Results of a Time and Motion Study of Two Next-Generation Sequencing Workflows in a Routine Oncology Biomarker Profiling Setting

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ABSTRACT

Introduction: Despite the growing adoption of next-generation sequencing (NGS) in molecular diagnostics, laboratories face operational challenges including complex workflows, skilled labor requirements , and resource constraints that can limit efficiency and scalability. A comparative assessment of two NGS workflows for oncology biomarker profiling as performed routinely in a clinical laboratory was conducted to better understand these barriers. The goal of this study was to quantify workflow demands and assess the impact on efficiency and labor requirements between systems used in molecular laboratories.

Methods: A time-and-motion study was performed by an independent consulting company, who observed and compared two NGS manufacturer-recommended workflows as used in routine for oncology biomarker profiling of formalin-fixed, paraffin-embedded (FFPE) tissue within the same clinical laboratory. The two workflows evaluated were: Oncomine Dx Express Test (ODxET) (CE-IVD, Thermo Fisher Scientific), a targeted, automated amplicon-based NGS workflow on the Ion Torrent Genexus Dx System, and a hybrid-capture workflow. The observed activities included sample extraction, quantification, library preparation, sequencing, data analysis, and reporting following the laboratory's established standard operating procedures over a period of 7 days. Each workflow was evaluated using a typical batch size of 6 FFPE patient samples and 1 control, as defined by the laboratory's standard practice. The methods included observational time-and-motion studies and process mapping. Time was captured and categorized into labor time, idle/waiting time, and total turnaround time. Analyses were conducted to assess workflow efficiency and scalability between the two NGS systems.

Results: The total turnaround time for ODxET was 26.8 hours, compared to 88.9 hours for the hybrid-capture workflow, a difference of 63 hours. For pre-processing, purification, quantification, library preparation, and sequencing, ODxET required 40.8 minutes of hands-on time, and the hybrid-capture workflow required 451.3 minutes of hands-on time; this represents a 91.0% reduction. The total attentive time required, including results data transfer, was 259.8 minutes for ODxET and 660.8 minutes for the hybrid-capture workflow. ODxET required 57 manual pipetting events for library preparation and sequencing, compared to 537 for the hybrid-capture workflow.

Conclusions: Effective implementation of genomic profiling is critical for patients to benefit from precision oncology. Turnaround time, hands-on time, and overall attentive time remain key barriers. This study demonstrated that an automated, targeted amplicon-based NGS assay substantially reduced both labor time and processing time compared to a manual hybrid-capture workflow.

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INTRODUCTION

- Next-generation sequencing (NGS) is a technology for determining the sequence of DNA or RNA, to study genetic variation associated with diseases or other biological phenomena. The speed, throughput, and accuracy of massively parallel sequencing with NGS has revolutionized genetic analysis and enabled new applications in clinical research, reproductive health, and environmental, agricultural, and forensics. NGS is the primary method of testing used for precision oncology.
- Despite the growing adoption of NGS in molecular diagnostics, laboratories face operational challenges including complex workflows, skilled labor requirements, and resource constraints that can limit efficiency and scalability.
- A comparative assessment of two manufacturer-recommended NGS workflows for oncology biomarker profiling as performed routinely in a clinical laboratory was conducted to better understand these barriers.
- The goal of this study was to quantify workflow demands and assess the impact on efficiency and any attentive time requirements between systems used in molecular laboratories.

METHODS

- A side-by-side direct observation and time and motion study was conducted as a part of routine laboratory work, by an independent consulting company (Argent Global Services).
- Sample purification, quantification, library preparation, sequencing, data analysis, and reporting were observed for two NGS workflows: Oncomine Dx Express Test (CE-IVD*) (ODxET, Thermo Fisher Scientific), a targeted automated amplicon-based NGS workflow on the Ion Torrent™ Genexus™ Dx System, and a hybrid-capture workflow.
- The same six FFPE patient samples were used for both workflows, along with one control, following the host laboratories standard operating procedures.
- Time requirements were captured and categorized into attentive time, idle/waiting time, and total turnaround time.
- Analyses were conducted to assess workflow efficiency and scalability between NGS systems.

*For *In Vitro* Diagnostic Use. Not available in all countries, including the United States.

Figure 1: Total Turnaround Time (TAT), for Six Samples

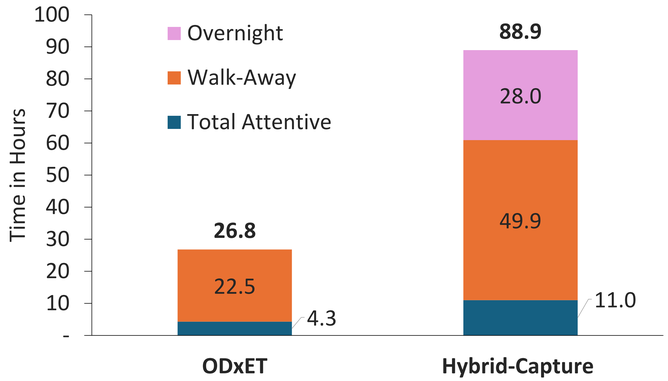


Figure 2: Hands-On Time Required for NGS Assay, for Six Samples

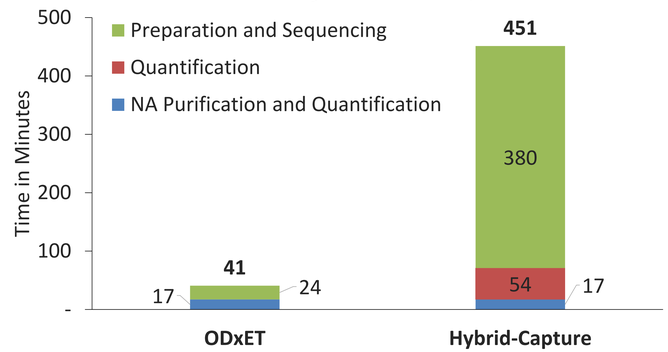
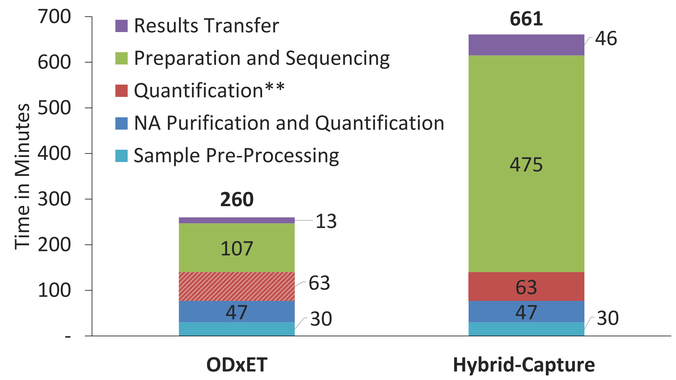


Figure 3: Total Attentive Time for Six-Sample Study Workflow Comparison



**Nucleic acid (NA) quantification for ODxET is done as part of the purification step on the Genexus Purification System, however in this study the laboratory opted to repeat it using the same method and system used for the hybrid-capture workflow.

RESULTS

- The total turnaround time was reduced by 63 hours with the ODxET, compared to the hybrid-capture workflow **(Figure 1)**.
- Hands-on time (defined here as active, manual steps directly required for starting the NGS workflow) was 91% lower with ODxET **(Figure 2)**.
- The total attentive time (including all labor and automation or waiting time for the tech, without the ability to walk away) required for pre-processing, purification, quantification, library preparation, sequencing and data transfer was 61% less for ODxET; library preparation and sequencing, specifically, required 77% less attentive time with ODxET **(Figure 3)**.
- Manual pipetting events were reduced by 89% with ODxET **(Table 1)**.

Note: Some terminology has been revised since submission of the abstract.

Table 1: Total Manual Pipetting Events

Workflow	Pipetting Events
ODxET	57
Hybrid-Capture	537

CONCLUSIONS

- ODxET required significantly less attentive and cycle time to prepare and sequence patient samples.
- ODxET provided much faster overall analytical turnaround times and greatly increased efficiency.
- Fewer manual pipetting events with ODxET results in fewer opportunities for errors, delay, and waste.
- Effective implementation of genomic profiling is critical for patients to benefit from precision oncology, and turnaround time and attentive time remain key barriers.
- An Automated, targeted amplicon-based NGS assay (ODxET) substantially reduced both attentive time and processing time compared to a manual hybrid-capture workflow.

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