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ORIGINAL RESEARCH

ADVANCES IN SURGICAL MANAGEMENT OF ORAL SQUAMOUS CELL CARCINOMA: CURRENT CONCEPTS AND FUTURE DIRECTIONS

Ahtesham Ahmad Qurishi[1], Vishwannath Hiremath[2], Mohamed S. Mohamed Morsy[3], Ahmed Mostafa Ahmed Mostafa[4], Mohamed Mansy[5], Dima Tarik Hassan Ibrahim[6]

[1]Department of maxillofacial surgery and diagnostic sciences, College of Dentistry, Jizan University , Saudi Arabia EMAIL- aqurishi@jazanu.edu.sa Orcid- 0000-0002-6943-7169

[2]Director, Department of Maxillofacial Surgery, Dr Hiremath Hospital (A Unit of Hiremath Hospitals Pvt Ltd),Vijayanagar, Bengaluru India drhiremathhospitals@gmail.com

[3]Department of Prosthodontics , College of Dentistry ,Jizan University, Saudi Arabia. mmorsy@jazanu.edu.sa

[4]Department of Maxillofacial surgery and diagnostic sciences College of Dentistry Jizan university, Saudi Arabia. Email- Ahmdmoustafa@yahoo.com

[5]Department of Maxillofacial surgery and diagnostic sciences, College of Dentistry, Jizan university, Saudi Arabia mmansy@jazanu.edu.sa Orcid-0000-0002-8488-2674

[6]Specialized Dental Centre , North Jeddah, Saudi Arabia. Email- dimatibrahim722@gmail.com

[*]**Corresponding author:** Ahtesham Ahmad Qurishi, Department of maxillofacial surgery and diagnostic sciences, College of Dentistry, Jizan University, Saudi Arabi aqurishi@jazanu.edu.sa

Oral squamous cell carcinoma (OSCC) represents the most common malignant neoplasm of the oral cavity, accounting for approximately 90% of all oral cancers. Despite advances in treatment modalities, the 5-year survival rate has remained relatively unchanged over the past few decades, highlighting the need for improved therapeutic strategies. This narrative review aims to synthesize current evidence on advances in the surgical management of OSCC, examining the evolution from conventional approaches to innovative techniques, and exploring future directions in the field. We comprehensively review the pathophysiology and molecular landscape of OSCC, recent diagnostic and staging advances, conventional and minimally invasive surgical approaches including robotic-assisted surgery, and contemporary reconstruction techniques. The literature reveals that while traditional surgical resection remains the cornerstone of treatment, technological innovations have enabled more precise tumor removal with better functional and aesthetic outcomes. Sentinel lymph node biopsy, transoral robotic surgery, and 3D-printed reconstruction represent significant advances that are reshaping the surgical paradigm. However, challenges remain in early detection, margin assessment, and personalized treatment approaches. The integration of molecular profiling with surgical decision-making holds promise for the future, potentially enabling more tailored interventions. This review underscores that multidisciplinary collaboration and continued technological innovation will be essential to improve survival outcomes and quality of life for OSCC patients.

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) constitutes a significant global health burden, ranking among the top ten most common cancers worldwide with approximately 377,713 new cases and 177,757 deaths annually [1]. Despite advances in diagnostic techniques and therapeutic modalities, the 5-year survival ratefor

OSCC remains disappointingly static at approximately 50-60% over the past three decades [2].

This plateau in survival outcomes underscores the urgent need for innovative approaches to improve patient prognosis.

The etiology of OSCC is multifactorial, with established risk factors including tobacco use, alcohol consumption, betel quid chewing, and oncogenic viruses such as human papillomavirus (HPV) [3]. The

anatomical complexity of the oral cavity, coupled with the critical functions of speech, mastication, and deglutition performed in this region, presents unique challenges in the management of OSCC. Surgical resection has historically been the mainstay of treatment for early-stage disease, while advanced cases often require multimodal approaches combining surgery, radiation, and chemotherapy [4].

Controversies persist in several aspects of OSCC management, including the optimal extent of surgical resection, the management of clinically negative necks, the role of elective neck dissection, and the integration of novel technologies into standard practice[5]. Furthermore, the balance between oncological control and functional preservation remains a central consideration in surgical decision-making.

The landscape of OSCC surgery has evolved considerably in recent years, driven by technological advancements and improved understanding of tumor biology. Innovations such as transoral robotic surgery (TORS), sentinel lymph node biopsy (SLNB), and computer-assisted surgical planning have revolutionized traditional approaches[6]. These developments have enabled more precise tumor removal with reduced morbidity and improved functional outcomes.

Given the rapid evolution of surgical techniques and the ongoing controversies in OSCC management, a comprehensive review of current evidence is warranted. This narrative review aims to synthesize the latest advances in the surgical management of OSCC, critically evaluate the evidence supporting various approaches, and identify future directions for research and clinical practice. By examining the pathophysiology, diagnostic advances, conventional and minimally invasive surgical techniques, and reconstruction methods, this review seeks to provide clinicians and researchers with an up-to-date understanding of the current state of OSCC surgery and the trajectory of its future development.

1. Pathophysiology and Molecular Landscape of Oral Squamous Cell Carcinoma

The pathogenesis of OSCC follows a multistep process of genetic and epigenetic alterations that drive the transformation of normal oral mucosa to invasive carcinoma [7]. This carcinogenic cascade involves the accumulation of molecular changes that disrupt critical cellular pathways controlling proliferation, differentiation, apoptosis, and genomic stability. Understanding these molecular mechanisms has important implications for surgical management, as they influence tumorbehavior, metastatic potential, and treatment response.The molecular landscape of OSCC is characterized by considerable heterogeneity, with distinct genomic profiles associated with different risk factors and clinical outcomes [8]. Tobacco and alcohol-related OSCCs typically exhibit a high mutational burden with frequent alterations in tumor suppressor genes such as TP53, CDKN2A, and NOTCH1 [9]. In contrast, HPV-positive OSCCs, which are increasing in incidence, particularly in the oropharynx, demonstrate a distinct molecular profile characterized by fewer mutations but frequent integration of viral oncogenes E6 and E7, which inactivate p53 and pRb, respectively [10].

Recent advances in next-generation sequencing have identified several keysignaling pathways that are frequently dysregulated in OSCC, including the PI3K/AKT/mTOR pathway, NOTCH signaling, and cell cycle regulation pathways [11]. These molecular insights have not only enhanced our understanding of OSCC pathogenesis but have also identified potential therapeutic targets that may complement surgical approaches.

The tumor microenvironment (TME) plays a crucial role in OSCC progression and metastasis [12]. The TME consists of various cellular components including cancer-associated fibroblasts, tumor-infiltrating lymphocytes, and tumor-associated macrophages, which interact with cancer cells through complex signaling networks. These interactions can promote tumor growth, invasion, and immune evasion. The composition and functional state of the TME have been shown to influence surgical outcomes and response to adjuvant therapies [13].

Field cancerization is another important concept in OSCC pathophysiology, referring to the molecular alterations in histologically normal mucosa surrounding the primary tumor [14]. This phenomenon explains the high rates of local recurrence and second primary tumors observed in OSCC patients. From a surgical perspective, field cancerization poses challenges in determining appropriate resection margins and has implications for the extent of surgical resection required to achieve local control.Emerging evidence suggests that molecular characterization of OSCC may help predict the likelihood of occult metastasis and the risk of recurrence, potentially guiding surgical decision-making [15]. For instance, specific gene expression signatures have been associated with lymph node metastasis, which could inform decisions regarding elective neck dissection in patients with clinically negative necks [16].

Despite these advances in understanding the molecular pathogenesis of OSCC, the translation of these findings into clinical practice remains limited. There is a need for prospective studies to validate molecular biomarkers for surgical decision-making and to develop targeted therapies that can be integrated with surgical approaches to improve outcomes.

2. Diagnostic Advances and Staging Modalities

Accurate diagnosis and staging are fundamental to

appropriate surgical planning for OSCC. Recent years have witnessed significant advances in diagnostic technologies and staging methodologies that have enhanced the precision of preoperative assessment and intraoperative decision-making [17].

Conventional examination under white light remains the initial step in the evaluation of suspicious oral lesions, but its limitations in detecting early malignant changes and determining tumor boundaries are well recognized [18]. To overcome these limitations, several adjunctive diagnostic tools have been developed. Vital staining with toluidine blue has been used for decades to highlight areas of abnormal epithelium, although its specificity remains suboptimal [19]. More recently, autofluorescence imaging has emerged as a promising technique for detecting dysplastic and malignant changes based on the differential fluorescence between normal and neoplastic tissues [20].

Optical coherence tomography (OCT) represents another technological innovation that enables cross-sectional imaging of oral mucosa at near-histological resolution, allowing for real-time assessment of tissue architecture[21]. This non-invasive technique has shown promise in differentiating between benign, dysplastic, and malignant lesions and may facilitate the delineation of tumor margins during surgical resection.

High-resolution imaging modalities play a crucial role in the preoperative assessment of OSCC. Contrast-enhanced computed tomography (CT) remains the workhorse for evaluating bone invasion and nodal metastasis, while magnetic resonance imaging (MRI) provides superior soft tissue contrast for assessing tumor extent and perineural invasion[22]. The integration of functional imaging techniques such as diffusion-weighted MRI and positron emission tomography (PET) with CT or MRI has further improved the accuracy of staging, particularly in detecting occult nodal metastasis and distant spread [23].

Sentinel lymph node biopsy (SLNB) has emerged as a minimally invasive alternative to elective neck dissection for staging the clinically negative neck in early-stage OSCC[24]. This technique involves the identification and removal of the first draining lymph node(s) from the primary tumor, which are then examined for metastatic deposits. Multiple studies have demonstrated the high accuracy of SLNB in detecting occult nodal metastasis, with sensitivity rates exceeding 90% in experienced centers[25]. The adoption of SLNB has the potential to reduce the morbidity associated with elective neck dissection while maintaining oncological safety.

Intraoperative margin assessment remains a critical challenge in OSCC surgery, with positive margins being a significant predictor of local recurrence and poor survival [26]. Conventional frozen section analysis has been the standard approach for intraoperative margin evaluation, but it is time-consuming and subject to sampling errors. Emerging techniques such as fluorescence imaging, optical coherence tomography, and Raman spectroscopy offer the potential for real-time, comprehensive margin assessment during surgery [27]. These technologies may enable more precise tumor resection with reduced rates of positive margins and decreased need for re-excision.

The integration of artificial intelligence (AI) and machine learning algorithms into diagnostic imaging represents a frontier in OSCC staging[28]. These computational approaches have shown promise in automating tumor detection, delineation, and classification, potentially improving the consistency and accuracy of staging. Furthermore, AI-based analysis of histopathological slides may provide additional prognostic information that could guide surgical decision-making.

Despite these technological advances, challenges remain in the widespread implementation of novel diagnostic techniques. Issues such as cost, accessibility, operator dependency, and the need for standardized protocols and validation studies limit their adoption in routine clinical practice. Future research should focus on addressing these barriers and establishing the clinical utility of emerging diagnostic modalities in improving surgical outcomes for OSCC patients.

3. Conventional Surgical Approaches and Their Evolution

Surgical resection remains the cornerstone of treatment for the majority of OSCC cases, particularly in early-stage disease. The evolution of conventional surgical approaches for OSCC has been characterized by a shift from radical, disfiguring procedures toward more conservative, function-preserving techniques without compromising oncological outcomes [29].

The traditional approach to OSCC surgery involved wide local excision with generous margins (1-2 cm) of normal tissue, often combined with radical neck dissection for regional control[30]. While this aggressive approach maximized local control, it resulted in significant functional and aesthetic morbidity. Over the past few decades, surgical philosophy has evolved to embrace the concept of "minimal effective resection," which aims to achieve clear margins while preserving as much normal tissue and function as possible [31].

The extent of surgical resection is primarily determined by tumor size, location, depth of invasion, and relationship to critical structures. For early-stage tumors (T1-T2), wide local excision with 1 cm clinical margins is generally recommended, with the goal of achieving at least 5 mm histological clearance [32]. For more advanced tumors, the resection may need to include adjacent structures such as bone, muscle, or skin to ensure complete tumor removal. The concept

of compartmental surgery, which involves en bloc resection of tumor along with the entire anatomical compartment, has gained traction for certain advanced OSCCs, particularly those involving the tongue or mandible [33].

Neck management is a critical component of OSCC surgery, as cervical lymph node metastasis is the most important prognostic factor [34]. The evolution of neck dissection techniques has progressed from the radical neck dissection described by Crile in 1906, which involved removal of all lymph node groups along with the sternocleidomastoid muscle, internal jugular vein, and spinal accessory nerve, to more selective and modified approaches [35]. Selective neck dissection preserves one or more non-lymphatic structures while removing specific lymph node groups at risk based on the primary tumor location. This approach has demonstrated equivalent oncological outcomes to radical neck dissection for appropriately selected patients, with significantly reduced morbidity [36].

The management of the clinically negative neck (cN0) in OSCC remains controversial. While elective neck dissection has traditionally been recommended for tumors with a high risk of occult metastasis (generally those with depth of invasion >4 mm), the emergence of sentinel lymph node biopsy has provided a less invasive alternative for staging the neck [37]. Several randomized controlled trials have compared elective neck dissection with watchful waiting in cN0 patients, with most showing improved regional control and survival with elective neck dissection for intermediate and high-risk tumors [38].

Intraoperative frozen section analysis has long been utilized to assess surgical margins, with the goal of reducing the rate of positive margins and the need for re-excision. However, the accuracy of frozen section analysis is influenced by several factors, including sampling error, interpretation challenges, and processing artifacts[39]. The development of more precise techniques for intraoperative margin assessment, such as specimen-oriented computed tomography and fluorescence-guided surgery, represents an important area of ongoing research[40].

The integration of laser surgery into the management of OSCC has enabled more precise tissue ablation with reduced bleeding and postoperative pain [41]. Transoral laser microsurgery (TLM) has been particularly valuable for tumors of the larynx and oropharynx, allowing for excellent access to tumors with minimal disruption to uninvolved tissues. The oncological outcomes of TLM have been shown to be comparable to those of conventional surgery, with the added benefits of reduced hospital stays and faster recovery [42].

Despite these advances in conventional surgical approaches, challenges remain in achieving the optimal balance between oncological control and functional preservation. The decision-making process for OSCC surgery requires careful consideration of multiple factors, including tumor characteristics, patient comorbidities, functional status, and patient preferences. A multidisciplinary approach involving surgeons, radiation oncologists, medical oncologists, and other specialists is essential to develop individualized treatment plans that optimize outcomes for each patient.

4. Minimally Invasive and Robotic Surgical Techniques

The past two decades have witnessed a paradigm shift in the surgical management of OSCC, with the emergence and refinement of minimally invasive and robotic techniques that aim to reduce treatment-related morbidity while maintaining oncological efficacy [43]. These technological advances have expanded the surgical armamentarium, offering new approaches to access and resect tumors in challenging anatomical locations.

Transoral robotic surgery (TORS) represents one of the most significant advances in minimally invasive head and neck surgery [44]. Approved by the FDA in 2009 for T1-T2 oropharyngeal tumors, TORS utilizes a robotic system that provides three-dimensional visualization, tremor filtration, and enhanced dexterity with wristed instruments that mimic human hand movements with seven degrees of freedom. This technology overcomes many of the limitations of traditional transoral surgery, including restricted access, limited visualization, and awkward instrument angles. TORS has been increasingly applied to OSCC in various subsites, including the base of tongue, tonsil, soft palate, and pharyngeal walls [45].

Multiple studies have demonstrated the feasibility and safety of TORS for selected OSCC patients, with favorable oncological outcomes and reduced morbidity compared to open approaches or chemoradiation[46]. A systematic review by de Almeida et al. reported 2-year overall survival rates ranging from 82% to 91% for TORS-treated oropharyngeal SCC, with locoregional control rates of 85-94% [47]. Functional outcomes have also been promising, with most patients achieving swallowing function without the need for a permanent tracheostomy or feeding tube. However, it is important to note that TORS is not without limitations, including the need for specialized training, high equipment costs, and challenges in certain patient populations such as those with limited mouth opening or prior radiation [48].

Endoscopic head and neck surgery (EHNS) encompasses a variety of minimally invasive techniques that utilize endoscopes and specialized instruments to access and resect tumors through natural orifices or small incisions[49]. Transoral

endoscopic head and neck surgery (TOEHNS) has been applied to selected OSCC cases, particularly those in the oropharynx and supraglottic regions. This approach offers advantages similar to TORS, including improved visualization and access, but at a lower cost. However, EHNS is technically challenging due to the two-dimensional view and limited maneuverability of instruments, which has restricted its widespread adoption [50].

Laser surgery has been an important component of minimally invasive OSCC management for several decades. Transoral laser microsurgery (TLM) utilizes CO2 lasers coupled with operating microscopes to precisely excise tumors with minimal thermal damage to surrounding tissues [51]. TLM has been particularly valuable for laryngeal and oropharyngeal tumors, with excellent oncological outcomes and functional preservation reported in multiple studies. The precision of laser surgery allows for layer-by-layer resection with immediate pathological assessment of margins, potentially reducing the rate of positive margins [52].

Non-excisional minimally invasive techniques such as photodynamic therapy (PDT) have also been explored for early-stage OSCC and premalignant lesions [53]. PDT involves the administration of a photosensitizing agent followed by exposure to specific wavelengths of light, resulting in selective destruction of neoplastic cells. While PDT offers the advantage of tissue preservation and minimal scarring, its role in OSCC management remains limited due to concerns about depth of penetration and long-term oncological control [54].

The integration of augmented reality (AR) and virtual reality (VR) technologies into OSCC surgery represents an emerging frontier [55]. These technologies can provide surgeons with real-time, three-dimensional anatomical information overlaid on the surgical field, potentially improving the precision of tumor resection and preservation of critical structures. Preoperative virtual planning and simulation can also enhance surgical preparedness and reduce operative times. While still in the early stages of development, AR and VR technologies hold promise for further advancing minimally invasive surgical approaches for OSCC [56].

Despite the enthusiasm surrounding minimally invasive and robotic techniques for OSCC, it is important to recognize that these approaches are not universally applicable. Patient selection is critical, with factors such as tumor size, location, depth of invasion, and patient anatomy influencing the suitability of minimally invasive approaches [57]. Furthermore, the learning curve associated with these technologies is steep, requiring specialized training and experience to achieve optimal outcomes. Ongoing research and technological refinements will likely expand the applications of minimally invasive techniques in OSCC management, but they should be viewed as complementary to rather than replacements for conventional surgical approaches.

5. Reconstruction and Rehabilitation After Surgical Resection

The surgical management of OSCC often results in significant defects that can impair speech, swallowing, mastication, and facial appearance. The reconstruction of these defects is a critical component of comprehensive OSCC care, with the goals of restoring form and function, minimizing morbidity, and improving quality of life [58]. The past few decades have witnessed remarkable advances in reconstructive techniques, driven by innovations in microsurgery, biomaterials, and tissue engineering.

The choice of reconstructive approach depends on multiple factors, including the size and location of the defect, the availability of recipient vessels, patient comorbidities, and surgeon expertise [59]. For small defects, primary closure, healing by secondary intention, or the use of local flaps may be sufficient. Local flaps, such as the buccal fat pad flap, palatal flap, or facial artery musculomucosal (FAMM) flap, offer the advantages of minimal donor site morbidity and good tissue match for small to moderate-sized defects [60].

Regional flaps, such as the pectoralis major myocutaneous flap, deltopectoral flap, or temporalis flap, have historically been workhorses for reconstructing moderate-sized defects in the head and neck [61]. These flaps provide reliable tissue coverage with relatively straightforward harvesting techniques. However, they are often bulky and may not provide optimal functional or aesthetic outcomes, particularly in complex defects.

The advent of microvascular free tissue transfer has revolutionized the reconstruction of complex OSCC defects [62]. Free flaps allow for the transfer of tissue from distant sites with their vascular supply, which is then anastomosed to recipient vessels in the head and neck. This approach enables the reconstruction of large, complex defects with tissues that are well-matched to the requirements of the defect. Commonly used free flaps for OSCC reconstruction include the radial forearm free flap (RFFF), anterolateral thigh (ALT) flap, fibula free flap, and rectus abdominis free flap [63].

The fibula free flap has become the gold standard for mandibular reconstruction following segmental mandibulectomy[64]. This flap provides a long segment of vascularized bone that can be osteotomized and shaped to recreate the mandibular contour, along with a skin paddle for intraoral and/or external soft tissue coverage. The incorporation of dental implants into the fibula flap enables dental rehabilitation, significantly improving functional outcomes [65].

Soft tissue free flaps such as the RFFF and ALT flap

are versatile options for reconstructing soft tissue defects in the oral cavity. The RFFF provides thin, pliable tissue ideal for reconstructing the tongue, floor of mouth, and buccal mucosa, while the ALT flap offers a larger amount of tissue with the option for varying thickness [66]. The choice between these flaps depends on the specific requirements of the defect and patient factors.

Functional outcomes following OSCC reconstruction have improved significantly with advances in surgical techniques and rehabilitation strategies[67]. Speech and swallowing therapy are essential components of postoperative care, helping patients to adapt to anatomical changes and maximize functional recovery. Prosthetic rehabilitation, including obturators and dental prostheses, can further improve speech, swallowing, and aesthetics [68].

DISCUSSION

The surgical management of OSCC has undergone remarkable evolution over the past few decades, transitioning from radical, disfiguring procedures to more refined, function-preserving approaches. This narrative review has synthesized current evidence on advances in the surgical management of OSCC, highlighting the interplay between technological innovations, improved understanding of tumor biology, and refinements in reconstructive techniques.

A key theme emerging from this review is the trend toward minimally invasive surgical approaches. Techniques such as TORS, TLM, and SLNB have demonstrated the potential to reduce treatment-related morbidity while maintaining oncological efficacy [45, 52, 25]. These approaches represent a paradigm shift from the traditional "one-size-fits-all" surgical philosophy to a more nuanced, patient-specific approach that considers both oncological control and functional preservation. However, it is important to recognize that minimally invasive techniques are not universally applicable, and patient selection remains critical to achieving optimal outcomes [57].

The integration of molecular profiling into surgical decision-making represents another significant advance. As our understanding of the molecular heterogeneity of OSCC improves, there is growing potential for personalized surgical approaches based on the biological behavior of individual tumors [15]. For instance, molecular markers may help identify patients at high risk of occult metastasis who would benefit from elective neck dissection, or those with aggressive tumors who might require more extensive resection or adjuvant therapies[16]. However, the translation of these molecular insights into clinical practice remains limited, highlighting the need for prospective validation studies.

Reconstructive techniques have also evolved considerably, with microvascular free tissue transfer becoming the standard of care for complex defects [62]. The advent of 3D printing technology and virtual surgical planning has further enhanced the precision of reconstruction, enabling better aesthetic and functional outcomes[71]. Despite these advances, challenges remain in achieving optimal reconstruction for all patients, particularly those with prior radiation or significant comorbidities. The emerging field of tissue engineering holds promise for addressing these limitations, although clinical applications remain largely experimental [69].

Several gaps in knowledge and areas for future research have been identified through this review. First, there is a need for prospective randomized trials comparing minimally invasive approaches with conventional surgery for specific OSCC subsites and stages. While retrospective studies have suggested equivalent oncological outcomes with reduced morbidity for techniques such as TORS, high-level evidence is lacking [47]. Second, the development and validation of molecular biomarkers to guide surgical decision-making represent a critical research priority. Such biomarkers could help personalize the extent of resection and neck management, potentially reducing overtreatment while ensuring oncological safety [5].

Third, the optimal integration of novel technologies such as fluorescence-guided surgery, AI-powered image guidance, and advanced robotic systems into clinical practice needs further investigation [7]. These technologies have the potential to enhance the precision of tumor resection and reduce complications, but their cost-effectiveness and impact on long-term outcomes require rigorous evaluation. Fourth, the development of targeted therapies and immunotherapies that can be effectively combined with surgical approaches represents an important frontier [6]. Such combinations may improve systemic control and reduce the risk of recurrence, particularly in high-risk patients.

CONCLUSION

The surgical management of oral squamous cell carcinoma has undergone significant transformation over recent years, marked by technological innovations, refined surgical techniques, and improved reconstructive approaches. This review has highlighted the evolution from radical, disfiguring procedures to more conservative, function-preserving strategies that aim to optimize both oncological control and quality of life.

Key advances include the emergence of minimally invasive techniques such as transoral robotic surgery and sentinel lymph node biopsy, which have reduced treatment-related morbidity while maintaining oncological efficacy. The integration of molecular profiling into surgical decision-making has opened

new possibilities for personalized approaches based on the biological behavior of individual tumors. Reconstructive techniques have also advanced considerably, with microvascular free tissue transfer and three-dimensional printing technology enabling better aesthetic and functional outcomes.

DECLARATIONS

Ethics approval and consent to participate

Not applicable

Conflicts Of Interests

None

Author Contribution

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