Full device assessment of trophoblastic cell surface antigen 2 (TROP2) normalized membrane ratio (NMR) in non-small cell lung carcinoma (NSCLC) using a computational pathology algorithm in real-world laboratories

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Objective

To assess the analytical reproducibility of the complete TROP2 (EPR20043) NSCLC research use only algorithm workflow in real-world laboratories.

Summary

These data demonstrate high inter-site reproducibility of TROP2 NMR assessment using the TROP2 (EPR20043) NSCLC research use only device in real-world laboratories, with agreement rates of 94.1% overall and 99.8% for non-borderline cases (TROP2 NMR score <0.553 or >0.573). This study can serve as a practical guide for organizing the deployment of artificial intelligence-based biomarkers.[1]

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Introduction

- TROP2 has been identified as a potential target for antibody-drug conjugates in NSCLC.[2]
- Conventional manual scoring of immunohistochemistry shows no relationship between TROP2 expression and response to TROP2 targeted antibody-drug conjugates.[3]
- The TROP2 NMR (EPR20043) NSCLC research use only (RUO) algorithm has been trained on pathologists' annotations to identify tumor areas and sub-cellular compartments of individual tumor cells (i.e. membrane and cytoplasm) across the whole slide image and measures TROP2 expression in the membrane relative to the cytoplasm to produce the TROP2 NMR.[4]

Methods

- Serial sections taken from 36 commercial NSCLC samples that qualified for the study (primary and metastatic) were distributed to 12 real-world pathology laboratories across eight countries, independently stained with the RUO TROP2 immunohistochemistry assay, scanned, and whole-slide images uploaded for analysis by 36 pathologists (thoracic and non-thoracic specialists). The workflow is illustrated in **Figure 1**.
- The full RUO device included the staining platform (VENTANA® TROP2 [EPR20043] RUO assay, OptiView® detection kit, BenchMark® ULTRA staining instrument), the digital platform (VENTANA DP200/DP600 scanners), the image management system (Navify® Digital Pathology), and the TROP2 NMR RUO algorithm (Roche Diagnostics, Tucson, Arizona, US).
- The case set included 18 negative (TROP2 NMR >0.563) and 18 positive (TROP2 NMR ≤0.563) cases; agreement rates were calculated between readers at each site and across sites with the case-level mode used as the reference status for comparing agreement.

Results

Figure 1. Each site stained, scanned, and analyzed 36 NSCLC cases. Concordance was measured at each individual site and overall (across all 12 sites).

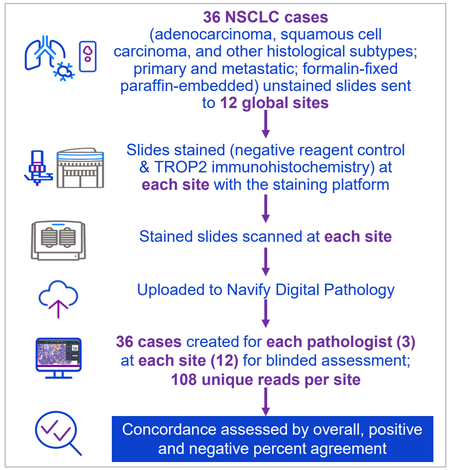
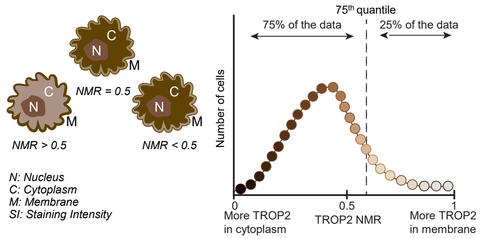


Figure 2. Calculation of the TROP2 NMR uses automated image analysis (Quantitative Continuous Scoring) to measure TROP2 sub-cellular (membrane and cytoplasm) distribution.[5]



TROP2 NMR = membrane SI / (membrane SI + cytoplasm SI)

Figure 3. Sites were located across the USA, Canada, and Western Europe.

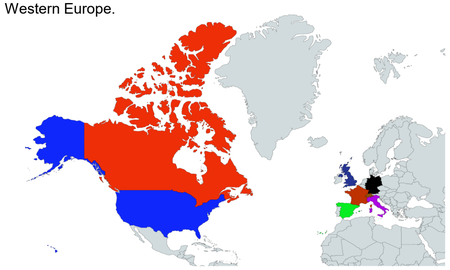


Figure 4. Six pathologist-driven steps in the image analysis workflow for computation of the TROP2 NMR using the whole slide image (WSI).

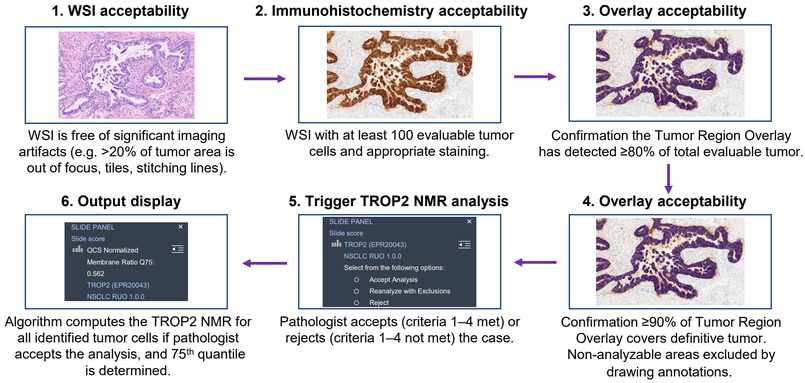


Figure 5. Distribution of TROP2 NMR scores for the 36 cases at each site; biomarker status was negative in 18 cases (TROP2 NMR >0.563) and positive in 18 cases (TROP2 NMR ≤0.563), ensuring equal distribution of cases above and below the 0.563 cutoff. The case qualification (median score of three sections from different regions of the tumor selected from 62 serial sections) is plotted for comparison.

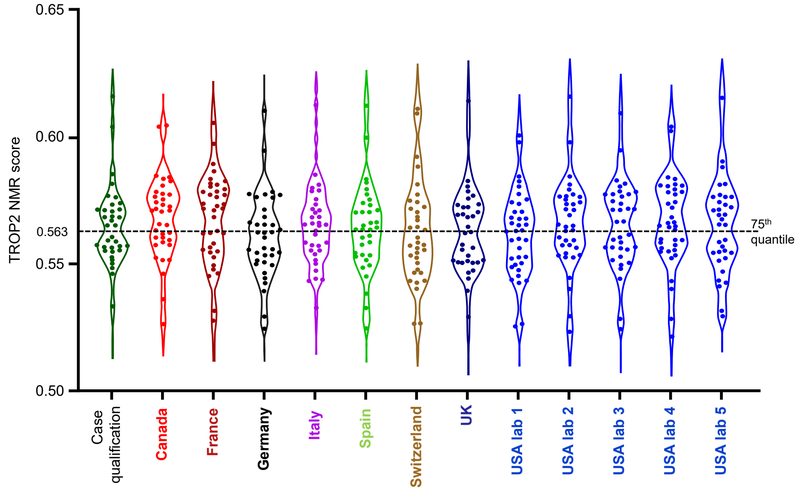


Figure 6. Negative (**NPA**), positive (**PPA**) and overall (**OPA**) percent agreement rates, (A) overall and per site and (B) for non-borderline (TROP2 NMR score <0.553 or >0.573) and borderline (TROP2 NMR score 0.553–0.573) cases. Overall % (95% confidence interval): NPA 92.5 (87.4, 97.4), PPA 96.1 (90.5, 99.6), and OPA 94.1 (90.3, 97.5).

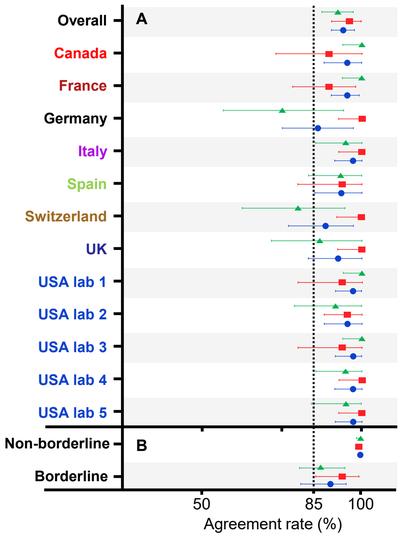


Figure 7. Number (%) of the 108 unique reads (from 36 cases) with positive or negative TROP2 status and the incidence of stain failure and analysis rejection (overall and per site).

	Positive	Negative	Stain failure	Analysis rejected
Overall	603 (46.5)	686 (52.9)	3 (0.2)	4 (0.3)
Canada	43 (39.8)	65 (60.2)	0	0
France	43 (39.8)	64 (59.3)	0	1 (0.9)
Germany	63 (58.3)	45 (41.7)	0	0
Italy	48 (44.4)	59 (54.6)	0	1 (0.9)
Spain	49 (45.4)	59 (54.6)	0	0
Switzerland	57 (52.8)	48 (44.4)	3 (2.8)	0
UK	55 (50.9)	52 (48.1)	0	1 (0.9)
USA lab 1	45 (41.7)	63 (58.3)	0	0
USA lab 2	53 (49.1)	55 (50.9)	0	0
USA lab 3	45 (41.7)	63 (58.3)	0	0
USA lab 4	51 (47.2)	56 (51.9)	0	1 (0.9)
USA lab 5	51 (47.2)	57 (52.8)	0	0

Disclosures

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