

# Laboratoire d'Imagerie Translationnelle en Oncologie

U1288 – groupe RIM

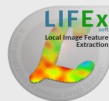
[www.lito-web.fr](http://www.lito-web.fr)

Frédérique Frouin / Fanny Orlhac /  
Christophe Nioche / Caroline Malhaire

- Meilleure compréhension des mécanismes oncologiques
- Amélioration de la prise en charge des patients
- Prédiction de la réponse au traitement et du pronostic

Intégration de **caractéristiques issues d'images médicales** avec des données cliniques, biologiques, histologiques, omiques pour une médecine de précision

- Méthodes pour l'intégration de données multi-omiques
- Développements en radiomique
- Instanciation : IRM mammaire dans le cancer du sein



## Organigramme nov 2024

Responsable : **Frédérique Frouin, CRHC Inserm**

Hervé Brisse, PH Curie

Caroline Malhaire, PH Curie

**Christophe Nioche, IR Inserm**

**Fanny Orlhac, CRCN Inserm**

Agnès Rouxel, PH Avicenne

Vincent Servois, PH Curie

Kibrom Girum, post-doc, Curie

Narinée Hovhannisyan, IR Curie

Hornella Fokem Fassio, CDD, IE Curie

Ghada Lemoudda, CDD, IE Curie

Julie Auriac, PhD student, Paris Saclay

Trung Kien Bui, PhD student, Paris Saclay

Juliette Dindart, PhD student, Paris Saclay

Pierre Loap, MD, PhD student, Paris Saclay

Charlotte Loisel, PhD student, Paris Saclay

Paul Steinmetz, PhD student, Paris Saclay

Joseph-Elias Al Khoury, M2, Univ Lille

- 3 chercheurs post-doctorants
- 1 chercheuse CNRS accueillie un an
- 4 CDD IE/IR (plus de 6 mois)
- 1 titularisation CRCN Inserm
- 1 promotion CRHC Inserm
- 1 CDD IR -> 1 CDI (CdR Curie)
- 17 Etudiants stages M2/M1/ fin école ingénieurs
- 16 Etudiants en thèse de sciences



Depuis 2020

17 stages M2/M1/ fin école ingénieurs

- 3 en 2020
- 4 en 2021
- 3 en 2022
- 2 en 2023
- 5 en 2024

1 formation par apprentissage (M2)  
(2024/2025)

2 M2 en cours de recrutement

9 soutenances de thèse de sciences

1. AS Dirand (oct 2020)
2. D Wallis (juin 2021)
3. AS Cottereau (jan 2022)
4. MJ Saint-Martin (nov 2022)
5. A Beddok (oct 2023)
6. T Escobar (nov 2023)
7. F Khalid (jan 2024)
8. L Rebaud, (mai 2024)
9. N Captier (mai 2024)

1 soutenance très prochainement  
C Malhaire (jan 2025)

6 thèses en cours



Unicancer 2020 award, 6th edition



Cancer Research

LIFEx: A Freeware for Radiomic Feature Calculation in Multimodality Imaging to Accelerate Advances in the Characterization of Tumor Heterogeneity

Christophe Nioche, Fanny Orhac, Sarah Boughdad, Sylvain Reuzé, Jessica Goya-Outi, Charlotte Robert, Claire Pellot-Barakat, Michael Soussan, Frédérique Frouin, and Irène Buvat



The Best of the AACR Journals 13





### Student Paper Competition Finalists

Marie-Judith Saint Martin  
Inserm – Institut Curie

*"Decrypting the Information Captured by MRI-Radiomic Features in Predicting the Response to Neoadjuvant Chemotherapy in Breast Cancer"*



### HECKTOR 2022

Head and neck tumor segmentation and outcome prediction in PET/CT images  
Third edition

MICCAI 2022 Singapore

The podium for Task 2 is


Rank	Team	C-index
1st	BDAV_USYD	0.6808
2nd	LITO	0.6815
3rd	ART	0.6726

BEST PAPER AWARD


HEALTHY 7

HEALTHY 7





SOCIETY OF NUCLEAR MEDICINE & MOLECULAR IMAGING

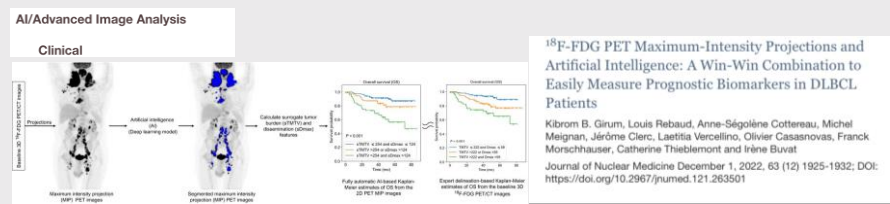


ERF  
The European Research Foundation for Nuclear Medicine and Molecular Imaging

May 24, 2023

Dear Kibrom B Gium:

It is with great pleasure that we inform you of being selected as a recipient of the Alavi-Mandell Award for your publication entitled, **"<sup>18</sup>F-FDG PET Maximum-Intensity Projections and Artificial Intelligence: A Win-Win Combination to Easily Measure Prognostic Biomarkers in DLBCL Patients"**.



**<sup>18</sup>F-FDG PET Maximum-Intensity Projections and Artificial Intelligence: A Win-Win Combination to Easily Measure Prognostic Biomarkers in DLBCL Patients**

Kibrom B. Gium, Louis Rebaut, Anne-Ségolène Cottreau, Michel Meignan, Jérôme Clerc, Laëtizia Vercellino, Olivier Casasnovas, Franck Morschhauser, Catherine Thieblemont and Irène Buvat

Journal of Nuclear Medicine December 1, 2022, 63 (12) 1925-1932; DOI: <https://doi.org/10.2967/jnumed.121.263501>

- Publications nombre (PCD) :
  - 3 (1) en 2020
  - 10 (6) en 2021
  - 10 (5) en 2022
  - 12 (6) en 2023
  - 12 (3) en 2024

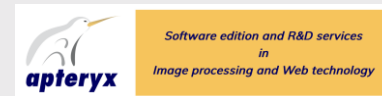
- 4 demandes de brevets
- 6 Dépôts Logiciels

## Liens industrie :

- 2 thèses CIFRE
- 1 projet BPI AI.DReAM
- 1 projet ANR PRCE

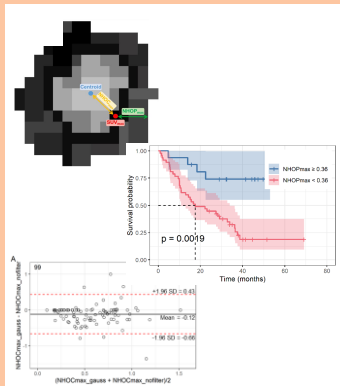


AI.DReAM





## Découverte et caractérisation de nouveaux biomarqueurs



# Découverte et caractérisation de nouveaux biomarqueurs

Proc Natl Acad Sci U S A. 2021 Feb 9;118(6):e2018110118. doi: 10.1073/pnas.2018110118.

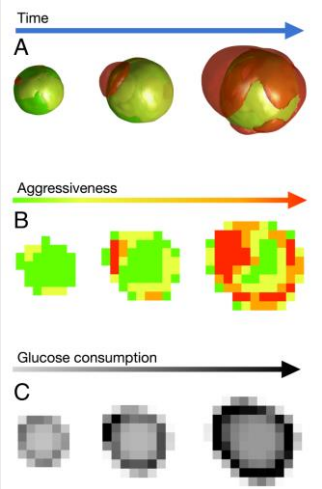
## Evolutionary dynamics at the tumor edge reveal metabolic imaging biomarkers

Juan Jiménez-Sánchez<sup>1</sup>, Jesús J Bosque<sup>1</sup>, Germán A Jiménez Londoño<sup>2</sup>, David Molina-García<sup>1</sup>, Álvaro Martínez<sup>1,3</sup>, Julián Pérez-Beteta<sup>1</sup>, Carmen Ortega-Sabater<sup>1</sup>, Antonio F Honguero Martínez<sup>4</sup>, Ana M García Vicente<sup>2</sup>, Gabriel F Calvo<sup>5</sup>, Víctor M Pérez-García<sup>5</sup>

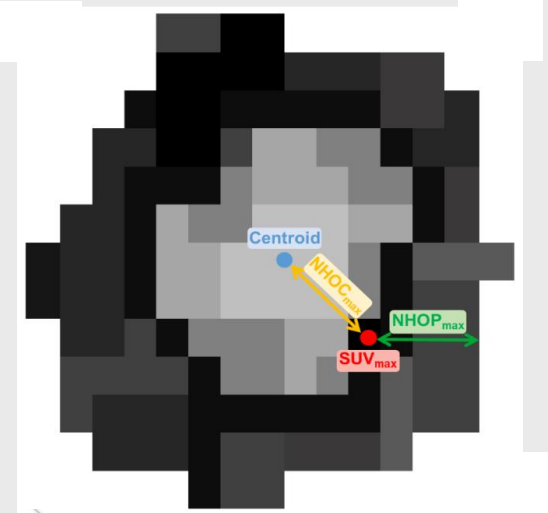
Eur Radiol. 2022 Jun;32(6):3889-3902. doi: 10.1007/s00330-021-08523-3. Epub 2022 Feb 8.

## SUVmax to tumor perimeter distance: a robust radiomics prognostic biomarker in resectable non-small cell lung cancer patients

Germán Andrés Jiménez Londoño<sup>1</sup>, Ana María García Vicente<sup>2</sup>, Jesús J Bosque<sup>3</sup>, Mariano Amo-Salas<sup>4</sup>, Julián Pérez-Beteta<sup>3</sup>, Antonio Francisco Honguero-Martínez<sup>5</sup>, Víctor M Pérez-García<sup>3</sup>, Ángel María Soriano Castrejón<sup>2</sup>



Evaluer de nouveaux biomarqueurs en imagerie TEP



**NHOC** : *Normalized distance from the **HO**t spot to the tumor **C**entroid*  
**NHOP** : *Normalized distance from the **HO**t spot to the tumor **P**erimeter*

Images TEP-FDG pré-traitement – cancer pulmonaire

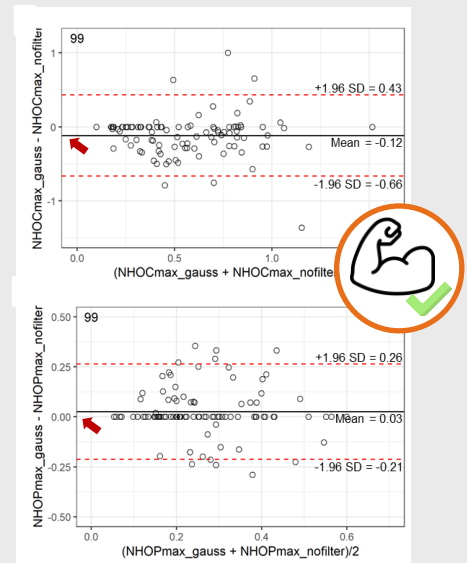


- Etude technique : 99 patients
- Analyse de survie : 244 patients

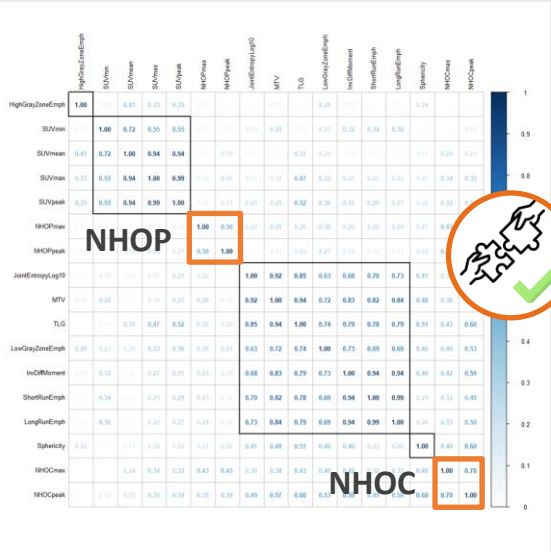
Promising candidate prognostic biomarkers in [18F] FDG PET images: evaluation in independent cohorts of NSCLC patients.  
N. Hovhannisyan-Baghdasarian, M. Luporsi, N. Captier, C. Nioche, V. Cuplov, E. Woff, N. Hegarat, A. Livartowski, N. Girard, I. Buvat, F. Orlhac.  
J Nucl Med. 2024; 65:635-642.



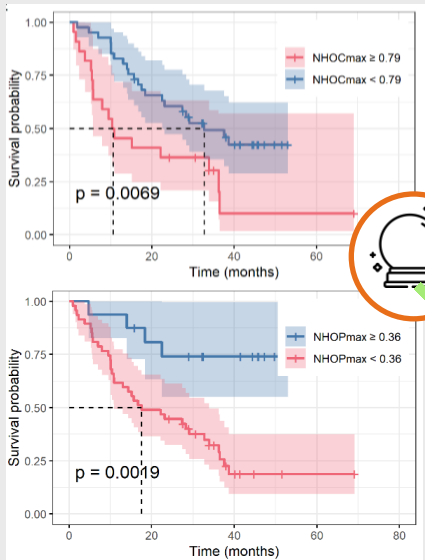
# Découverte et caractérisation de nouveaux biomarqueurs



Robustes



Complémentaires



Pronostiques

Promising candidate prognostic biomarkers in [18F] FDG PET images: evaluation in independent cohorts of NSCLC patients.

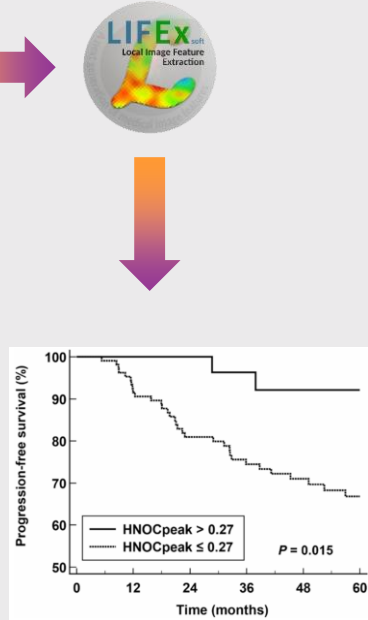
N. Hovhannisyan-Baghdasarian, M. Luporsi, N. Captier, C. Nioche, V. Cuplov, E. Woff, N. Hegarat, A. Livartowski, N. Girard, I. Buvat, F. Orlhac.

J Nucl Med.2024; 65:635-642.

> Cancer Imaging. 2024 Oct 11;24(1):136. doi: 10.1186/s40644-024-00787-4.

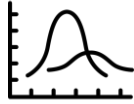
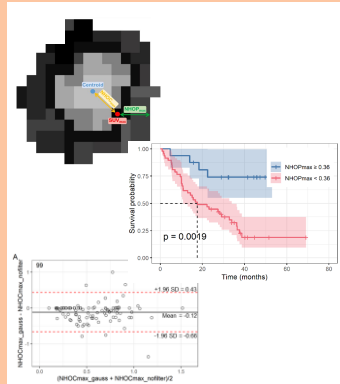
**Clinical value of SUVpeak-to-tumor centroid distance on FDG PET/CT for predicting neoadjuvant chemotherapy response in patients with breast cancer**

Sun-Pyo Hong <sup>#1</sup>, Sang Mi Lee <sup>#1</sup>, Ik Dong Yoo <sup>1</sup>, Jong Eun Lee <sup>2</sup>, Sun Wook Han <sup>2</sup>, Sung Yong Kim <sup>2</sup>, Jeong Won Lee <sup>3</sup>

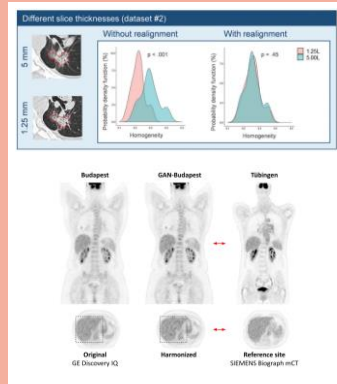




## Découverte et caractérisation de nouveaux biomarqueurs



## Harmonisation des biomarqueurs d'imagerie



# Harmonisation des biomarqueurs d'imagerie

1) Utiliser **uniquement** les indices radiomiques **robustes** (ex : indices de forme)



2) Utiliser une **stratégie d'harmonisation**

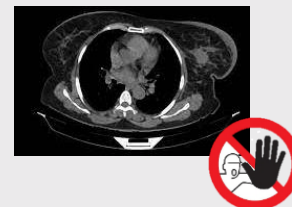
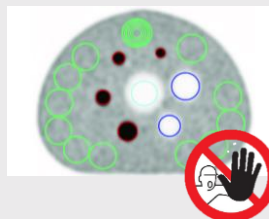


Etude prospective :

- Harmoniser les protocoles d'imagerie avant le début de l'étude
- Respecter les standards (ex : protocole EARL en imagerie TEP)



Etude rétrospective :



# Harmonisation des biomarqueurs d'imagerie

- **ComBat** pour *Combating Batch effects* [Johnson et al. *Biostatistics* 2007]



*Biostatistics* (2007), 8, 1, pp. 118–127

**Adjusting batch effects in microarray expression data  
using empirical Bayes methods**

- Initialement décrite en génomique pour corriger des effets “batches”

Index  $y$  mesuré dans une région d'intérêt ( $j$ ) pour le scanner  $i$

$$y_{ij} = \alpha + \gamma_i + \delta_i \varepsilon_{ij}$$

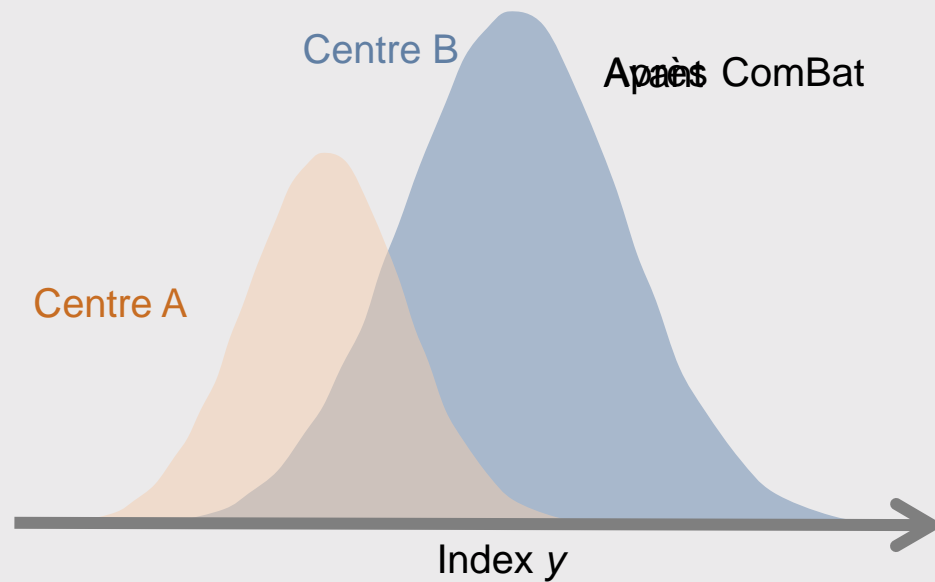
Terme d'erreur

Valeur moyenne de l'index  $y$

Effet scanner additif

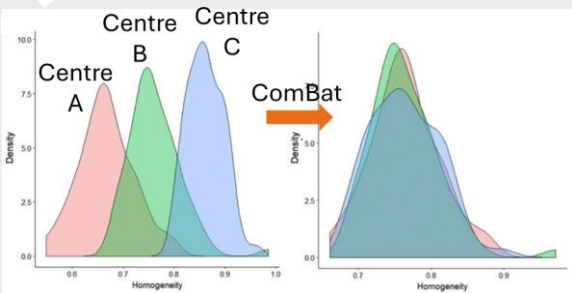
Effet scanner multiplicatif

# Harmonisation des biomarqueurs d'imagerie



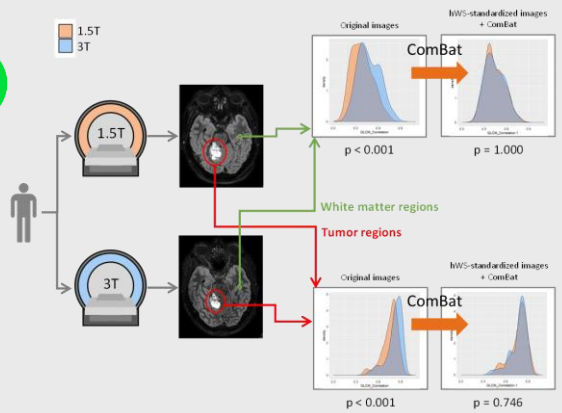
# Harmonisation des biomarqueurs d'imagerie

• TEP 



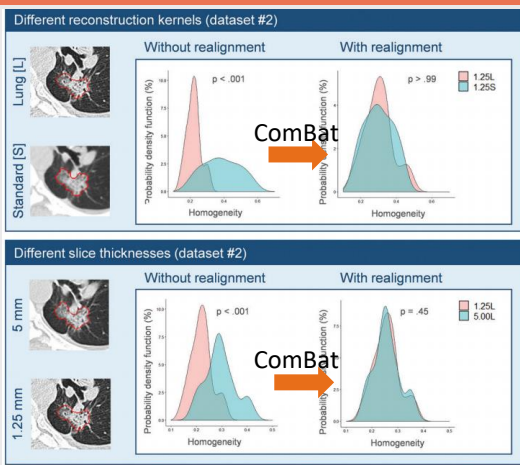
A post-reconstruction harmonization method for multicenter radiomic studies in PET. F. Orlhac, S. Boughdad, C. Philippe, H. Stalla-Bourdillon, C. Nioche, L. Champion, M. Soussan, F. Frouin, V. Frouin, I. Buvat. J Nucl Med. 2018;59:1321-1328.

• IRM 

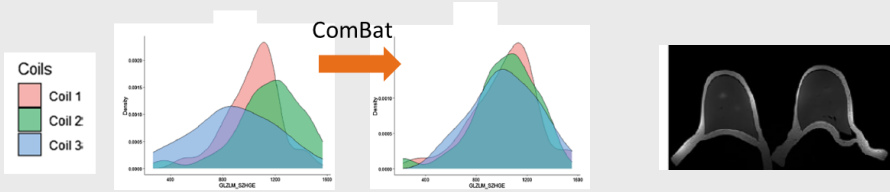


How can we ComBat multicenter variability in MR Radiomics? Validation of a correction procedure. F. Orlhac, A. Leclerc, J. Savatovski, J. Goya-Outi, C. Nioche, F. Charbonneau, N. Ayache, F. Frouin, L. Duron, I. Buvat. Eur Rad. 2021;31:2272-2280.

• TDM 



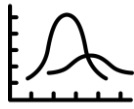
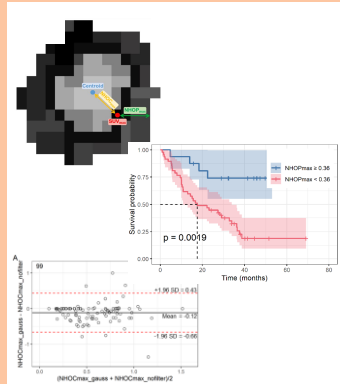
Validation of a method to compensate multicenter effects affecting CT Radiomics. F. Orlhac, F. Frouin, C. Nioche, N. Ayache, I. Buvat. Radiology. 2019;291:53-59.



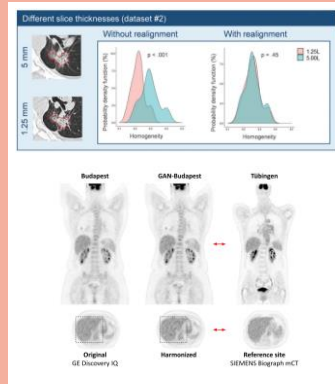
A radiomics pipeline dedicated to Breast MRI: validation on a multi-scanner phantom study. M-J. Saint Martin, F. Orlhac, P. Akl, F. Khalid, C. Nioche, I. Buvat, C. Malhaire, F. Frouin. MAGMA 2021;34:355-366.



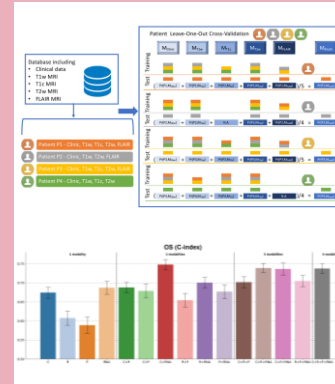
## Découverte et caractérisation de nouveaux biomarqueurs



## Harmonisation des biomarqueurs d'imagerie



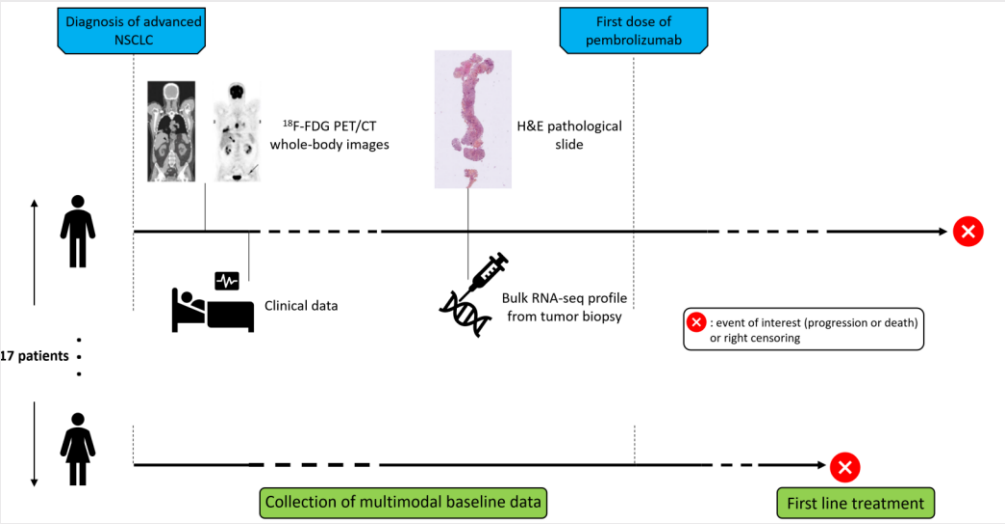
## Construction de modèles radiomiques ou multi-modaux



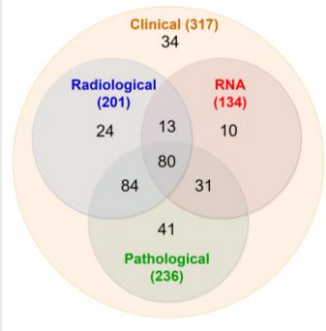
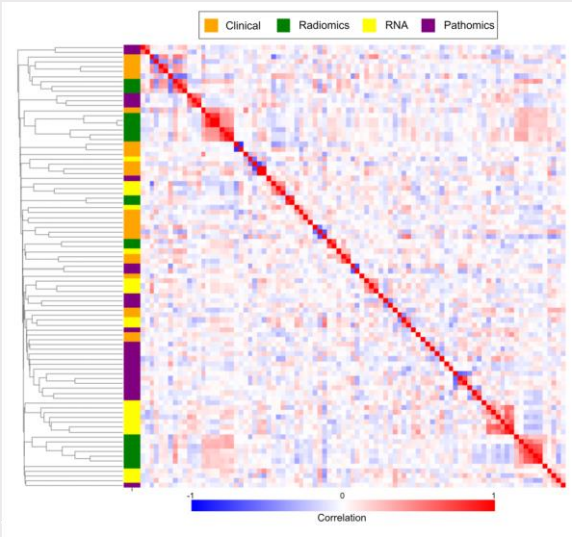
# Construction de modèles radiomiques ou multi-modaux



Prédire la réponse à l'immunothérapie pour des cancers pulmonaires non à petites cellules (TIPIT)



→ Complémentarité des biomarqueurs extraits

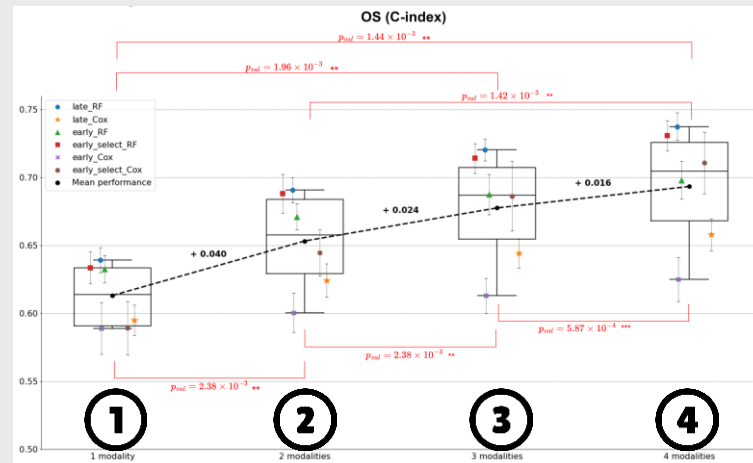
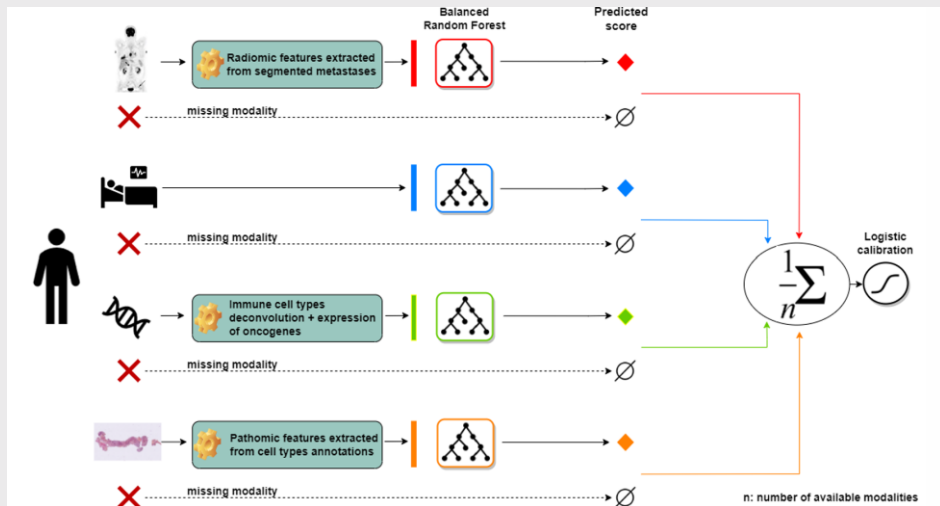


Integration of clinical, pathological, radiological, and transcriptomics data improves the prediction of first-line immunotherapy outcome in metastatic non-small cell lung cancer. N. Captier, M. Lerousseau, F. Orlhac, N. Hovhannisyan-Baghdasarian, M. Luporsi, E. Woff, S. Lagha, P. Salamoun Feghali, C. Lonjou, C. Beaulaton, H. Salmon, T. Walter, I. Buvat, N. Girard, E Barillot. En revision. Nature Communications.



# Construction de modèles radiomiques ou multi-modaux

- Stratégie de fusion tardive des modèles unimodaux avec gestion des modalités manquantes
- Modèles multimodaux > modèles unimodaux

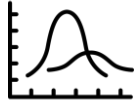
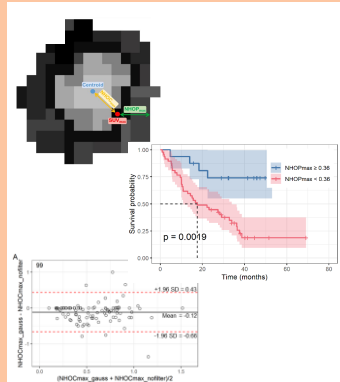


→ Collecte de grandes cohortes multimodales indispensable pour développer et valider des biomarqueurs d'immunothérapie robustes et puissants.

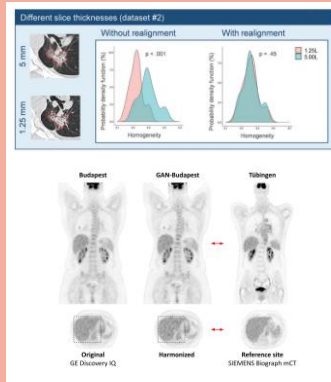
Integration of clinical, pathological, radiological, and transcriptomics data improves the prediction of first-line immunotherapy outcome in metastatic non-small cell lung cancer. N. Captier, M. Lerosseau, F. Orlhac, N. Hovhannisyan-Baghdasarian, M. Luporsi, E. Woff, S. Lagha, P. Salamoun Feghali, C. Lonjou, C. Beaulaton, H. Salmon, T. Walter, I. Buvat, N. Girard, E Barillot. En revision. Nature Communications.



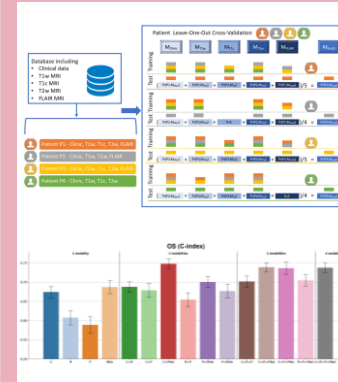
Découverte et  
caractérisation de  
nouveaux  
biomarqueurs



Harmonisation des  
biomarqueurs  
d'imagerie



Construction de  
modèles  
radiomiques ou  
multi-modaux

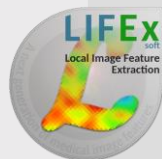


Développement et  
mise à disposition  
de nouveaux outils



# Local Image Feature Extraction Project

C. Nioche



Viewer

Image viewer of mono or multi-modalities (PET, SPECT, CT, MRI, US)



Texture

Textural features: radiomic features reflecting tissue heterogeneity



MTV

MTV: metabolic tumor volume over the whole body



Predictive models



Quality Control

LITO

Inserm

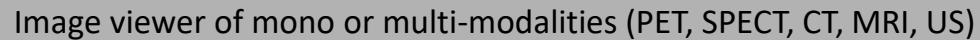


université  
PARIS-SACLAY

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Curie

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Curie

RÉPUBLIQUE  
FRANÇAISE  
Liberté  
Égalité  
Fraternité







# LIFEx, producer of image texture analysis results

C. Nioche, F. Orhlaç, I. Buvat

The screenshot displays the LIFEx software interface, which is used for image texture analysis. The interface is divided into several panels:

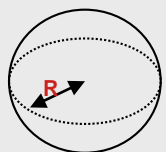
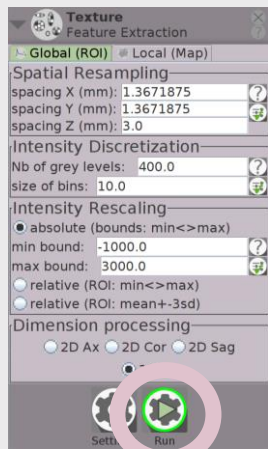
- Texture Panel (Left):** This panel is highlighted with a pink circle. It contains settings for texture analysis, including:
  - Spatial Resampling:** spacing X (mm): 1.3671875, spacing Y (mm): 1.3671875, spacing Z (mm): 3.0
  - Intensity Discretization:** Nb of grey levels: 400.0, size of bins: 10.0
  - Intensity Rescaling:** absolute (bounds: min<=>max), min bound: -1000.0, max bound: 3000.0, relative (ROI: min<=>max), relative (ROI: mean+-3sd)
  - Dimension processing:** 2D Ax, 2D Cor, 2D Sag, 3D
- Applied to selected series:** A list of series with checkboxes for applying texture analysis.
- Measure:** A section with various measurement tools like Max, Histo, Dist, etc.
- Display:** A section with display options like Auto, Trans, FlipAP, etc.
- Operations between series:** A section with operations like SA+SB, SA-SB, etc.
- Tools:** A section with tools like Merge, Add se..., Subtra..., etc.
- INFO:** A section with information about the current series.
- Drag images or scripts:** A section with a 'Drop here' button and a list of supported file formats (dcm, nii, DICOMDIR, etc.).
- Notification(s):** A section with a 'Drop here' button and a list of supported file formats (dcm, nii, DICOMDIR, etc.).
- Main View:** A large central area showing a PET/CT scan with texture analysis results. It includes a list of series on the left, a central image area, and a right panel with measurement results.
- Right Panel:** A section with measurement results, including ROI ID, min, mean, max, peak, nbVx, and volume.



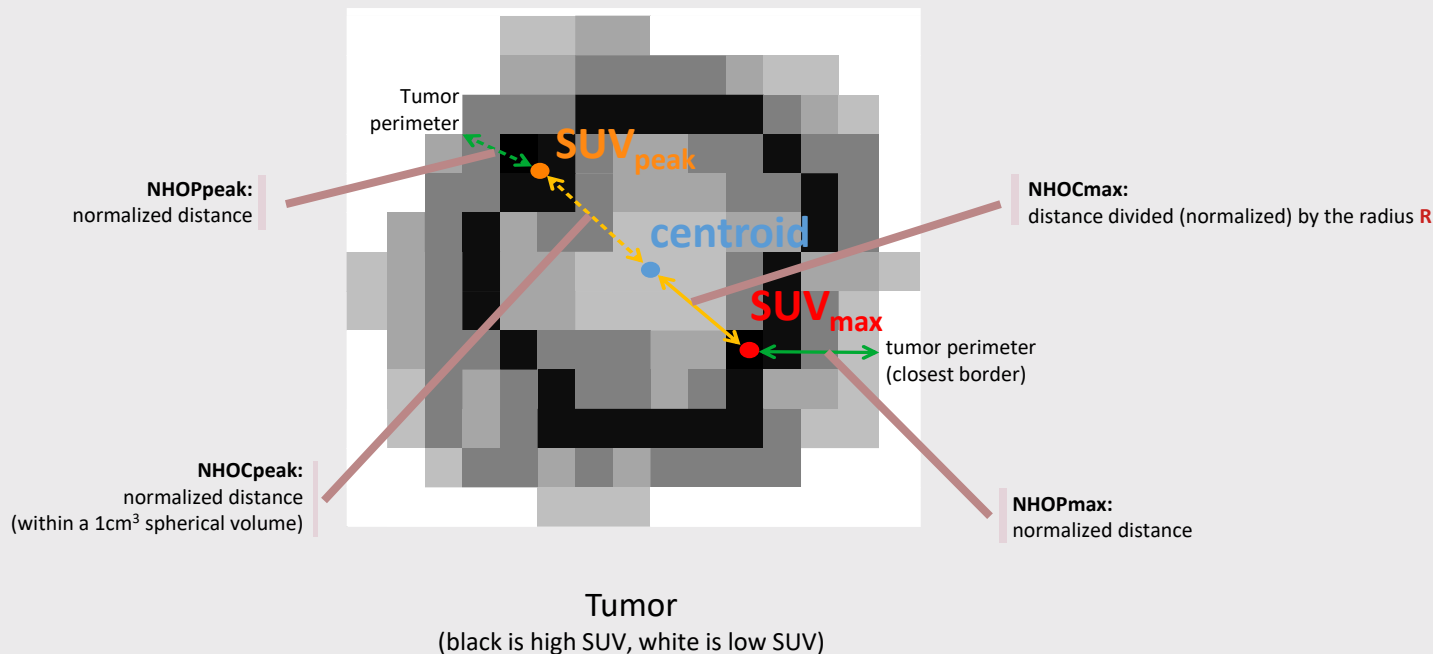
# LIFEx, producer of image texture analysis results

C. Nioche, N. Hovhannisyan-Baghdasarian, I. Buvat, F. Orlhac

## Always adding new radiomic features



Hypothetical sphere of radius  $R$   
having the same volume as the tumor

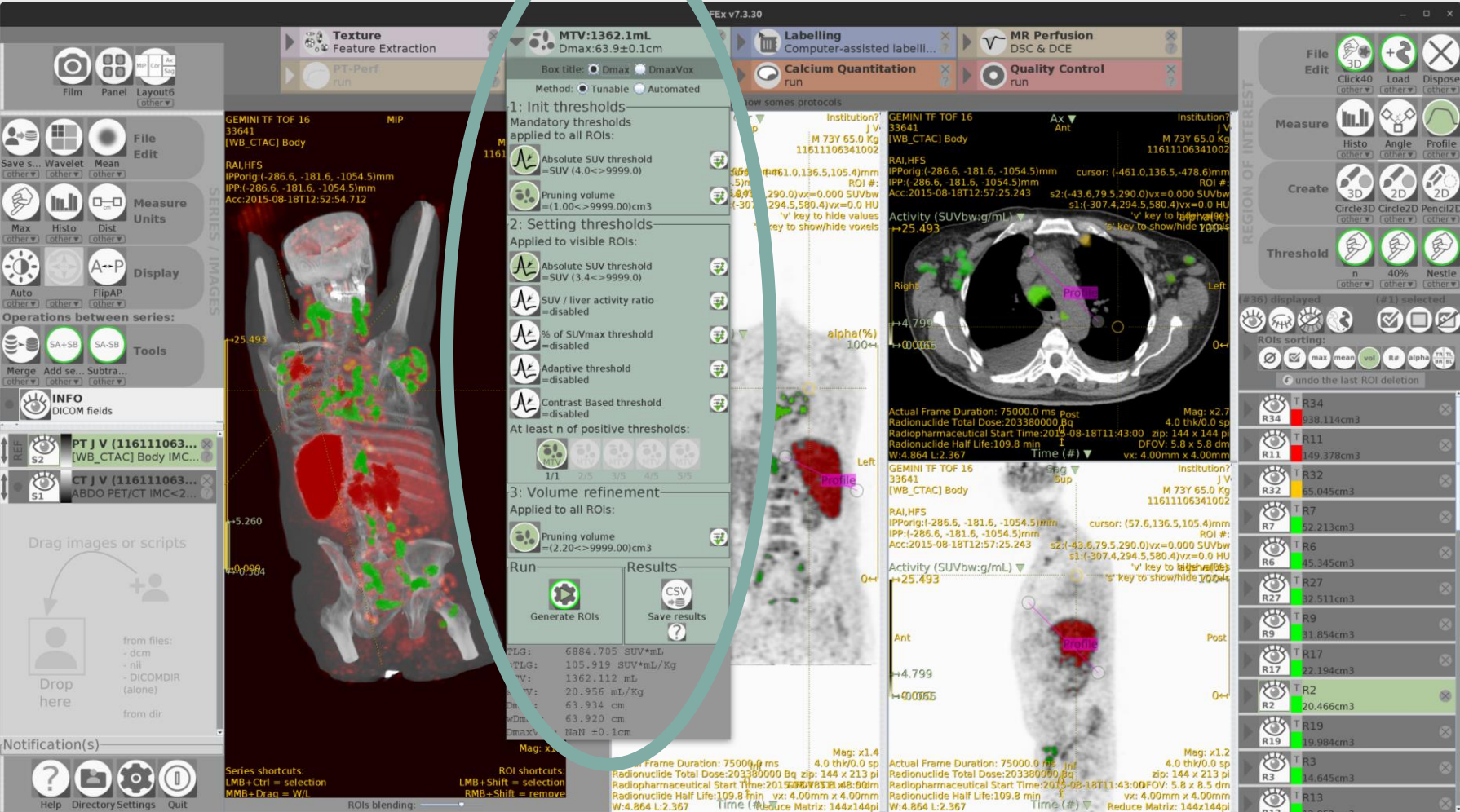


Narinée Hovhannisyan-Baghdasarian, Marie Luporsi, Nicolas Captier, Christophe Nioche, Vesna Cuplov, Erwin Woff, Nadia Hegarat, Alain Livartowski, Nicolas Girard, Irène Buvat, Fanny Orlhac. Promising candidate prognostic biomarkers in [18F]FDG-PET images: Evaluation in independent cohorts of Non-Small Cell Lung Cancer Patients. Journal of Nuclear Medicine March 2024, jnumed.123.266331; DOI: <https://doi.org/10.2967/jnumed.123.266331>



# LIFEx, analysis of total metabolic volume

C. Nioche, I. Buvat





# LIFEx, analysis of total metabolic volume

C. Nioche, AS. Cottureau, I. Buvat

Always adding new radiomic features

MTV:1362.1mL  
Dmax:63.9±0.1cm

Box title: DmaxVox

Method: ☒ Tunable ☐ Automated

1: Init thresholds

Mandatory thresholds applied to all ROIs:

Absolute SUV threshold  
=SUV (4.0<>9999.0)

Pruning volume  
=(1.00<>9999.00)cm3

2: Setting thresholds

Applied to visible ROIs:

Absolute SUV threshold  
=SUV (3.4<>9999.0)

SUV / liver activity ratio  
=disabled

% of SUVmax threshold  
=disabled

Adaptive threshold  
=disabled

Contrast Based threshold  
=disabled

At least n of positive thresholds:

Dmax





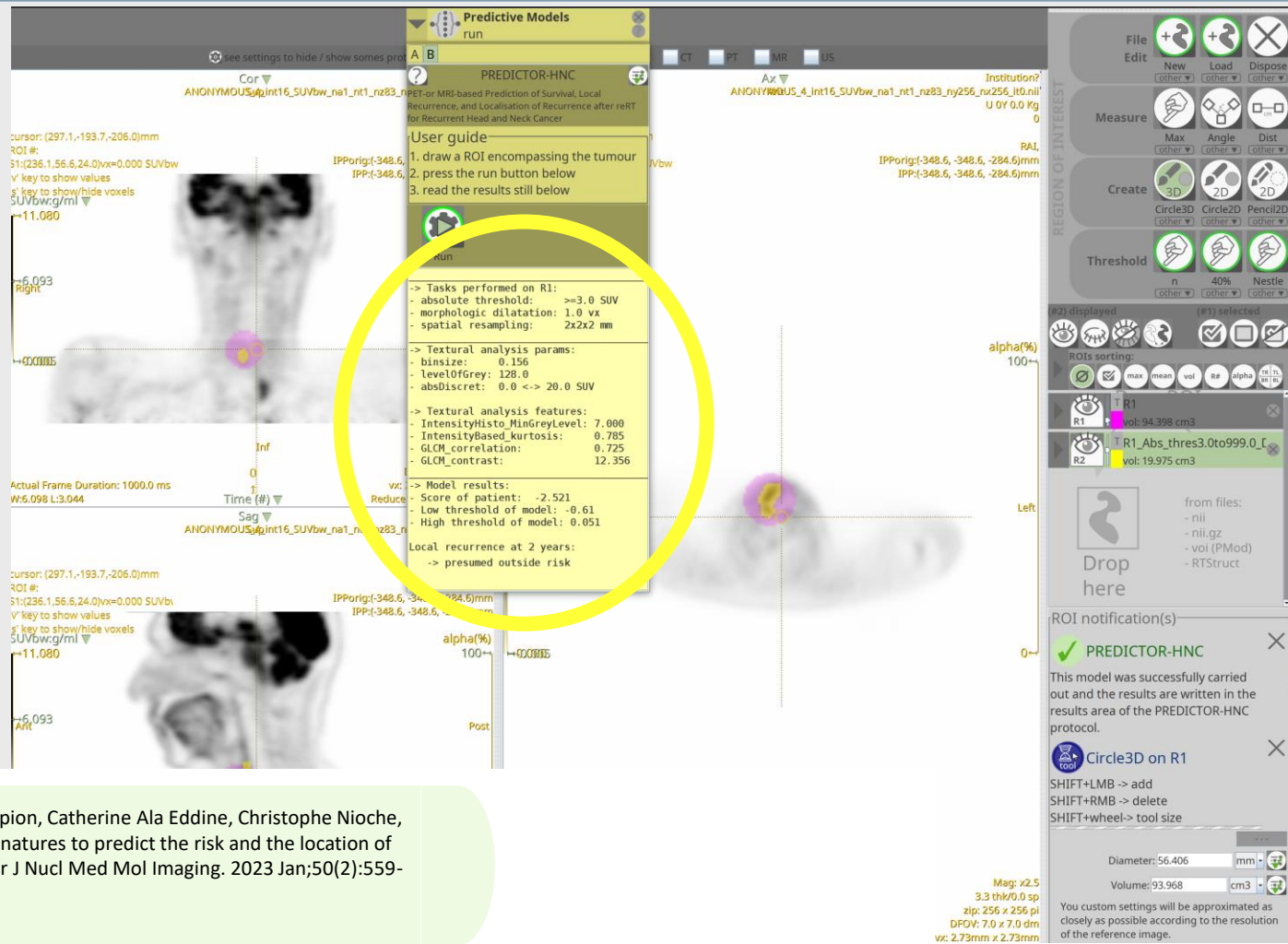
# LIFEx, its predictive models

## PREDICTOR-HNC

C. Nioche, A. Beddok, I. Buvat

### Purpose:

To evaluate whether radiomics from [18F]-FDG PET before re-irradiation (reRT) of recurrent head and neck cancer (HNC) could predict the occurrence and the location “in-field” or “outside” of a second loco-regional recurrence (LR).



Arnaud Beddok, Fanny Orlhac, Valentin Calugaru, Laurence Champion, Catherine Ala Eddine, Christophe Nioche, Gilles Créhange, Irène Buvat. [18F]-FDG PET and MRI radiomic signatures to predict the risk and the location of tumor recurrence after re-irradiation in head and neck cancer. Eur J Nucl Med Mol Imaging. 2023 Jan;50(2):559-571. doi: 10.1007/s00259-022-06000-7

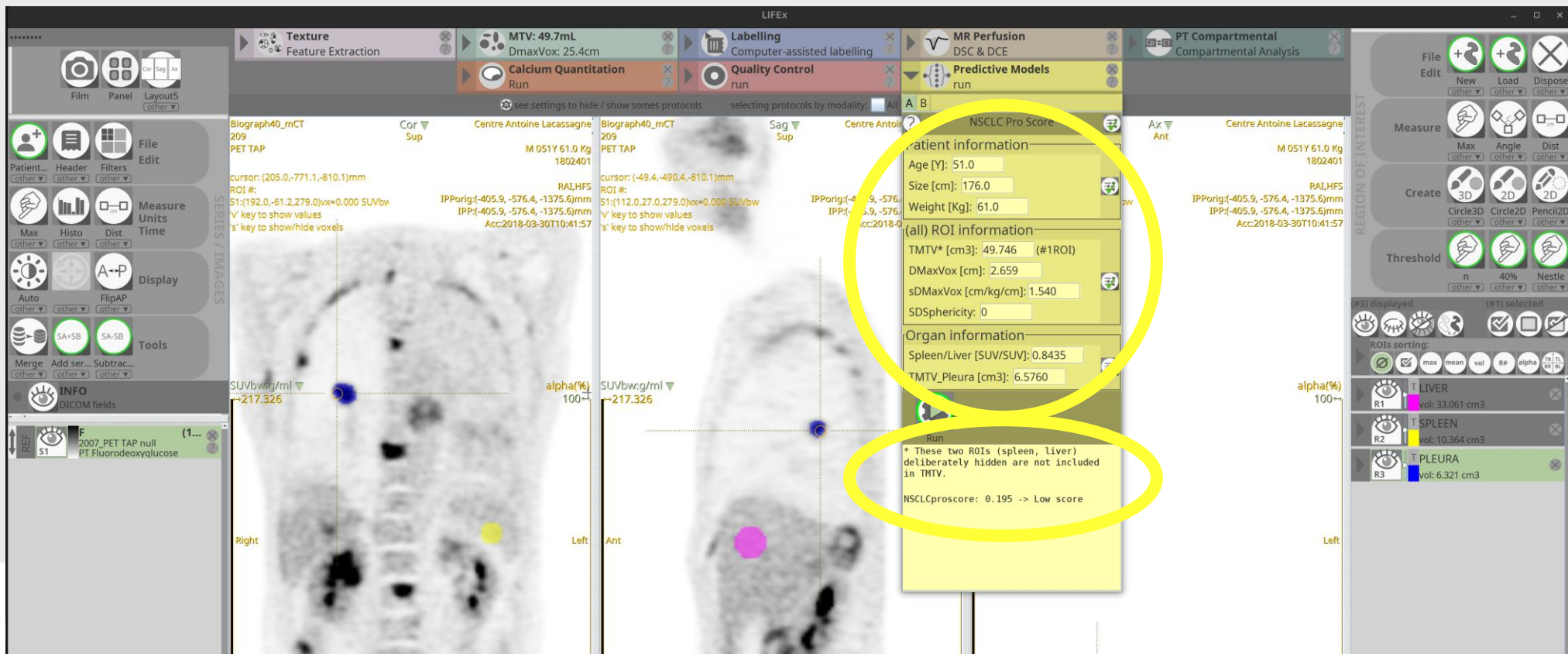


# LIFEx, its predictive models

## NSCLC Pro Score

C. Nioche, H. Fokem-Fosso, F. Orlhac

Purpose: Prediction of survival in NSCLC patients  
treated by immunotherapy alone  
or in combination with chemotherapy





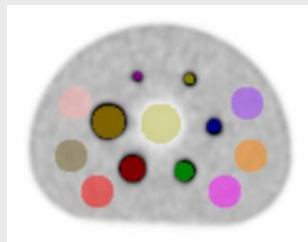
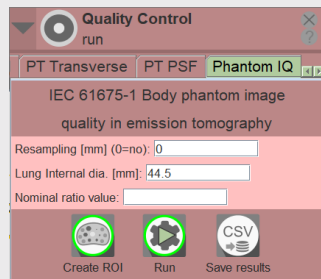
# LIFEx, PET-CT Quality Control

## NEMA IEC PET Body Phantom Set + Calibration and Axial/Transverse uniformity test

C. Nioche, M. Soret, C. Comtat

### Main:

- Evaluation of the PET system image quality in a standardized situation representative of a typical clinical condition.
- It follows the guidelines of the PET working group of the French Society of Medical Physics (SFPMP).



### 1.3.1 Calibration and axial uniformity test

A centered circular ROI is automatically drawn in yellow in each slice of the cylinder (see Figure 1.3).

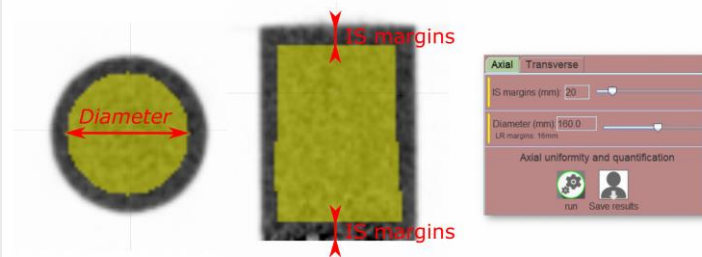


Figure 1.3: Definition of the ROIs for the calibration and axial uniformity test

### 1.3.2 Transverse uniformity test

A centered circular ROI in green and four peripheral circular ROIs in red are automatically drawn in each slice of the cylinder (see Figure 1.5).

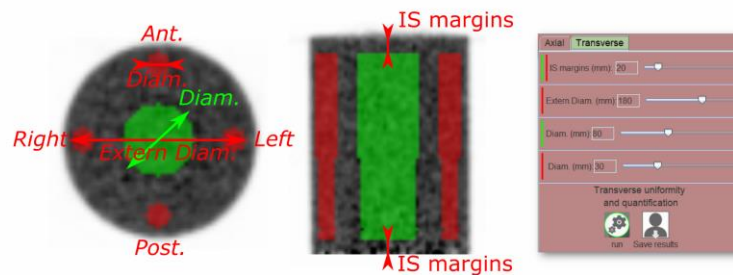
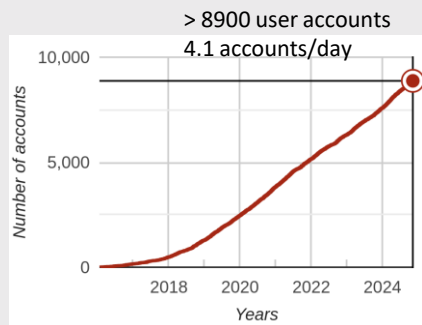
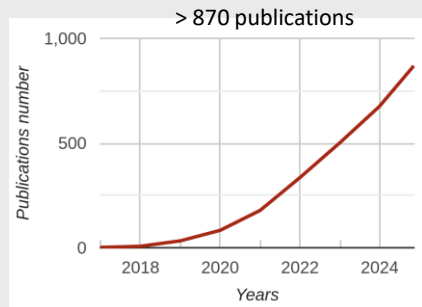


Figure 1.5: Definition of the ROIs for the transverse uniformity test



# LIFEx Analytics - since 2016

C. Nioche



C Nioche, F Orlhac, S Boughdad, S Reuzé, J Goya-Outi, C Robert, C Pellot-Barakat, M Soussan, F Frouin, and I Buvat.  
LIFEx: a freeware for radiomic feature calculation in multimodality imaging to accelerate advances in the  
characterization of tumor heterogeneity. Cancer Research 2018; 78(16):4786-4789

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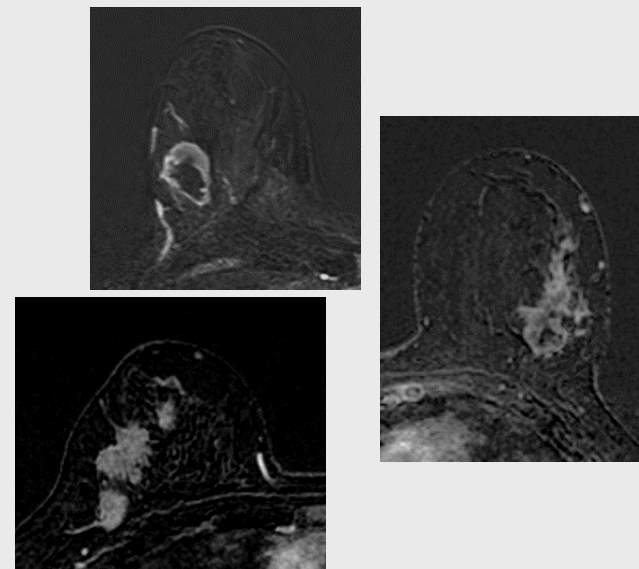
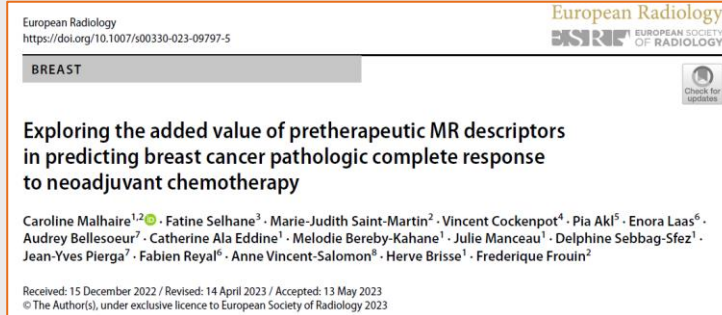
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RÉPUBLIQUE  
FRANÇAISE  
Liberté  
Égalité  
Fraternité

- Prédire la réponse à la chimiothérapie néoadjuvante dans des cancers localement avancés ou agressifs à partir d'IRM pré-thérapeutique et à mi-parcours
- Segmenter les cancers sur les IRM mammaires avec des méthodes « deep learning » pour le monitoring des traitements
- Constitution progressive de bases de données multi-critères (imagerie, biologie, suivi longitudinal, etc)
- Combiner BI-RADS (radiomique) et paramètres histomoléculaires
- **Meilleure compréhension des mécanismes oncologiques**
- **Accélération et optimisation de la recherche sur la radiomique en IRM mammaire**
- **Amélioration de la prise en charge des patients**

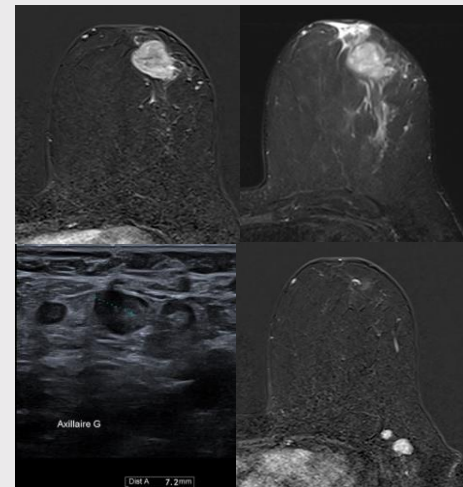
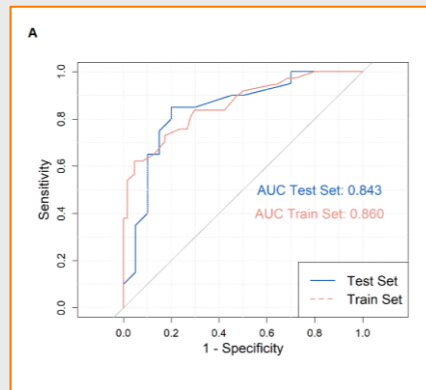
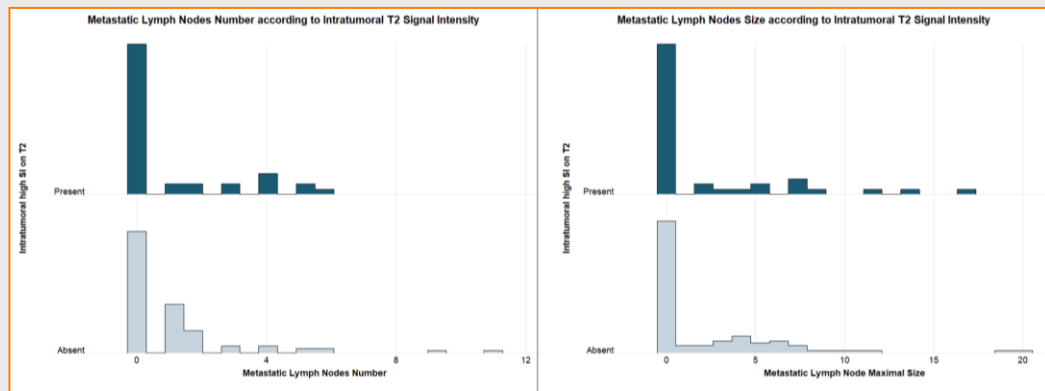


- Etude des critères sémantiques BI-RADS
- Associés en univarié à la réponse tumorale dans la population globale
  - Forme globale
  - Contours
  - Présence de multiples foyers
  - Taille tumorale globale en IRM
- Les contours spiculés et la multifocalité IRM sont des paramètres indépendamment associés à la réponse incomplète
- Amélioration des performances de prédiction par Random Forest



# Prédire la réponse ganglionnaire incomplète

- Évaluer la valeur de l'échographie axillaire et de l'IRM initiales pour prédire la maladie résiduelle axillaire après CNA
- Étudier la charge axillaire post-NAC en relation avec les caractéristiques d'imagerie

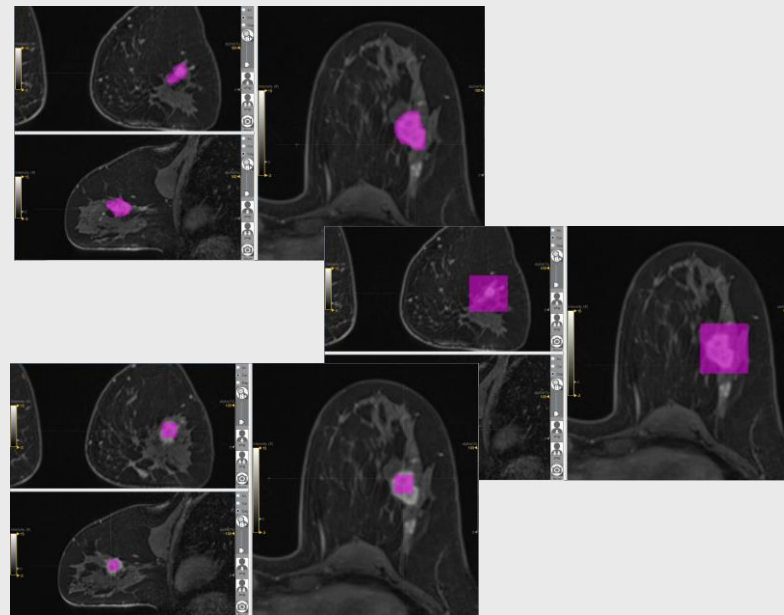


European Radiology  
Predicting Axillary Residual Disease to Neoadjuvant Therapy in Breast Cancer Using  
Baseline MRI and Ultrasound  
--Manuscript Draft--

Révision en cours

# Décrypter les paramètres predictifs de la reponse tumorale

- Décrypter les sources d'information issues des images IRM qui contribuent le plus à prédire la réponse à la CNA
- A l'aide d'analyses radiomiques basées sur différents types de VOI 3D
- La boîte englobante binaire améliore les performances des modèles prédictifs



2022 44th Annual International Conference of  
the IEEE Engineering in Medicine & Biology Society (EMBC)  
Scottish Event Campus, Glasgow, UK, July 11-15, 2022

**Decrypting the information captured by MRI-radiomic features in  
predicting the response to neoadjuvant chemotherapy in breast cancer\***

Marie-Judith Saint Martin<sup>1</sup>, Frédérique Frouin<sup>1</sup>, Caroline Malhaire<sup>1,2</sup> and Fanny Orlhac<sup>1</sup>



# Segmenter automatiquement les cancers mammaires

## Evaluation vis-à-vis d'un expert

Passage sur d'autres BDD:

Tumeur de petite taille

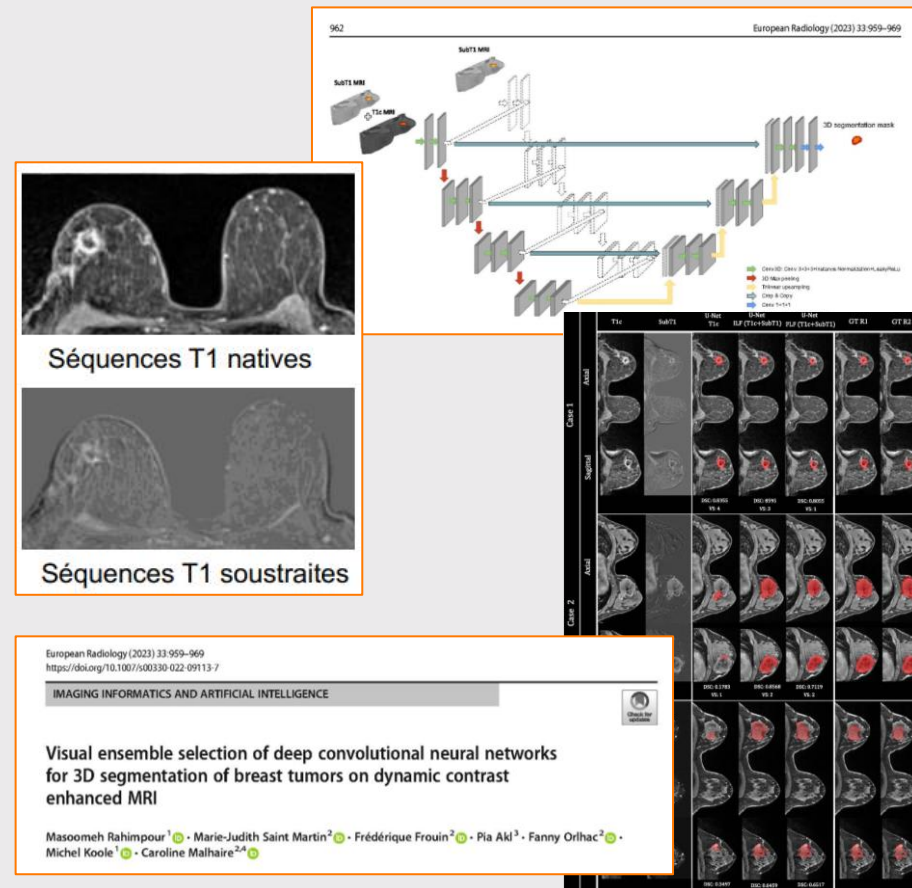
Confusions, eg. kyste, PAC

*Droquet M, Stage EFREI, 2023*

## Défi : augmenter la robustesse

1. Poursuite de la constitution de la base d'apprentissage (augmenter le nombre de sujets, le nombre d'images en considérant l'examen dans sa globalité)
2. Trouver des critères quantitatifs prédictifs des échecs

*Steinmetz P, AI DReAM oct 2023*



- Recherche de facteurs pronostiques
- Corrélations aux biomarqueurs réponse tumorale : TILs
- Caractérisation de l'hétérogénéité tumorale (IHU Cancers des femmes & Womens' atlas)
- Etude de la réponse des carcinomes luminaux a la chimioimmunothérapie combinée à la radiothérapie pre-opératoire (Neo-checkray)
  - Collaboration KU Leuven, Centre Georges François Leclerc

