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COMMENT

New frontiers in O-MFS: omic-maxillofacial surgery toward a translational approach to patient care

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Abstract

The integration of omics sciences into maxillofacial surgery marks a transformative step toward a new model of personalized and translational patient care. Recent advances in genomics, transcriptomics, and epigenomics are reshaping the understanding and management of head and neck squamous cell carcinoma (HNSCC), one of the most challenging malignancies in the maxillofacial region due to its biological heterogeneity and poor prognosis. Omics sciences offer unprecedented insight into the molecular landscape of these tumors, allowing the identification of specific biomarkers that predict patient outcomes and guide tailored surgical strategies. A landmark study by Ribeiro et al. demonstrated the clinical value of a nine-gene multi-omics signature capable of distinguishing HNSCC patients with markedly different survival rates, independent of metastasis status. This signature integrates copy number alterations, gene expression profiles, and methylation patterns linked to key cellular processes such as DNA repair, cytoskeletal dynamics, and immune response. The concept of "Omic-Maxillofacial Surgery" (O-MFS) envisions a future where molecular data complement anatomical, pathological, and functional criteria to refine surgical planning, intraoperative decision-making, and postoperative surveillance. Despite challenges related to data complexity, clinical validation, and cost, this emerging approach promises to revolutionize maxillofacial oncology by enabling more accurate patient stratification and truly personalized surgical care.

Keywords Omics sciences · Maxillofacial surgery · Translational surgery · Personalized oncology · Molecular biomarkers.

Introduction

Maxillofacial surgery (MFS) is traditionally perceived as an anatomical and technical discipline—where success depends on precise surgical technique, preoperative imaging, and biomechanical reconstruction. However, in recent years, a revolution has begun to reshape this field: the incorporation of *omics sciences*—genomics, transcriptomics, proteomics, metabolomics, and epigenomics—into clinical decision-making [1]. This evolving landscape, which we propose to call for the first time "O-MFS" (Omic-Maxillofacial Surgery), represents a new paradigm where surgery becomes deeply integrated with molecular, cellular, and bioinformatics knowledge.

Omics-based approaches promise to bridge the gap between surgical practice and personalized, predictive, and preventive medicine. Nowhere is this integration more pressing than in head and neck oncology, particularly head and neck squamous cell carcinoma (HNSCC), which represents a significant challenge in maxillofacial surgery due to its heterogeneity, poor prognosis, and resistance to standard treatments [2].

This paper theorizes how omics data, including genomics, epigenomics, and transcriptomics, may shape the future of maxillofacial surgery with significant impact. We argue that "Omic-MFS" represents a critical translational frontier, offering new biomarkers, prognostic tools, and therapeutic targets for individualized surgical oncology in the maxillofacial region.

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The omics revolution

Omics technologies have fundamentally changed cancer biology. Genomics identifies DNA-level alterations such as mutations and copy number variations (CNVs); transcriptomics measures gene expression patterns; proteomics and metabolomics profile proteins and metabolites; and epigenomics assesses changes such as DNA methylation that modulate gene activity without altering the DNA sequence. Integrated together, these datasets provide an unprecedented multi-dimensional view of tumor behavior [1].

The integration of omics data allows the classification of tumors not only by their histology or location but also by their molecular profiles. This is especially important in HNSCC, where the clinical behavior of tumors is highly variable—even among tumors of identical stage and histological subtype.

One recent study by Ribeiro et al. demonstrated the power of multi-omics integration by analyzing head and neck cancer using The Cancer Genome Atlas (TCGA) data [3]. By applying genomics, transcriptomics, and DNA methylation data, the researchers identified a nine-gene signature associated with survival in HNSCC patients, independent of metastasis development.

Implications for maxillofacial surgery: towards omic MFS

How does this molecular knowledge translate into clinical practice in maxillofacial surgery?

1. Patient stratification for surgery
   Multi-omics data can divide patients into high-risk and low-risk groups, guiding surgical aggressiveness. For instance, tumors with a genetic signature indicating poor prognosis may justify more extensive resection, prophylactic neck dissection, or combined modality therapy—even in early stages. Conversely, low-risk molecular signatures could support more conservative surgery, preserving function and aesthetics. Future studies could use genomic or transcriptomic panels to identify maxillofacial cancer patients most likely to respond to specific pre-operative (neoadjuvant) therapies, such as immunotherapy or targeted chemotherapy. For instance, the presence of certain gene mutations or the expression of specific immunological markers might indicate a better response, thereby avoiding ineffective treatments in non-responsive patients.
2. Biomarker-Based Surgical Planning
   Omics-derived biomarkers could predict complications such as wound healing disorders, recurrence, or radiation resistance. Surgeons could tailor flap selection, reconstruction strategies, and perioperative therapies based on the molecular profile of both the tumor and the host tissues. An example can be laboratory parameters, such as the HALP score, used to calculate the preoperative risk of possible failure of a free flap for the reconstruction of facial defects[3].
3. Post-Surgical Surveillance
   Liquid biopsy technologies (e.g., circulating tumor DNA) rooted in omics can enable minimally invasive monitoring of residual disease or early recurrence, potentially replacing or complementing imaging in the postoperative follow-up of maxillofacial cancer patients. Liquid biopsies (analysis of circulating tumor DNA - ctDNA or circulating tumor cells - CTCs) could be used also to monitor the effectiveness of neoadjuvant or adjuvant therapies in real-time. A decrease in ctDNA or CTCs might indicate a good response, while an increase could signal treatment resistance or disease relapse, allowing for a more timely change in therapeutic strategy. After surgery, proteomic or metabolomic analysis of residual tumor tissues or peripheral blood could reveal biomarkers associated with a higher risk of recurrence or metastasis. This would allow for patient stratification for more intensive follow-up or the adoption of personalized adjuvant therapies, improving treatment efficacy and reducing unnecessary side effects.
4. Translational Surgical Trials
   Future clinical trials in maxillofacial oncology will increasingly incorporate omics stratification as inclusion criteria or as endpoints, ensuring that surgical innovations benefit molecularly defined patient subgroups rather than heterogeneous populations. A deeper understanding of the tumor's molecular profile could influence surgical decisions themselves. For example, tumors with particular genetic signatures associated with high local invasiveness might require wider resection margins or the inclusion of prophylactic lymphadenectomies, whereas tumors with a less aggressive profile could benefit from more conservative surgical approaches.

The nine-gene signature: A model of translational omics

The study by Ribeiro et al. represents a clear example of how omics sciences can be translated into practical applications in maxillofacial oncology. Through an integrated analysis that combined genomic, transcriptomic, and epigenetic data, the researchers succeeded in identifying a molecular signature capable of distinguishing head and neck squamous cell carcinoma (HNSCC) patients with markedly different survival prospects [4].

At the genomic level, they highlighted alterations in the copy number of two genes—*LMCD1-AS1* and *GRM7*, both located on chromosome 3p26.1—whose structural variations appeared to have a significant impact on disease prognosis. In terms of gene expression, differences in the activity of four genes—*RPL29*, *UBA7*, *FCGR2C*, and *RPSAP58*—were found to effectively separate patients into distinct survival groups, suggesting that the deregulation of these genes plays a role in tumor behavior and progression.

This molecular portrait thus offers a comprehensive view of the mechanisms underlying tumor heterogeneity and patient outcome, underscoring the potential of omics-driven approaches to transform prognostic evaluation and therapeutic planning in the field of maxillofacial surgery [5].

Interestingly, this molecular signature provided prognostic separation independent of metastatic status or clinical staging—a crucial feature for surgical decision-making, where anatomical criteria alone often fail to capture biological behavior.

Looking ahead, omics sciences may soon become the "fourth dimension" of surgery, complementing anatomy, pathology, and functional expertise. In this emerging model of Omic Maxillofacial Surgery, molecular biology will be seamlessly integrated into every phase of patient care. It is not difficult to imagine a scenario in which preoperative planning meetings include not only CT scans and histological slides but also detailed molecular profiles of each tumor. Surgeons will use this information to assess the tumor's biological behavior—its potential for aggression, its likely response to radiation or chemotherapy, and its risk of recurrence—and adjust the surgical plan accordingly to avoid both overtreatment and undertreatment [8].

Moreover, the future may bring real-time molecular diagnostics directly into the operating room. The concept of "molecular navigation surgery" could allow surgeons to assess resection margins at the genetic or epigenetic level during the procedure itself, ensuring complete removal of malignant tissue with unprecedented precision.

Challenges in implementing omic MFS

Although the integration of omics sciences into maxillofacial surgery holds extraordinary promise, several practical challenges must be addressed before this approach can become part of daily clinical practice. One of the most significant obstacles is the sheer complexity of the data involved. Multi-omics analyses generate vast quantities of information that require advanced bioinformatics platforms for interpretation—systems that are not yet standardized or universally accessible in hospital settings. Without reliable and validated pipelines, translating this information into clinically meaningful guidance remains a difficult task.

Timing is also a crucial factor. For omics data to genuinely inform surgical planning, results must be generated and interpreted rapidly—ideally before the operation takes place. Current sequencing technologies and data processing methods are improving, but the turnaround time is still not always compatible with the fast pace of clinical workflow [6]. Until sequencing, analysis, and reporting can be performed within a timeframe relevant to preoperative discussions, the impact of omics on surgical practice will remain limited [1, 7].

Finally, cost and accessibility represent significant barriers. At present, comprehensive multi-omics profiling is expensive and available only in specialized centers. To justify widespread adoption in surgical oncology—including maxillofacial surgery—future studies must demonstrate that these techniques are not only clinically useful but also cost-effective, improving patient outcomes enough to warrant the investment.

Conclusion

The integration of omics sciences into maxillofacial surgery is not merely a research curiosity but a necessity in an age where personalization of oncologic care is imperative. The concept of Omic MFS—the application of genomics, transcriptomics, and epigenomics in surgical oncology of the maxillofacial region—marks the beginning of a translational shift towards molecularly guided surgery.

While technical, economic, and educational barriers remain, the potential to improve survival, reduce morbidity, and optimize resource utilization is immense. Maxillofacial surgeons must embrace this molecular dimension, transforming their practice from one based on form and function alone to one that incorporates the rich complexity of tumor biology.

In this new frontier of O-MFS, the scalpel will be guided not only by the surgeon's hand but also by the molecular signature of each individual tumor.

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Declarations

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors. The treatment of the presented patient was not in any way influenced due to this article.

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