High-Precision Tissue Extraction: QuantumCyte integrated with Roche navify® Digital Pathology

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FROM PIXELS TO PATIENTS

OBJECTIVES

The objective was to evaluate the integration of the QuantumCyte **QCPRECISE** high precision extraction platform with the Roche navify digital pathology (DP) and image management system* (Figure 1). The integration enables a seamless workflow, starting with digitization of the tissue sections on glass slides, manual or AI-based automated annotations on the navify DP platform, and precision tissue extraction, including on-slide tissue extraction, using the QCPRECISE platform. Here we demonstrate:

- An integrated digital workflow requiring no adjustment from scan to lysis.
- Precise extraction from regions of interest (ROI), minimizing contamination from adjacent non-ROI areas.
- Enhanced cellular purity, demonstrated by increased signal to noise leading to higher variant allele frequencies (VAF)* vs. the manual macrodissection workflows used in current molecular pathology settings.

Figure 1: Integration between systems for fast, precise tissue extraction: Navify is used to define the desired ROI and QCPRECISE automatically extracts that tissue from standard slides. The tissue was then sequenced using Roche AVENIO assays.

ABSTRACT / INTRODUCTION

Digital pathology has gained significant popularity in recent years, enabling advanced image analysis and digital workflows. At the same time, sequencing and proteomic diagnostics have reached an accuracy ceiling, usually due to sample purity limitations. Therefore, precise tissue extraction is the next frontier in personalized diagnostics and translational research.

QuantumCyte's QCPRECISE platform addresses this need by offering high-resolution extraction down to 50 microns resolution while maintaining high throughput, processing up to 40 slides per hour. In this work, we validate the integration of Roche's navify DP platform, AI and QPRECISE, showing:

- Precise extraction from regions of interest (ROI), minimizing contamination from adjacent non-ROI areas.
- Enhanced cellular purity and increased signal to noise thus enabling detection of low-frequency variants.
- Capability to extract viable tissue from highly compromised samples, such as those with >80% necrosis, where standard methods would fail.
- High-resolution extraction from small tissue biopsies, targeting regions as small as 50 microns.

Additionally, samples with low tumor content - historically challenging for NGS - demonstrated highly enhanced diagnostic yield.

This integrated workflow represents a significant advancement in digital pathology and precision medicine, enhancing biomarker discovery, improving diagnostic accuracy, and enabling RNA, DNA and proteomic applications even in low-quality or small biopsy samples.

METHODS

We evaluated the integration of the QCPRECISE platform (QuantumCyte) with the navify Digital Pathology solution* (Roche) in a study on 10 lung cancer samples.

- Reference H&E slides were scanned on the VENTANA DP600 scanner* (Roche).
- 4 of the 10 samples were annotated by a board-certified pathologist through the navify DP system.
- The rest of the samples were annotated using a Roche internal AI-model that performs tumor-stroma segmentation, wherein we utilized the tumor segmentation output for this study.
- Digital annotation files were processed using QuantumCyte's QCPRECISE platform, ensuring precise extraction that preserves spatial resolution down to a few cells.
- For each sample, three tissue sections/sample were manually macro dissected (MMD) (all tissue was harvested using a scalpel), theses samples were used to compare the two digital annotation processes for VAF differences.
- Following tissue extraction and purification of genomic DNA, downstream DNA sequencing was performed on 8 of the 10 samples using the AVENIO Tumor Tissue Surveillance V2 panel.**
- Sequencing results from the QCPRECISE-navify DP-integrated process were then compared to MMD results by dividing the VAF from MMD samples vs the precision extracted samples.

RESULTS

Precision Microdissection Yields Higher VAF versus Manual Microdissection

Figure 2 shows successful lysing of the regions of interest annotated on Navify DP via the integrated platform.

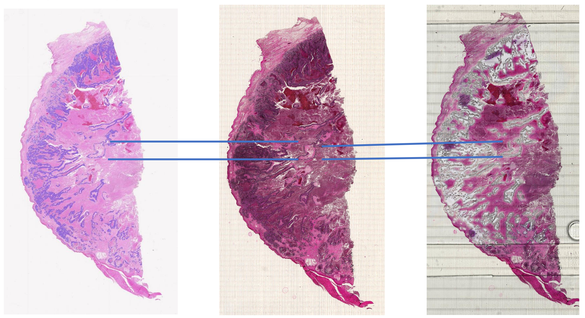

Figure 2: Images from precision extraction process, from annotation to post-lysis

Figure 2a: AI-annotation overlay on tissue. Annotations are shown in Purple.

Figure 2b: Masked slide. The open regions correlate to the annotations (see highlights for an example.

Figure 2c: Post lysis image. Open areas are the lysed regions that correlate to the AI annotations

Figures 3 and 4 show that the samples run on the AVENIO CGP panel, after the integrated precision extraction workflow, had higher VAFs than samples run though the traditional MMD process. Improvements in VAF were seen for almost all samples, indicating that the integrated process results in increased signal to noise.

Further, there was a notable difference in sensitivity increases observed in samples that were annotated using AI vs manual annotation.

These results show that the QuantumCyte method of precision extraction provided a high cellular purity sample for sequencing, which was further improved by AI annotation, leading to the signal to be boosted resulting in higher VAF: Table 1 shows a set of biologically-significant variants that were highly enriched by the navify DP-QC technology. For example, for gene CDKN2A, the VAF for the MMD sample was 7.96% and for the precision extraction, it was 34.39%, leading to a 3.3x increase in VAF.

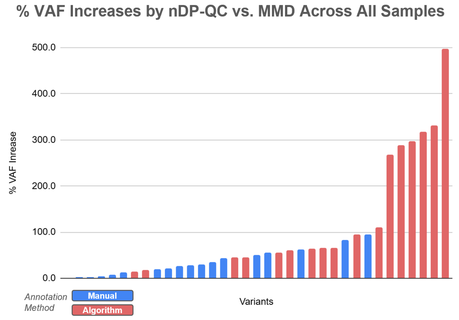

Figure 3: % increase in VAF (VAF from purified samples divided by VAF from MMD). AI annotated samples saw larger improvements in VAF

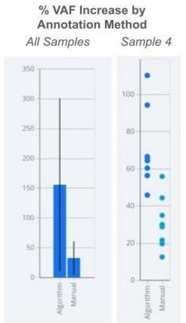

Figure 4. % VAF increases for multiple genes inside a sample (each dot is one variant)

Gene	Variant	% VAF Increase
KRAS	p.Gly12Cys	66.4
TP53	p.Glu294*	110.1
CDKN2A	p.Gly101Trp	332
TP53	p.Trp53*	45
KRAS	p.Gly12Asp	288.5
TP53	c.920-2A>T	496.7
KRAS	p.Gly12Ala	94.8
TP53	c.1101-2A>T	82.8

Table 1: % Increase in VAF in variants of known significance

CONCLUSIONS

QuantumCyte's QCPRECISE platform has been shown to be well integrated with Roche navify DP digital platform.

The QuantumCyte precision extraction process, informed by the Roche navify DP annotation software (manual and AI-model) for lung cancer:

- Showed successful annotation to extraction of regions of interest in the integrated workflow
- Consistently resulted in significantly higher VAF, up to 5-fold increase in signal

This means that:

- Samples that are difficult to analyze can now be regularly processed and in volume leading to better diagnostics, particularly for difficult samples such as those with low percentage of tumor content, e.g., needle biopsies
- Potentially, fewer failed samples and increased revenue for laboratories from low tumor content samples that could not be sequenced previously
- Accelerated biomarker discovery and clinical trials for Pharma companies, which have been limited by the low accuracy of manual methods and the laborious, time-consuming legacy processes that yield high precision such as laser capture microdissection (LCM)

These results highlight the potential of this integrated platform to yield higher precision results at scale for genomics applications.

REFERENCES

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CONTACT/ ACKNOWLEDGEMENTS/ RESOURCES

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* Variant Allele Frequency (VAF) measures the proportion of DNA sequences that contain a specific mutation within a sample. Higher VAF improves the sensitivity and reliability of molecular testing.
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