



Laboratoire d'Imagerie Translationnelle en Oncologie

U1288 – groupe RIM

www.lito-web.fr

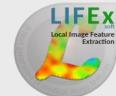
Frédérique Frouin / Fanny Orlhac /
Christophe Nioche / Caroline Malhaire



- 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 Fasso, 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)
- 17 Etudiants stages M2/M1/ fin école ingénieurs
- 16 Etudiants en thèse de sciences



- 1 titularisation CRCN Inserm
- 1 promotion CRHC Inserm
- 1 CDD IR -> 1 CDI (CdR Curie)



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

Radiomique Intégrative pour une Médecine de précision - Bilan « Prix »

5



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

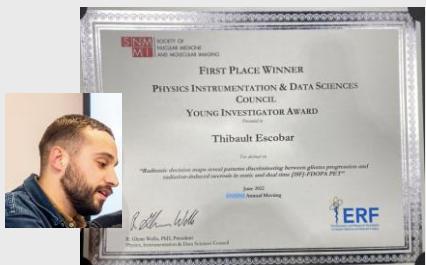
Christophe Nioche, Fanny Orlhac, Sarah Boughdad, Sylvain Reuzé, Jessica Goya-Outi, Charlotte Robert, Claire Pellet-Barakat, Michael Soussan, Frédérique Frouin, and Irène Buvat



Irène Buvat

The Best of the AACR Journals 13

AACR American Association for Cancer Research



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"



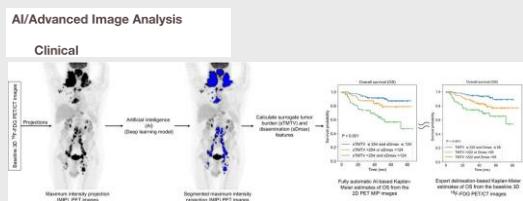
SOCIETY OF
NUCLEAR MEDICINE &
MOLECULAR IMAGING



May 24, 2023

Dear Kibrom B Girum:

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



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

Kibrom B. Girum, Louis Rebaud, Anne-Ségolène Cottereau, Michel Meignan, Jérôme Clerc, Laetitia Vercellino, Olivier Casarnovas, 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

SIEMENS
Healthineers

DOSI soft

 GE HealthCare

AI.DReAM



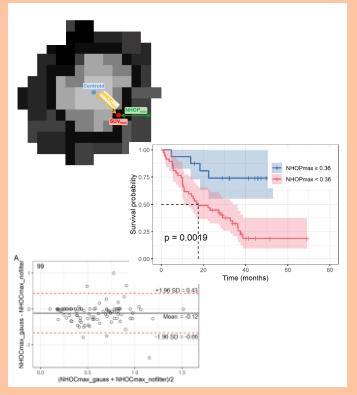
Mindray soutient une recherche pionnière sur l'échographie à l'Assistance Publique - Hôpitaux de Paris et à l'Institut Curie



 **apteryx**
Software edition and R&D services
in
Image processing and Web technology



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.

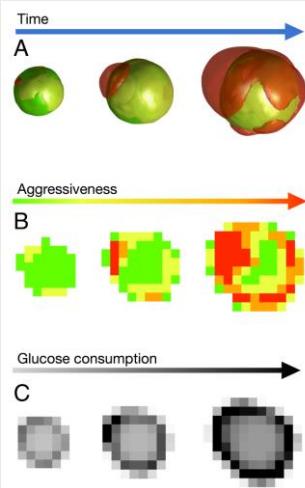
Evolutionary dynamics at the tumor edge reveal metabolic imaging biomarkers

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

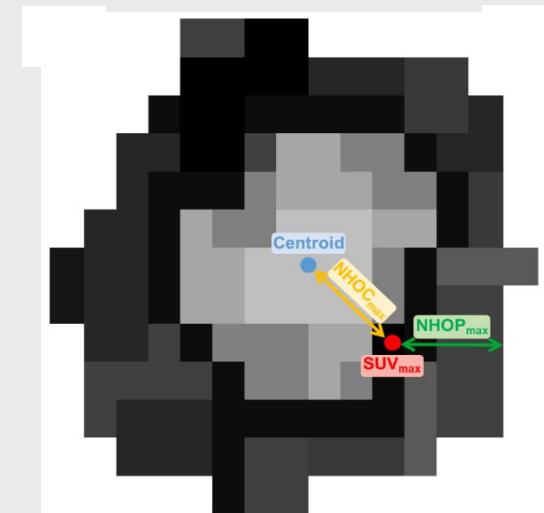
> Eur Radiol. 2022 Jun;32(6):3889-3902. doi: 10.1007/s00330-021-08523-3. Epub 2022 Feb 8.

SUV_{max} to tumor perimeter distance: a robust radiomics prognostic biomarker in resectable non-small cell lung cancer patients

Germán Andrés Jiménez Londoño ¹, Ana María García Vicente ², Jesús J Bosque ³, Mariano Amo-Salas ⁴, Julián Pérez-Beteta ³, Antonio Francisco Honquero-Martínez ⁵, Victor M Pérez-García ³, Ángel María Soriano Castrejón ²



Evaluer de nouveaux biomarqueurs en imagerie TEP



NHOC : *Normalized distance from the **HOt** spot to the tumor **Centroid***

NHOP : *Normalized distance from the **HOt** spot to the tumor **Perimeter***

Images TEP-FDG pré-traitement – cancer pulmonaire



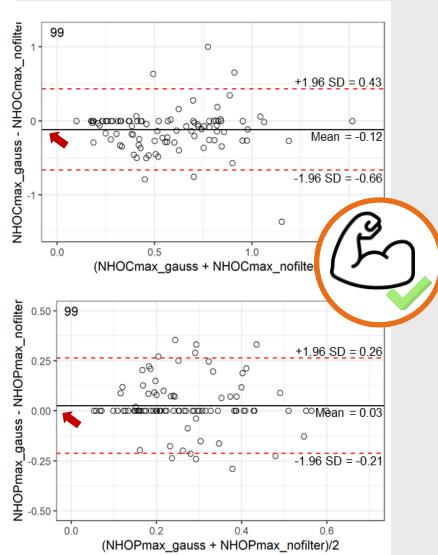
- Etude technique : 99 patients
- Analyse de survie : 244 patients

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

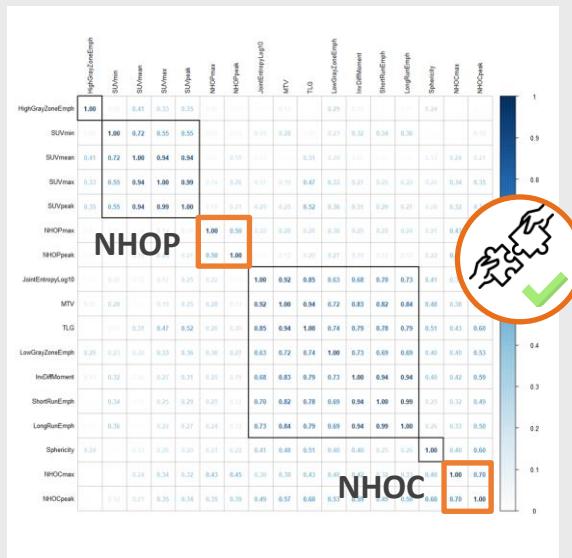
N. Hovhannisan-Baghdasarian, M. Luporsi, N. Captier, C. Nioche, V. Cuplov, E. Woff, N. Hegarat, A. Livartowski, N. Girard, I. Buvat, F. Orlhac.

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

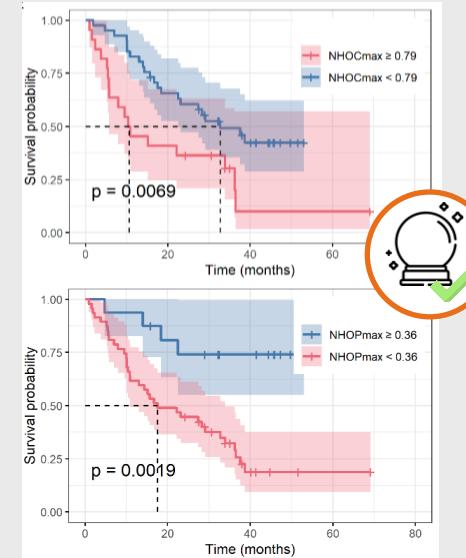
Découverte et caractérisation de nouveaux biomarqueurs



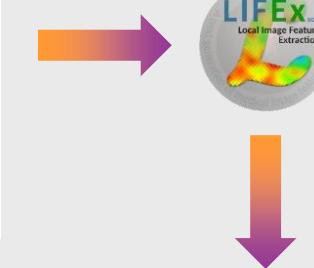
Robustes



Complémentaires



Pronostiques



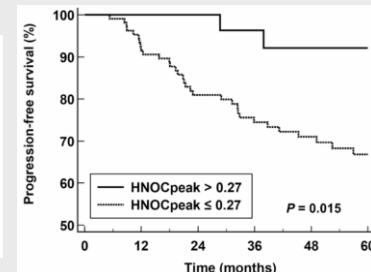
Promising candidate prognostic biomarkers in [18F] FDG PET images: evaluation in independent cohorts of NSCLC patients.

N. Hovhannisan-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.

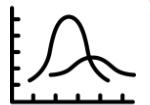
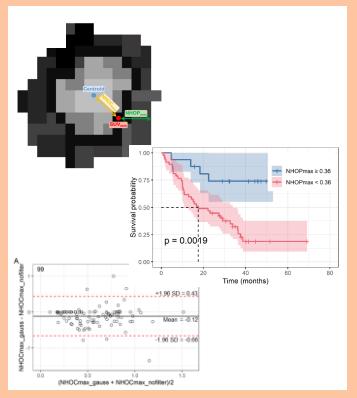
Clinical value of SUVpeak-to-tumor centroid distance on FDG PET/CT for predicting neoadjuvant chemotherapy response in patients with breast cancer

Sun-Pyo Hong ^{# 1}, Sang Mi Lee ^{# 1}, Ik Dong Yoo ¹, Jong Eun Lee ², Sun Wook Han ², Sung Yong Kim ², Jeong Won Lee ³

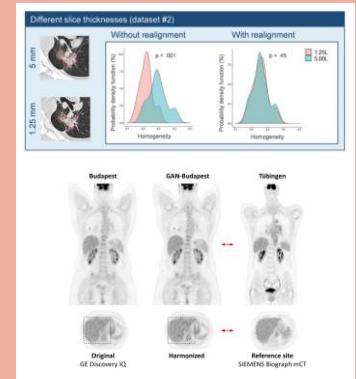




Découverte et caractérisation de nouveaux biomarqueurs



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**

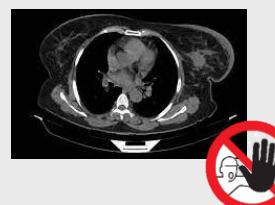
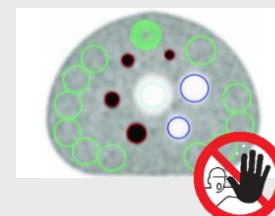


Etude prospective :

- 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 “batchs”

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

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

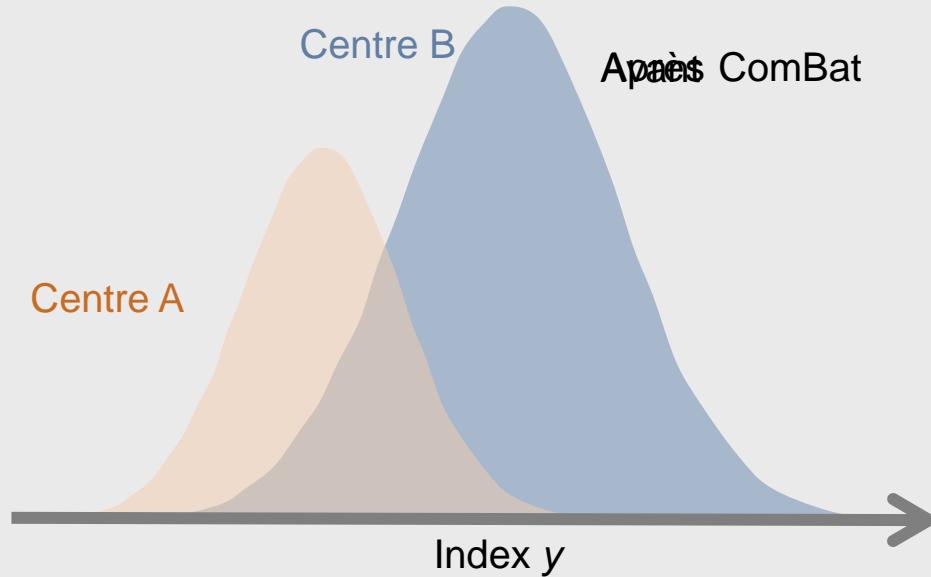
Valeur moyenne de l'index y

Effet scanner additif

Effet scanner multiplicatif

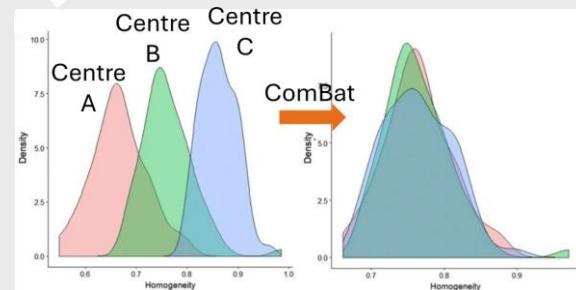
Terme d'erreur

Harmonisation des biomarqueurs d'imagerie



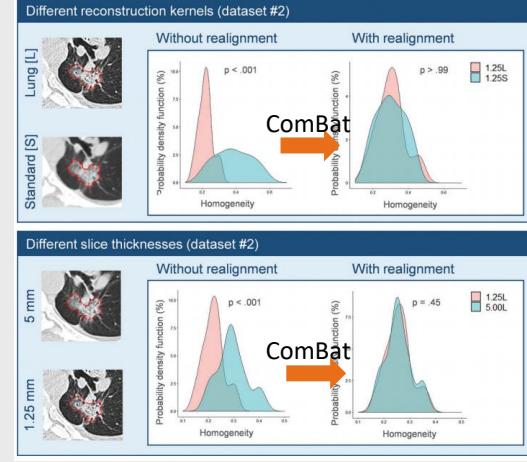
Harmonisation des biomarqueurs d'imagerie

- TEP



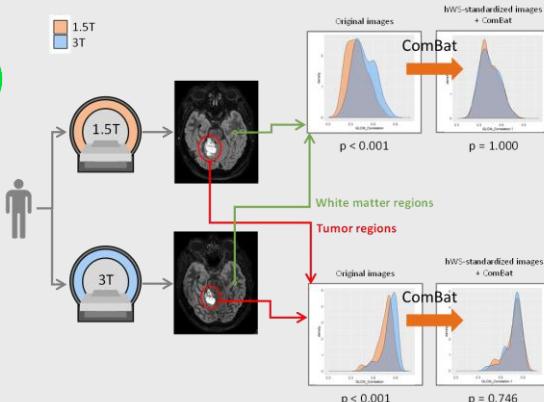
A post-reconstruction harmonization method for multicenter radiomic studies in PET.
F. Orlac, S. Boughdad, C. Philippe, H. Stalla-Bourdillon, C. Nioche, L. Champion,
M. Soussan, F. Frouin, V. Frouin, I. Buvat. J Nucl Med. 2018;59:1321-1328.

- TDM

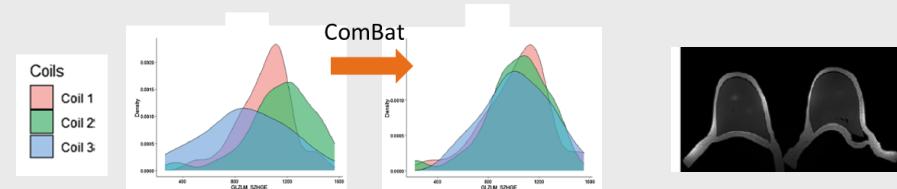


Validation of a method to compensate multicenter effects affecting CT Radiomics. F. Orlac, F. Frouin, C. Nioche, N. Ayache, I. Buvat. Radiology. 2019;291:53-59.

- IRM



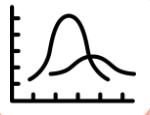
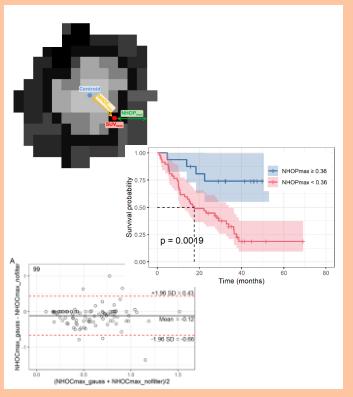
How can we ComBat multicenter variability in MR Radiomics? Validation of a correction procedure. F. Orlac, A. Lecler, J. Savatovski, J. Goya-Outi, C. Nioche, F. Charbonneau, N. Ayache, F. Frouin, L. Duron, I. Buvat. Eur Rad. 2021;31:2272-2280.



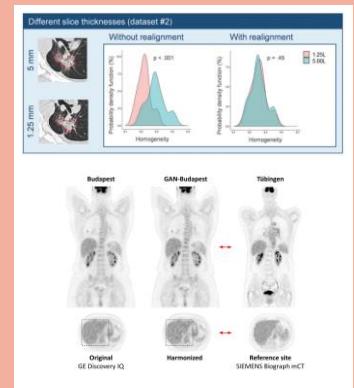
A radiomics pipeline dedicated to Breast MRI: validation on a multi-scanner phantom study. M-J. Saint Martin, F. Orlac, P. Akl, F. Khalid, C. Nioche, I. Buvat, C. Malhaire, F. Frouin. MAGMA 2021;34:355-366.



Découverte et caractérisation de nouveaux biomarqueurs



Harmonisation des biomarqueurs d'imagerie



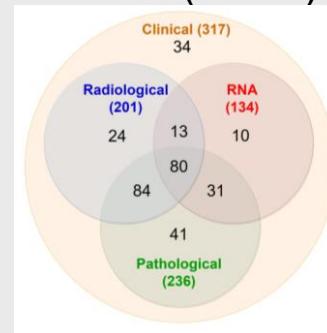
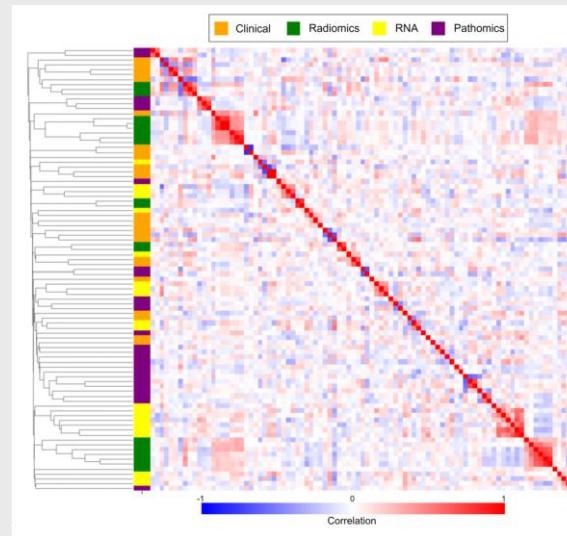
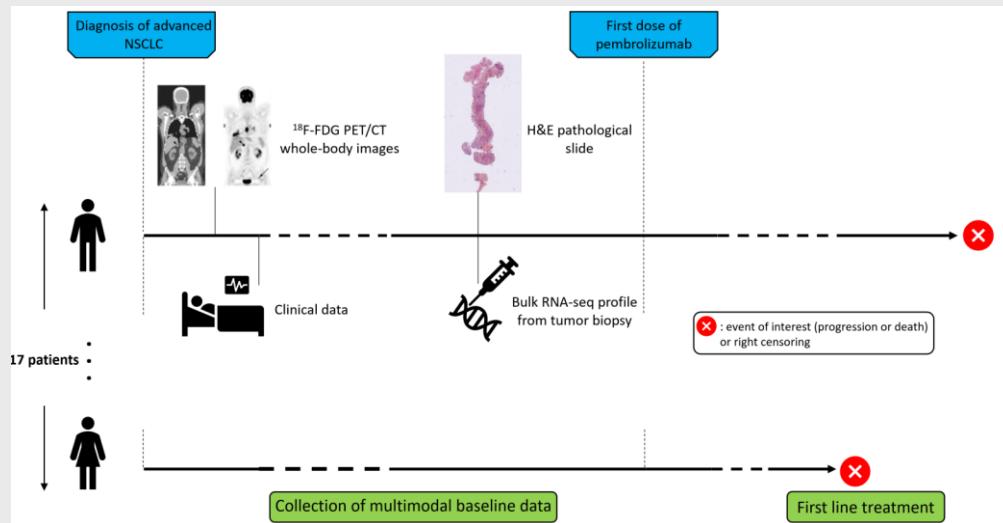
Construction de modèles radiomiques ou multi-modaux



Construction de modèles radiomiques ou multi-modaux



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

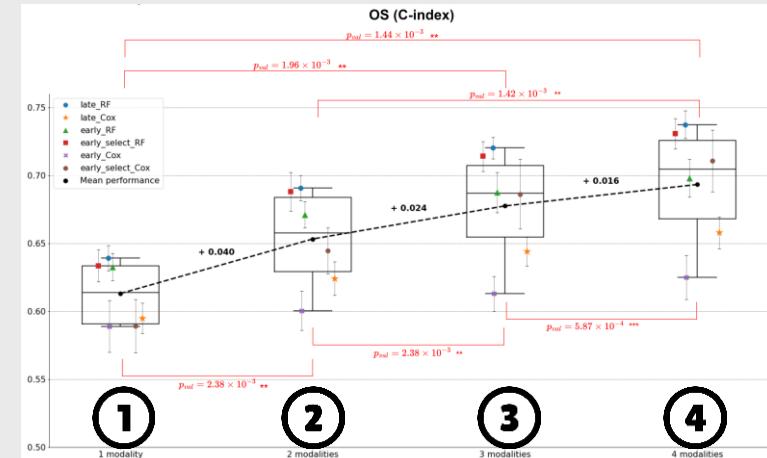
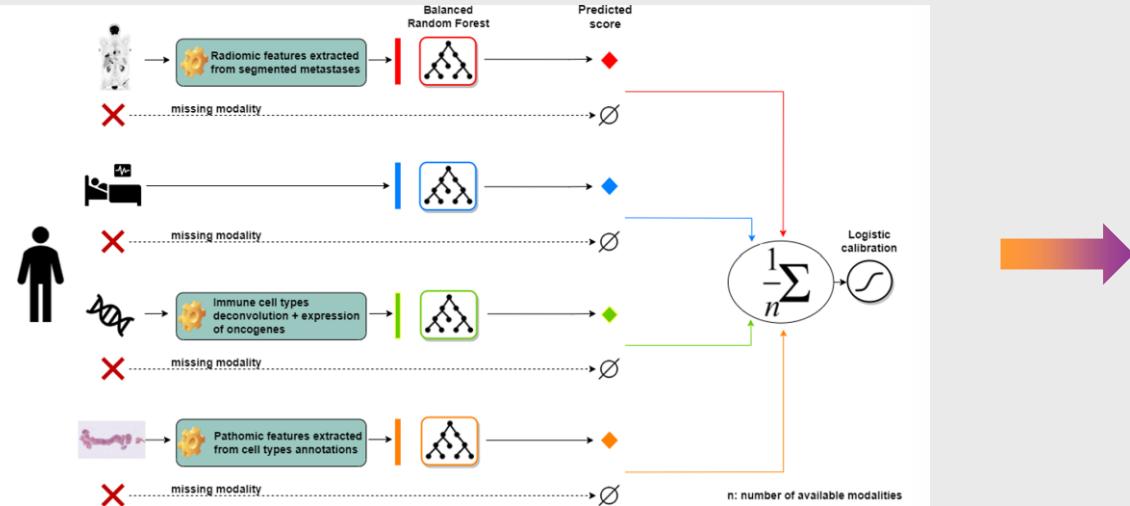


→ Complémentarité des biomarqueurs extraits

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. Hovhannisan-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

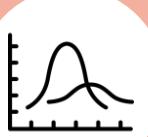
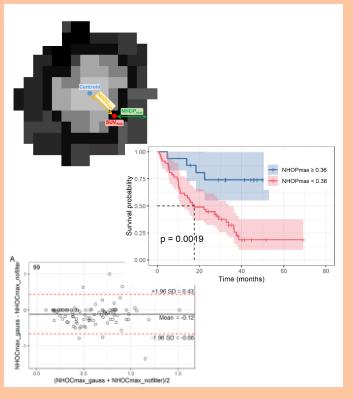


→ Collecte de grandes cohortes multimodales indispensable pour développer et valider des biomarqueurs d'immunothérapie robustes et puissants.

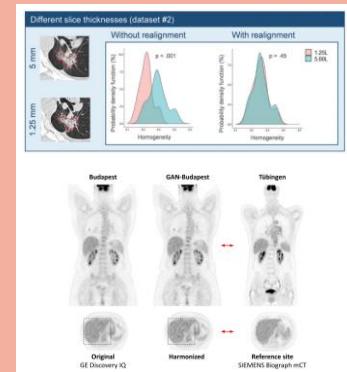
Integration of clinical, pathological, radiological, and transcriptomics data improves the prediction of first-line immunotherapy outcome in metastatic non-small cell lung cancer. N. Captier, M. Lerousseau, F. Orlhac, N. Hovhannisan-Baghdasarian, M. Luporsi, E. Woff, S. Lagha, P. Salamoun Feghali, C. 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 Projet

C. Nioche



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



Textural features: radiomic features reflecting tissue heterogeneity



MTV: metabolic tumor volume over the whole body



Predictive models



Quality Control

LITO

Inserm

cnrs
Centre National de la Recherche Scientifique

université
PARIS-SACLAY

institut
Curie



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

FREE



The screenshot displays a medical imaging software interface with three axial slices of a patient's torso. The left slice is a PET/CT fusion image (LIFEx) showing red hotspots. The middle slice is a grayscale CT scan (LIFEx) showing yellow Hounsfield units. The right slice is a grayscale CT scan (LIFEx) showing red hotspots. A histogram window on the right shows the distribution of voxel values.

Applied to selected series:

- Film
- Panel
- Layouts
- Other
- File
- Edit
- Measure Units
- A-P Display
- Display
- Operations between series:
- Merge
- Add se...
- Subtra...
- Tools

INFO DICOM fields

PT LIFEx (LIFEx)
S2 2006_PET_TAP_68SG5...

CT LIFEx (LIFEx)
S1 3_AC_CT_LIFEx

Drag images or scripts

Drop here

Notification(s)

Series shortcuts:
LMB+Ctrl = selection
LMB+Shift = selection
MMB+Drag = W/L
RMB+Shift = remove

ROI shortcuts:
LMB+Drag = ROI
RMB+Shift = remove

ROIs blending:

Mag: x1.9

MTV: 12.7mL
Dimax: 5.8±0.1cm

Biograph 6 MIP

LIFEx F OY Y 74.0 Kg AC_CT

RAI,HFS IPPorig(-349.3,-513.3,-1670.5)mm IPP(-349.3,-513.3,-1670.5)mm Acc:2018-04-13T10:01:18.938484

see settings to hide / show some protocols

Labeling Computer-assisted labelling

MR Perfusion DSC & DCE

PT Compartmental Compartmental Analysis

Applied to selected ROI:

File Edit New Load Dispose

Measure Histo Angle Dist

Create 3D 2D Circle3D Circle2D Pencil2D

Threshold n 40% other

Blending: S1 S2

1 selected ROI, all: select unselect

undo the last ROI deletion

PT_Anonym_RoiVolume_ R1 0.107cm³

PT_Anonym_RoiVolume_ R2 0.241cm³

Blending: S1 S2

ROI ID: 2 min: -930.0 HU mean: -813.90±51.0 HU max: -461.0 HU peak: NaN (see settings) nbVx: 1113 Vx volume: 6.241 cm³

Histogram

Number of voxels (#)

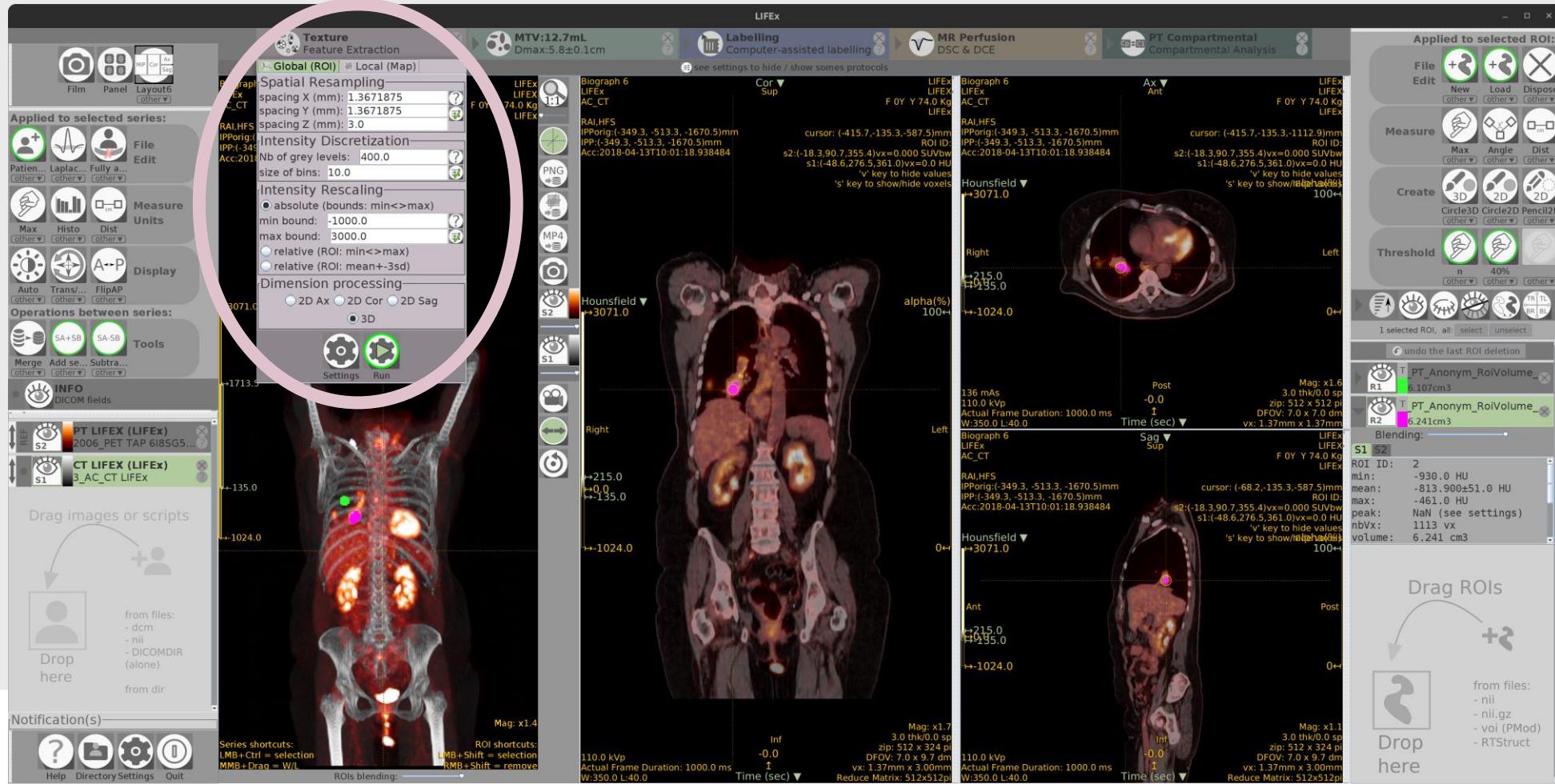
HU

DataFile1_PT_Anonym_RoiVolume_ DataFile1_PT_Anonym_RoiVolume_



LIFEx, producer of image texture analysis results

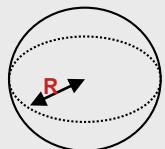
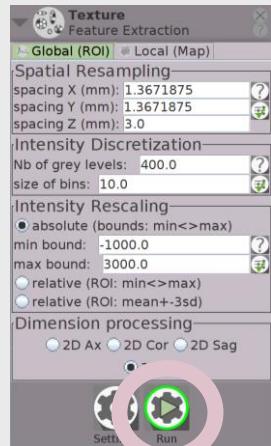
C. Nioche, F. Orhlac, I. Buvat



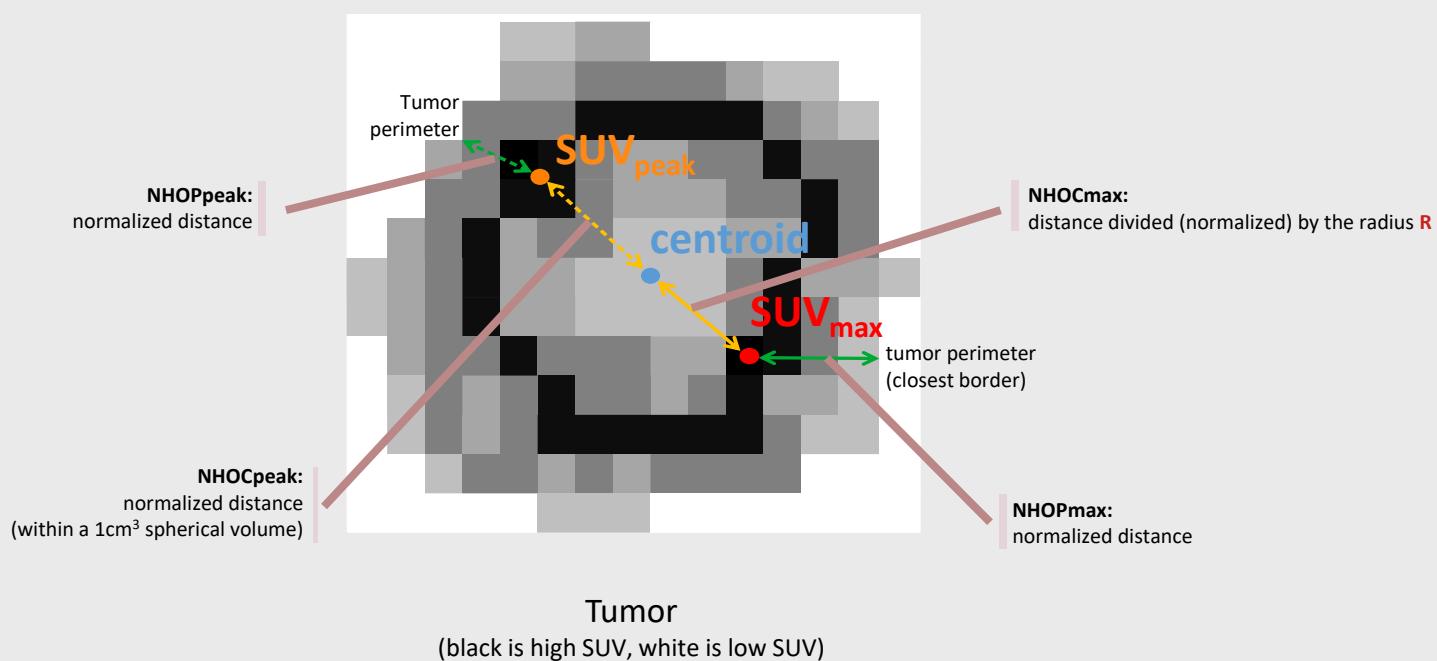
LIFEx, producer of image texture analysis results

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

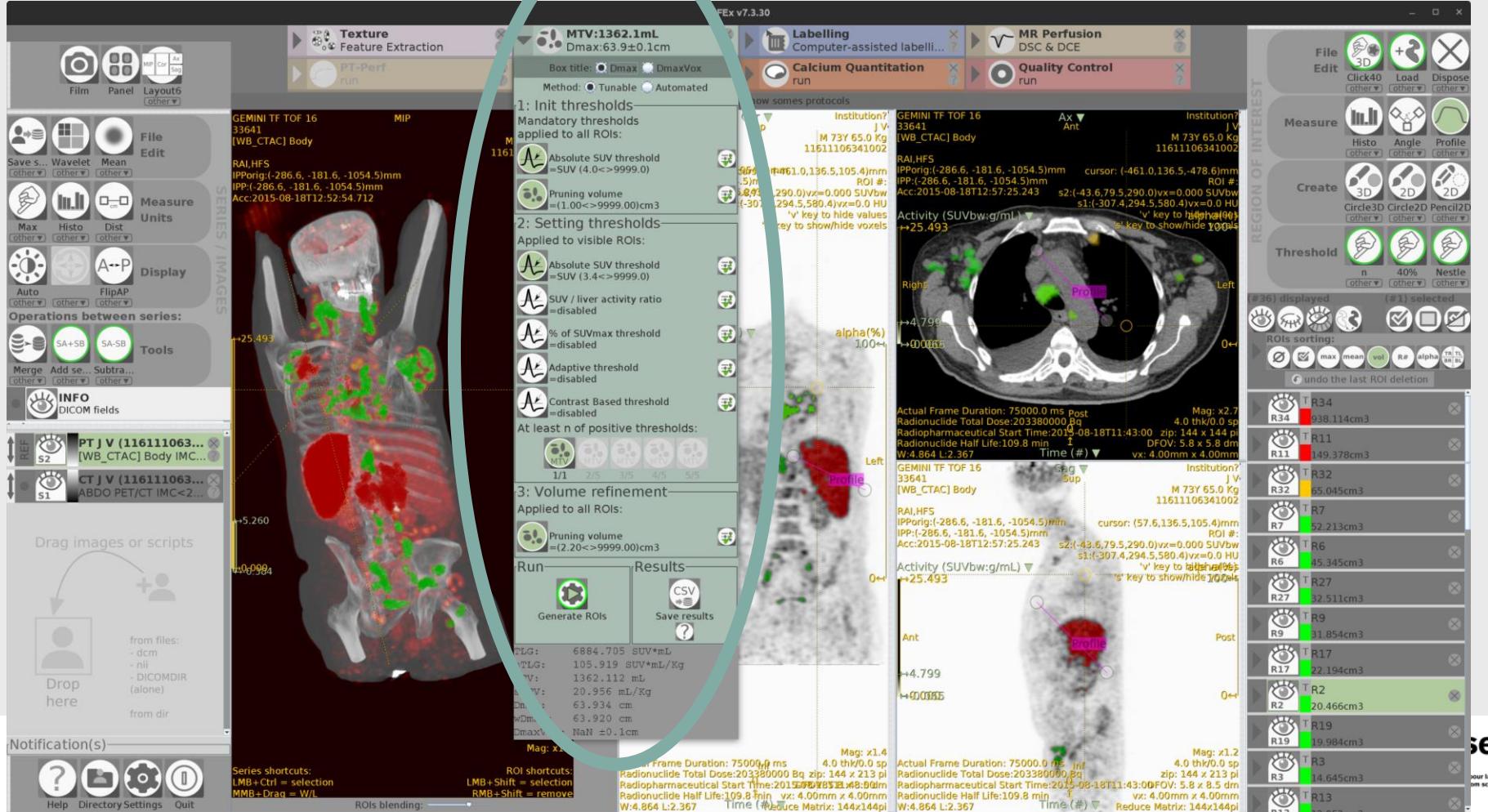


Narinée Hovhannisyan-Baghdasarian, Marie Luporsi, Nicolas Captier, Christophe Nioche, Vesna Cuplov, Erwin Woff, Nadia Hegarai, Alain Livartowski, Nicolas Girard, Irène Buvat, Fanny Orlhac. Promising candidate prognostic biomarkers in [18F]FDG-PET images: Evaluation in independent cohorts of Non-Small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



LIFEx, analysis of total metabolic volume

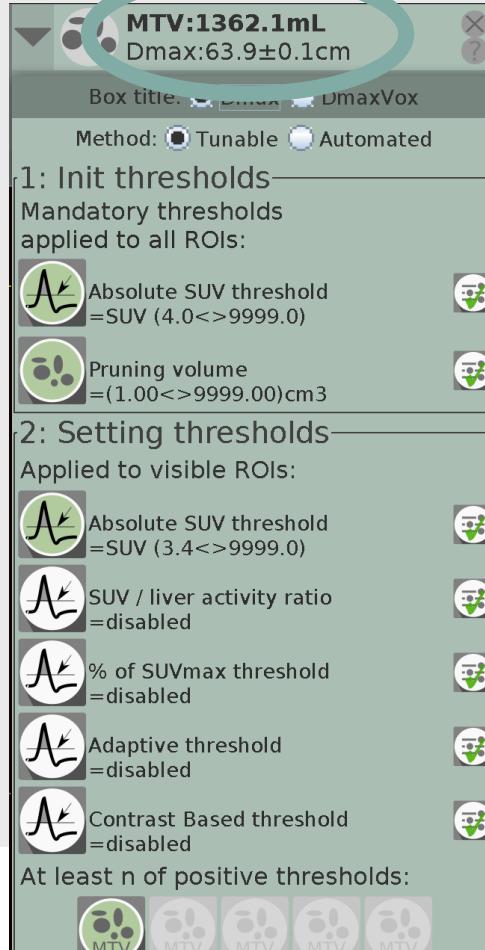
C. Nioche, I. Buvat





LIFEx, analysis of total metabolic volume

C. Nioche, AS. Cottreau, I. Buvat



Always adding new radiomic features

Dmax



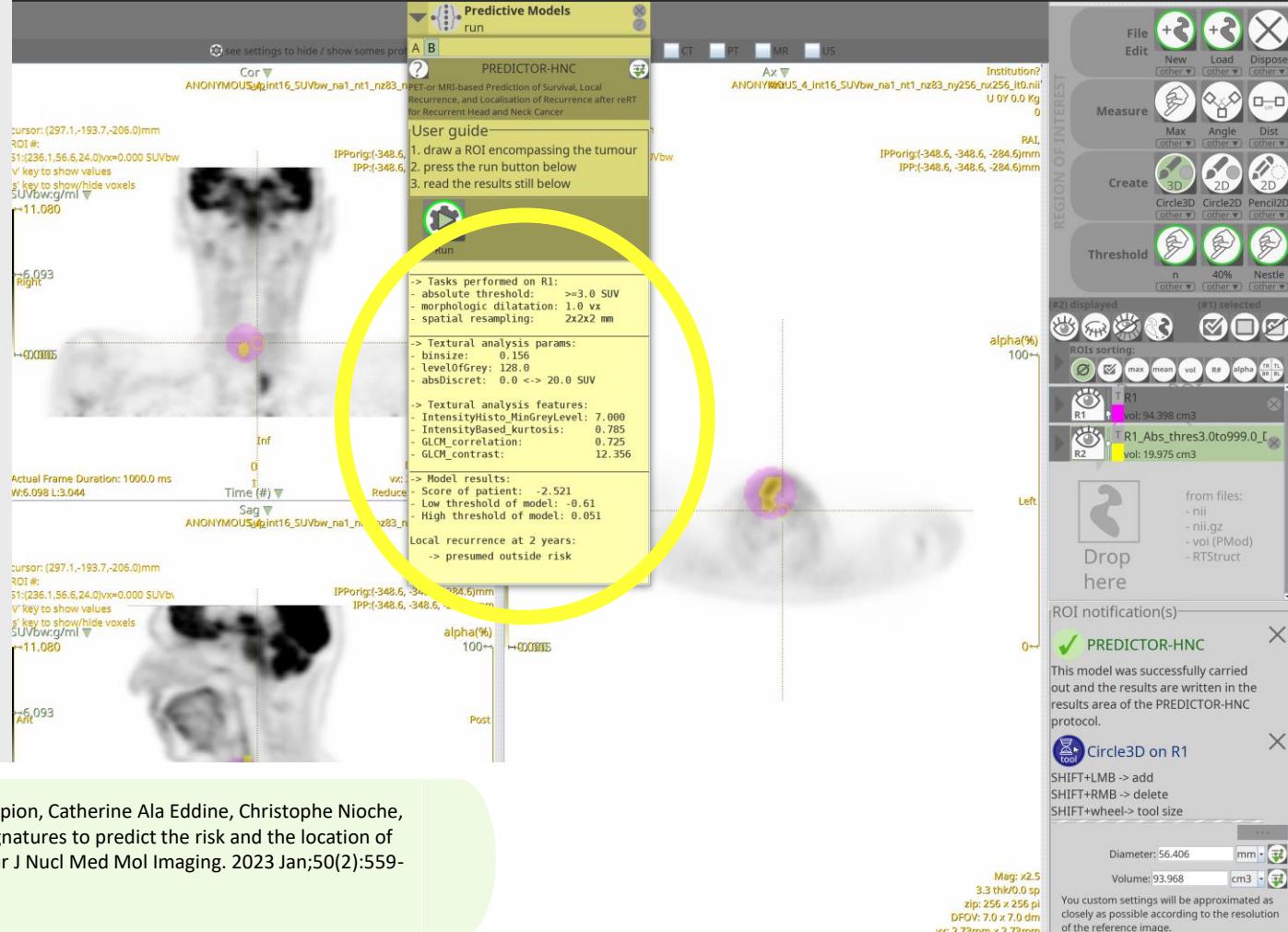
LIFEx, its predictive models

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

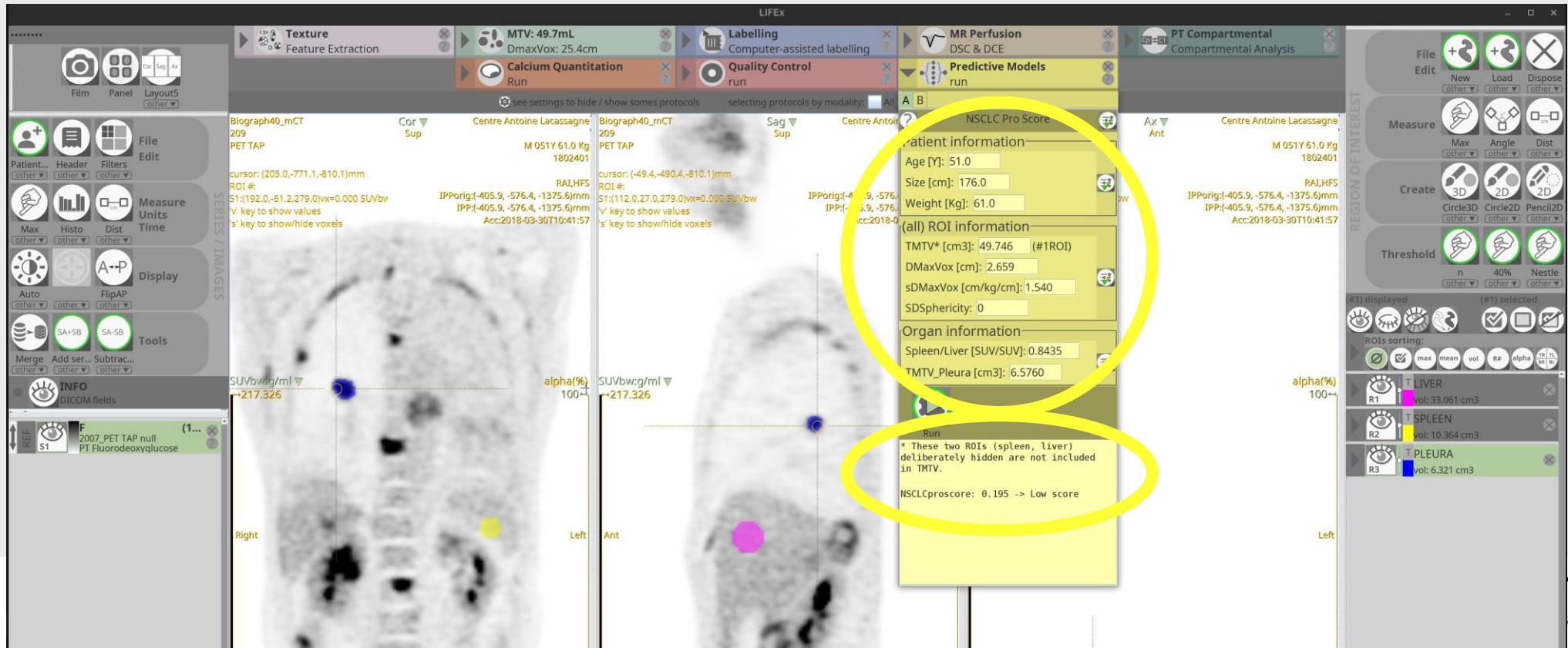


LIFEx, its predictive models

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





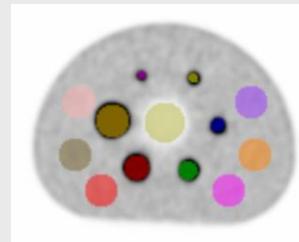
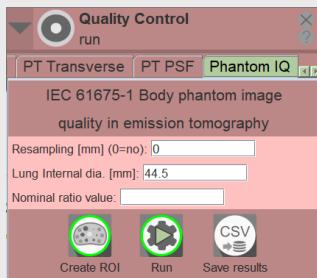
LIFEx, PET-CT Quality Control

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 (SFPM).



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).

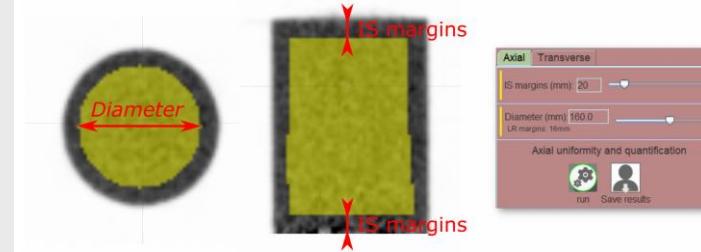


Figure 1.3: Definition of the ROIs for the calibration and axial uniformity test

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).

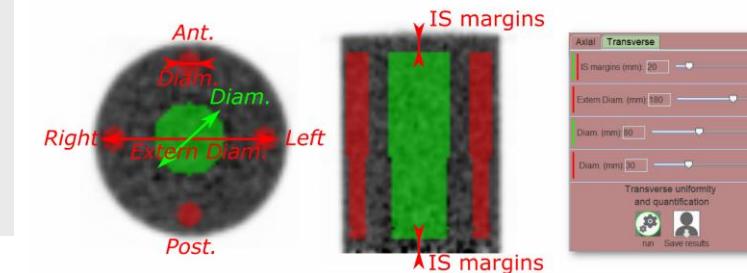
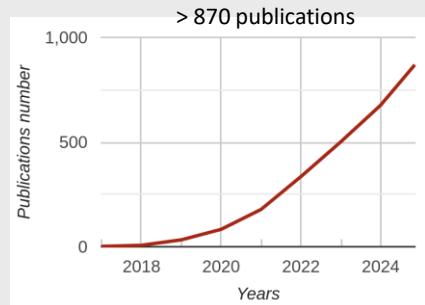


Figure 1.5: Definition of the ROIs for the transverse uniformity test



LIFEx Analytics - since 2016

C. Nioche



- 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

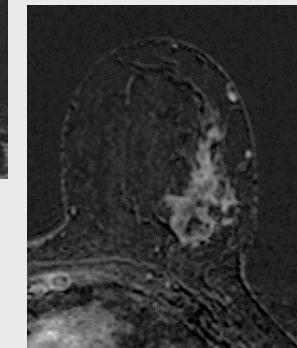
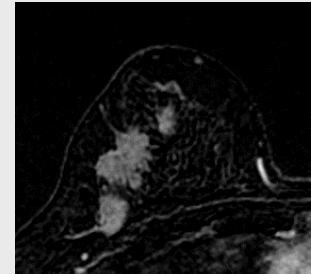
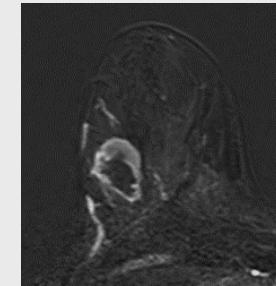
European Radiology
<https://doi.org/10.1007/s00330-023-09797-5>

BREAST

Exploring the added value of pretherapeutic MR descriptors in predicting breast cancer pathologic complete response to neoadjuvant chemotherapy

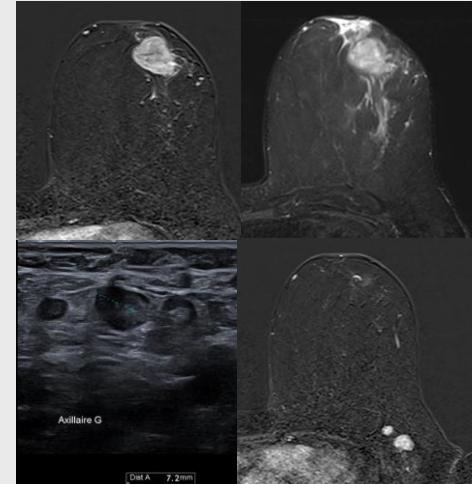
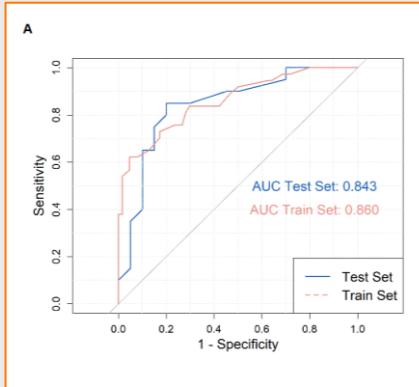
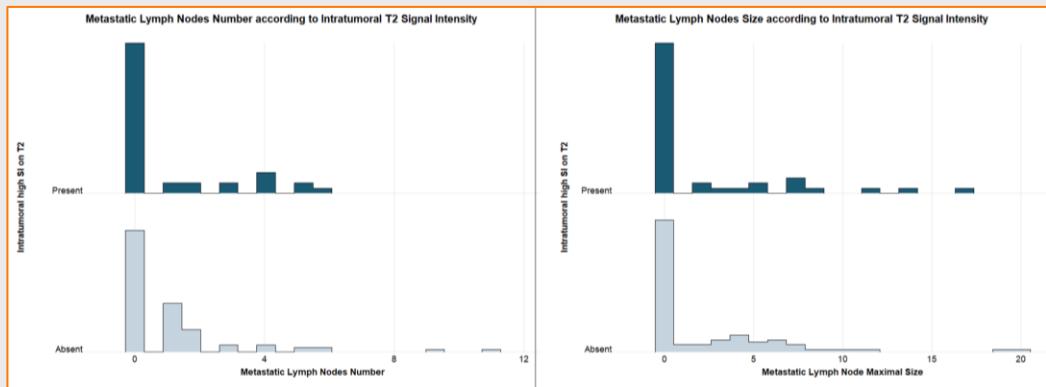
Caroline Malhaire^{1,2} , Fatiha Selhane³ · Marie-Judith Saint-Martin² · Vincent Cockenpot⁴ · Pia Aki⁵ · Enora Laas⁶ · Audrey Bellesoeur⁷ · Catherine Ala Eddine¹ · Melodie Bereby-Kahane¹ · Julie Manceau¹ · Delphine Sebbag-Sfez¹ · Jean-Yves Pierga⁷ · Fabien Reynal⁶ · Anne Vincent-Salomon⁸ · Hervé Brisse¹ · Frédérique Frouin²

Received: 15 December 2022 / Revised: 14 April 2023 / Accepted: 13 May 2023
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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

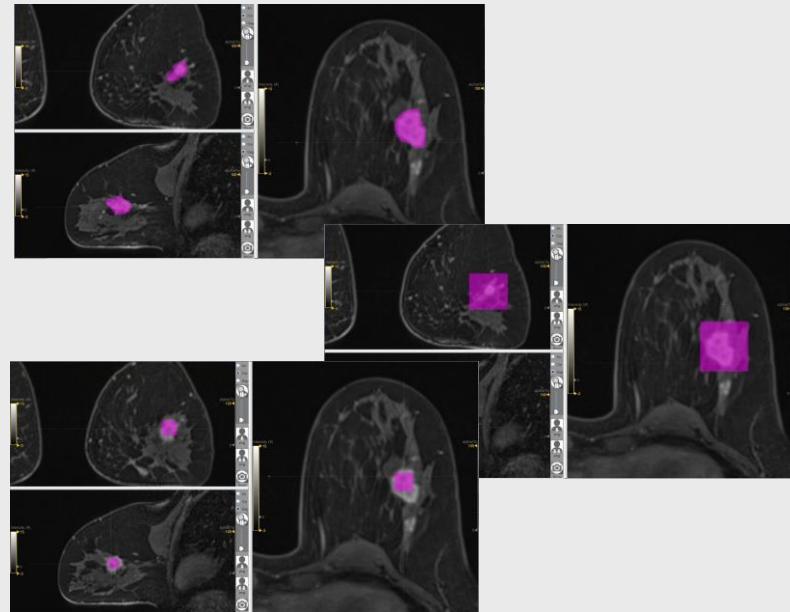
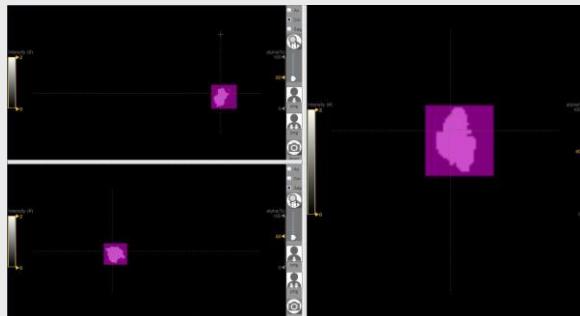


European Radiology
Predicting Axillary Residual Disease to Neoadjuvant Therapy in Breast Cancer Using Baseline MRI and Ultrasound
--Manuscript Draft--

Révision en cours

Décrypter les paramètres prédictifs de la réponse 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 Martin¹, Frédérique Frouin¹, Caroline Malhaire^{1,2} and Fanny Orlhac¹

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

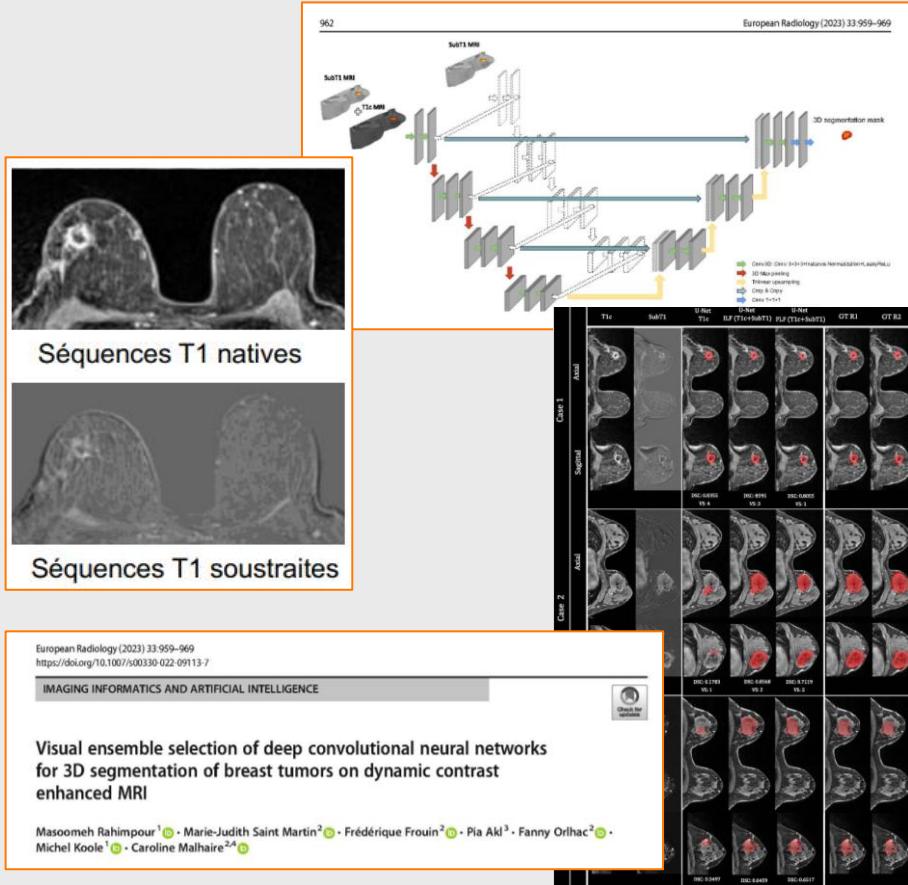
Droguet M, Stage EFREI, 2023

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)

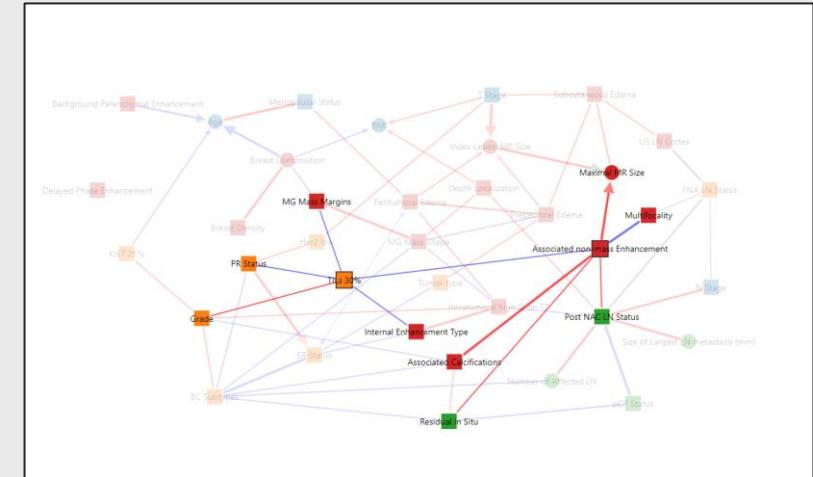
2. Trouver des critères quantitatifs prédictifs des échecs

Steinmetz P, AI DReAM oct 2023



Perspectives

- 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 à la chimioimmunothérapie combinée à la radiothérapie pré-opératoire (Neo-checkray)



- Collaboration KU Luewen, Centre Georges François Leclerc