



Leveraging artificial intelligence in next generation sequencing for head & neck cancer: opportunities and challenges

Carlos M. Chiesa-Estomba^{1,5,6} · Antonino Maniaci^{2,5,6} · Luigi Angelo Vaira^{3,5,6} · Jerome R. Lechien^{4,5,6}

Received: 6 January 2025 / Accepted: 22 January 2025 / Published online: 1 March 2025
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2025

Comment

The advent of Next Generation Sequencing (NGS) has revolutionized our understanding of cancer genomics, enabling clinicians and researchers to establish the foundations to decode the genetic underpinnings of these diseases with unparalleled precision. Head and Neck (H&N) cancers pose diagnostic and therapeutic challenges due to their heterogeneous and multifactorial nature. Integrating Next-Generation Sequencing (NGS) and Artificial Intelligence (AI), particularly Natural Language Processing (NLP), into clinical workflows offers opportunities to overcome these challenges [1, 2]. As artificial intelligence (AI) technologies, including natural language processing (NLP), mature, their integration with NGS workflows has become a subject of growing interest. But how AI, specifically NLP, can support

NGS-based applications for H&N cancers, and which could be its capabilities and limitations?

Regarding capabilities, these will include parsing raw sequencing data and integrating findings with established databases such as COSMIC, ClinVar, and dbSNP to annotate variants with functional and clinical relevance [3]. Moreover, they will be able to summarize complex datasets into actionable insights for clinicians and researchers, improving communication and decision-making. Automation of essential NGS processes, including quality control, read alignment, variant calling, and tumor-specific metric calculations such as Tumor Mutational Burden (TMB) and Microsatellite Instability (MSI), is another area where AI excels [4, 5]. Recognizing mutational signatures and recurrent genetic patterns specific to H&N cancers, including HPV-related mutagenesis and smoking-induced mutations, as well as identifying actionable pathways and networks affected by driver mutations such as those involving TP53, NOTCH1, FBXW7 or PI3K signaling, are among NGS and AI's advanced insights generation capabilities [5–7].

AI can match patient-specific genetic profiles to targeted therapies, immunotherapy options, and clinical trials using curated databases like OncoKB and FDA-approved drug repositories. This demonstrates significant value in personalized therapy recommendations [8]. Interactive support for clinicians and researchers is another critical aspect, with AI generating real-time Q&A responses, providing tutorials, assisting with tool selection for bioinformatics workflows, and producing human-readable reports tailored to the needs of multidisciplinary teams. Tracking clonal architecture to predict resistance mechanisms and assess treatment strategies is crucial for longitudinal studies. AI's ability to analyze tumor dynamics in response to therapy could revolutionize adaptive treatment approaches [6].

Despite its computational strengths, AI remains dependent on foundational laboratory processes of NGS analysis for H&N cancers, such as library construction or sequencing itself. These foundational steps remain reliant

✉ Carlos M. Chiesa-Estomba
chiesaestomba86@gmail.com

- ¹ Department of Otorhinolaryngology, Donostia University Hospital, Biodonostia Research Institute, Osakidetza, San Sebastian 20014, Spain
- ² Faculty of Medicine and Surgery, University of Enna “Kore”, Enna 94100, Italy
- ³ Maxillofacial Surgery Operative Unit, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy
- ⁴ Department of Otolaryngology and Head and Neck Surgery, Division of Laryngology and Broncho-Esophagology, UMONS Research Institute for Health Sciences and Technology, EpiCURA Hospital, University of Mons, Mons, Belgium
- ⁵ Head & Neck Study Group of Young-Otolaryngologists of the International Federations of Oto-rhino-laryngological Societies (YO-IFOS), Mons, Belgium
- ⁶ Young-Otolaryngologists of the International Federation of Oto-Rhino-Laryngological Societies (YO-IFOS) Study Group, Paris, France

on laboratory workflows. Sequencing platform variability, including differences in error rates between Illumina and Oxford Nanopore technologies, requires tailored bioinformatics pipelines. AI models must be adapted and validated for these specific contexts to ensure reliability and reproducibility, complementing but not replacing these technologies [9]. While AI offers data-driven recommendations, the final interpretation of results and their integration into a patient's clinical context require human clinical and scientific expertise. Moreover, ethical considerations and individual patients' factors necessitate clinician oversight during the decision-making process. Harmonizing data from diverse sources, such as multi-omics datasets and sequencing platforms, remains a challenge. AI developers must prioritize standardization efforts to enable seamless integration and accurate biological interpretations. For example, differences in read lengths and error rates between Illumina and Oxford Nanopore platforms can significantly affect variant calling and assembly accuracy. Cross-platform validation strategies, such as combining results from multiple platforms or using benchmark datasets, can mitigate these discrepancies and improve robustness in data interpretation. Also, the variability among NGS protocols and sequencing platforms can complicate data processing and analysis, requiring tailored pipelines and validation across different settings to ensure consistency and reliability [8].

The integration of AI, particularly NLP-based systems, into NGS workflows has the potential to accelerate advancements in H&N cancer research as well as clinical management. By automating repetitive tasks, annotating complex datasets, and facilitating personalized therapy recommendations, AI acts as a powerful adjunct to human expertise. Fostering collaboration between AI developers, bioinformaticians, and clinicians will be critical. Establishing interdisciplinary task forces can ensure that AI tools align with clinical needs while addressing ethical considerations and real-world challenges. Moving forward, the synergy between AI and NGS holds great promise for transforming cancer care. Developing globally recognized validation standards for AI models in NGS workflows will enhance trust and facilitate broader adoption. Initiatives like open-source benchmarking datasets could accelerate these efforts. In this vein, expert feedback and collaborative opportunities will be necessary to refine these technologies further and expand their real-world impact [7].

The synergy between AI and NGS has the potential to redefine cancer care, but its success depends on addressing current limitations and fostering interdisciplinary collaboration. As these technologies continue to evolve, the oncology community must work together to ensure their ethical and impactful integration into clinical practice.

Declarations

Competing interests The author Jerome R. Lechien was not involved with the peer review process of this article.

References

1. Zehir A, Benayed R, Shah RH et al (2017) Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients. *Nat Med* 23:703–713
2. Chu YH, Katabi N, Sukhadia P, Mullaney KA, Zaidinski M, Cracchiolo JR, Xu B, Ghossein RA, Ho AL, DiNapoli SE, Ladanyi M, Dogan S (2024) Targeted RNA sequencing in diagnostically challenging head and neck carcinomas identifies novel *MON2::STAT6*, *NFATC2::NUTM2B*, *POC5::RAF1*, and *NSD3::NCOA2* gene fusions. *Histopathology*. Dec 4
3. Tsang H, Addepalli K, Davis SR (2017) Resources for interpreting variants in Precision genomic oncology applications. *Front Oncol* 7:214
4. Dotolo S, Esposito Abate R, Roma C, Guido D, Preziosi A, Tropea B, Palluzzi F, Giaco L, Normanno N (2022) Bioinformatics: from NGS data to Biological complexity in variant detection and oncological clinical practice. *Biomedicine* 10(9):2074
5. Nadal A, Cardesa A, Agaimy A, Almangush A, Franchi A, Hellquist H, Leivo I, Zidar N, Ferlito A (2024) Massive parallel sequencing of head and neck conventional squamous cell carcinomas: a comprehensive review. *Virchows Arch* 485(6):965–976
6. Qureshi MA (2024) Integration of Next Generation sequencing, Artificial Intelligence and Machine Learning in Cancer Diagnostics: a Major Leap Forward. *J Coll Physicians Surg Pak* 34(2):127–128
7. Park Y, Heider D, Hauschild AC (2021) Integrative analysis of Next-Generation sequencing for Next-Generation Cancer Research toward Artificial Intelligence. *Cancers (Basel)* 13(13):3148
8. Guan M, Cho S, Petro R, Zhang W, Pasche B, Topaloglu U (2019) Natural language processing and recurrent network models for identifying genomic mutation-associated cancer treatment change from patient progress notes. *JAMIA Open* 2(1):139–149
9. Lu H, Giordano F, Ning Z (2016) Oxford Nanopore MinION sequencing and Genome Assembly. *Genomics Proteom Bioinf* 14(5):265–279

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.