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# L'apport des jumeaux numériques dans la recherche clinique

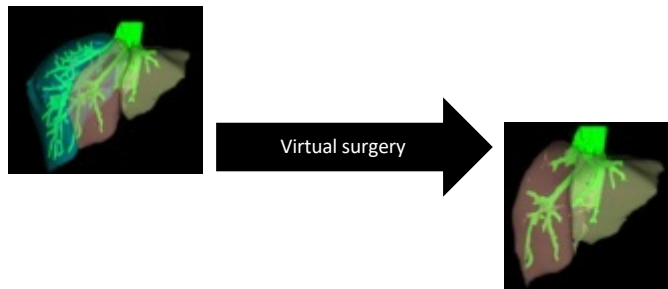


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Directrice de recherche, INRIA

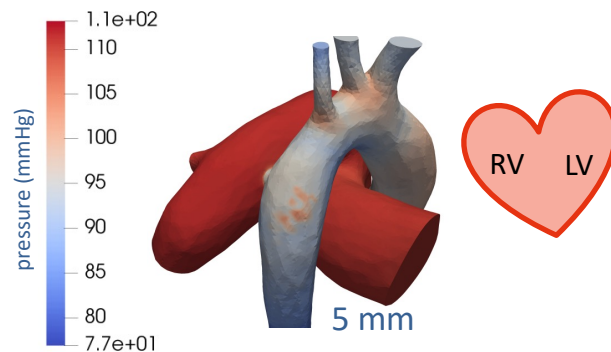


## I had a dream...

Anticiper le risque de chirurgie du foie?



Design d'un pontage artificiel pour palier à l'hypertension pulmonaire & comprendre l'effet sur le coeur?



Prédire le risque de croissance d'anévrisme?



1

# METHODES: MODELES MATHEMATIQUES & NUMERIQUES



100 000 km

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# Modèles mathématiques : physique & IA

Math & numerical complexity



$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + \nabla \cdot \mu(\nabla \mathbf{u} + \nabla \mathbf{u}^T)$$

**3D**  $\nabla \cdot \mathbf{u} = 0$   
rigid walls or Fluid-Solid Interaction

$$\partial_t(Au) + \partial_x(Au^2) = -\frac{A}{\rho} \partial_x p - f(A, A_0, u)$$

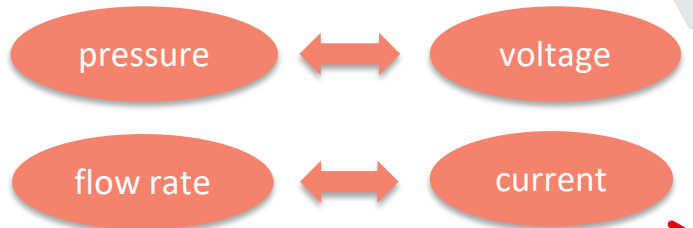
**1D**  $\partial_t A + \partial_x(Au) = 0$

$$p = p_0 + \psi(A, A_0, \beta)$$

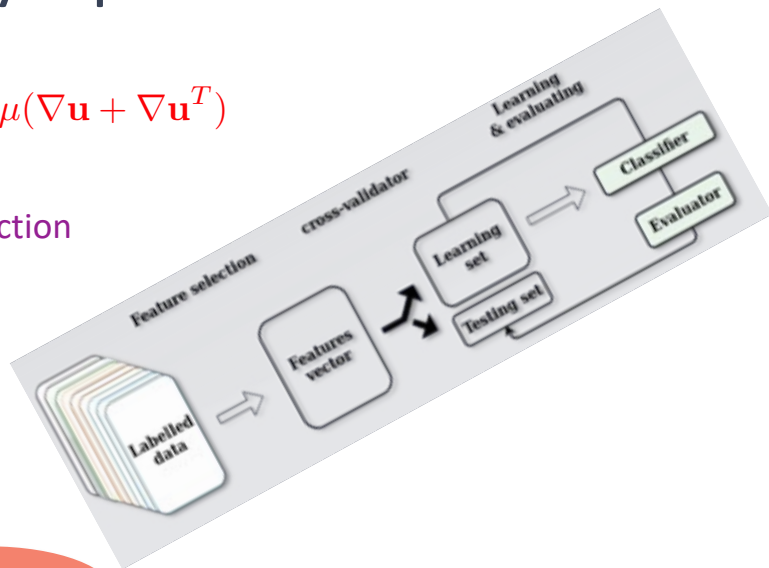
$$P_{in} - P_{out} = RQ$$

$$L \frac{dQ}{dt} = P_{in} - P_{out}$$

**0D**  $C \frac{dP}{dt} = Q_{in} - Q_{out}$

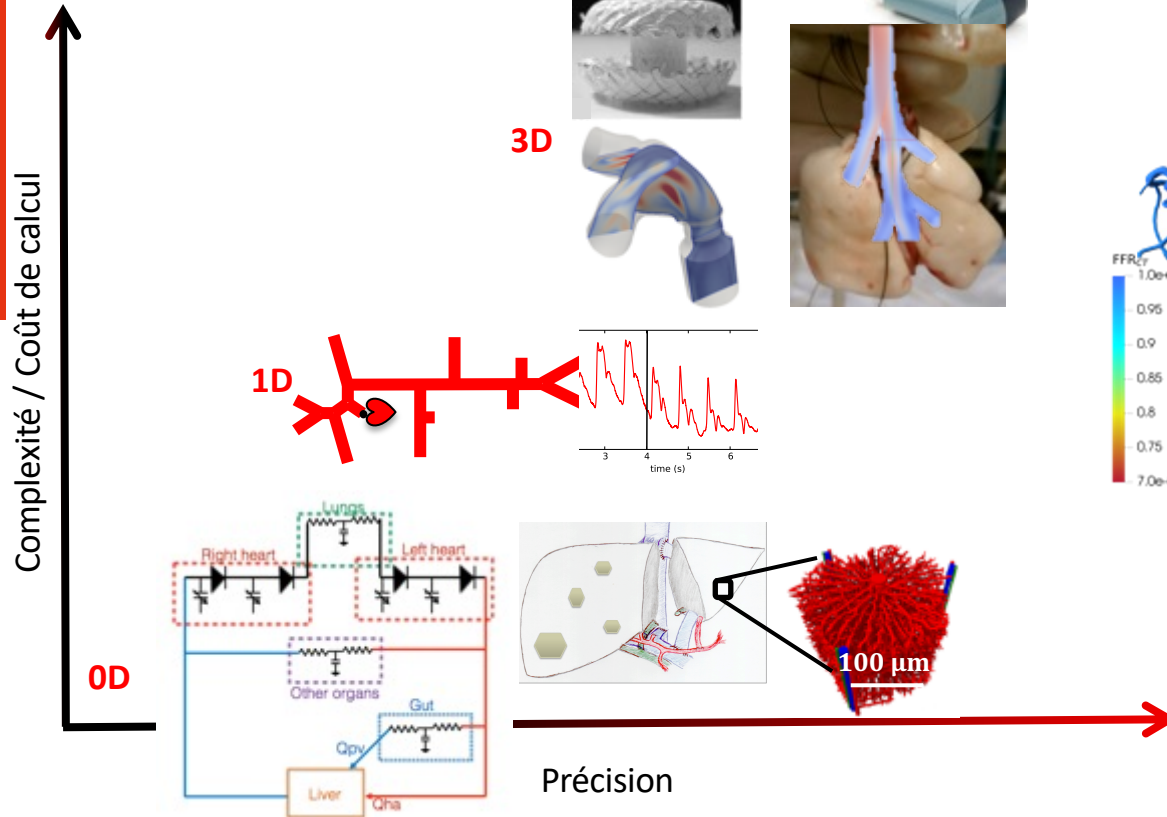


Precision





# A chaque application médicale son modèle



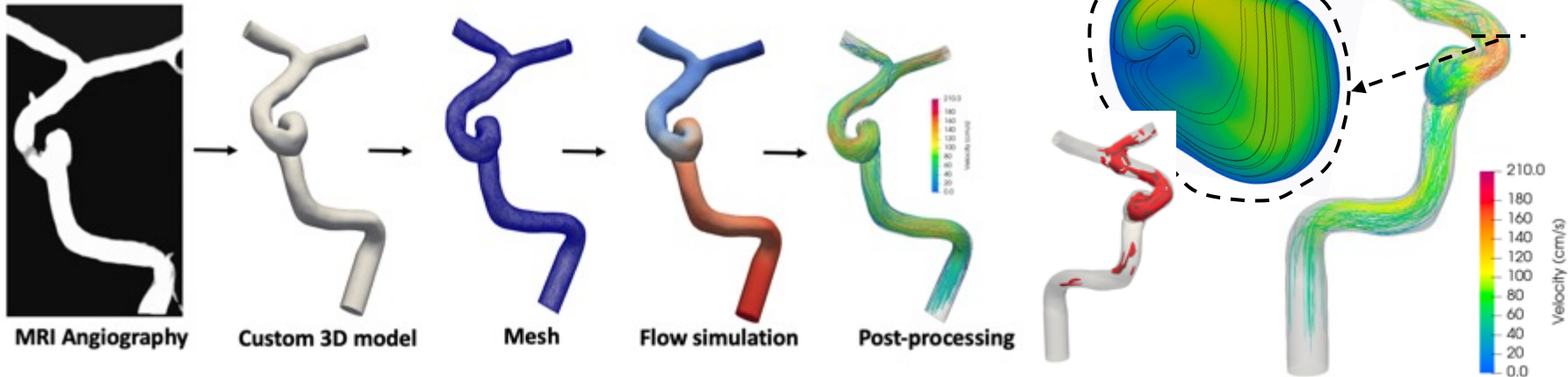
VC et al., CMAME 2006; CMBBE 2010  
 Oakes et al., J. Biomech 2015  
 Papamanolis et al., Annals Biomed Eng 2021

Vignon & Taylor, Wave  
 Motion 2004  
 Audebert et al., CMAME 2017

Pant et al., J. Biomech 2016  
 Golse et al., Clinical Biomechanics 2020  
 Boissier et al., IJNMBE 2021

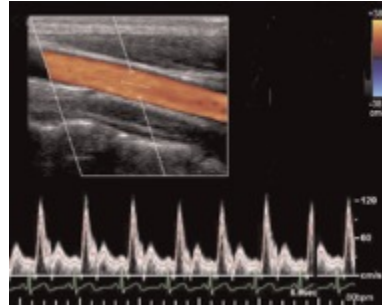
# Le jumeau numérique d'un patient

- **Un modèle** qui représente la circulation du sang **d'un patient**
- Au **niveau de fidélité** cohérent avec la question biomédicale posée
- Qui, paramétré à partir de **données** à un état précis peut générer une **nouvelle information** ou **prédire un autre état**

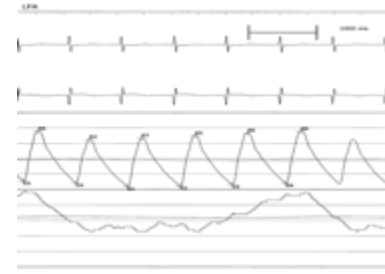




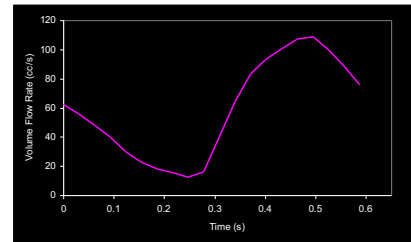
## Pression directe ou bloquée, débits, vitesses



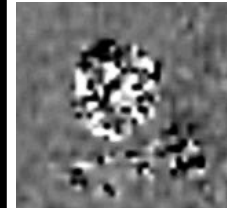
Doppler ultrasound  
(max) velocities



Catheterization



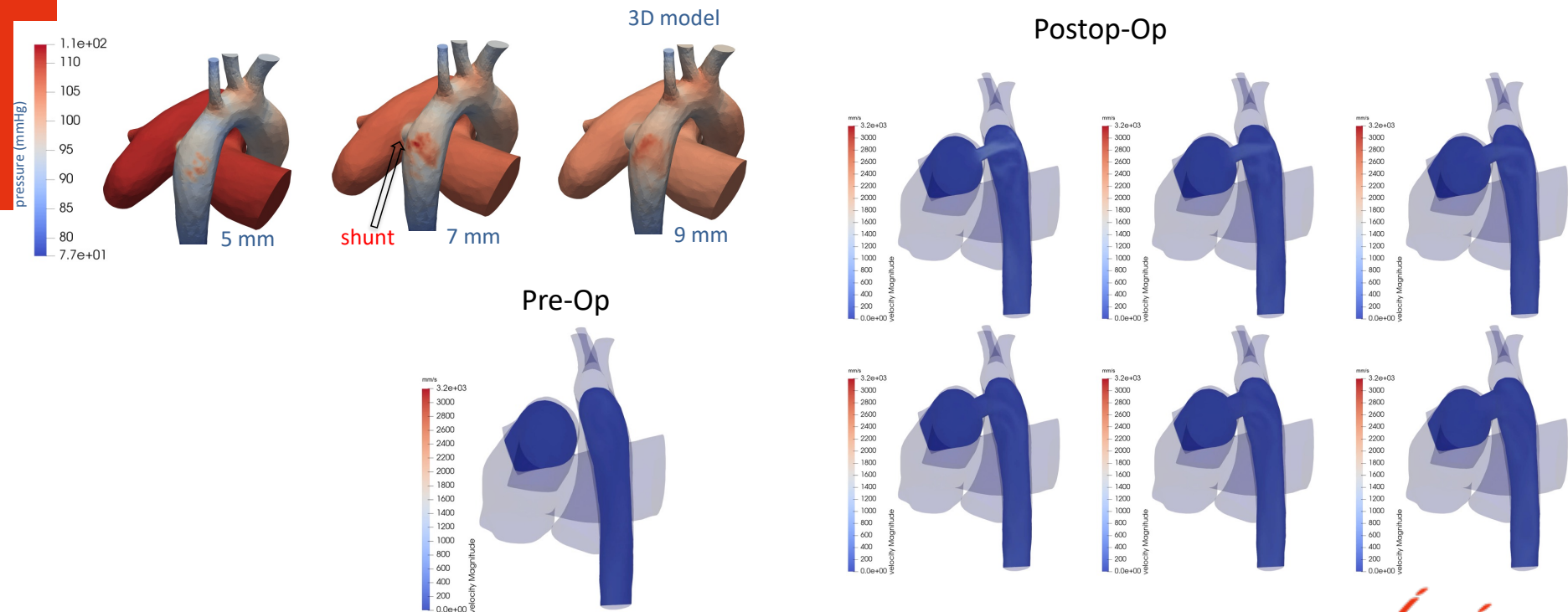
PC-MRI flow rate



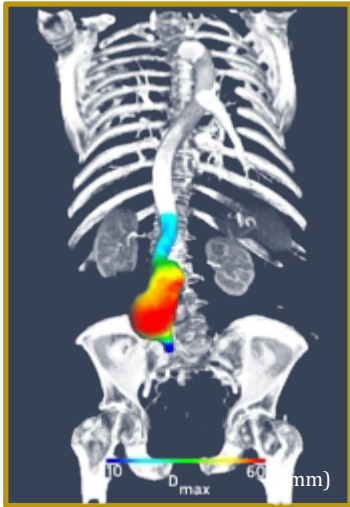
# 2

## AVANTAGES DES Jumeaux NUMERIQUES

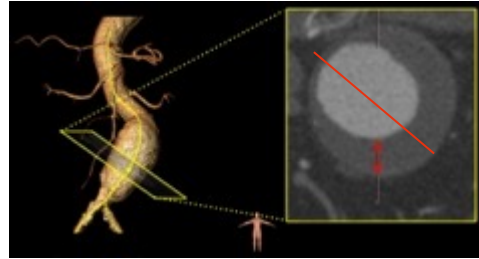
# Aspect design de Shunt: test in-silico de différentes options = **force du numérique** !



# Abdominal aortic aneurysms: clinical overview

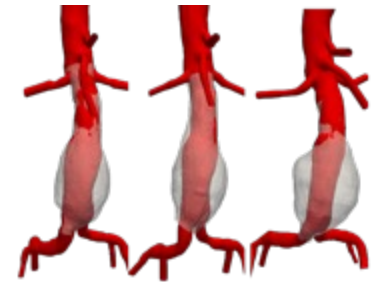
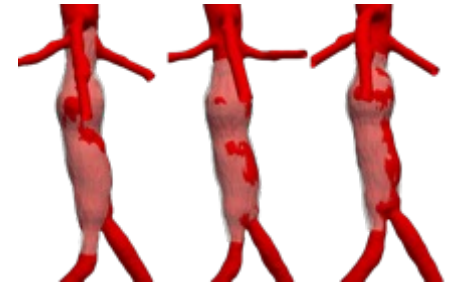


- **Localized expansion of the arterial wall**
- Usually asymptomatic
- If ruptures: mortality > 80% (US CDC)



- **Treatment (ideally only for high risk patients)**
  - Stent-graft
  - Open-surgery

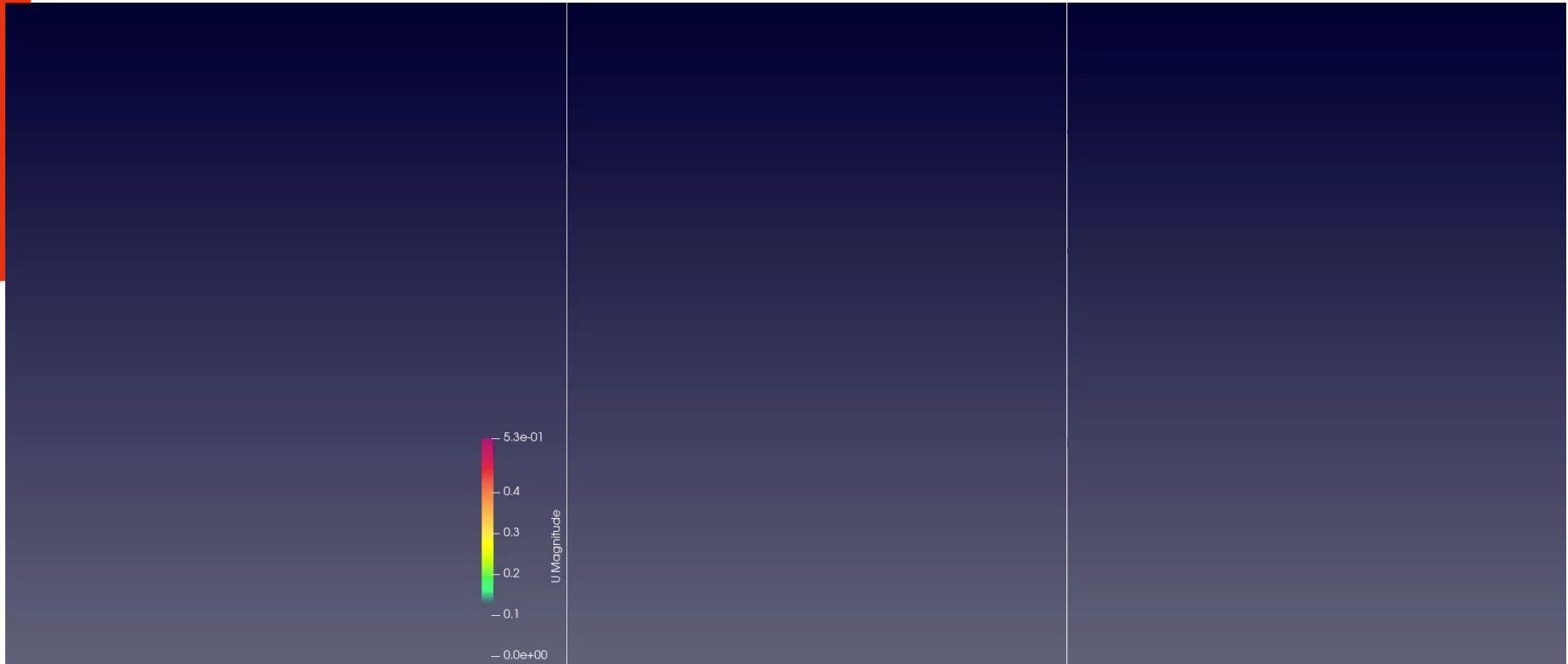
AAA follow-up on 2 patients:  
~ 6 months between each



Can we predict AAA progression?

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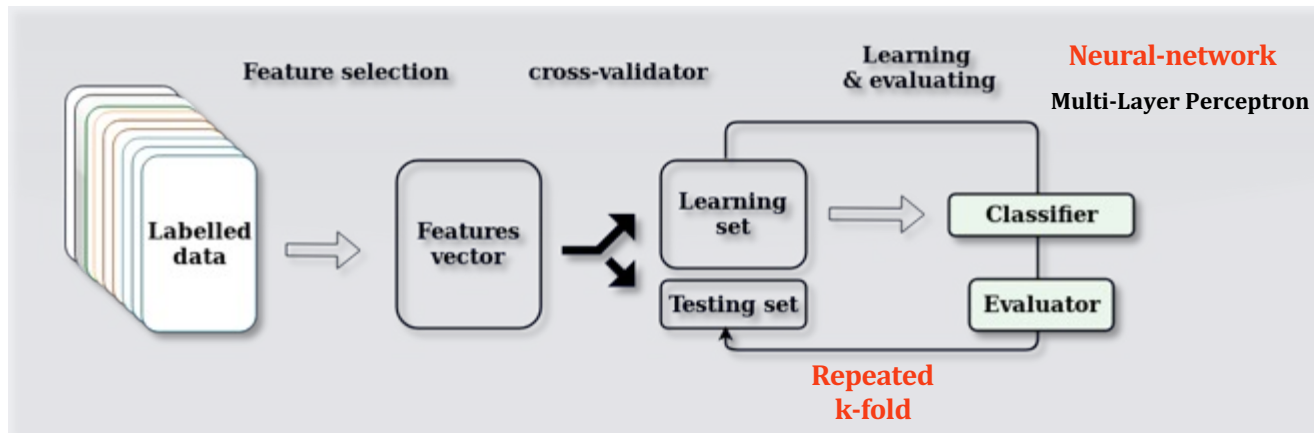
# Morphologie & écoulement dans un anévrisme



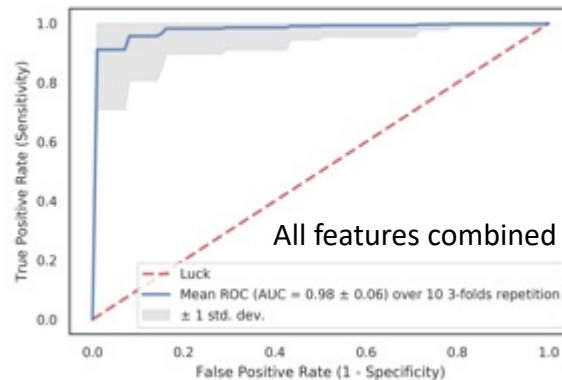
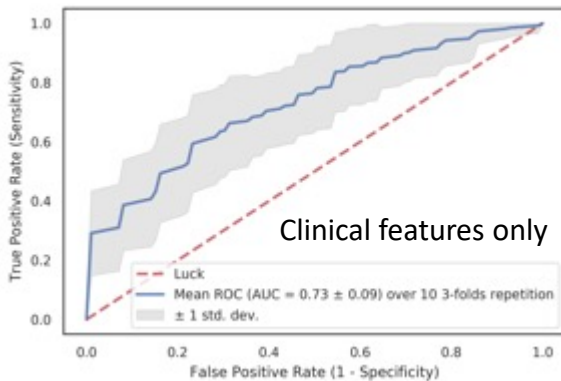
- Goal: **prediction of risk change** from low risk to high risk based on current data (n)
- Machine learning process



- Clinical data
- Dmax
- Morphological analysis
- Hemodynamics (CFD)



- Results



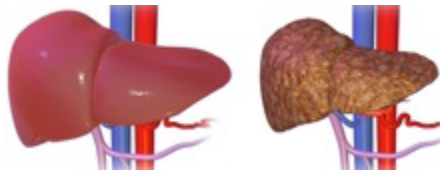




Hôpital  
Paul-Brousse  
AP-HP

3

## APPLICATIONS: EXEMPLE DE LA CHIRURGIE DU FOIE

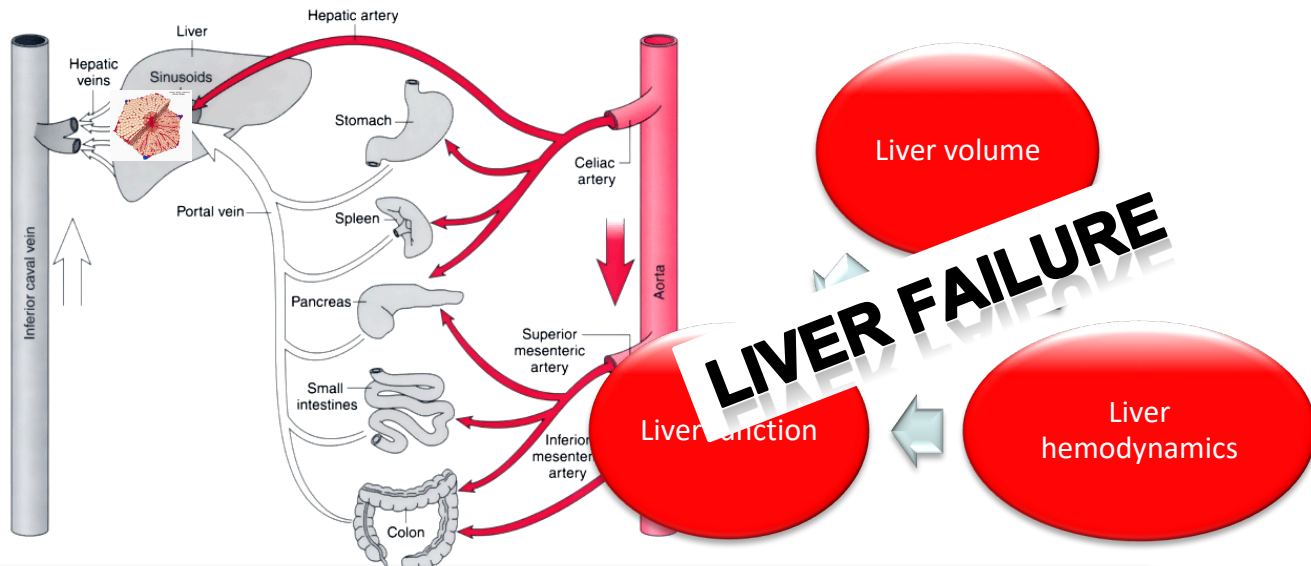


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# Medical context: liver surgery



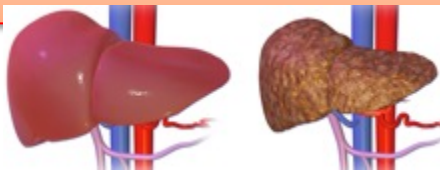
- 25% cardiac output
- regeneration capacity
- metabolism and storage
- drugs and hormones processing



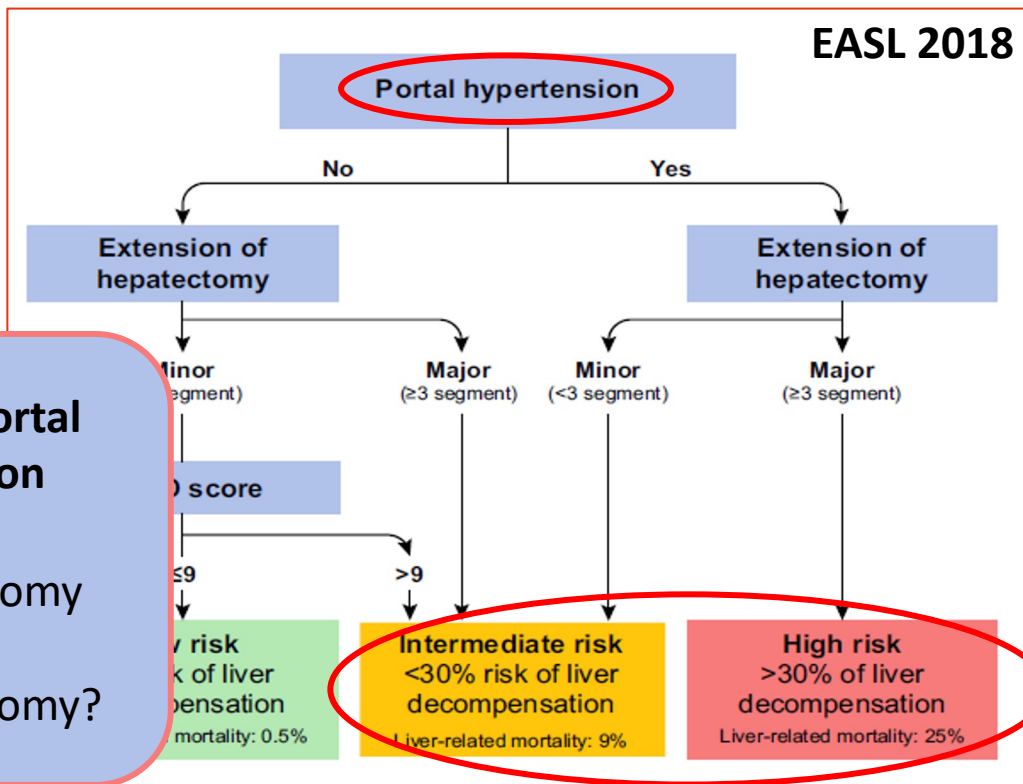
Liver cancer  
Chronic liver disease



Partial liver resection (partial hepatectomy)  
Liver transplantation (total liver or split liver)

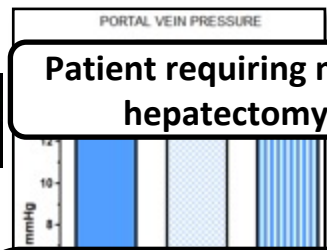
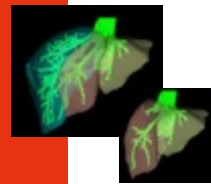


# New guidelines for patient selection



		Extension of hepatectomy	
		Major	Minor
Portal hypertension	Yes		
	No		MELD score >9 MELD score ≤9

# Jumeau numérique pour le risque chirurgical du foie

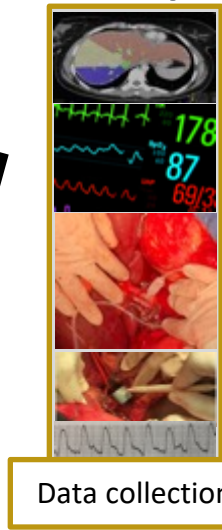


Patient requiring major hepatectomy

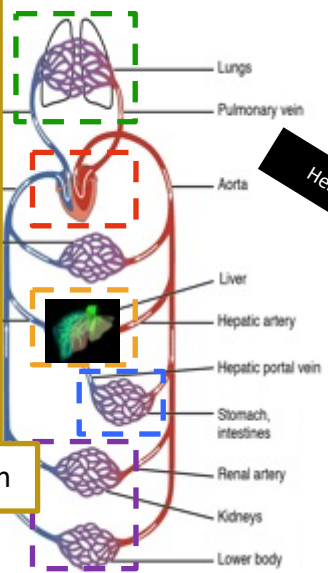
Preoperative concern about **surgical risk** (portal hypertension)

Validation on a first cohort

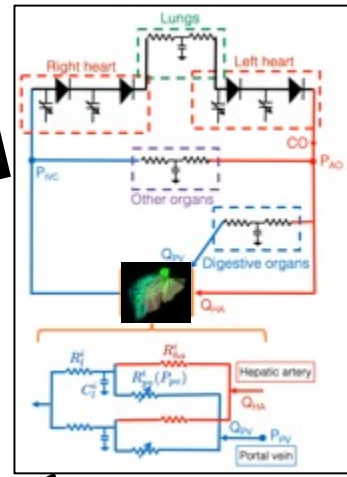
Current work



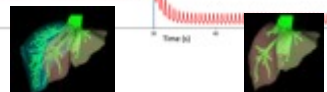
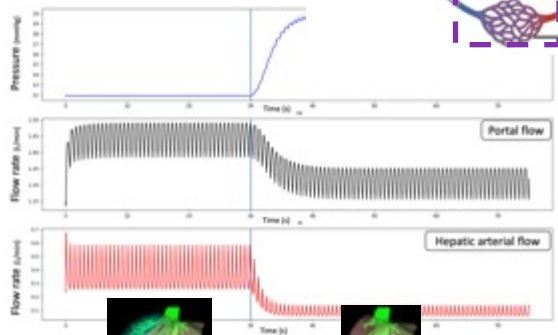
Data collection



Hemodyn. model



Virtual surgery: Anticipation of risk

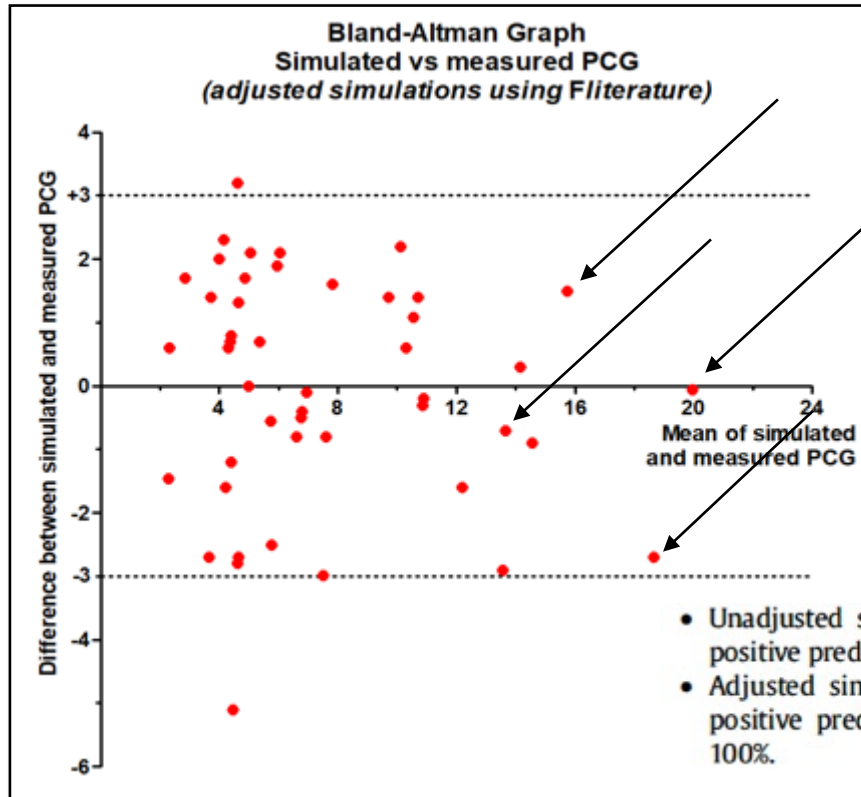


## Another way to look at results



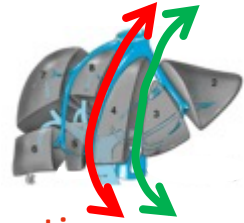
European Research Council  
Established by the European Commission

Sensitivity analysis: linking decision criteria and necessary data



Postop death  
(PHLF)

10 mmHg  
cutoff

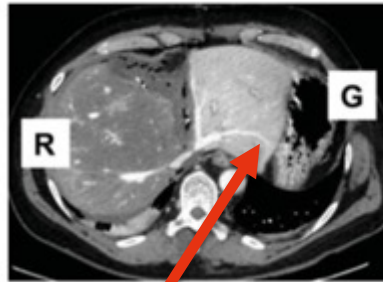


# A new surgical idea: the RAPID

- Main issue = **organ shortage** -> **graft split**: adult/child ok, but 2 adults **problematic**
- **RAPID**: tests in Northern Europe for unresectable liver metastases but non-consensual indication



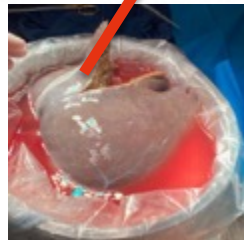
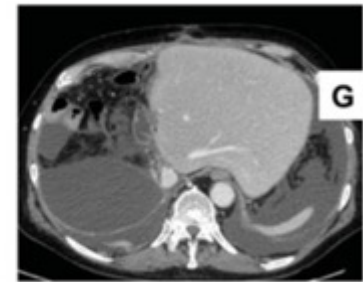
Immediately after 1<sup>st</sup> stage  
(remnant + graft)



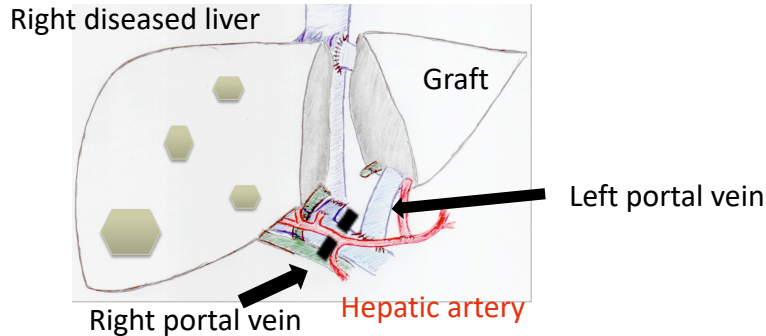
One month later



After right hepatectomy  
(2<sup>nd</sup> stage)



# Crucial step: right portal vein clamping



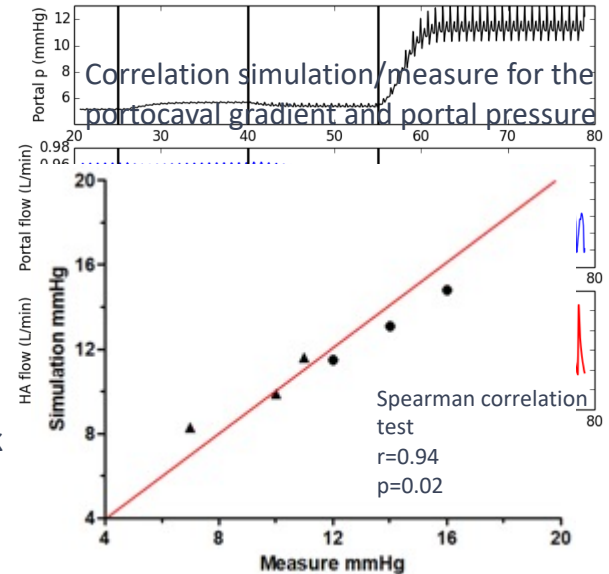
- Right portal vein ligation to deviate portal flow to the graft (hypertrophy+++)
- Requires CLOSE monitoring of portal vein PRESSURE (PPv) !

So far, no possibility of predicting the occurrence of Portal Hypertension

Biophysical in-silico simulation could help to predict the portal hypertension risk and need for portal flow modulation

Continuing with RAPID multicentric clinical study

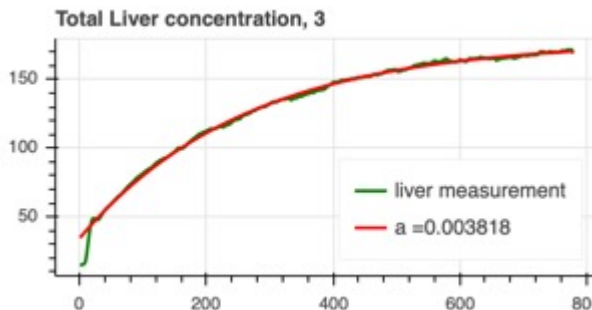
**Goal:**  
 PPv < 20 mmHg  
 (to avoid graft failure, ascitis, death...)





# Evaluation of liver @end transplantation

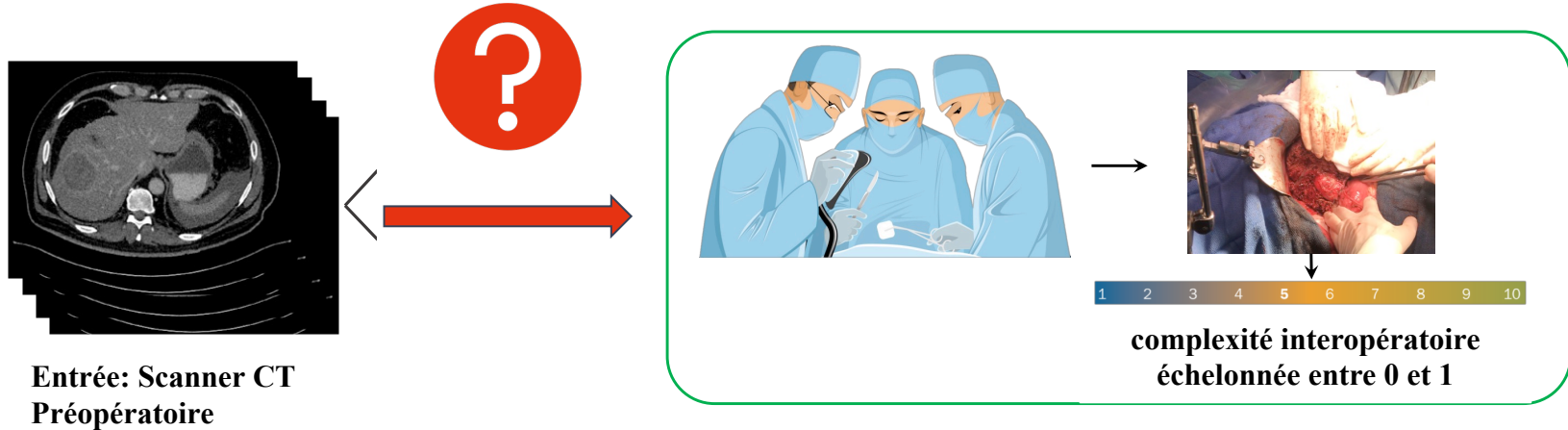
- Primary non-function of a liver graft after transplantation:
  - Major concern
  - Use of marginal grafts
  - Few early predictors
- Indocyanine green (ICG) fluorescence:
- Finding: **Graft fluorescence during transplantation can predict the graft survival at 3 months**



Variables	Value
Sensitivity	83.3 %
Specificity	78.6 %
AUROC (95 % CI)	0.824 [0.669; 0.979]
p	0.009
Positive likelihood ratio	3.89
Negative likelihood ratio	0.21
Youden index	0.619
Cut-off Parameter $\alpha_{150}$	0.0155

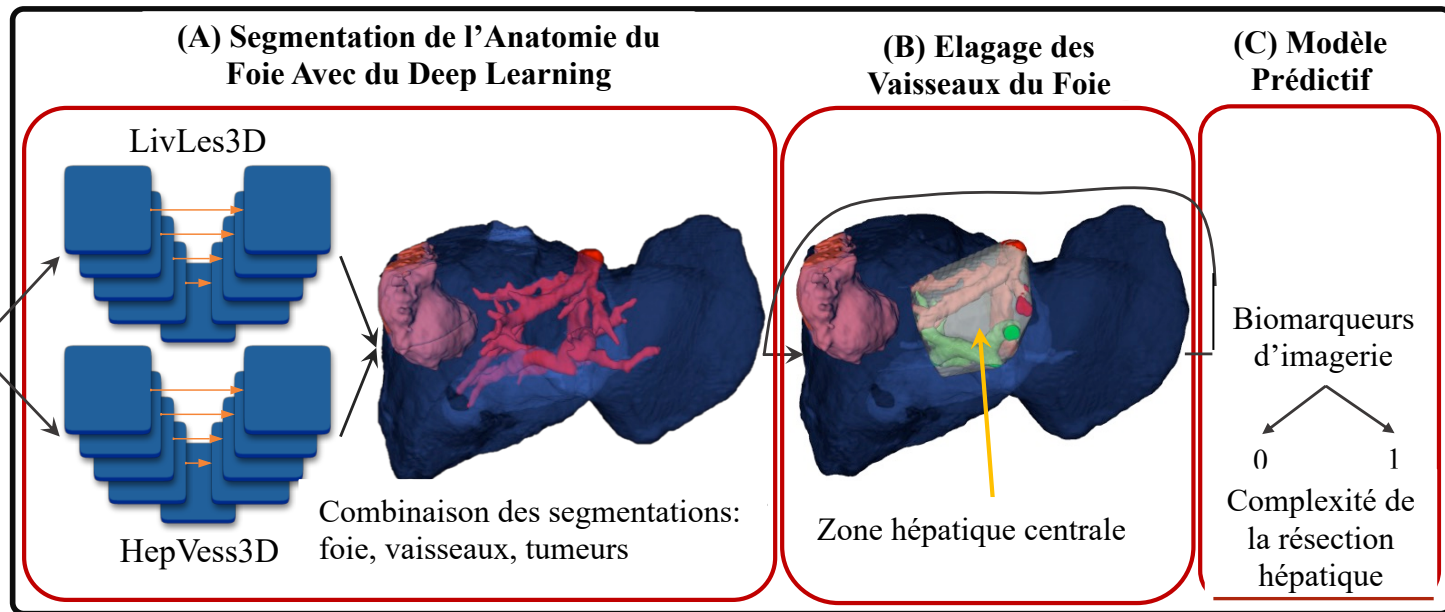


# Analyse d'image pour la prédiction de la complexité de la résection du foie



**Objectif : Développer un pipeline d'apprentissage automatique basé sur l'imagerie pour prédire en préopératoire la complexité de la résection hépatique**

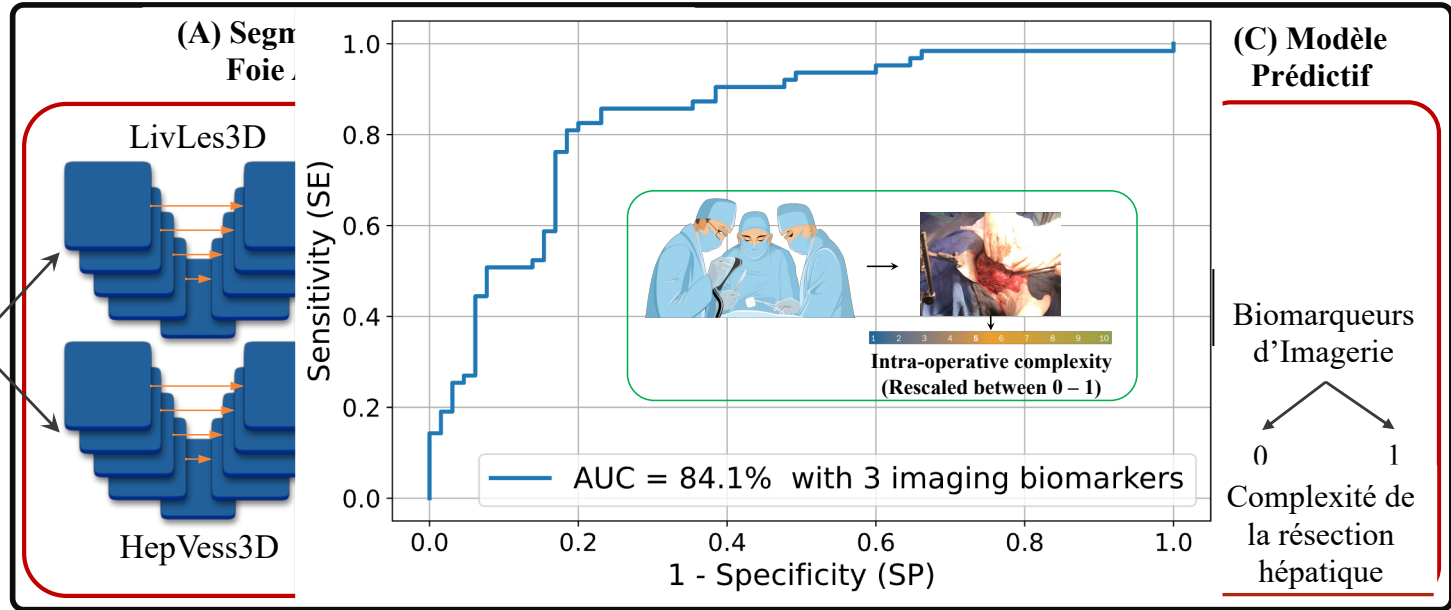
## CoRe Automatic Pipeline



Détails du pipeline CoRe

Entrée: Scanner CT  
Préopératoire

## CoRe Automatic Pipeline



Détails du pipeline CoRe

# Inria @Saclay IDF

## MEDISIM

Modèles  
biophysiques,  
coeur,  
monitorage  
anesthésie

## SIMBIOTX

Modèles biophysiques,  
cardiovasculaire, foie,  
plannification  
chirurgie/intervention

## OPIS

Imagerie  
médicale, IA,  
optimisation

## MIND

IA, neuro-  
imagerie

## GEOMERIX

Analyse de signaux,  
prediction de perte  
de connaissance

## TROPICAL

Analyse de système,  
contrôle, centre  
d'appels d'urgence

## SODA

Data-science, IA,  
population,  
santé & société

Conclusion: jumeaux numériques & IA sont  
complémentaires pour répondre à des  
questions cliniques

Des questions?  
[Irene.vignon-clementel@inria.fr](mailto:Irene.vignon-clementel@inria.fr)