Prolaris Kit Cell-Cycle Risk Scores are Reproducible across External Molecular and Pathology Laboratories

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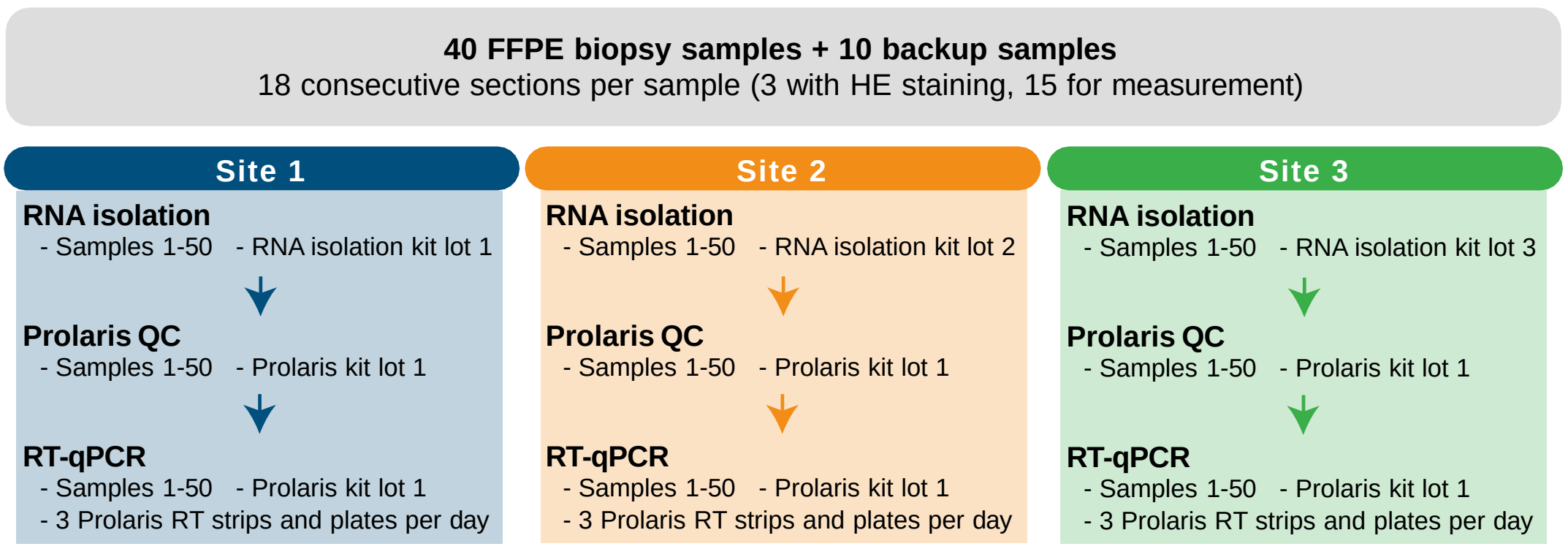
Background

- The Prolaris test predicts the aggressiveness of prostate cancer.
- The kit was developed and validated to be used as a decentralized solution.
- Here, we assessed the reproducibility of the Prolaris kit Cell-Cycle Progression score (CCP) across three different laboratory sites.

Methods

- At each site, operators isolated RNA from 50 formalin-fixed, paraffin-embedded (FFPE) samples, performed RT-qPCR, and determined the CCP Score using the Prolaris Biopsy Report Generator (Figure 1).
- Each sample was analyzed once at each site.
- Potential outliers were identified using a threshold of 4 MAD (mean absolute deviation).
- Overall reproducibility was estimated using a random intercepts model. Site-to-site variability was then calculated by subtracting variance components estimated from previous work.

Figure 1. Schematic overview of study performance.



Results

- Only samples that provided valid results in all 3 laboratories were used for statistical analysis. 43/50 samples met this criteria and were used for statistical analysis.
- No outliers were identified.
- Variance decomposition using these samples, along with previously calculated variance component estimates,[1] demonstrated a site-to-site variability of 0.115 CCP Score units (CCPsu) (Table 1).
- As acceptance criterion for the overall reproducibity, a standard deviation of at most 0.31 CCPsu was defined as it leads to a clinically relevant absolute shift of disease-specific mortality risk at the active surveillance threshold of less than 1%.
- The overall reproducibility for the Prolaris test was 0.184 CCPsu, which fulfilled the defined acceptance criterion (Table 1).

Table 1. Variability of the CCP Score provided as standard deviation of each variance component.

Variance Component	All measurements
Measurements (n)	129
Site-to-site*	0.115
Day-to-day**	0.000
Instrument-to-Instrument**	0.000
Lot-to-lot**	0.114
Operator-to-Operator**	0.016
Repeatability**	0.085
Overall reproducibility	**0.184**

Values for day, instrument, lot, operator and the repeatability originated from previous work.
*Current Study
**Kuhl V, Clegg W, Meek S, et al., Biomark Med. 2022 Apr;16(6):449-459.

Conclusions

- The variance in CCP Scores across the three external sites was within the acceptable range, indicating that Prolaris kit results are reliable and reproducible when performed locally by trained laboratory staff.

Reference: 1. Kuhl V, Clegg W, Meek S, et al., Biomark Med. 2022 Apr;16(6):449-459.