

Accelerating Minimal Residual Disease (MRD) Detection Through GPU-Accelerated Genomic Analysis Using NVIDIA Parabricks

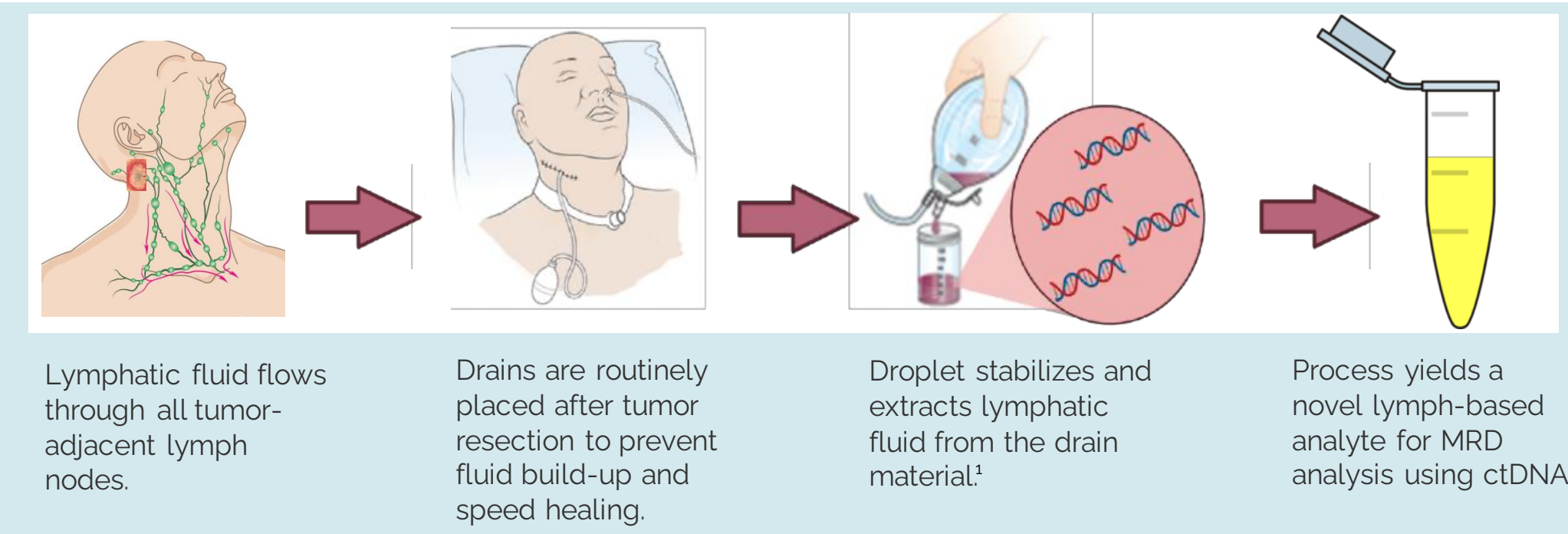
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Introduction

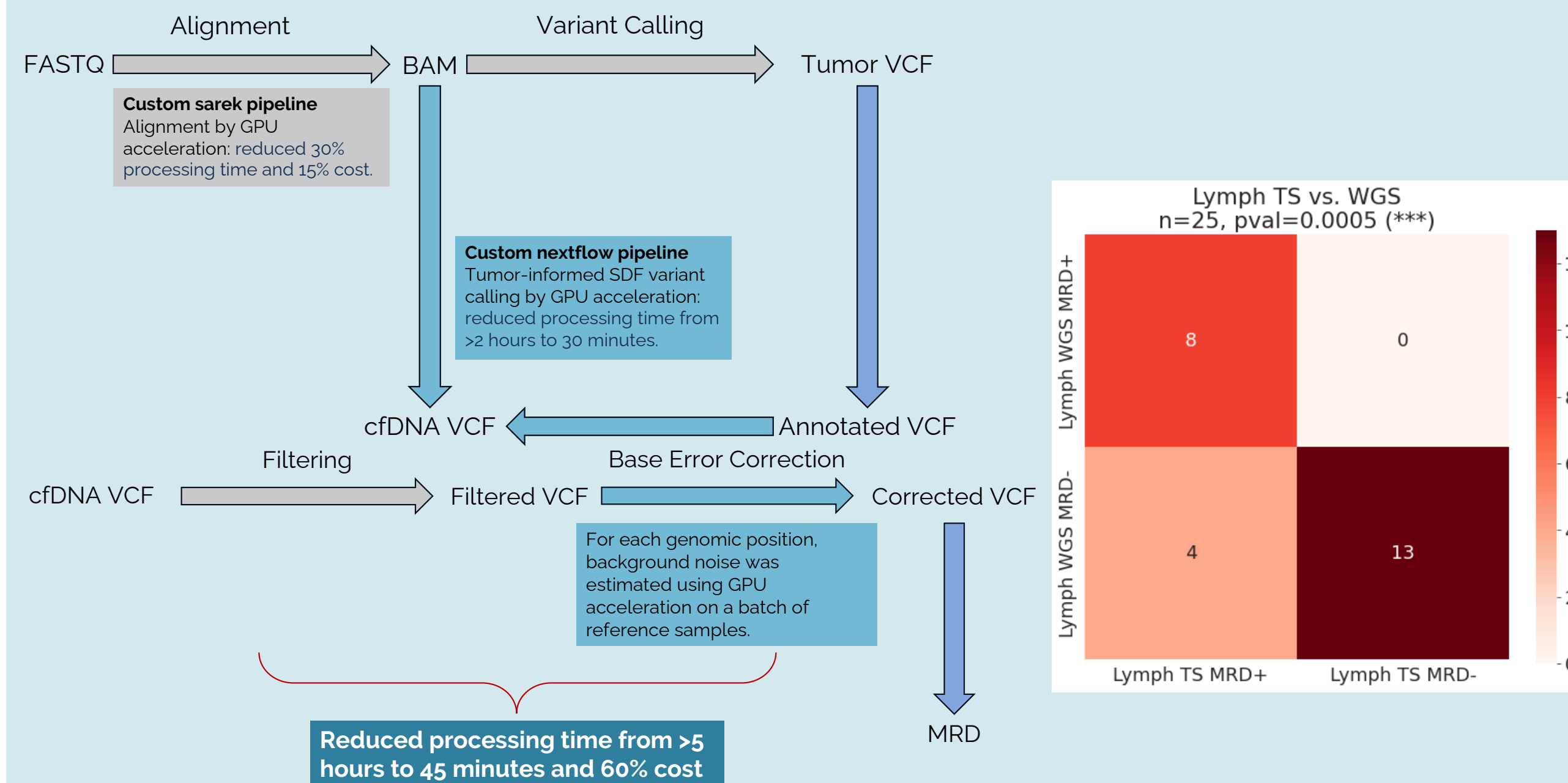
Previously we demonstrated that ctDNA present in lymphatic exudate collected via surgical drains ("lymph") outperformed plasma for detecting MRD in head and neck squamous cell carcinoma (HNSCC) patients through a targeted sequencing (TS) approach¹. However, detecting ultra low frequency variants requires deep sequencing coverage and computationally intensive workflows, often resulting in long turnaround times. To enhance the performance of the TS approach, we implemented an MRD detection pipeline optimized with NVIDIA Parabricks² to accelerate computation and enable faster, scalable molecular analysis without compromising accuracy.

Methods and Materials

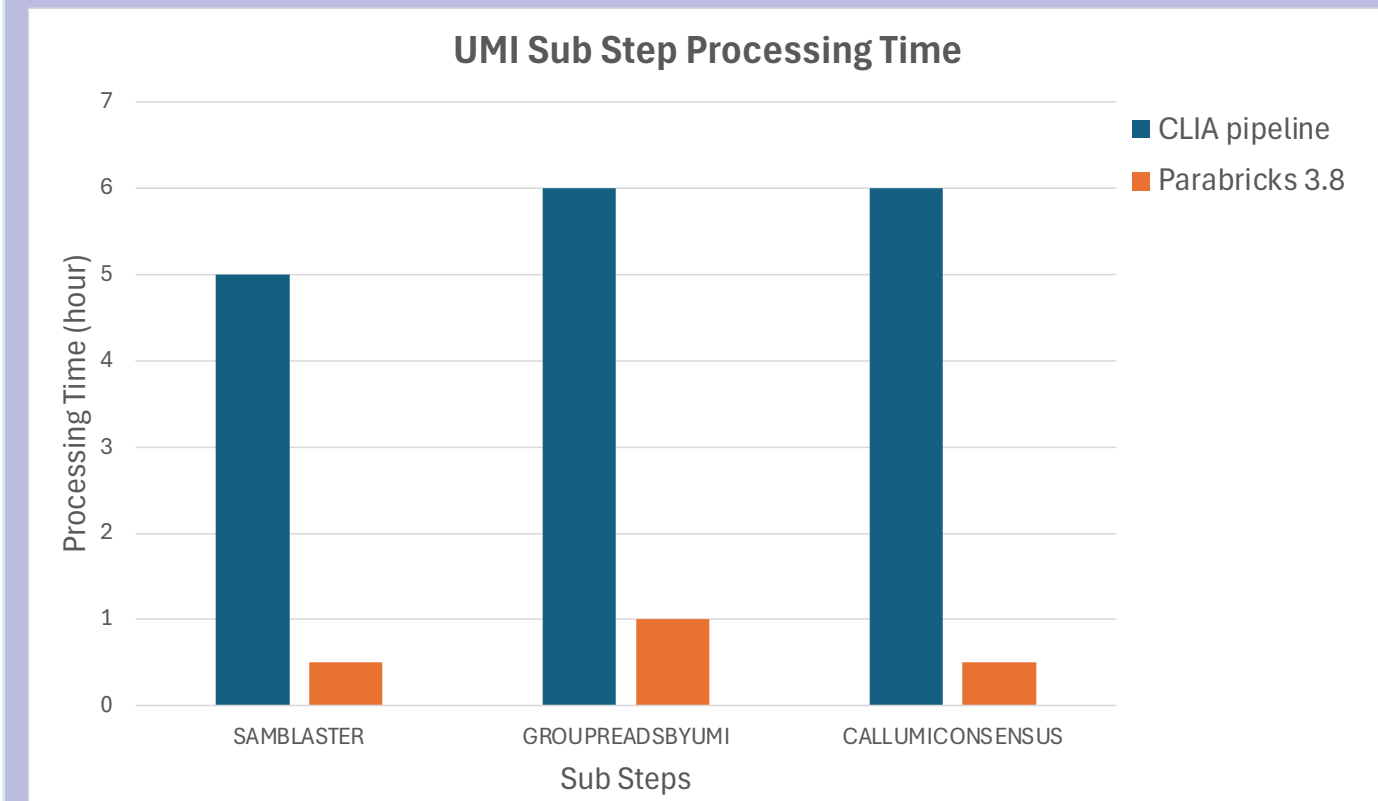


25 unique patients with HPV-independent HNSCC were included in the cohort to demonstrate the performance improvements by porting our MRD workflow from a CPU-based infrastructure to GPU-accelerated Parabricks. Clinical validity was assessed by testing those same 25 patients who each had a minimum of 1 year of clinical follow up data and using the determined mean variant allele fraction (VAF) to classify them as MRD-positive or MRD-negative. MRD classifications were compared to a CLIA / CAP-validated orthogonal tumor-informed whole-genome sequencing-based ctDNA MRD assay. Additionally, as artifacts introduced during library preparation and sequencing remain challenges to sensitive low VAF mutation detection, a base-error model (BEM) that reduces sequencing artifacts and maximizes ctDNA signal was built using a series of high-quality lymph reference samples to quantify the background noise of each tumor variant³. A GPU-accelerated pipeline was implemented for this step when generating the baseline. Tumor-derived variants in lymph samples were considered artifacts if the VAF was not greater than BEM cutoff controlled by false discovery rate.

Results



We observed significant reduction on processing time and cost at the steps that implemented GPU acceleration. At alignment step, we were able to reduce processing time by 30% and computation cost by 15%. At the tumor-informed variant calling step, we reduced average processing time from over 2 hours to 30 minutes per sample. For BEM, combining with optimization on the VCF filtering step, we reduced processing time from over 5 hours to 45 minutes along with a 60% reduction in computation cost. Furthermore, the comparison between our method and the CLIA / CAP-validated assay showed high concordance with p-val = 0.0005 using Fisher's exact test. We achieved 84% percent agreement, demonstrating the accuracy of GPU-accelerated pipeline.



We are currently working with the Parabricks team to further boost our pipeline performance at alignment and tumor variant calling step. More specifically, we are implementing a GPU-accelerated UMI tool to reduce the processing time. In the figure above, we showed significant time reduction for 3 major sub steps for UMI from CPU-based infrastructure to GPU-accelerated Parabricks v3.8. With this implementation, we will be able to reduce the processing time for alignment step to under 8 hours. For tumor variant calling, Parabricks allows us to finish within an hour while it takes over 10 hours on the CPU environment. These speedups will also be translated into cost savings even though the per-hour rate is higher for the GPU instance.

Conclusions

We demonstrated that our GPU-accelerated MRD pipeline using NVIDIA Parabricks delivers clinical-grade accuracy with significant performance boost, enabling scalable, rapid molecular insights for adjuvant decision making. Given its advantages, we envision that GPU acceleration will prove useful to be a general strategy for deep sequencing applications.

References

- ¹Lazare, S. et al. Postoperative Lymph is a Proximal Source of ctDNA for Detection of Recurrence in HPV-independent Head and Neck Cancer. Clin Cancer Res. 2025 Nov 3.
- ²Zhu, T., Vats, P. et al. Parabricks: GPU Accelerated Universal Pan-Instrument Genomics Analysis Software Suite. bioRxiv 2025.07.23.666378; doi: <https://doi.org/10.1101/2025.07.23.666378>.
- ³Newman, A. M. et al. Integrated digital error suppression for improved detection of circulating tumor DNA. Nat. Biotechnol. 34, 547–555 (2016).

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