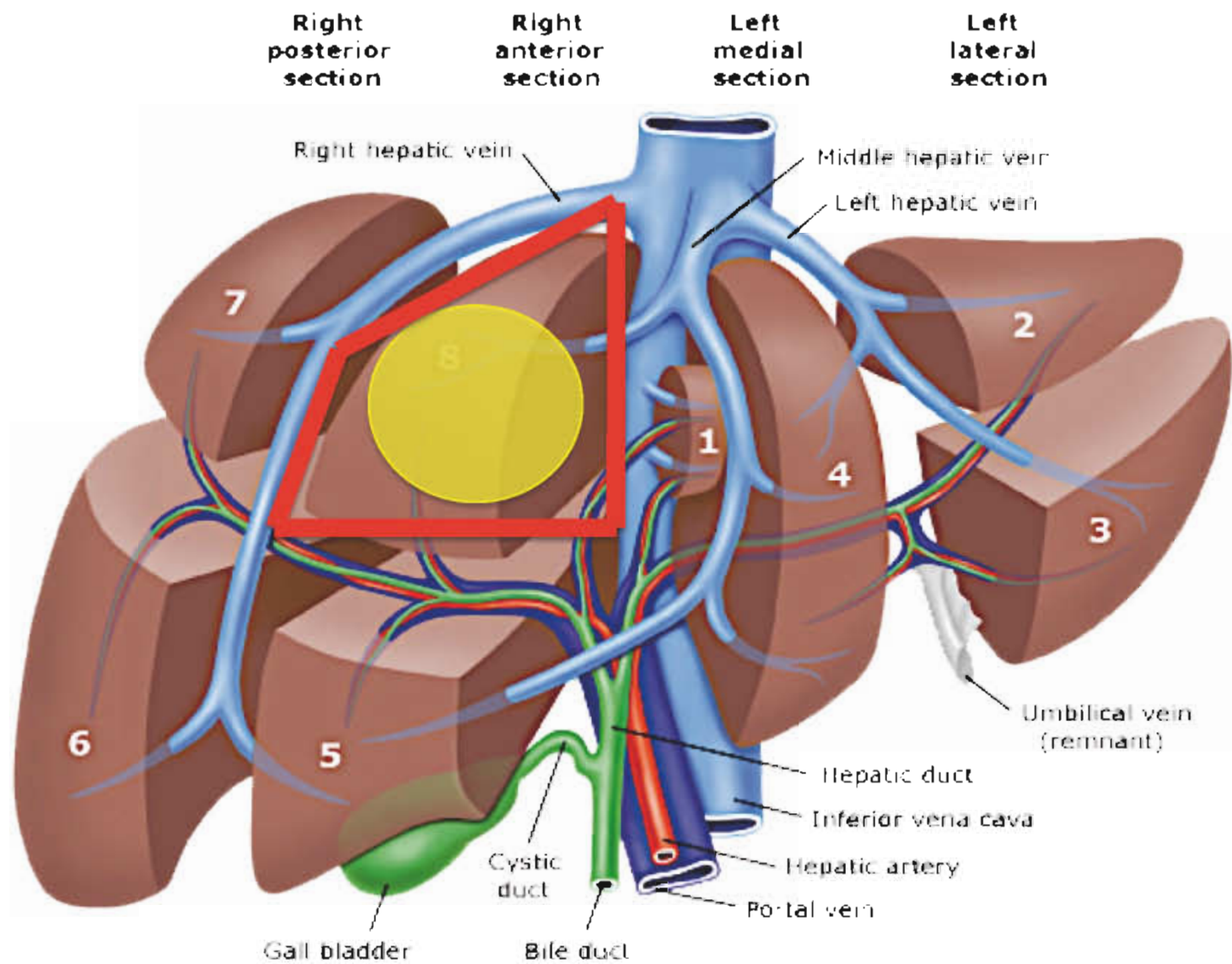
# Chirurgie du cancer du foie chez l'homme

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- *Laboratoire LINA EA 4624 (Saint Etienne)*
- *Equipe 5 Institut Albert Bonniot INSERM 823*

## *Participants*

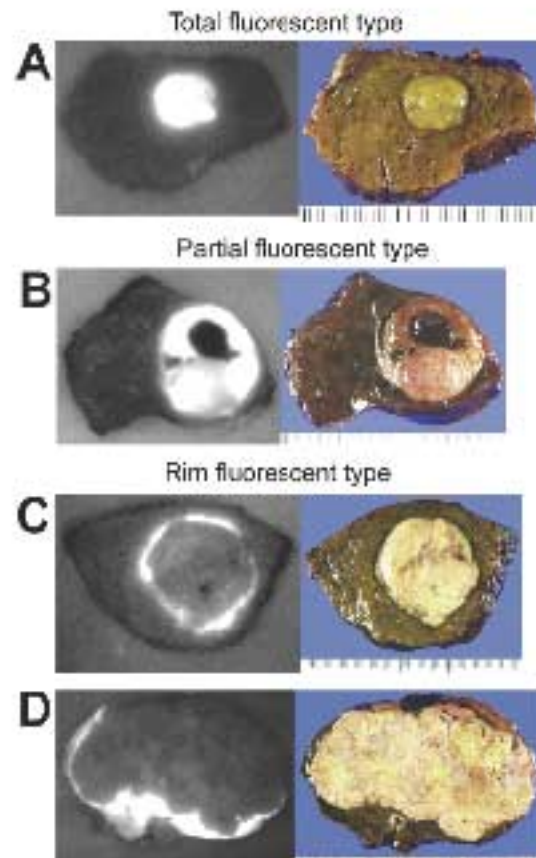
*Michelle Keramidas (INSERM U823)*

*Jean-Guillaume Coutard (CEA-LETI Grenoble)  
Michel Berger*

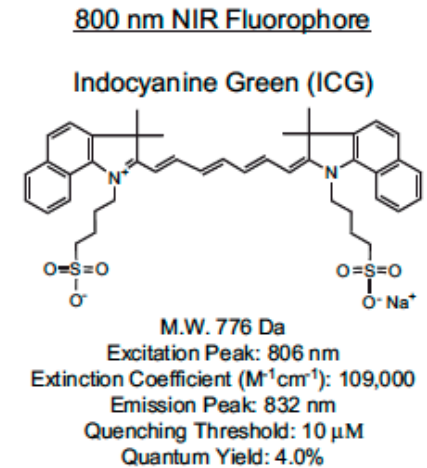


# Real-Time Identification of Liver Cancers by Using Indocyanine Green Fluorescent Imaging

Takeaki Ishizawa, MD<sup>1</sup>, Noriyoshi Fukushima, MD, PhD<sup>2</sup>, Junji Shibahara, MD, PhD<sup>2</sup>, Koichi Masuda, MD<sup>1</sup>, Sumihito Tamura, MD<sup>1</sup>, Taku Aoki, MD, PhD<sup>1</sup>, Kiyoshi Hasegawa, MD, PhD<sup>1</sup>, Yoshifumi Beck, MD, PhD<sup>1</sup>, Masashi Fukayama, MD, PhD<sup>2</sup>, and Norihiro Kokudo, MD, PhD<sup>1</sup>



# - ICG –(Infracyanine)



## INDICATIONS

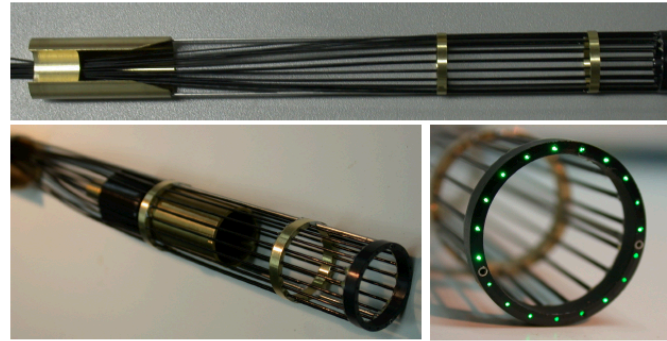
- **Evaluation du débit cardiaque:** amm/indiqué, smr: niveau insuffisant - le 2005-04-13: le 2006-09-21, révisé le 2006-09-21
- **Evaluation du débit sanguin hépatique:** amm/indiqué, smr: niveau insuffisant - le 2005-04-13: le 2006-09-21, révisé le 2006-09-21
- **Evaluation du volume sanguin:** amm/indiqué: le 2006-09-21, révisé le 2006-09-21
- **Exploration de la fonction hépatique:** amm/indiqué: le 2006-09-21, révisé le 2006-09-21
- **Exploration des vaisseaux choroïdiens:** amm/indiqué, smr: niveau important - le 2005-04-13: le 2006-09-21, révisé le 2006-09-21

# Imaging systems :

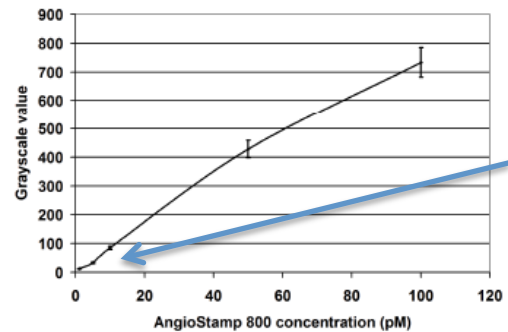
## Fluobeam



## Fluostic



Detection Curve



pmoles détectées  
( $\pm$  PET)



Gioux S. et al. *Journal of Biomedical Optics* in press







# Plateforme d'imagerie optique du petit animal

Véronique Josserand

**Bioluminescence**

**2D  
Fluorescence**

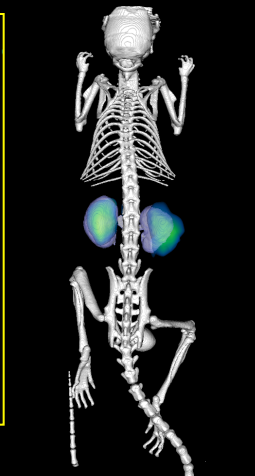
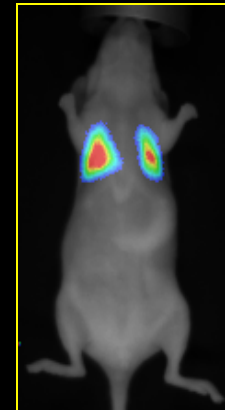
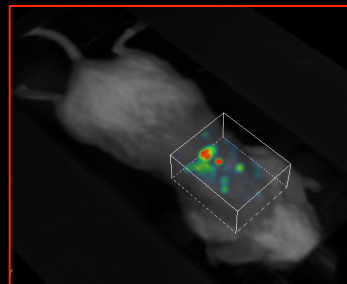
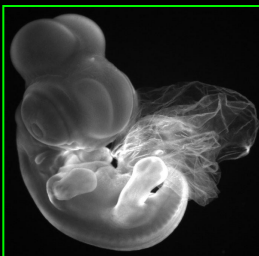
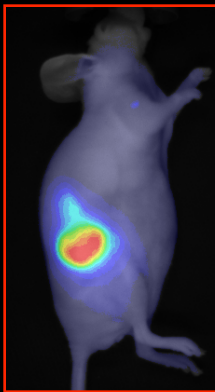
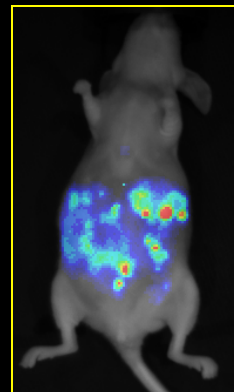
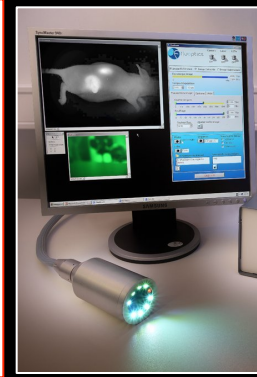
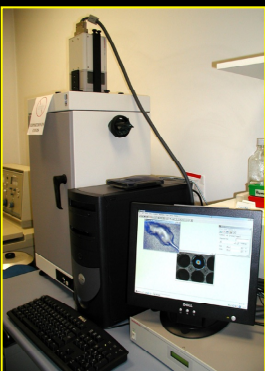
**Macroscopie de  
Fluorescence**

**3D Fluorescence  
(Tomographie)**

**Fluorescence  
per opératoire**

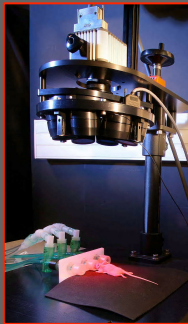
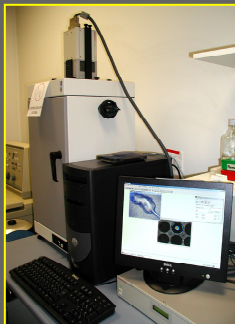
**Bioluminescence  
Fluorescence**

**Scanner  
Micro CT**



Un parc d'instruments pour l'imagerie optique in vivo

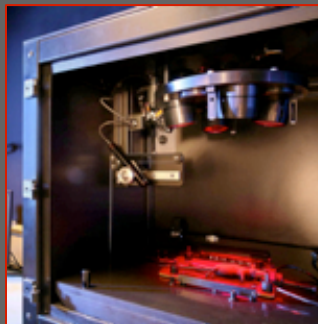
Bioluminescence **2D**  
**Fluorescence**



Macroscopie de  
**Fluorescence**



**3D Fluorescence**  
(Tomography)



**Fluorescence**  
per opérateur



Bioluminescence  
**Fluorescence**



Scanner  
Micro CT



## Grenoble Imaging Facility

### MRI



7T



4.7T

### Nuclear/US Imaging



**SPECT/CT**  
γ-Imager Biospace



**Echographie**  
VisualSonics



**SPECT/CT**  
NanoSPECT/CT Bioscan

**TEP/CT**  
NanoTEP/CT Bioscan

A level 2 technical plateau in the Hospital

Optics



## Prototype instruments

- femto laser
- bimodal US/laser endorectal probe
- 2 photon microscope
- Vibratome, hood...biol. Lab.



Centre for Clinical Investigation  
& Technological Investigation  
(test of Medical devices in patients)

Centre for Clinical Investigation  
Pharmacologie  
(prep of injectable molescs)

## Test of prototypes & molecules

- On patients
- On fresh human tissues

Industrials  
&  
Academics

PROJECTS

# Thanks

## INSERM U823



**Michelle Kéramidas**  
**Christiane Wenk**  
**Veronique Josserand**

**Jean-Marc Dinten**  
**Jean-Guillaume Coutard**  
**Sylvain Gioux**  
**Michel Berger**

**Philippe Rizo**  
**Stéphanie Guillemet**

**Pascal Dumy**  
**Didier Boturyn**

**Olivier Tillement**  
**François Lux**

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