



1er
COLLOQUE
onco
NOUVELLE-AQUITAINE



INNOVATIONS
EN CANCÉROLOGIE
Parcours et organisations

onco
NOUVELLE-AQUITAINE
Dispositif spécifique régional du cancer

Bordeaux

12 déc. 2024

Innovation en Pathologie:

Le projet eNovA-Path

ou la **pathologie numérique**

au service des patients et des pathologistes en
région Nouvelle Aquitaine

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Anatomie et Cytologie Pathologiques (ACP) en 2020

en France et en NoVa: état et enjeux...



Démographie

Perte séniorisation
Difficulté formation DES
Attractivité privé/région

Complexité

- Hyperspécialisation/
polycompétence
- Médicale et technique

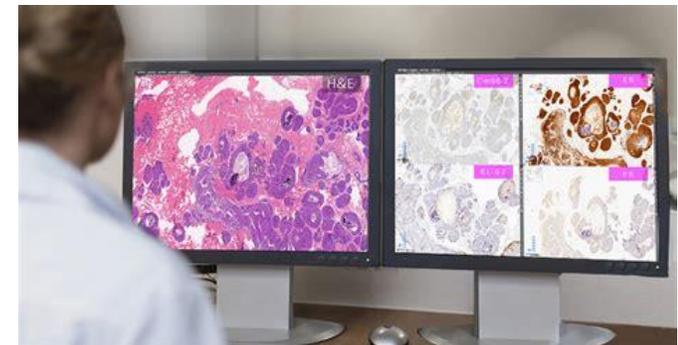
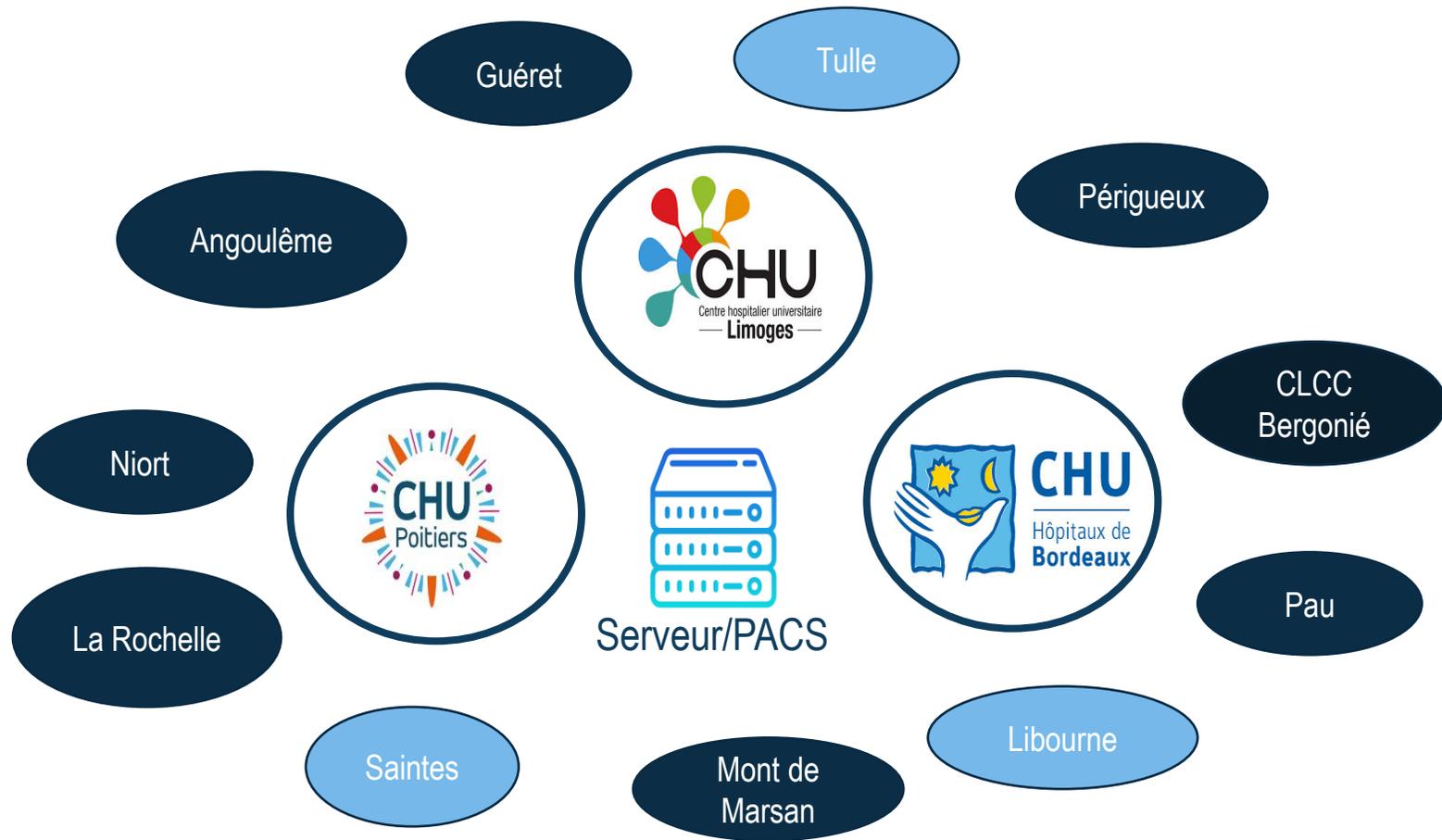
Recours en CHU

Avis/ 2ème lecture
Hyperspécialité/niches
Routine
Valorisation CNAM

**Perte attractivité et
difficultés des services
d'ACP service public
(national / Aquitaine)**



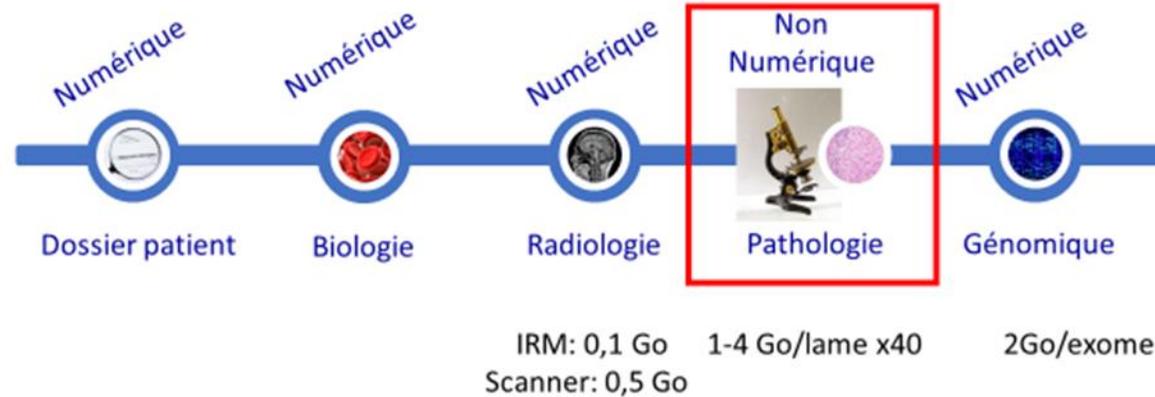
L'idée du projet eNovA-Path débute en 2020 avec les médecins des 3 CHU du GCS Nova





Le numérique pour le diagnostic en ACP

Pourquoi si tard ?... Une question de TAILLE



1 lame = 1 à 4 Go à l'objectif x 40
1 cas = 1 à 100 lames (x100-1000 un dossier radio)

**Et donc d'infrastructure informatique
et de coût**

Le flux analytique d'un laboratoire ACP avant et après le passage numérique : c'est quoi ?

1 - Fixation
(+/-décalcification)



3 heures... à 3 jours
(12 à 48 heures)

2 - Macroscopie



Photos

30 sec.... à 3 heures

3 - Déshydratation



4 -Inclusion en
paraffine

environ 12 heures

J+1 (J+4)

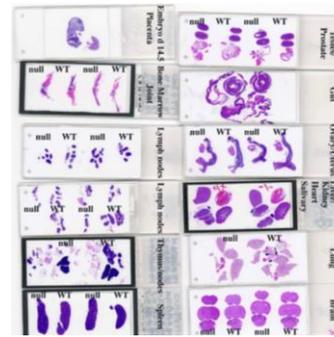
5 - Coupe



5 min à >1
heure/cas

**Qualité technique optimale
requisse pour pathologie
numérique**

6 - Coloration



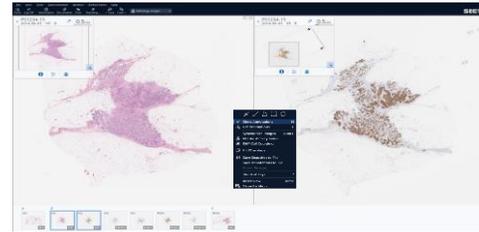
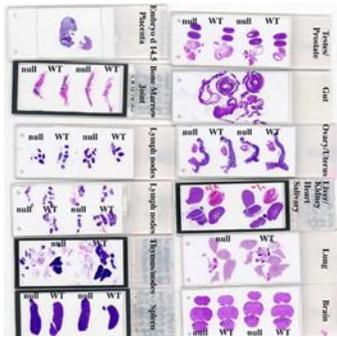
20 minutes

**7 - Lecture au microscope
photonique: interprétation**



qq minutes...à des heures !

8- Rédaction du compte rendu et transmission



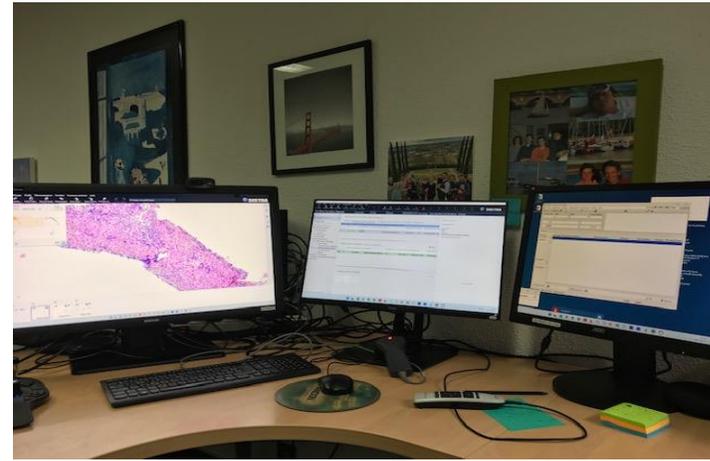
★	Block B, HE	2.47 mm	Margin
★	Block B, HER2		Tumor board
	Block B, HER2	(Draft)	
★	Block C, HE	HER2 IHC 2+ (84.1% [CI: ...	M1



EN PRATIQUE ce qui change dans le flux d'un service ACP !

7 - Numérisation haut débit (+4h à terme) : scanners de lames

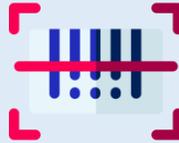
8 - Passage au microscope numérique avec plateau de lames virtuel



Diagnostic en flux continu



Fin 2024...

				
	18 septembre 2023	155 110 lames scannées	18 stations de travail, 3 écrans chacun	3 scanners de lames (2 à fond clair, 1 à IF)
	05 février 2024	92 340 lames scannées	18 stations de travail, 3 écrans chacun	4 scanners de lames (2 à fond clair, 2 à IF)
	21 mai 2024	112 965 lames scannées	44 stations de travail, 3 écrans chacun	4 scanners de lames (3 à fond clair, 1 à IF)



Du microscope à l'écran...

The screenshot displays the CaloPix software interface, which is used for digital pathology. The main window shows a grid of images, including a reference HES (H&E) stain and several immunohistochemical (IHC) stains. The IHC stains are labeled with markers such as IPCD3, IPCD4, IPCD56, IPCD8, HES a, HES b, HES c, and HES m. The interface includes a toolbar at the top with various icons for navigation and analysis. The main display area is divided into four quadrants, each showing a different IHC stain. Each quadrant includes a digital overlay with a QR code, patient information (19AH05226, BOU, 12/09/2019), and a small thumbnail of the original image. The zoom level is set to 41%, and the coordinates are x=271, y=-34.

19AH05226
01
HES c
BOU
12/09/2019 12

19AH05226
01
IPCD3
BOU
12/09/2019 12

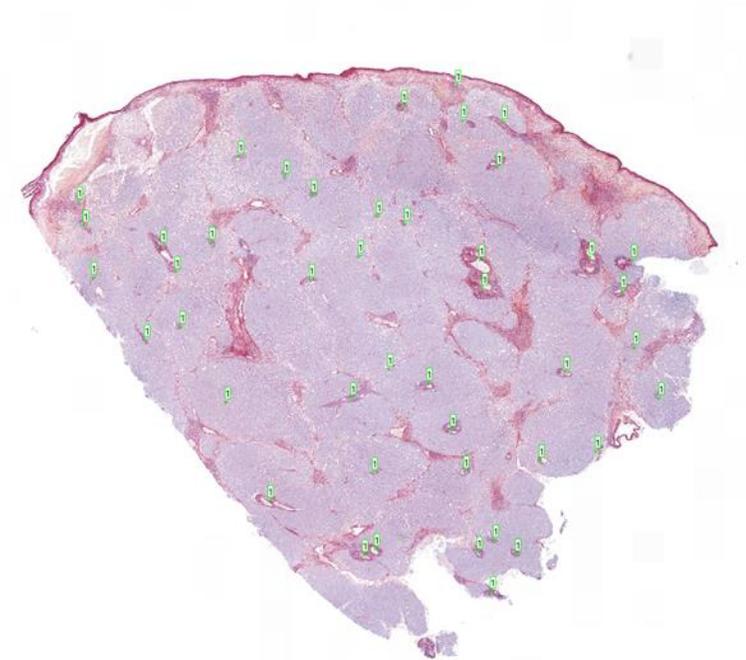
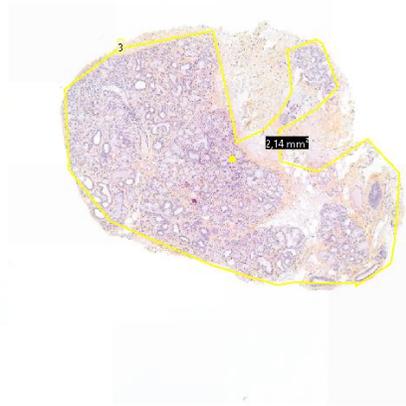
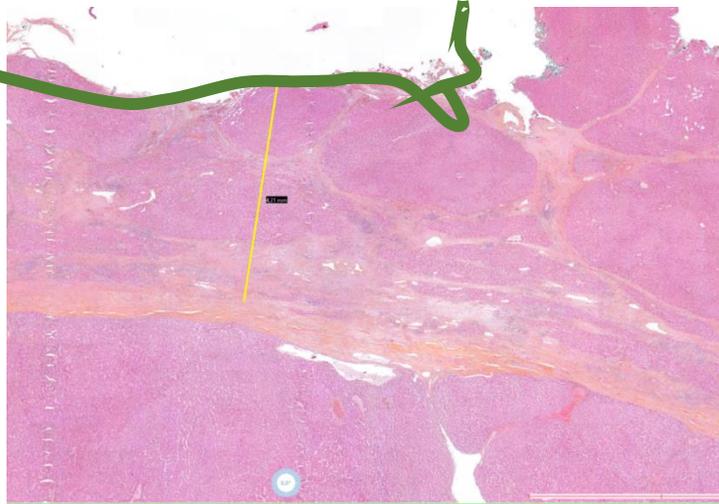
19AH05226
01
IPCD4
BOU
12/09/2019 12

19AH05226
01
IPCD8
BOU
12/09/2019 12

Zoom : 41% x = 271 y = -34

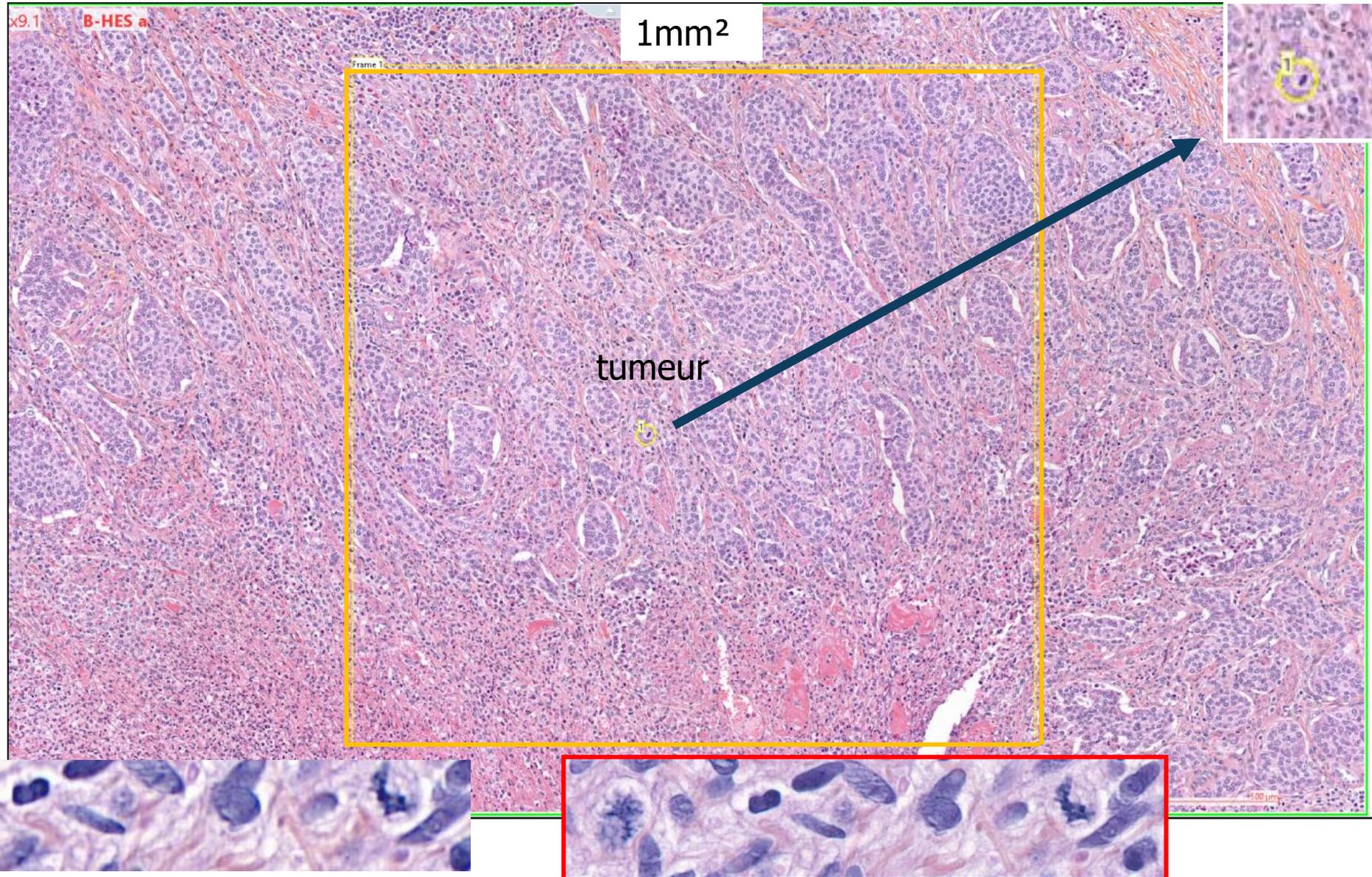


En pratique : une aide à toutes les mesures...





au comptage...





Une corrélation macro-histo (et même radio !)

The screenshot displays the CaloPix software interface, which is used for correlating macroscopic and histological images. The main window is divided into several panels:

- Top Panel:** A row of small thumbnail images representing different sections of the specimen, labeled from 20PH00608_1_1 to 02I.
- Left Panel:** Metadata for the specimen, including the ID **20PH00608**, the slide label **02S HES a LEMO**, and a QR code. Below this is a small thumbnail of the histological slide.
- Center Panel:** A large histological image of a tissue section stained with HES (Hematoxylin-Eosin-Safran), labeled **02S-HES a**. The magnification is **x0.3**. A scale bar at the bottom indicates **5000 µm**. Patient information is displayed: **20PH00608**, **NIP : 8001969780**, **Nom d'usage : LEMONNIER**, **Prénom : JOSIANE**, **Sexe : F**, and **Date de naissance : 19 mai 1950**. A blue box contains the year **2013**.
- Right Panel:** A macroscopic image of the specimen, labeled **20PH00608 1 5**, with a magnification of **49,9%**. A yellow box highlights a specific area of the specimen. Patient information is repeated: **20PH00608**, **NIP : 8001969780**, **Nom d'usage : LEMONNIER**, **Prénom : JOSIANE**, and **Organe :** Viewed. A blue box contains the year **2013**.



Une intégration possible d'outils d'IA dans notre pratique quotidienne

Aide au diagnostic

- assistance dans les tâches fastidieuses
- objectivité accrue (screening)
- amélioration de la qualité
- sécurisation du diagnostic
- productivité

Aide prédictive

- statut génomique (MSI, BRCA...)
- susceptibilité aux traitements (théranostic)
- évolution de la maladie (risques métastatiques, de récurrence...)

Applications au domaine de la recherche, au dépistage...



Aide au diagnostic : le repérage de lésions...

IA app 612
IA vendor 612

Microcalcifications

Page(s) 1 1-16 out of 16 patches

Microcalcifications Already verified

Microcalcifications

EF4N93J1CP
03/05/2024 - 0,5/20x

Annotations
Created by Everyone Favorites only Off On

There are hidden annotations. Click to remove filter.

- Analyse terminée
- Microcalcifications

RF4N93J1DP - 20x

H&E

Calcification Detection

Automatic detection of the calcification on a patient case
Each potential calcification is displayed to help the pathologist to quickly identify each calcification



La détection de zones tumorales...

Automatic detection of IC/ISC

An heatmap is displayed to automatically detect the regions of Invasive and In Situ Carcinoma

EF4N93J1CP
03/05/2024 - 0,4/20x

Annotations

Created by: Everyone Favorites only: Off On

There are hidden annotations. Click to remove filter.

- ★ - Analyse terminée
- ★ - Carcinomes

RF4N93J1DP - 20x

H&E



Le décompte mitotique...

Mitosis Detection

Every mitosis in the invasive carcinoma identified by the algorithm are displayed in the tiles panel and identified on the slide

Mitosis automatic counting

An automatic counting is performed by the algorithm in the invasive carcinoma regions

The screenshot shows a software interface for mitosis detection. The top left panel displays the application name 'IA app 612' and 'IA vendor 612'. Below this, the word 'Mitosis' is shown. A 'Page(s)' indicator shows '1' selected, with other pages 2, 3, 4, 5, and 6 visible. A status bar indicates '1-48 out of 262 patches'. A green checkmark icon is next to the word 'Mitoses', and a blue button labeled 'Already verified' is present. Below this is a grid of small thumbnail images, each showing a magnified view of a mitotic cell. The right panel shows a large histological slide at 1.5x magnification. The slide is annotated with several red rectangular boxes highlighting specific regions. Small orange dots are scattered across the slide, representing detected mitoses. The top right of the slide view shows the file name 'EF4N93J1CP', the date '03/05/2024', and the magnification '1,5/20x'. A vertical toolbar on the far right contains various navigation and tool icons.

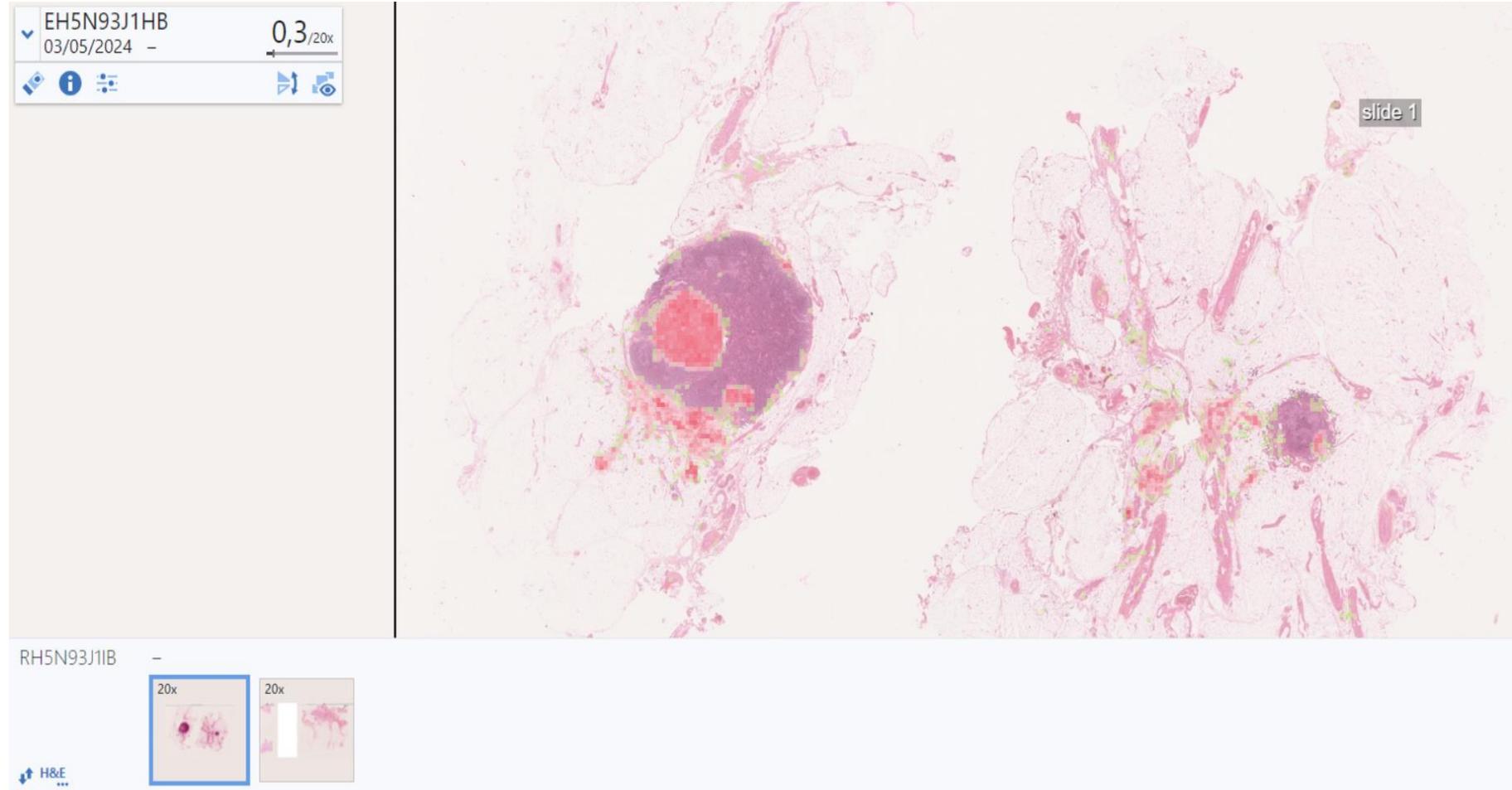


la détection de micrométastases...

Metastasis Detection

Automatic detection of the macro metastasis on the lymph node slides.

An heatmap is displayed to help the pathologist to quickly identify the metastasis on the lymph node





Début d'utilisation d'outil IA dans e Nova Path

- Système de gestion d'images IDS7 de la société SECTRA
- Intègre un outil de comptage pour le comptage Ki67

The screenshot displays the e Nova Path software interface. On the left, a histology image is shown with a toolbar at the top. The toolbar includes a dropdown menu with '24A10105', '24/06/2024', 'HES', 'A/1', a refresh icon, and a zoom level of '3,8/38x'. Below the toolbar are icons for navigation and zoom. The main image area shows a histology slide with a purple and pink stain.

On the right, a second window is open, showing the same histology image but with a 'Index Ki67' tool overlay. The tool has a toolbar with the same dropdown menu and zoom level. Below the toolbar, there is a section titled 'Index Ki67' with a close button. It contains the following elements:

- 'Sélectionner une zone' (Select a zone)
- 'Nombre de cellules:' (Number of cells:)
- A row of buttons: '100', '200', '500', '1000', '2000'.
- A text instruction: 'Choisissez le nombre de cellules à compter et placez le cercle sur le hotspot que vous souhaitez calculer.' (Choose the number of cells to count and place the circle on the hotspot you want to calculate.)
- 'Corrigez le résultat' (Correct the result)
- 'Types de cellules visibles:' (Types of cells visible:)
- A row of buttons: '* Tout' (selected), '+ Positi...', '- Néga...'
- A text instruction: 'Pour basculer entre l'affichage de toutes les cellules, des cellules positives seulement et des cellules néantives seulement pour une aide visuelle.' (To toggle between displaying all cells, only positive cells, and only negative cells for visual aid.)
- A green checkmark icon and the text: '7,7% (77 sur 1000 sont positives)' (7.7% (77 out of 1000 are positive)).

The main image area on the right shows the histology slide with a circular hotspot overlaid, containing many red dots representing positive cells.



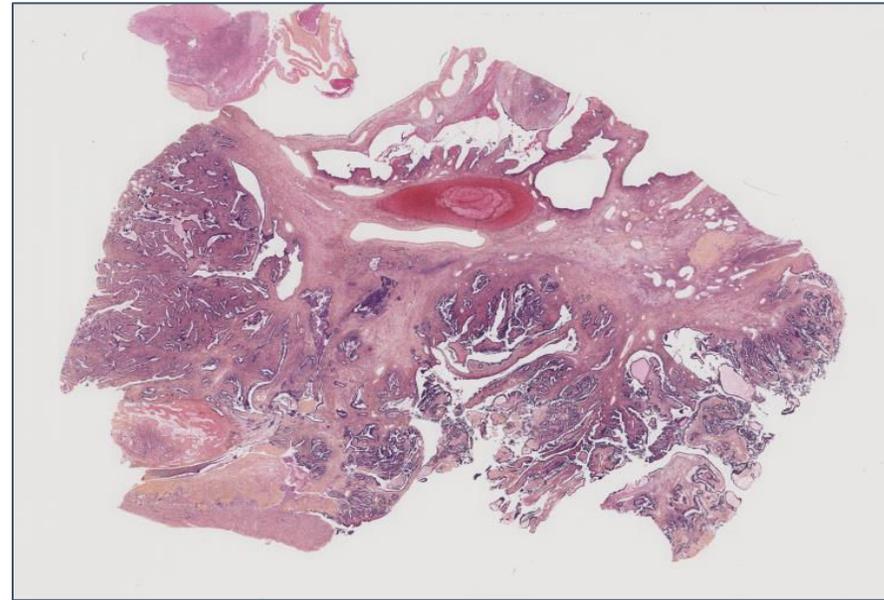
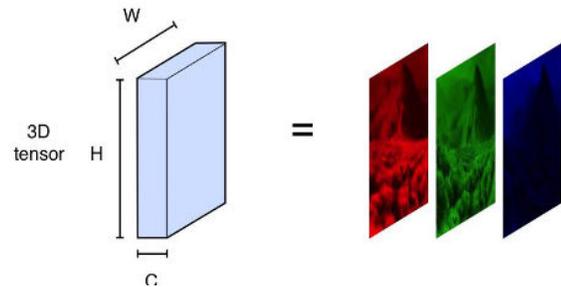
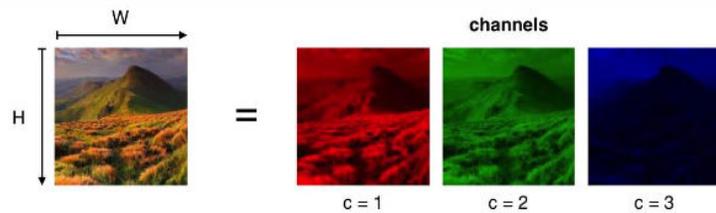
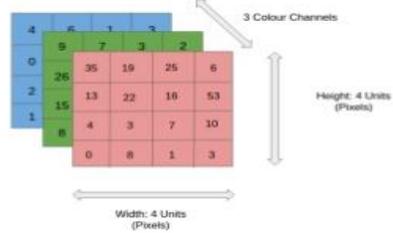
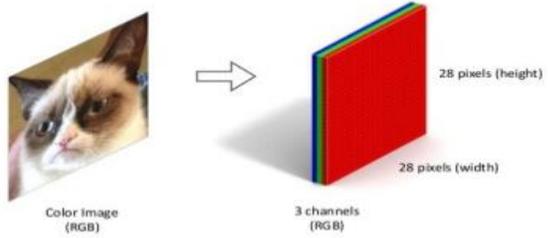
L'univers du prédictif en anatomopathologie...

Deep learning for detecting BRCA somatic mutations in high-grade ovarian cancer based on an innovative tumor segmentation method from Whole-Slide Images.

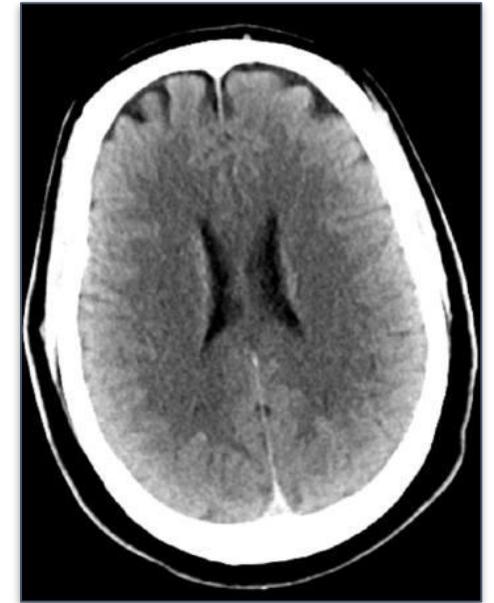
Raphaël Bourgade
Dr Delphine Loussouarn
Anatomie Pathologique CHU de Nantes



Par décomposition d'une image complexe



$200.000 \times 100.000 \times 3 = 60.000$
Mpx

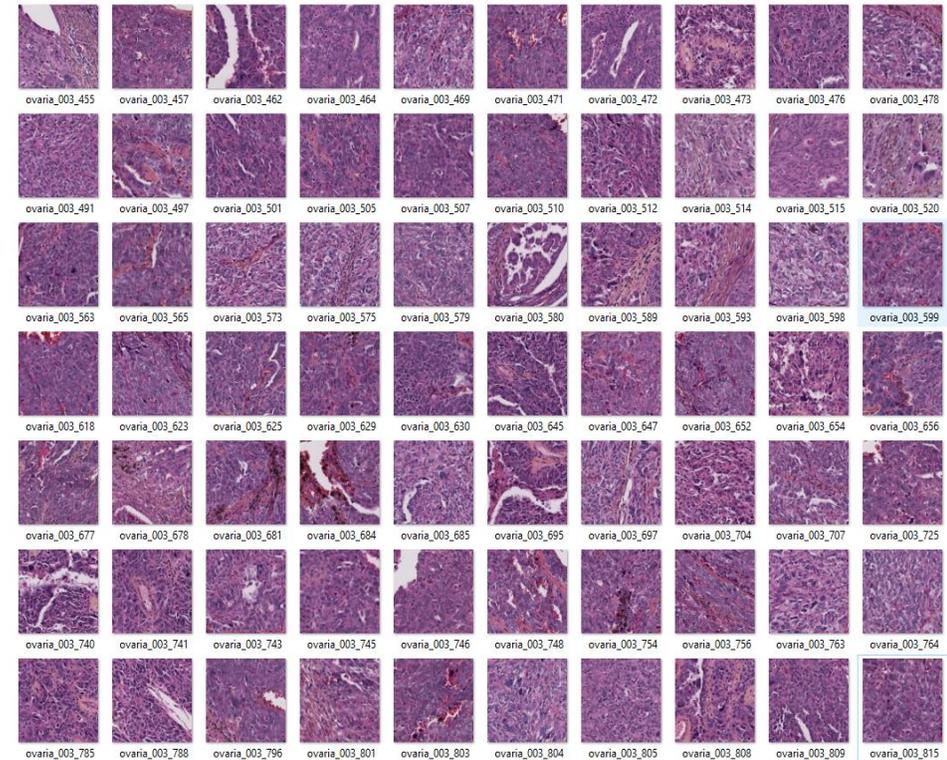
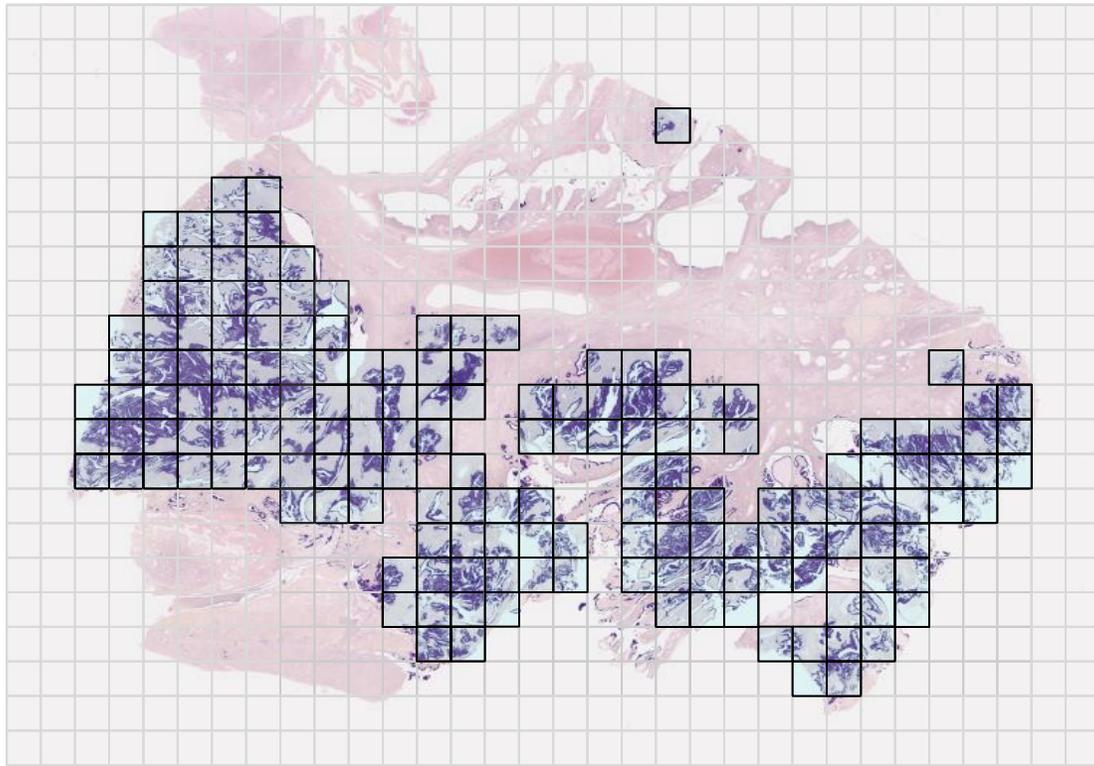


$512 \times 512 \times 100 \times 1 = 26$ Mpx

Due to their high dimensionality, WSI require preprocessing steps.



Tuilage (tiling...) de l'image



WSI size of 200K x 100K x 3 px → 512 x 512 x 3 px tumor tiles

- ❑ **Goal**: reduce the dimensionality of WSI for process
- ❑ The tiles retained are those which contain **at least 50% of tumor area** based on the predicted tumor mask.



codification en octets de chaque point

```
1.083916333e-02, 6.65431842e-03, 1.48833198e-02, 1.83468754e-03,  
8.30330100e-05, 1.77248404e-03, 3.77870747e-05, 4.66463994e-03,  
7.02315103e-03, 5.37262112e-03, 7.43276067e-03, 8.59884545e-03,  
5.67436852e-02, 3.46514676e-03, 3.94016244e-02, 9.74502531e-04,  
8.98182276e-04, 1.74174011e-02, 2.04124339e-02, 1.26710860e-04,  
6.57500792e-03, 3.43532860e-02, 1.06369946e-02, 4.20637242e-02,  
9.77508165e-03, 8.21832940e-03, 1.31977769e-02, 2.61034444e-02,  
9.56259109e-03, 7.79939676e-03, 9.59301740e-03, 2.18877979e-02,  
1.52148437e-02, 1.82728167e-03, 6.83128089e-03, 9.36573744e-03,  
4.16146824e-03, 1.94973815e-02, 1.14029590e-02, 4.06450033e-02,  
5.90699911e-03, 1.55246370e-02, 5.78293875e-02, 4.21503838e-03,  
3.85129522e-03, 3.62235829e-02, 2.28800811e-03, 3.13826166e-02,  
3.63471219e-03, 7.60105299e-03, 7.61656789e-03, 2.00632960e-02,  
4.23341931e-04, 8.91206134e-03, 1.56855565e-02, 6.50411006e-03,  
1.26371942e-02, 3.29926275e-02, 4.25170846e-02, 1.56503115e-02,  
6.62918296e-03, 1.53685585e-02, 1.14911171e-02, 1.93001702e-03,  
3.05106267e-02, 2.23482735e-02, 1.58879831e-02, 1.34749226e-02,  
7.32441545e-02, 3.04484088e-03, 1.07906788e-04, 4.01106197e-03,
```



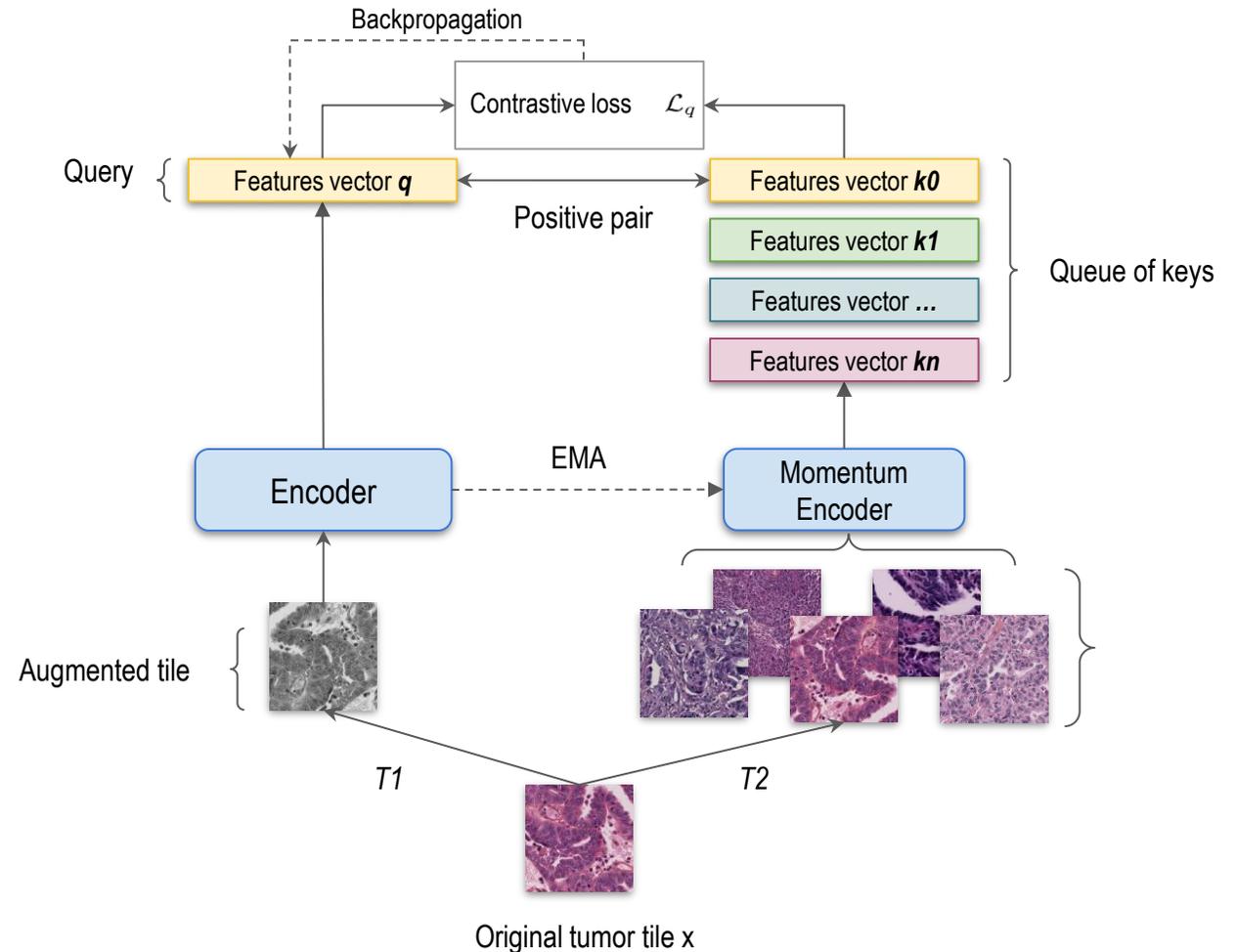
et enfin une formule mathématique !

Momentum Contrast :

- **Self-supervised learning** algorithm.
- Batch of tiles goes through two **ResNet-50** encoders with different data augmentations.
- The encoded query image is compared to a **queue of mini-batches** (key images) encoded by the momentum encoder.
- The **contrastive loss function** maximizes similarity of positive pairs while **minimizes** it for negative pairs.
- Backpropagation is then performed **through the encoder network** whose weights will be used to update those of the momentum encoder by a **momentum-based moving average**.

The **contrastive loss function** looks like a softmax-based classifier loss :

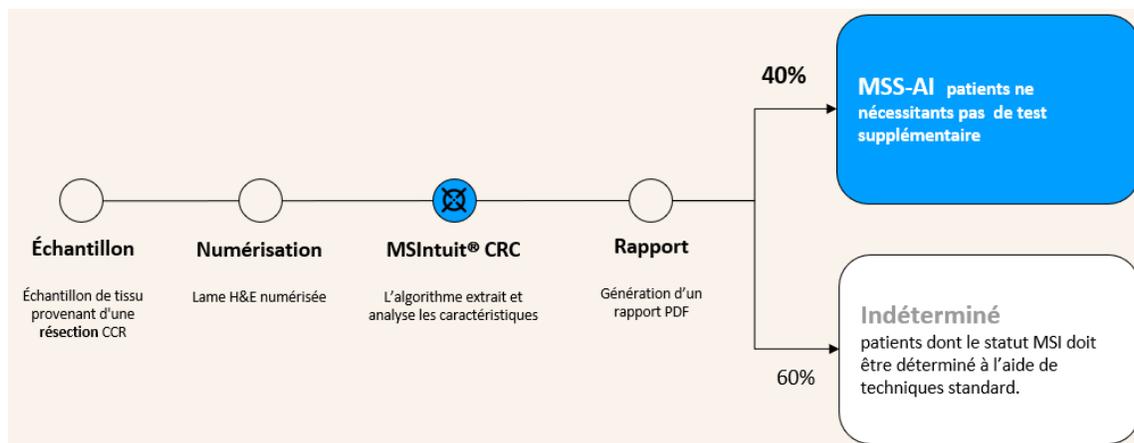
$$\mathcal{L}_q = -\log \frac{\exp(q \cdot k_r / \tau)}{\sum_{i=0}^K \exp(q \cdot k_i / \tau)}$$





Autre exemple pour les MSI...

- IA pour le pré-screening MSI dans le cancer colorectal



Mise en évidence des régions prédictives par l'algorithme d'IA



RESULT REPORT MSIntuit CRC OWKIN

Case ID: 000A14085-003
Block ID: /
Location: Colorectal
Specimen type: Resection
Report name: 000A14085-003_MSIntuit_CRC
Creation date: 2023-12-06 17:16:00
Product software version: v1.3.0
Scanner: 2000305

RESULT
MSS-AI

INTERPRETABILITY

Information presented in this section is intended to provide a better understanding of the analytical process by which the MSIntuit CRC software made its prediction. This information is not intended to be used for diagnostic purposes.

Tiles with the highest MSI risk scores

Tiles with the lowest MSI risk scores

RESULT REPORT MSIntuit CRC OWKIN

Case ID: 000A13966-004
Block ID: /
Location: Colorectal
Specimen type: Resection
Report name: 000A13966-004_MSIntuit_CRC
Creation date: 2023-12-07 10:19:34
Product software version: v1.3.0
Scanner: 2000305

RESULT
Undetermined

INTERPRETABILITY

Information presented in this section is intended to provide a better understanding of the analytical process by which the MSIntuit CRC software made its prediction. This information is not intended to be used for diagnostic purposes.

Tiles with the highest MSI risk scores

Tiles with the lowest MSI risk scores



La patience étant mère de toutes les vertus... restent deux grandes difficultés à dépasser

L'utilisation de l'IA ne peut se faire qu'en respectant les réglementations liées au numérique :

- contraintes RGPD
- collaboration avec les RSSI /DPO

Un modèle économique qui reste à définir :

- coût élevé du passage au numérique
- coût supplémentaire de l'accès aux algorithmes



Mais d'ores et déjà :

- Réussite pour les 3 CHU et 4 sites
- > 90% des lames scannées; délais adaptés (malgré des re-scan)
- Pathologistes seniors conquis et attractivité pour les jeunes : productivité, ergonomie, facilité pour enseignement, staffs, télépathologie...
- Echanges inter-site : débutés, convaincants
- Entraide entre les 3 CHU : création de 2 postes d'assistants partagés (novembre 2024) et projet de mutualisation pour les activités d'astreintes pour greffe (agence biomédecine)
- Partenariat, innovations avec industriels : projets R&D en cours, valorisation du patrimoine numérique
- Projet d'accès du groupe à une plateforme d'outils d'IA (pour screening des lésions cancéreuses, comptage-mesures, scores-grading...)
- Valorisation possible (protocoles de recherche industrielle, actes RIHN/CCAM?...)
- Thèses d'internes DES (4)
- Communications (interview, congrès, articles...).

MERCI
