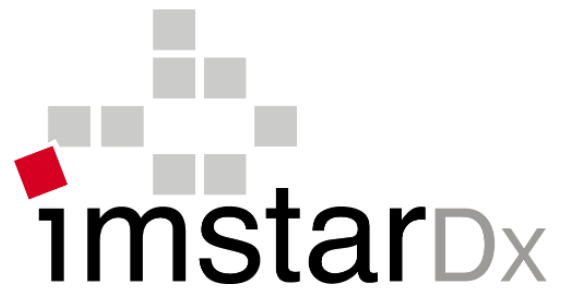


Automated evaluation of Ki67 index in breast cancer and in neuroendocrine tumor by quantitative image analysis

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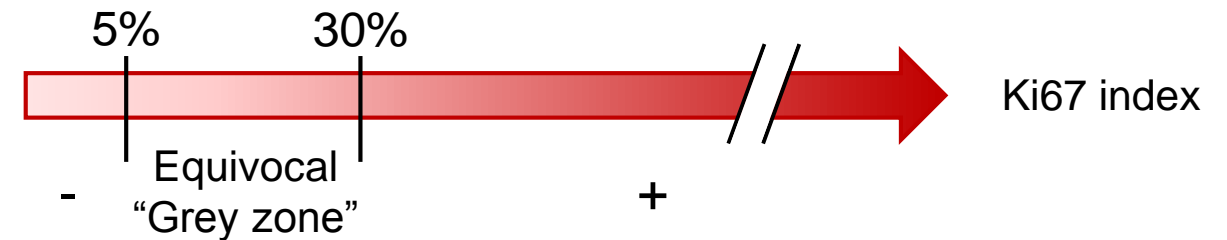
PhD | Cell & Molecular Biology

Lead Scientist

Ki67 index evaluation by immunohistochemistry (IHC) depends on:

- The spatial intra-tumoral heterogeneity of Ki67 expression
- The immunostaining quality
- The staining interpretation by the pathologist

Ki67 clinical utility thresholds for breast cancer (1) require high accuracy:



Ki67 index evaluation in heterogeneous tumors relies on 3 quantitative parameters (AFAQAP), estimated for each tumor zone :

- Ki67 index
- Cancer cell density
- Area

➤ **Need for an automated, robust, and objective method** (International Ki67 in breast cancer Working Group IKWG 2019)

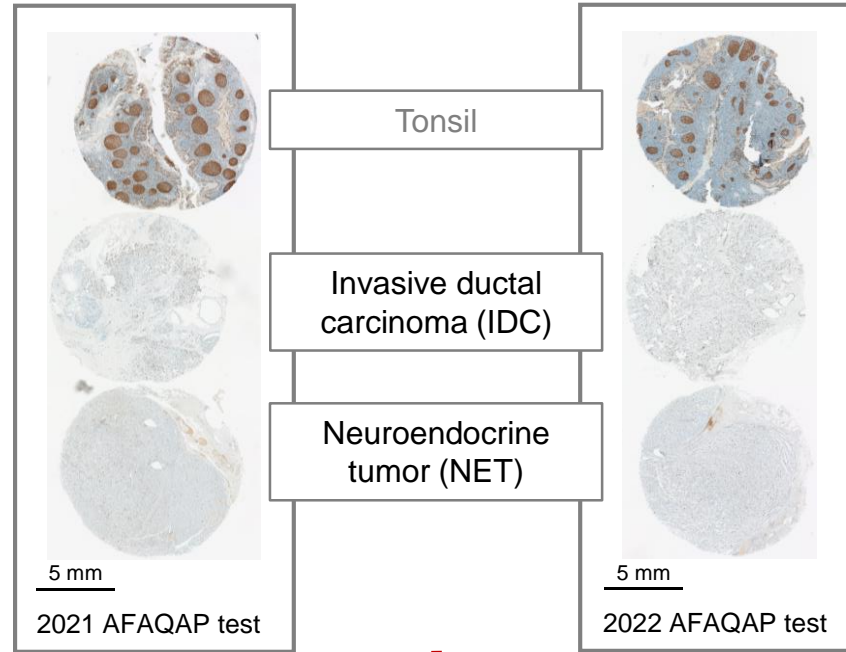
Objective

To develop a quantitative image analysis (QIA) algorithm for Ki67 index assessment by IHC in breast cancer and neuroendocrine tumor

(1) IKWG 2019, published in Nielsen TO, et al. *J Natl Cancer Inst.* 2021;113(7)

55 pathology laboratories

55 Ki67 IHC slides



66 pathology laboratories

66 Ki67 IHC slides

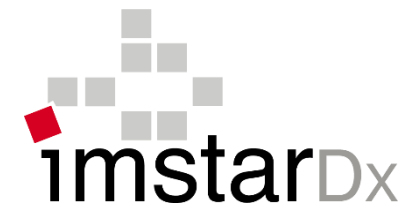


Visual interpretation (eyeballing)

Physical slide reading (multi-head microscope)

Ki67 index + IHC technical quality

- 3 levels without therapeutic impact : **optimal, good, borderline**
- 1 level with therapeutic impact: **insufficient**

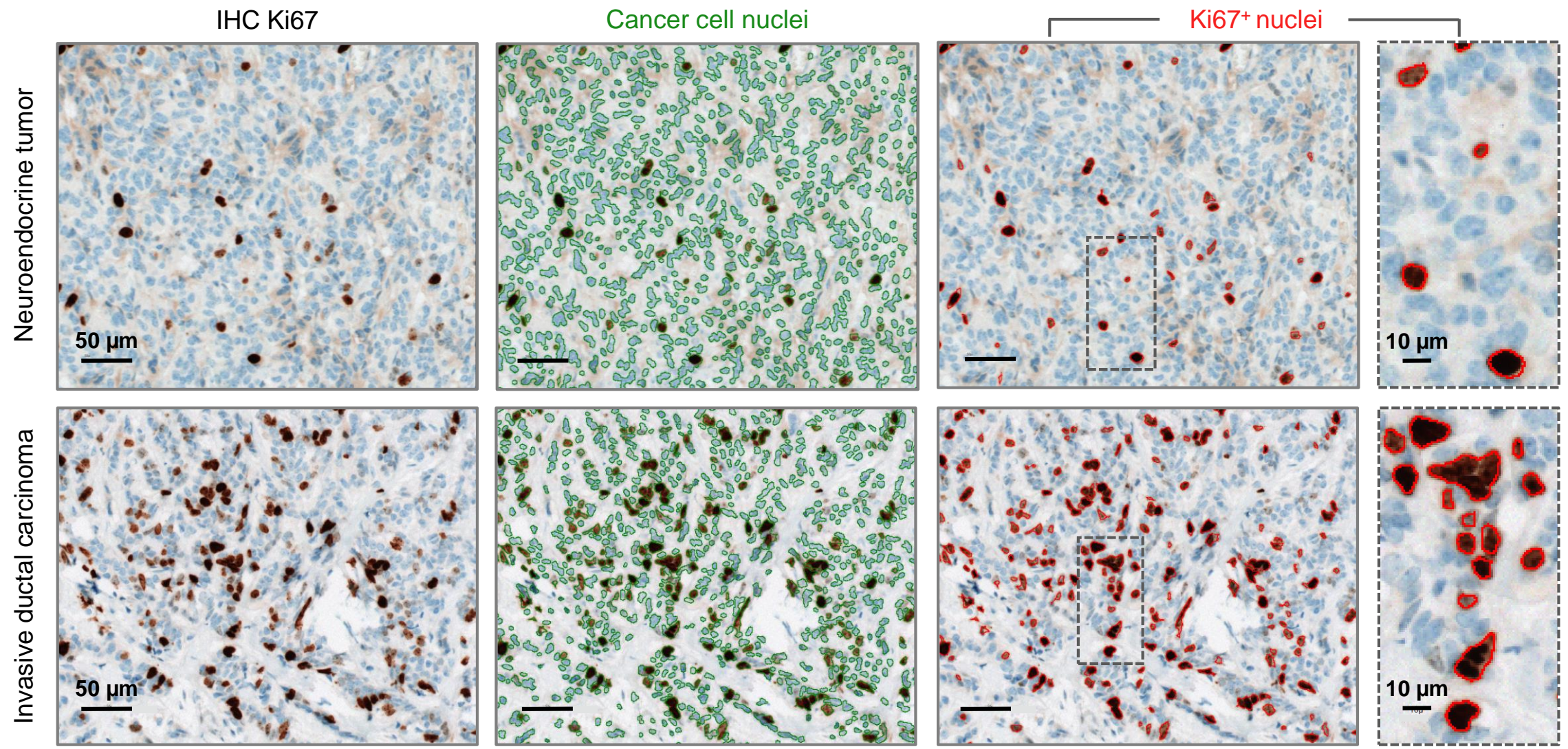


Quantitative Image Analysis (QIA)

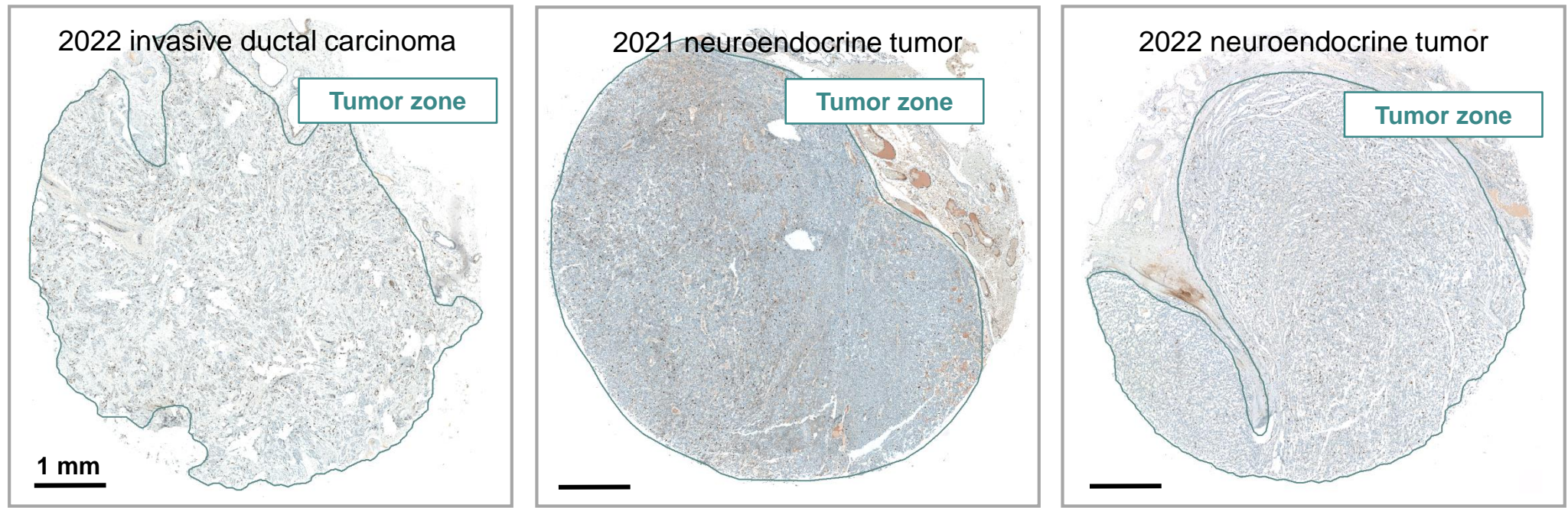
Automated scanning + quantification (Ki67 index)

IMSTAR PathoScan software

- **VS-Emage** module: virtual slide viewing + sharing
- **Tumor-Marker Ki67 IHC** module: Ki67 IHC quantification



➤ QIA performs an automated detection of total and Ki67+ cancer cell nuclei in tumors from different organs

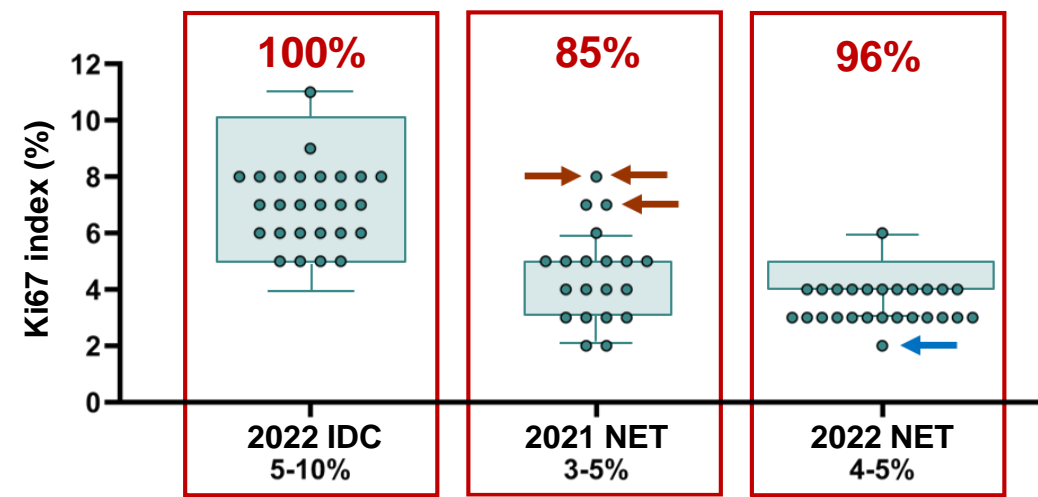


Homogeneous tumors:

- Low stroma
- Low intra-tumoral spatial heterogeneity of Ki67 expression

46 slides with an “optimal technique” for both IDC and NET:

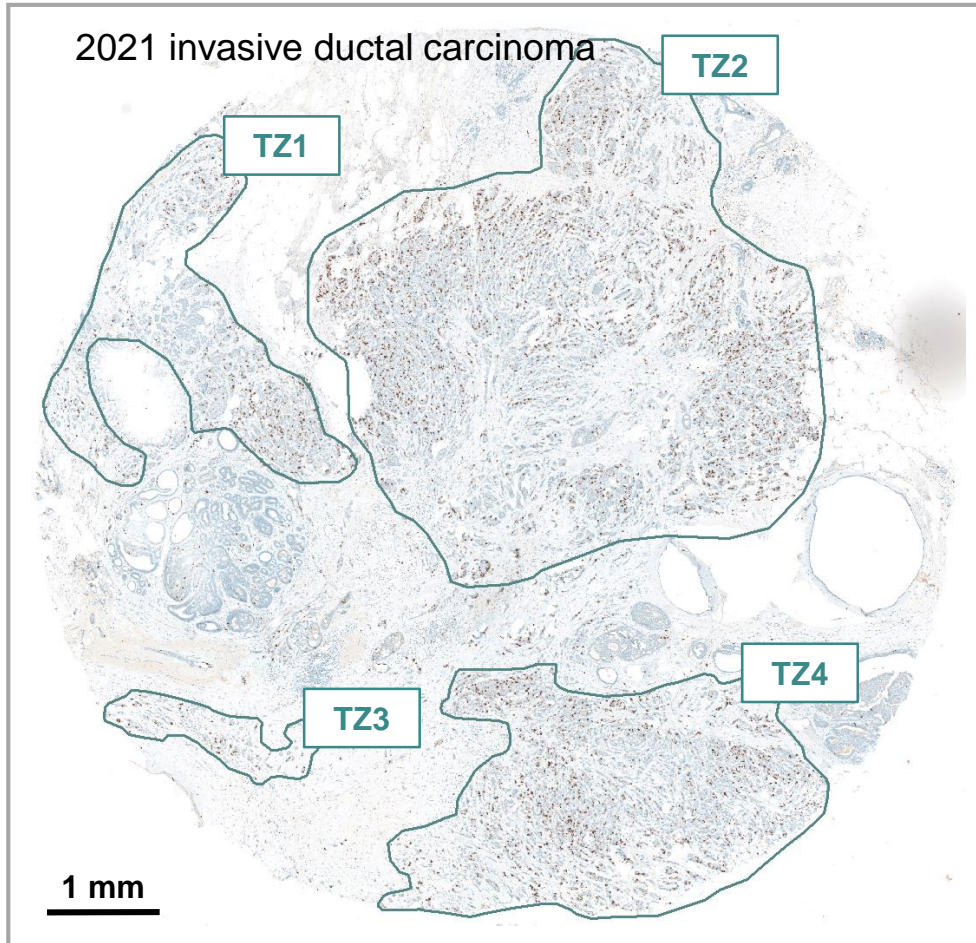
- 2021 | n = 20 slides
- 2022 | n = 26 slides



- Agreement with the visual interpretation of the expert panel
- QIA performs an automated evaluation of Ki67 index in heterogeneous tumors

Heterogeneous tumor:

- Stroma
- 4 main tumor zones (TZ)
- Intra-tumoral spatial heterogeneity of Ki67 expression

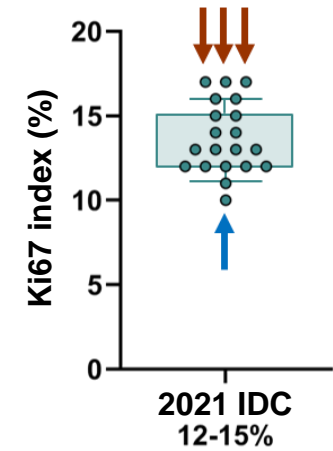


3 parameters automatically quantified by QIA (AFAQAP reference slide)

	Area (mm ²)	Nucleus number	Ki67 index (%)
TZ1	2.08	4200	10.7
TZ2	8.83	17533	16.4
TZ3	0.46	633	12.9
TZ4	3.83	7856	16.6

Average Ki67 index for the 4 tumor zones:

- QIA: 15.4%
- Experts: 12-15%



Agreement rate: 80%

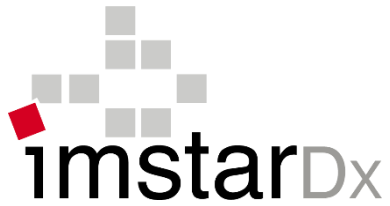
- **Agreement with the visual interpretation of the expert panel**
- **Significant cell recruitment (high statistics)**
- **Evaluation of Ki67 index by selected area in heterogeneous tumors**

- QIA-based Ki67 IHC Tumor-Marker module is:
 - **Universal** - adaptation to multiples technical conditions (autostainer, antibodies, ...)
 - **Accurate** – agreement with the AFAQAP experts for the interpretation of Ki67 IHC in IDC and NET

- QIA allows to measure and visualize tumor heterogeneity:
 - **High recruitment** of cancer cell analyzed
 - Automated quantification of **the area and the cell density of each tumor zone**
 - Display of **the Ki67 expression level for each tumor zone** automatically detected or annotated by the pathologist

- QIA is a quantitative, and objective tool able to adapt to technical variations and to participate in the improvement of Ki67 index interpretation, especially for heterogeneous tumors and for tumors close to the clinical thresholds

- QIA sustains pathologists for Ki67 IHC interpretation:
 - Robustness of interpretation
 - Time-saving
 - Training support for junior pathologists



IMSTAR team

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Mélanie Cossutta

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Charles Homsy

The expert pathologists of AFAQAP

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With the help of Caroline Egele

Thank you for your attention



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