TSO500 Local App Software Release Notes

V2.0.0

For TruSight Oncology 500 Assay

November 25, 2019

Introduction

These Release Notes detail the key features and known limitations to software components for the Local TSO500 App v2.0.0

This software is intended for use with the TruSight Oncology 500 Assay.

- Software Version: 2.0.0
- Docker Image ID: 826b3e42373d

The software package includes:

- trusight-oncology-500-ruo-2.0.0.70.zip

New Features:

- Support of RNA Variant Calling (Splice and Fusion Variants)
- Support of Gene Amplification Calling
- Algorithmic Improvements for DNA Small Variants
- Combined Variant Output – Paired RNA and DNA variants
- Update to FASTQ Generation (BCL Converter)

Defect Repairs:

- None

Known Issues:

- Indel Realignment and Read Stitching algorithm can produce output stitched BAM files that vary by as many as 5 reads due to a reproducibility issue with sorting order, which can lead to variation in DNA QC Metrics less than .01%
- Across multiple analyses on the same compute environment, the phased variant algorithm can produce different variant calls for variants with equal levels of supporting evidence within EGFR exon 19 region (seen in less than 1/100 samples)
- Local app may use additional available hardware/compute resources, recommendation is to not run multiple local app instances on a single node
- Performance not verified using read lengths other than 2 x 101

Product Limitations:

- Unmapped long insertions are not likely to occur on shorter indels because there is sufficient reference-matching sequence in the reads. Product claims only indels up to 25 base pairs.

- Complex variants are specifically output only for a specific region of the EGFR gene, component and phased variants would both be contained in the output
- Incorrect calculation of variant allele frequency can occur in variants near the start and end of genomic reads, but variation in read start and end positions in an enrichment assay is sufficient to make incorrect variant allele frequency in output variants a low-probability situation.
- Germline estimation using high tumor purity (>70%) can impact estimation, due to somatic and germline variants appearing with similar variant allele frequency.
- Germline estimation uses latest publicly available population data and estimated to be representative of targeted population, the impact of rare germline mutations is expected to be limited
- Poor quality wild type reads may align as chimeric and be miscalled during RNA analysis

Release History

Version	ER#	Author	Description of Change
00	1030343	Kyle Cutler	Initial Release
01	DIR Workflow	Kyle Cutler	Updates for version 2.0.0 - RNA Support - CNV Support - Algorithm Updates - Combined Variant Output