NEXT-GENERATION SEQUENCING APPLICATION WITH WASAI ON QCT POD FOR MEDICAL (QPM)

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Executive Summary

Next Generation Sequencing (NGS), also known as massive parallel sequencing, is a form of DNA sequencing that analyzes individual strands of DNA simultaneously, which allows it to analyze DNA at a much faster rate than other forms due to the parallel nature of the analysis. Sequencing provides information about the kind of genetic information that is carried in a particular DNA segment. However, due to the advancement NGS provides to the field, the technology used to analyze the NGS results has not kept up with the increase in processing speed. The quantity of DNA data being processed has only continued to increase in volume and cost in the last decade.

With the abundance of raw data from the rapid sequencing, various processing steps are required. Secondary analysis is the process for genome alignment and variant calling. It can identify variants and differences in an individual's genome by comparing it through a DNA reference sequence. As this process is the most time-consuming of the stages of NGS, high-performance computing (HPC) is required for secondary analysis.

Quanta Cloud Technology (QCT) is a leading cloud datacenter solution provider with extensive experience in developing HPC solutions. QCT has expertise on end-to-end HPC and Deep Learning (DL) solutions for companies in a wide variety of fields such as higher education and research, medical, and manufacturing.

QCT developed a platform called QCT POD for medical (QPM) that is specifically designed to meet the needs for life science. QCT cooperates with its technology partner-WASAI Technology Inc, a company that specializes in Big Data acceleration, to process the massive amounts of data in NGS. "Running NGS with WASAI-Lightning™ on QPM, enables our customers to get a significant performance boost during DNA sequencing and leads to a better return on investment (ROI) while requiring less computer processing time," states Stephen Chang, R&D director of QCT.

QCT Focusing on Precision Medicine

QPM (QCT POD for Medical) is a Platform on Demand (POD) solution, which provides an on-premises rack-level system for the healthcare industry. To reach greater flexibility and scaling, QPM offers common building blocks to meet different medical demands, like Next Generation Sequencing (NGS), Molecular Dynamics (MD), and Image Recognition.

Benefits of QPM

- **For Users:** Speeds up productivity with best-fit system design to get insights faster and deeper
- **For Administrators:** Streamlines system monitoring and management with intelligent management tools
- **For Developers:** Accelerates development with a comprehensive environment

QCT realizes Information Technology (IT) staff are facing a number of challenges in the medical and related research industries. In general, there are usually limited IT resources to support complex system deployment, management, and monitoring. There are often isolated platforms and limited resources to fulfill medical workload demands efficiently. The rapid growth of data volume and data protection requirements also places a strain on IT staff. QCT ensures the quality and serviceability of the infrastructure, which could accelerate time-to-value for customers.

The QPM solution addresses the challenges commonly faced by IT:

- **Easy management and rapid deployment:** QPM provides a full software stack, various administrative tools and monitoring dashboards for rapid system deployment and easy system management.
- **Best practice converged system for medical workloads:** QPM is tailored for medical applications with the best-fit hardware and software combination to meet diverse workload demands including data processing / analytics, high-performance computing, and deep learning within a converged platform. QCT also offers pre-defined and pre-installed software components to fulfill NGS, MD, and medical image recognition workloads.
- **Simplified storage management to minimize overall cost:** Since data is ever- increasing in volume and demands high availability nowadays, QPM provides diverse scalable storage building blocks with advanced technologies and hierarchical storage management system to manage hot data and cold data in a cost-effectively manner.

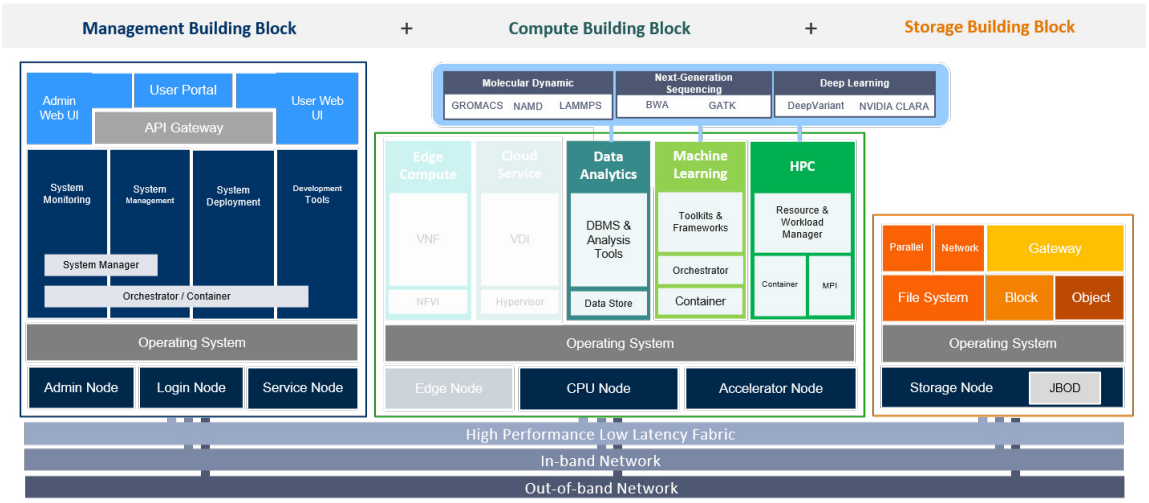

Figure 1. QPM Building Blocks

QCT provides the infrastructure which is suitable for medical researcher and they can focus on Next Generation Sequencing, image recognition and molecular dynamics workloads to support on precision medicine under the QPM platform. "WASAI-Lightning running on QPM is one of our medical workloads, under the trends of precision medicine," states Stephen Chang, R&D director of QCT.

QCT partners with WASAI on Next Generation Sequencing

QCT collaborates with WASAI Technology Inc, a company that specializes in Big Data acceleration on Next Generation Sequencing. WASAI provides a revolutionary solution to DNA and NGS problems through its newly launched WASAI-Lightning™ accelerators. The WASAI-Lightning™ Family is an All-in-one DNA Sequencing Acceleration solution, which addresses challenges caused by growing volumes of genomics data. Through using field programmable gate arrays (FPGAs), WASAI-Lightning™ is capable of significantly reducing the analysis time of DNA data while maintaining a high level of accuracy and consistency of GATK Best Practice workflow from Broad Institute.

WASAI-Lightning targets the BWA-MEM and Haplotypecaller algorithm using a specialized memory hierarchy and pipeline design. This product enhances the efficiency for frequent memory accesses and provides an accurate and high-speed solution. The WASAI-Lightning solution massively accelerates the secondary analysis of NGS data. This pipeline harnesses the tremendous power of the WASAI-Lightning™ Bio-IT Platform and includes highly optimized algorithms for aligning, sorting, mark-duplication, and haplotype variant calling. It also includes a full set of platform tools to match the GATK Best Practice pipeline workflow. "With its powerful integration with FPGA accelerators

on QCT accelerated server QuantaGrid D52BV-2U and QuantaGrid D52G-4U, WASAI-Lightning is implemented with a state-of-the-art technology of memory hierarchy and pipeline design to conquer the issue of frequent memory accesses. This is accomplished by analyzing FASTQ datasets through mapping and variant calling pipeline to create the VCF file. Consequently, we can provide a highly accurate solution with significantly decreased execution time," states Calvin Hung, CEO of WASAI.

QPM Platform with WASAI Lightning performance results

The WASAI Lightning Acceleration solution running on QPM can efficiently lower time required by the GATK Best Practices pipeline. Using the same BWA-MEM + GATK4 software tools and the same CPU computing, WASAI Lightning integrates the Intel® Programmable Acceleration Card (PAC) with the Intel FPGA D5005 to enhance whole pipeline acceleration. While processing a WGS (whole genome sequencing) workflow by GATK Best Practices, it usually takes more than 32 hours with CPU-only computation. WASAI's acceleration cards can significantly reduce total execution time. With a Genome-in-a-Bottle (GIAB) genome sample (NA12878 30x) under the same BWA-MEM and GATK4 pipeline, the Intel PAC FPGA D5005 WASAI Lightning can process a WGS in 2 hours and 58 minutes, while Intel PAC Arria 10 could process a WGS in 4 hours and 58 minutes. The combination of the Intel® CPU and Intel® PAC FPGA D5005 on QCT's accelerated server QuantaGrid D52G-4U is approximately 11 times faster comparing to the CPU-only solution.

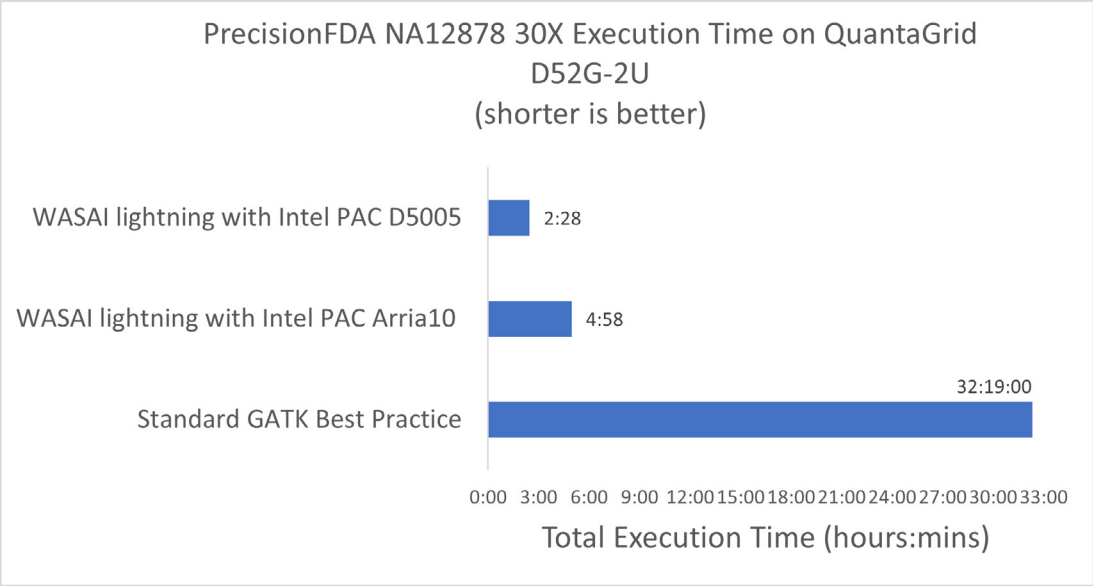

Figure 2. PrecisionFDA NA12878 30X execution time on QuantaGrid D52G-4U and WASAI Lightning with Intel® FPGA PAC D5005 and Intel® FPGA PAC Arria 10

Under QPM Platform, QCT has validated QuantaGrid D52G-4U and QuantaGrid D52BV-2U servers with WASAI Lightning:

- QuantaGrid D52G-4U support high performance demands
    - Support Intel® Xeon® Platinum CPU
    - Support x8 dual-width Intel® FPGAs/GPUs or x16 single-width Intel® FPGAs/GPUs
- QuantaGrid D52BV-2U support high performance demands
    - Support Intel® Xeon® Platinum CPU
    - Support x4 dual-width Intel® FPGAs/GPUs within 2U chassis

QCT Servers support Programmable Acceleration Cards (FPGAs)

In order to keep up with the genomic data growth, FPGA accelerators are the best hardware accelerators to use because they can drastically decrease secondary analysis times. FPGAs can better match the demands of the rise of genomic data, while they serve as an alternative for traditional high-performance computing. The FPGA is capable of processing HPC workloads and is also able to perform parallel operations on a single chip. This omits any latency responses that occur with an input/output computing system. The FPGA is flexible because it can be reprogrammed for workload matching. FPGAs are not limited to processing a single design. A design stored on an FPGA can be instantly overwritten for accelerating different applications with very low latency responses.

QCT has validated Intel® FPGA D5005 and Intel Arria 10 on QCT QuantaGrid D52G-4U and QuantaGrid-D52BV servers. With the supports on FPGAs, QPM provides a comprehensive platform to promise performance potential for medical NGS processing.

WASAI Lightning, equipped with superior memory and input/output optimization, uses Intel® FPGA integration on the QCT servers to optimize the pipeline acceleration processing speed more than five times on average. Users can increase their sample volumes and rely on the accuracy and efficiency that the QPM platform and WASAI Lightning provides. With improved efficiency in sequencing data analysis, users could analyze more than 10,000 genomes a year.

Figure 3. WASAI Lightning BWA& GATK with Intel® PAC FPGA D5005 on QuantaGrid D52G-4U

Accuracy Comparison

The NA12878 and NA24385 comparison is between our NA12878 and NA24385 VCF and the NIST/GiaB v3.3.2 benchmark VCF file for the same sample, constrained within the coordinates of the accompanying GiaB v3.3.2 BED file. The PrecisionFDA website provides NISTv3.3.2.vcf.gz (to be used as benchmark VCF) and NISTv3.3.2.bed (to be used as benchmark BED). This comparison is meant to estimate the accuracy of your pipeline within the "confident" regions of the Genome in a Bottle NA12878 truth dataset — therefore you must leave the test BED entry blank.

The following table summarizes the comparison entries, and the results of the comparison against the NA12878(HG001) PrecisionFDA truth data, using the reference genome of GRCh38 and GRCh37. Not only does the WASAI lightning solution deliver with spectacular acceleration in data processing, it also upholds a 99.99% accuracy in sensitivity and precision in comparison to the standard GATK best practice. These can be seen for both sections of the single nucleotide polymorphism (SNP) and insertion-deletion (INDEL) procedures. While running the genome sample of NA12878 with 50X coverage, it can be seen on the table comparison that the standard GATK best practices vs WASAI's Lightning solution accuracies are virtually identical.

Figure 4. NA12878 50x GRCh38

Figure 5. NA12878 50x GRCh37

Sample	Reference	Compare	SNP-Recall	SNP-Precision	SNP-F-Score	INDEL-Recall	INDEL-Precision	INDEL-F-Score
NA12878 50x	GRCh38	Lightning	98.24%	99.62%	98.90%	97.67%	99.30%	98.50%
		Standard	98.24%	99.70%	99.00%	97.67%	99.34%	98.50%
NA12878 50x	GRCh37	Lightning	99.95%	99.09%	99.50%	99.51%	99.14%	99.30%
		Standard	99.96%	99.33%	99.60%	99.52%	99.26%	99.40%

Figure 4 and Figure 5 show that WASAI solution acceleration cards can maintain the accuracy of the industry standard of GATK software tools while speeding up genome processing during secondary analysis by 10 times.

Conclusion

Next Generation Sequencing (NGS) is a high-throughput DNA sequencing technology constructed based on the technical paradigm of massively parallel sequencing to reach up to enormous numbers of DNA sequences. It has the capability to sequence millions of DNA molecules to multiple individuals simultaneously. Many hardware advances have made genomics analysis faster but with lower cost. With the abundance of raw data from the rapid sequencing, various processing steps require the use of HPC systems to process and analyze data. This is especially true in the secondary analysis used for genome alignment and variant calling.

QCT has expertise on end-to-end HPC and Deep Learning (DL) solutions for companies in a wide variety of fields such as academic research, life science, and manufacturing. QCT developed a platform called QCT POD which provides flexible building blocks to meet diverse industrial demands. QPM is a one of the QCT POD solutions that is specifically designed to meet the needs of the medical field.

QCT is working with WASAI, a company that specializes in Big Data acceleration. WASAI provides a revolutionary solution to DNA and NGS problems through its newly launched WASAI-Lightning™ accelerators. WASAI provides a revolutionary solution to DNA and NGS problems through its newly launched WASAI-Lightning™ accelerators. WASAI is using the QCT QPM solution which helps meet the NGS processing needs. QPM provides the required building blocks for customers to integrate their software with QCT in-house designed hardware to build solutions for a variety of workloads.

The QPM solution along with the WASAI all-in-one accelerated solution used an Intel® PAC (Programmable Acceleration Card), Arria10, D5005 and Intel® Xeon Gold processor, it ran approximately 11 times faster compared to the CPU-only solution.

In this age of AI and DL, medical researchers are focusing on real time health data capture, precise data analysis, as well as machine assisted analysis. Due to the trend of increasing data volumes, a scalable storage and data management system is more important than ever. Time and cost efficiency of medical resources are also critical issues when addressing complex medical tasks. Modernizing the infrastructure of servers, racks, storage, and networking is key to realizing medical innovation. The QPM and WASAI solution provides the infrastructure and data management needed to meet the processing and storage requirements of NGS and DNA sequencing.

Learn more about QCT POD please find here

About Quanta Cloud Technology (QCT)

Quanta Cloud Technology (QCT) is a global datacenter solution provider. We combine the efficiency of hyperscale hardware with infrastructure software from a diversity of industry leaders to solve next-generation datacenter design and operation challenges. QCT serves cloud service providers, telecoms and enterprises running public, hybrid, and private clouds.

Product lines include hyper-converged and software-defined datacenter solutions as well as servers, storage, switches, integrated racks with a diverse ecosystem of hardware component and software partners. QCT designs, manufactures, integrates and services cutting edge offerings via its own global network. The parent of QCT is Quanta Computer, Inc., a Fortune Global 500 corporation.

http://www.QCT.io

About WASAI Technology Inc.

WASAI Technology's mission is to deliver acceleration technologies of High-Performance Data Analysis (HPDA) in future data centers for targeted vertical applications with massive volumes and high velocities of scientific data. To strengthen and advance scientific discovery and technological research via big data-intensive acceleration in high-performance computing, WASAI Technology aims to improve commercialization and commoditization of scientific and technological applications