

ORAL METASTASIS REVEALING OCCULT SMALL CELL LUNG CANCER: A CASE REPORT AND SYSTEMATIC REVIEW

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Aim: the aim was to describe a rare case of oral metastasis from small-cell neuroendocrine carcinoma of an unknown primary tumor. Also, a systematic review of literature was conducted.

Methods: a female patient was referred at the Oral Medicine department of Fondazione Policlinico A. Gemelli IRCCS, Rome for severe pain in the attached gingiva in the 3.5 region, where the tooth had been extracted one month earlier. The clinical exam revealed a swollen and erythematous lesion. An incisional biopsy was performed. Histological and immunohistochemical analyses revealed a small-cell neuroendocrine carcinoma, suggesting of metastasis. The patient underwent PET-CT and MRI, revealing a subsolid mass with irregular margins in the right upper and lower lobe. A systematic review was conducted

using PubMed, Scopus, and Web of Science, following the PRISMA 2020 guidelines.

Results: the systematic review identified 1,532 records; after deduplication, screening, and full-text review, 5 studies were included. Out of 5 patients, 3 were males and 2 females; 3 cases located in the attached gingiva; 1 in the tongue and 1 in the mandible. The onset occur within 6 and 12 months following primary diagnosis and the survival time ranges from 3-12 months.

Conclusions: oral metastases from SCLC are rare and only 6 cases are reported. This case was particularly complicated as it involved a metastasis with an unknown primary. Histological and immunohistochemical examination remains the gold standard in the diagnostics of benign and malignant lesions of the oral cavity.

PERSISTENT MANDIBULAR BONE EXPOSURE IN AN IMMUNOSUPPRESSED PATIENT AND ANTIRESORPTIVE THERAPY: DIFFERENTIAL DIAGNOSIS BETWEEN MRONJ AND EBV-POSITIVE MUCOCUTANEOUS ULCER - A CASE REPORT

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Aim: to report a case of oral ulcer and persistent mandibular bone exposure in an immunosuppressed patient receiving antiresorptive therapy, ultimately diagnosed as Epstein-Barr Virus-Positive Mucocutaneous Ulcer (EBVMCU).

Methods: a 72-year-old woman with a history of kidney transplantation for autoimmune glomerulonephritis, on chronic immunosuppressive therapy and Denosumab (Prolia) for osteoporosis, was referred to the oral medicine department of Fondazione Policlinico universitario A. Gemelli IRCCS, Rome, for suspected MRONJ of the right mandible. She presented with persistent pain, grade III mobility of tooth 4.4, bone exposure, and adjacent mucosal swelling. Although CBCT findings were suggestive of MRONJ, the short duration of antiresorptive therapy and the clinical conditions were not fully convincing. Surgical debridement,

marginal bone resection, extraction of the involved tooth, and biopsy of adjacent soft tissues were performed.

Results: histopathology did not unequivocally support MRONJ. Bone specimens showed remodeling changes, focal necrosis, and chronic nonspecific inflammation. In contrast, mucosal biopsy revealed an ulcerated polymorphous lymphoid infiltrate with Eber-positive cells. Thus, a final diagnosis of EBVMCU was achieved. Hematologic evaluation was requested, and PET-CT is pending.

Conclusions: in immunosuppressed patients receiving antiresorptive therapy, persistent ulcer and bone exposure is not necessarily synonymous with MRONJ. EBVMCU should be considered in the differential diagnosis of non-healing oral lesions with bone exposure.

OSTEONECROSIS OF THE JAW OR BONE METASTASIS? CLINICAL PROTOCOL AND CASE REPORT

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Aim: in patients with solid malignancies receiving therapies associated with osteonecrosis of the jaw, the detection of an osteolytic lesion of the jawbones may pose a diagnostic challenge. This finding should raise a differential diagnosis between osteonecrosis and metastatic bone disease. Distinguishing between these two entities is complex due to their overlapping clinical and radiological features: both may show a mixed “leopard spot” pattern, with radiopaque and radiolucent areas. The case presented outlines a structured diagnostic approach.

Methods: a 72-year-old-male patient with prostate adenocarcinoma (PRAD), presenting multiple skeletal uptakes in sacral and mandibular regions, and treated with Zometa (03/2025-09/2025), was referred for evaluation. OPT and CBCT revealed

an osteolytic lesion with sclerotic margins in the right hemimandible, with cortical thickening and periosteal reaction. In agreement with the oncology team, exploratory surgery was performed under antibiotic prophylaxis. The procedure consisted of a ~2 cm cortico-medullary resection using piezosurgery, with removal of multiple medullary fragments.

Results: histology was consistent with metastatic PRAD. Bone lacunae contained neoplastic cells with round nuclei, prominent nucleoli, and clear cytoplasm. Immunohistochemistry was positive for a PSA, PSMA, androgen receptor, and racemase, and negative for PAX-8 and cytokeratin-7.

Conclusions: early and accurate differential diagnosis of jaw lesions in oncological patients is crucial, as it directly guides therapeutic strategies and improves clinical management.

LANGERHANS CELL HISTIOCYTOSIS PRESENTING WITH ORAL MANIFESTATIONS IN AN ADULT: A CASE REPORT

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Aim: Langerhans cell histiocytosis (LCH) is a rare disorder characterized by a clonal proliferation of dendritic cells expressing CD1a and CD207, with S-100 positivity, infiltrating various tissues and organs. The disease may present as either single-system, more commonly involving skin and bone, or multisystem, which is associated with a worse prognosis. We present a case of LCH in which oral manifestations represented early clinical signs of the disease and led to the initial diagnosis.

Methods: we report the case of a 52-year-old male in good general health presenting with ulcerative gingival lesions and osteolytic involvement of the mandibular premolar-molar region, initially diagnosed as periodontal disease and unresponsive to conventional therapy. Biopsy revealed a chronic inflam-

matory infiltrate composed of lymphocytes, plasma cells, and eosinophils, along with numerous cells with irregular, grooved nuclei and abundant eosinophilic cytoplasm, immunohistochemically positive for S-100 and CD1a, consistent with LCH. The patient was referred to Oncology for further evaluation.

Results: MRI and PET imaging revealed multisystem disease involving the lungs, perirenal region, and abdominal adipose tissue. The patient is currently undergoing treatment with the BRAF inhibitor Vemurafenib.

Conclusions: LCH may mimic common oral conditions such as periodontitis, making diagnosis challenging. Early recognition is essential and highlights the key role of dentists in multidisciplinary patient management.

VANISHING BONE: THE RARE DISEASE OF CHERUBISM

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Aim: this case report aims to present the clinical and radiological features of a 7-years-old female with the rare disease of Cherubism.

Methods: the patient's diagnostic pathway began during a routine dental evaluation at her dentist, where an orthopantomography was performed. The radiograph revealed bilateral "soap bubble" lesions in the mandible. A CBCT was also made for further investigation. The patient was then referred to our clinic for a consultation. A clinical examination and an imaging review led to a blood tests prescription, including phosphorus and calcium profile. An orthopedic evaluation, genetic counseling and a second opinion from the radiologist were requested too.

Results: blood tests results showed an increased bone alkaline

phosphatase, an increased serum levels of vitamin B12, and positive anti-nuclear antibodies. The radiologist's report confirms the radiological diagnosis of Cherubism. The orthopedic evaluation indicates that there are no signs of illness in the rest of the body. The genetic counseling is not available yet.

Conclusions: cherubism is a rare genetic disorder, often with autosomal dominant inheritance, in which the normal bone is replaced by cellular fibrous and immature bone, resulting in painless enlargement of the jaws. Cherubism needs regular follow-up to see if it stabilizes or regresses with the passing of the years, as reported in literature. In this case, in this specific moment, no surgical treatment is needed, and regular follow-up examinations until the end of the growth stage are recommended to the patient.

PERSISTENT ORAL ULCER REVEALING MUCOSAL LEISHMANIASIS: A DIAGNOSTIC CHALLENGE

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Aim: Leishmaniasis is an infectious disease caused by protozoa of the genus *Leishmania* and transmitted through the bite of infected sandflies. Clinical manifestations may involve skin, mucous membranes, or present as visceral disease. This report describes a case of leishmaniasis presenting solely as a persistent oral ulcer, underscoring the need to include this condition in the differential diagnosis of treatment-resistant oral ulcers.

Methods: an 81-year-old woman with dilated cardiomyopathy, hypercholesterolemia, and remote breast cancer presented in October 2025 with a painful, non-healing ulcer at the left labial commissure that had been present for five months. The lesion had initially been interpreted as traumatic in origin but failed to resolve despite the removal of local irritative factors.

On clinical examination, a yellowish ulcer with irregular margins, covered by a whitish pseudomembrane and showing firm consistency on palpation, was observed.

Results: incisional biopsy showed non-necrotizing granulomatous inflammation composed of histiocytes (CD68+) and Langhans-type giant cells, set within a fibrous stroma and associated with a lymphoplasmacytic infiltrate (CD138+). Within the histiocytes, small punctate intracellular elements compatible with *Leishmania* amastigotes were observed, consistent with subacute chronic mucosal leishmaniasis.

Conclusions: although rare, oral leishmaniasis should be considered in the differential diagnosis of persistent oral ulcers, emphasizing the key role of histopathological examination.

MALIGNANT TRANSFORMATION OF AN ORAL LICHENOID REACTION INDUCED BY DURVALUMAB (ANTI-PD-L1) THERAPY IN A PATIENT WITH BREAST CANCER: A CASE REPORT

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Aim: immunotherapy represents an effective precision medicine approach for treating various types of cancer, but it may be associated with immune-mediated oral adverse effects. This report describes a case of an oral lichenoid reaction (OLR) related to immunotherapy for breast cancer that subsequently progressed to oral squamous cell carcinoma (OSCC).

Methods: a 65-year-old patient presented with bilateral and symmetrical white-red lesions of the oral mucosa. Her medical history revealed prior breast cancer treated with adjuvant therapy consisting of datopotamab deruxtecan (anti-TROP2) and durvalumab (anti-PD-L1) completed six months earlier.

Results: an incisional biopsy of the right cheek was performed. Histological examination showed a band-like lymphocytic inflammatory infiltrate, damage of basal layer of the epi-

thelium, apoptotic bodies and keratinocytes with vacuolated cytoplasm, in the absence of dysplasia. Fourteen months later, an ulcerated non-homogeneous lesion on the left lateral border of the tongue was observed. Histopathological analysis of the lesion revealed a moderately differentiated microinvasive OSCC associated with lichenoid inflammation.

Conclusions: to the best of our knowledge, this is the first reported case of OSCC arising from lichenoid reactions developed as an adverse effect to durvalumab (anti-PD-L1). Patients who develop such reactions should undergo strict follow-up program, as there may be a risk of malignant transformation. Further studies are needed to clarify the specific risk of oral cancer in patients that develop an ORL related to immunotherapy.

MLPA AS A MOLECULAR TOOL FOR STRATIFYING LEUKOPLAKIA AND PROLIFERATIVE VERRUCOUS LEUKOPLAKIA BY COPY NUMBER ALTERATIONS ANALYSIS

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Aim: the risk of malignant progression of oral potentially malignant disorders (OPMDs) into squamous cell carcinoma (OSCC) is inadequately predicted by current clinical and pathological criteria; Multiplex ligation-dependent probe amplification (MLPA)-based analysis of copy number alterations (CNAs) offers a practical approach to identify high-risk lesions through molecular characterization.

Methods: 52 retrospective cases were examined: benign alveolar ridge keratosis (bARK, n = 5) served as controls; leukoplakia (n = 12, including 7 non-dysplastic and 5 dysplastic cases); proliferative verrucous leukoplakia (PVL, n = 10); and oral squamous cell carcinoma (OSCC, n = 25), including 5 cases of verrucous carcinoma. OSCC cases were further classified as arising from OPMD or as *de novo* lesions.

Results: non-dysplastic leukoplakia has a CNA frequency of 16.7%, dysplastic leukoplakia of 23.3%, and OSCC of 30%, all of which are higher than the 3.3% recorded in bARK. PVL demonstrated greater genomic instability than leukoplakia, whereas verrucous carcinoma showed fewer CNAs than conventional OSCC. *De novo* OSCC displayed a higher CNA burden, in contrast to OSCC arising in OPMD. This difference may reflect earlier detection and a more favorable prognosis in the latter group.

Conclusions: MLPA-based CNA profiling identifies PVL as a highly genomically unstable lesion and demonstrates a progressive increase in genomic instability across OPMD, supporting the presence of clinically relevant genomic alterations even in non-dysplastic leukoplakia.

ORAL MANIFESTATIONS OF RARE NEUROENDOCRINE TUMORS: A CASE REPORT WITH MULTISCIPLINARY MANAGEMENT

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Aim: to report the case of a patient presenting with an atypical oral lesion and a medical history of neuroendocrine tumor.

Materials and methods: a 45-year-old male patient with a malignant ileal neuroendocrine tumor, previously underwent right hemicolectomy, hepatic metastasectomy and combined liver-kidney transplantation and currently receiving ocreotide, methylprednisolone, everolimus and tacrolimus, was referred from the ENT team to the Oral Pathology Unit of the Dental Clinic of Padua. The patient presented a large ulcerative exo-endophytic lesion with poorly defined margins, which involved the right retromolar trigone, anterior palatal pillar, posterior buccal mucosa, and maxillary tuberosity, measuring 30 x 20 mm, protruding into the oral cavity and contacting the ipsilateral pterygoid muscle and the right vestibular aspect, associated with trismus.

Following dental evaluation, the patient was referred back to the ENT specialist for further diagnostic assessment due to PET scan showing positivity for somatostatin receptors SSTR2-SSTR5, and to schedule a biopsy. CT scan revealed a mass with heterogeneous vascularization. Laboratory blood tests, including measurement of chromogranine A were performed, which was found to be elevated (198 ug/L). Based on these findings, paraganglioma was suspected; therefore, an incisional biopsy was performed.

Results: the biopsy findings, based on morphological and immunophenotypic features, are consistent with metastatic Small Cell Neuroendocrine Carcinoma.

Conclusions: small Cell Neuroendocrine Carcinoma is a rare neuroendocrine neoplasm, especially in the oral cavity, and its diagnosis may be challenging. This case report highlights the role of the dentist in the early detection of atypical lesions.

SCHWANNOMA OF THE LEFT DORSAL TONGUE: CLINICAL, RADIOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSTIC WORKFLOW

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Aim: Schwannomas are benign tumors arising from Schwann cells. Their occurrence in the oral cavity accounts for 1-12% of head and neck cases, with the tongue being the most frequently affected site (~50%). We describe the diagnostic process of a schwannoma of the left tongue, highlighting the importance of a multidisciplinary approach.

Methods: a 76-year-old female presented with an exophytic mass on the left dorsal tongue, mobile, covered by normal mucosa, and firm. An initial biopsy was non-diagnostic due to inadequate sampling.

After MRI evaluation, a second biopsy was performed, provid-

ing sufficient tissue for histological and immunohistochemical analysis (S-100, SOX10).

Results: MRI showed a well-circumscribed lesion with contrast enhancement. Histology revealed Antoni A areas with nuclear palisading (Verocay bodies) and Antoni B areas. Immunohistochemistry showed diffuse positivity for S-100 and SOX10, excluding other neural tumors.

Conclusions: lingual schwannoma should be considered in the differential diagnosis of asymptomatic oral masses. Diagnosis requires combined radiological and histological evaluation. Surgical excision is the treatment of choice.

BILATERAL PALATINE TONSIL TRAUMATIC ULCERATIVE GRANULOMA WITH STROMAL EOSINOPHILIA: A CASE REPORT AND REVIEW OF ATYPICAL SITES

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Aim: Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) is a rare, benign, self-limiting lesion of the oral mucosa characterized by granulation tissue with an eosinophil-rich inflammatory infiltrate. The lateral tongue is the most common site. This study describes a case of TUGSE occurring in an unusual location and reviews the literature on atypical sites.

Materials and methods: a 39-year-old man presented with a painful ulcerative lesion of the left palatine tonsil, which regressed after incisional biopsy and was initially diagnosed histopathologically as squamous papilloma. The patient reported recent acute streptococcal pharyngotonsillitis before lesion onset. One month later, a similar lesion appeared on the right tonsil and the patient was referred to our service. Because the

initial diagnosis was inconsistent with the clinical findings, histological slides were reviewed and confirmed the clinical suspicion of TUGSE based on the lesion history and appearance. A literature review was performed using PubMed, Scopus, and Google Scholar.

Results: the review confirmed the tongue as the most frequent site of TUGSE, followed by the buccal mucosa. Less common locations included the hard palate, lip, retromolar area, and palatoglossal arch. To our knowledge, this is the first reported case involving palatine tonsils.

Conclusions: although TUGSE is usually related to local trauma, the metachronous contralateral lesion after streptococcal pharyngotonsillitis suggests a possible role of infection; further studies are needed.

ORAL ULCERATION AS A MANIFESTATION OF A LYMPHOPROLIFERATIVE DISORDER

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Aim: Lymphomatoid Papulosis (LyP) is a rare, chronic, recurrent cutaneous disorder characterized by papulo-nodular eruptions that undergo spontaneous regression. Despite its histologically malignant appearance (CD30+), it exhibits a clinically benign course. It is associated with an increased risk of developing lymphomas. Recognizing LyP in dental patients is essential in order to enroll them in an appropriate lymphoma-specific follow-up program. The aim is to present a case of Lymphomatoid Papulosis and to illustrate its diagnostic approach.

Methods: a 68-year-old male patient presented with a whitish-yellow, exophytic, infiltrative, and non-painful lesion located on the right ventral surface of the tongue. He is a former smoker in therapy for arterial hypertension and dyslipidemia.

An incisional biopsy was performed for histological typing, and the specimen was sent for pathological examination.

Results: the histological report revealed: "The morphological and immunohistochemical features are consistent with a CD30-positive T-cell lymphoproliferative disorder of the oral mucosa, referable to type A lymphomatoid papulosis". Spontaneous resolution of the lesion was observed two months after diagnosis. No treatment was prescribed during the follow-up period. The patient was referred for an onco-hematological consultation.

Conclusions: this case highlights the importance of an accurate diagnostic approach and the need for specialist consultation. It is crucial for dentists to be aware of this condition to ensure appropriate and timely management.

ORAL LYMPHATIC MALFORMATION: CLINICAL, HISTOPATHOLOGIC, AND MOLECULAR RE EVALUATION UNDER THE ISSVA 2025 UPDATE

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Aim: to report a case of recurrent oral lymphatic lesion and to classify it according to the ISSVA classification criteria of vascular anomalies.

Methods: a 50-year-old male patient presented with a soft, translucent, exophytic lesion on the right lateral border of the tongue. Scarring was evident at previous surgical sites on the tip and right ventral surface, with suspected recurrence due to increased tissue consistency. A new biopsy was performed and showed thin-walled vascular channels with dilated lumina lined by flattened endothelial cells, surrounded by fibrous stroma rich in capillary and post-capillary venular proliferation. Immunohistochemical assay demonstrated CD31 positivity, WT-1 negativity, and variable podoplanin expression. The lesion was consistent with a microcystic lymphatic malformation (LM), according to the ISSVA 2025 criteria.

Results: the term lymphangioma, abandoned since 1996, has been replaced by LM, distinguishing vascular tumors (endothelial proliferative) from vascular malformations (structural, non-proliferative). LMs are simple slow-flow lesions including macrocystic, microcystic, mixed, and angiokeratoma forms, as well as complex combined variants. From 2014 to 2025, ISSVA updates incorporated molecular data identifying PIK-3CA and related PI3K-AKT-mTOR pathway mutations, which support the use of targeted therapies in extensive or recurrent lesions.

Conclusions: knowledge of ISSVA classification criteria is crucial for clinicians, pathologists, and surgeons to achieve accurate diagnosis and therapy aligned with current molecular advances.

OZONIZED GEL IN MRONJ MANAGEMENT: A CASE REPORT

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Introduction: Medication-related osteonecrosis of the jaw (MRONJ) is a challenging condition associated with antiresorptive and antiangiogenic therapies, characterized by bone necrosis, pain, inflammation, and risk of secondary infection. Management includes both surgical and conservative approaches aimed at controlling symptoms and promoting mucosal healing. Topical ozonized gel has recently drawn interest because of its antimicrobial and regenerative properties.

Objective: to describe the clinical outcome of a conservative protocol based on topical ozonized gel delivered through a custom-made thermoformed splint in a patient with Stage II MRONJ.

Case report: a 77-year-old man receiving intravenous zoledronate for multiple myeloma presented with Stage II MRONJ according to AAOMS criteria. Clinical examination revealed exposed necrotic bone on the lingual aspect of the left posterior mandible, adjacent to tooth 37, associated with local in-

flammation and pain. A conservative home-based protocol was initiated using ozonized gel applied once daily through a patient-specific thermoformed splint for approximately 8 minutes over 28 days. The patient was instructed to avoid eating, drinking, or rinsing for at least 1 hour after each application.

Results: after 1 week, sequestrum formation and early re-epithelialization were observed. Progressive clinical improvement continued throughout follow-up, with complete mucosal healing at 4 weeks. No adverse events were reported and patient compliance was good.

Conclusions: in this case, ozonized gel delivered through a thermoformed splint appeared to be a useful adjunct in the conservative management of Stage II MRONJ, allowing targeted topical delivery and favorable mucosal healing. Further studies are needed to confirm the reproducibility and clinical value of this approach in larger cohorts.

ORAL ULCERATIONS AND PERIODONTAL DISEASE IN KOSTMANN SYNDROME: A CASE REPORT

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Aim: this report describes oral manifestations in a young adult with Kostmann syndrome, a rare genetic disorder classified as severe congenital neutropenia (SCN), characterized by granulocytic maturation arrest and predisposition to recurrent bacterial infections and an increased risk of MDS/AML transformation.

Methods: a 21-year-old male with SCN due to HAX1 mutation, on treatment with pegfilgrastim, a long-acting granulocyte colony-stimulating factor (G-CSF), with a history of recurrent aphthous lesions and oral candidiasis since early infancy, reported worsening oral lesions associated with febrile episodes, upper respiratory tract symptoms, and perianal abscesses.

Results: oral examination revealed a deep, painful ulcer with

well-defined margins on the left labial commissure mucosa, along with cicatricial lesions on the buccal mucosa and lower lip. Diffuse linear gingival erythema with persistent inflammation involved the vestibular gingiva of both jaws. Hematological reassessment revealed a further decline in absolute neutrophil count, prompting escalation of systemic therapy. Adjunctive management included topical corticosteroids, ozonized oil-based formulations, re-epithelializing agents, and supportive periodontal therapy at 2-month recall intervals.

Conclusions: as in SCN, aphthous ulcerations and periodontal disease are part of a broader systemic disease spectrum. Oral health specialists play a key role in early detection, as well as in active surveillance and long-term management.

A NON-HEALING POST-EXTRACTION LESION REVEALING MULTIFOCAL SQUAMOUS CELL CARCINOMA: A DIAGNOSTIC CHALLENGE

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Aim: to present a misleading non-healing post-extraction lesion with an atypical clinical presentation and to highlight the diagnostic challenges in distinguishing reactive from malignant conditions.

Methods: a 64-year-old female patient presented with a non-healing lesion in the posterior maxilla following extraction of tooth 2.8. The patient's medical history included diabetes mellitus, hyperlipidemia, non-Hodgkin lymphoma treated with hematopoietic stem cell transplantation, and oral lichen planus under clinical follow-up. Clinical examination revealed a hyperplastic and irregular lesion at the post-extraction alveolar site. In addition, a granular erythematous lesion was observed on the left buccal mucosa, along with an ulcerative erythematous

area extending to the palatal aspect of tooth 2.7. Similar mucosal changes had been present prior to extraction, as confirmed by clinical photographs. Incisional biopsies were obtained from different anatomical sites.

Results: histopathological examination revealed keratinizing squamous cell carcinoma (grade 2) identified in distinct sampled sites, showing invasive features in the alveolar region and superficially invasive characteristics in the buccal mucosa.

Conclusions: this case demonstrates that non-healing post-extraction lesions involving multiple oral sites may conceal underlying malignancy with variable invasive patterns. The presence of additional mucosal lesions should raise clinical suspicion and prompt early biopsy for accurate diagnosis.

FROM OVER-REHABILITATION TO NEUROPATHIC PAIN: BURNING MOUTH SYNDROME AFTER EXTENSIVE MAXILLARY IMPLANT PLACEMENT

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Aim: to describe the onset of burning mouth syndrome (BMS) following extensive maxillary implant rehabilitation and to highlight a potential association with neuropathic mechanisms.

Methods: we report the case of a 64-year-old male patient with a history of cardiovascular disease who developed persistent oral burning symptoms following the placement of 11 implants in the maxillary arch. Clinical evaluation included a comprehensive oral examination, salivary assessment, and brain magnetic resonance imaging.

Results: the patient presented with a burning sensation predominantly involving the tip of the tongue, associated with dysgeusia. Symptoms exhibited circadian variation and improved with mastication.

Oral examination showed normal mucosa without morphological or chromatic alterations. The clinical picture was consistent with a dysesthetic variant of BMS. A multidisciplinary approach including topical antiepileptic therapy and systemic pharmacologic management was initiated.

Conclusions: this case highlights a potential association between extensive implant rehabilitation and the onset of neuropathic oral pain. While causality cannot be definitively established, the cumulative surgical burden of placing multiple implants, together with procedure-related local trauma and patient-related stress, may have contributed to the development of burning mouth syndrome through peripheral and/or central sensitization mechanisms.

UNCOMMON GINGIVAL PIGMENTATION AS A DIAGNOSTIC CHALLENGE: A CASE REPORT

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Aim: gingival discoloration is an uncommon clinical finding that may be associated with local or systemic conditions and can represent a diagnostic challenge. This study reports a case of blue gingival pigmentation related to a traditional cultural practice, highlighting the importance of accurate diagnosis.

Methods: a 39-year-old female presented with diffuse blue-gray pigmentation symmetrically distributed on the maxillary alveolar mucosa. She reported no oral or odontogenic pain and denied tobacco, alcohol, or drug use. Her medical history was significant for well-controlled diabetes. During anamnesis, the patient disclosed having undergone intentional gingival tattooing as part of a traditional practice known as “diamou,” commonly performed in Senegal. An incisional biopsy was performed to confirm the diagnosis.

Results: histological analysis showed stratified squamous epithelium overlying fibroadipose and muscular tissue with coarse brownish granular deposits, partly perivascular and adherent to collagen fibers. Perls staining was negative. Findings were consistent with non-melanocytic exogenous pigmentation compatible with gingival tattooing.

Conclusions: cultural gingival tattooing should be considered in the differential diagnosis of diffuse maxillary pigmentation. Careful correlation between clinical findings and patient history is essential to guide appropriate management. While histopathological examination may be required to confirm the diagnosis and rule out other conditions, increased awareness of this practice can support a more targeted diagnostic approach.

SURGICAL TREATMENT OF SEVERE GINGIVAL HYPERPLASIA IN STURGE-WEBER SYNDROME USING ND:YAG LASER: A CASE REPORT

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Introduction: Sturge-Weber Syndrome (SWS) is a rare, non-hereditary congenital neurocutaneous disorder characterized by capillary vascular malformations. At the oro-facial level, it typically presents with “Nevus Flammeus” and angiomas that can involve soft tissues and maxillary areas. In severe cases, gingival hyperplasia and intraoral angiomas can compromise vital functions such as mastication.

Aim: this study analyzes the clinical management and therapeutic evolution of a 25-year-old patient with SWS and a severe phenotype, focusing on resolving odontostomatological complications that prevented proper nutrition.

Materials and methods: the patient presented a complex clinical picture including hemiplegia, glaucoma, cognitive deficit, and severe diffuse gingival hyperplasia with nodular angiomas on the lips and tongue. Surgery was performed under general

anesthesia following infiltration of 2% adrenaline. An Nd:YAG laser (400-micron fiber, 40 Hz frequency, 130 mJ energy, 4W power) was used for the resection of hyperplastic tissues. Hemostasis was optimized using tranexamic acid and a specific laser protocol (200 Hz, 20 mJ, 4W).

Results: the use of laser technology allowed for a bloodless surgical field, which is fundamental in patients with a high risk of hemorrhage. A significant reduction in surgical time was observed, along with high-quality tissue healing and improved post-operative compliance.

Conclusions: the Nd:YAG laser is confirmed as a tool of choice for treating the oral manifestations of Sturge-Weber Syndrome. Its ability to combine cutting precision with excellent hemostasis drastically reduces recurrence rates and recovery times, significantly improving the patient's quality of life.

TOPICAL DRUG DELIVERY USING A CUSTOM-MADE TRANSPARENT TRAY IN THE TREATMENT OF MUCOUS MEMBRANE PEMPHIGOID: A CASE REPORT

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Aim: Mucous membrane pemphigoid (MMP) is an autoimmune disease characterized by blistering lesions that, in the oral cavity, often progress to erosions, ulcerations, and desquamative gingivitis. The aim of this case report is to evaluate the clinical effectiveness of a custom-made transparent tray equipped with micro-reservoirs for controlled topical drug delivery in the treatment of oral lesions in a patient affected by MMP.

Methods: the clinical case involves a patient with a histological diagnosis of oral blistering disease consistent with pemphigoid, with gingival and palatal involvement. Initially, classic therapy with a corticosteroid (clobetasol propionate 0.05%) was prescribed, combined with an antifungal oral suspension, yielding limited results. Subsequently, a custom-made trans-

parent tray was fabricated using an intraoral scanner (MEDIT i700), incorporating micro-reservoirs for the placement of the drug in ointment form. This device enabled targeted and prolonged drug release, increasing contact time with the lesions and reducing salivary dispersion.

Results: after 15 days of treatment, a marked clinical improvement of the lesions was observed; complete resolution was achieved after 40 days. The device demonstrated high tolerability and excellent patient compliance.

Conclusions: custom-made oral trays with micro-reservoirs represent an innovative and effective approach for the topical treatment of oral mucosal diseases, significantly enhancing therapeutic efficacy compared to direct drug application alone.

KAPOSI'S SARCOMA OF THE ORAL CAVITY IN AN HIV-POSITIVE PATIENT: IMPORTANCE OF EARLY DIAGNOSIS AND MULTIDISCIPLINARY MANAGEMENT

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Aim: to describe a clinical case of HIV infection diagnosed after the observation of oral lesions, highlighting the central role of the oral medicine specialist in the early detection of apparently silent diseases.

Methods: we report a case of 32-year-old male patient who was attended at the Oral Medicine Unit V. Margiotta of AOUP P. Giaccone in Palermo who underwent an incisional biopsy with histological diagnosis of Kaposi's sarcoma, together with immunohistochemical findings of HHV-8, was enabled the initiation of a multidisciplinary management pathway involving the Infectious Diseases Unit.

Results: clinical examination revealed two red lesions on the posterior palate, characterized by regular margins and surfaces. Biopsy represents a crucial step in the diagnosis of Kaposi's

si's sarcoma, as it allows differentiation from other clinically similar conditions. The "patch" stage was diagnosed in this case. Immunohistochemical identification found out HHV-8+. Following diagnosis, the patient was referred to the Infectious Diseases Unit, where antiretroviral therapy was initiated. After 4 months of treatment, complete remission of the oral lesions was observed. Antiretroviral therapy, by improving immune function and reducing HIV viral replication, can promote regression of Kaposi's Sarcoma lesions.

Conclusions: the oral cavity can represent an initial site of HIV manifestation. Oral mucosal examination should be considered a fundamental component, especially in the presence of atypical, persistent, pigmented, or vascular lesions not attributable to evident traumatic causes.

FIELD CANCERIZATION IN A YOUNG PATIENT WITHOUT CONVENTIONAL RISK FACTORS: A CASE REPORT WITH OCT AS A COMPLEMENTARY TOOL

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Aim: to describe a case of field cancerization in a young patient without known risk factors, highlighting the role of OCT as a useful tool in the longitudinal evaluation of oral mucosal changes and in guiding targeted biopsy.

Methods: we report a case of patient with a history of OSCC who was referred to Oral Medicine Unit of A.O.U.P. Paolo Giaccone of Palermo, for follow-up.

Case presentation: a 36-year-old man, with no risk factors, with previous diagnosis of OSCC of the left lateral tongue, was enrolled in a follow-up program. The follow-up consists of quarterly clinical evaluations, complemented by OCT assessment. In May 2025, patient developed a new OSCC at the same site of the primary tumor; then, surgical excision, including left-sided cervical and submandibular lymph node dissec-

tion, was performed. Histological finding confirmed the OSCC diagnosis. In December 2025, a new lesion was detected in the same area; an incisional biopsy revealed low-grade epithelial dysplasia. In March 2026, intraoral examination shows a new erythematous area on the same site. OCT examination revealed suspicious epithelial and subepithelial architectural changes confirmed by vital staining with toluidine blue. An incisional biopsy was performed, confirming diagnosis of carcinoma *in situ*. The patient was referred to Plastic Surgery and Oncologic Units for management.

Conclusions: this case highlights the importance of surveillance in patients with previous OSCC, even in the absence of conventional risk factors and supports the use of OCT for monitoring oral lesions and guiding targeted biopsy.

ORAL VIDEOCAPILLAROSCOPY IN SJÖGREN'S SYNDROME: MICROVASCULAR ALTERATIONS IN A CASE REPORT

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Aim: to describe microvascular alterations detected by oral videocapillaroscopy in Sjögren's syndrome and assess its diagnostic value through comparison with healthy subjects and literature.

Methods: a patient with primary Sjögren's syndrome underwent oral videocapillaroscopy (200×) of selected mucosal sites. Evaluated parameters included capillary morphology and tortuosity, microhemorrhages, loop caliber, and density (loops/mm²). Findings were qualitatively compared with healthy subjects from the same center and published data.

Results: videocapillaroscopy revealed increased tortuosity, irregular loop course, heterogeneous distribution, and reduced capillary density. Microhemorrhages, caliber variability, and areas of reduced perfusion were observed. These findings differed from healthy patterns and aligned with those reported in Sjögren's syndrome.

Conclusions: oral videocapillaroscopy is a non-invasive method to detect microvascular alterations in Sjögren's syndrome. Consistent differences *versus* healthy subjects and literature support its role as an adjunctive diagnostic and monitoring tool.

INTRAORAL ULTRASOUND IN THE ASSESSMENT OF A FOREIGN BODY GRANULOMA OF THE TONGUE MARGIN

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Aim: to describe the application of intraoral ultrasound (IOUS) as a real-time diagnostic adjunct in the assessment of a tongue nodular lesion.

Methods: an 81-year-old man presented with a three-month history of a painful nodular lesion on the left lateral border of the tongue associated with reduced mobility. Magnetic Resonance Imaging (MRI) was performed due to suspicion of malignancy. IOUS was subsequently carried out using an 18 MHz linear probe in second harmonic mode with standardized focal depth.

Results: MRI revealed a solid lesion without excluding malignancy. IOUS demonstrated a well-defined, roundish hypoechoic lesion within the submucosal layer, with preserved epithelial continuity. A focal hyperechoic structure was identified within the lesion, associated with mild reverberation artifact

and marked posterior acoustic shadowing, suggesting strong attenuation from dense material and supporting a foreign-body component. Posterior acoustic enhancement and edge shadowing were also observed. Surgical excision revealed a shrimp leg embedded within the lesion. Histopathological examination confirmed a foreign body granuloma. The IOUS examination was well tolerated, rapidly performed, and provided high-resolution real-time imaging.

Conclusions: foreign body granulomas may clinically and radiologically mimic neoplastic lesions. While MRI remains essential in the evaluation of tongue masses, IOUS is a feasible, non-invasive, and readily applicable technique that enhances diagnostic accuracy by enabling detection of intralesional foreign bodies and characteristic ultrasound artifacts, thereby supporting clinical decision-making.

PERIPHERAL AMELOBLASTOMA: CASE REPORT AND SYSTEMATIC REVIEW OF THE LITERATURE

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Aim: the study reports the case of an old man with histologically diagnosed of peripheral ameloblastoma (PA) and provides a systematical review of the literature regarding PA.

Methods: the systematic review was conducted according to PRISMA statement and PICOS criteria. Comprehensive search of databases including PubMed, Web of Science, Scopus for eligible studies published between 1950-2025 was performed. Two reviewers carried out the evaluations independently. The methodological quality of the studies was assessed with the Cochrane Collaboration tool for risk of bias. The outcome was the assessment of the clinic-pathological, follow-up data and therapeutic strategies of PA.

Results: a total of 119 studies and 160 cases are included in the review. Male and mandible are the most involved gender

and site, and the mean age at diagnosis is equal to 53.6 ± 20.1 years. Clinically, PA appears as a slow-growing, painless, exophytic gingival mass, with rare bone depression due to the local compression. The gold standard is the surgical excision with free margins. The recurrence rate ranges from 5% to 15%, related to incomplete excision. Malignant transformation has been documented in 6 studies.

The case report showing a longstanding, slow-growing, painless, firm exophytic gingival mass of the maxillary tuberosity, treated by partial maxillectomy and Bichat fat flap. No relapses were observed in the first year from the surgical treatment.

Conclusions: PA exhibits benign behaviour; however, a long-term follow-up is highly suggested to detect relapse or malignant transformation.

NECROTIZING SIALOMETAPLASIA IN A 15-YEAR-OLD FEMALE WITH BULIMIA NERVOSA: CASE REPORT

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Aim: Necrotizing sialometaplasia (NS) is a rare benign ischemic lesion of minor salivary glands that may clinically mimic malignancy. It is uncommon in adolescent patients. The aim of this report is to describe the clinical and diagnostic management of a suspected case of NS in a 15-year-old female patient with a history of bulimia nervosa.

Methods: a 15-year-old female patient presented to the Department of Oral and Maxillo-Facial Sciences, Sapienza University of Rome, with an asymptomatic ulcerative lesion of the left posterolateral hard palate. Clinical examination identified a solitary oval lesion measuring 10×4 mm. No cervical lymphadenopathy or swelling of the major salivary glands was detected. Maxillofacial CT imaging showed no abnormalities. Incisional biopsy was undertaken two weeks after the first visit.

Conservative management with Aminogam gel and mouthwash was prescribed.

Results: at the time of biopsy, partial healing was evident. Clinical evolution, absence of radiological abnormalities, and lesion site were strongly suggestive of necrotizing sialometaplasia. Histopathological findings are pending at the time of submission.

Conclusions: Necrotizing sialometaplasia should be considered in the differential diagnosis of palatal ulcerative lesions in younger patients. Correlation of clinical findings, imaging, healing pattern and histopathology is essential to avoid over-treatment and unnecessary aggressive procedures. A multidisciplinary approach may be particularly valuable when systemic or behavioral factors are present.

PERIODONTAL STATUS IN PATIENTS WITH ORAL LICHEN PLANUS: A CASE-CONTROL STUDY

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Aim: to evaluate whether oral lichen planus (OLP) patients have a higher prevalence and severity of periodontitis than healthy patients, and secondarily to assess the prevalence of RT1 gingival recessions compared with controls.

Methods: the study was conducted at the Oral Medicine Unit, Fondazione Policlinico Universitario A. Gemelli, Rome. Patients were matched for age and sex. Periodontal status was assessed using major clinical indices and classified per the 2017 AAP/EFP definition. The study was approved by the Ethics Committee of Catholic University of the Sacred Heart, (ID-7603) and registered at ClinicalTrials.gov (NCT06934863).

Results: the final sample consisted of 176 subjects: 88 with histologically confirmed OLP and 88 matched controls. Perio-

donitis was significantly more prevalent in OLP patients than in controls (71.6% vs 51.1%; $p = 0.002$), with a more than two-fold increased risk (OR = 2.64; 95% CI: 1.41-4.92). Severe periodontitis (stages III-IV) was also more frequent in the OLP group (48.9% vs 30.7%; $p = 0.001$). RT1 gingival recessions were significantly more common in OLP patients (9.12 ± 4.52 vs 5.60 ± 5.51 ; $p = 0.008$).

Conclusions: OLP patients show a higher prevalence and severity of periodontitis, supporting shared immune-inflammatory mechanisms. The higher prevalence of RT1 recessions suggests a possible direct effect of mucosal inflammation on periodontal tissues, underscoring the need to include periodontal assessment in OLP management.

EVALUATION OF SALIVARY METABOLIC PROFILE FROM HEALTHY ORAL MUCOSA TO SQUAMOUS CELL CARCINOMA

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Aim: the present multicenter pilot study aimed to evaluate salivary metabolomic changes across the progression from healthy mucosa to oral leukoplakia (OL) and oral squamous cell carcinoma (OSCC), identifying potential biomarkers for early diagnosis and clinical monitoring.

Methods: fifty-two subjects were enrolled in 3 centers (two in Modena and one in Parma): 13 with non-dysplastic OL, 13 with dysplastic OL, 13 with OSCC, and 13 healthy controls (HC). Demographic, anamnestic, clinical data, and risk factors were recorded for each patient. Tissues and saliva samples (the four groups) were collected prior to surgery and analyzed by High Resolution Magic-Angle Spinning (HR-MAS) and Hydrogen Nuclear Magnetic Resonance spectroscopies (¹H-NMR), respectively. Multivariate and univariate analyses were performed using MetaboAnalyst 6.0.

Results: in tissues, 32 metabolites were identified. ROC

curves showed four relevant metabolites with AUCs ≥ 0.80 for HCs vs OSCC comparison: glycerol, choline, fumarate, and glutamate. In saliva, total of 72 salivary metabolites were identified. PLS-DA showed a progressive shift in salivary metabolic profiles by groups, with a clear separation of the groups. Some of the metabolites, such as pyroglutamate, desaminotyrosine, succinate, and glycerol showed progressively varying average concentrations across the groups (from HC to OSCC). On the other hand, N-acetyl-glucosamine, and indole-3 acetate were detected only in HCs and 4-OH-phenyllactate was in all the groups except in OSCC.

Conclusions: overall, valuable tissue biomarkers of OSCC emerged from ROC analysis of tissue samples. Salivary metabolomic profiling may support risk stratification and a potential early detection of OSCC. Larger studies are needed to validate these biomarkers and their clinical application.

FRAILITY IN BURNING MOUTH SYNDROME: A MULTIDIMENSIONAL CASE-CONTROL STUDY

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Aim: to investigate frailty in patients with Burning Mouth Syndrome (BMS) through a multidimensional assessment of physical, cognitive, psychological, and social domains, compared with healthy controls.

Materials and methods: a multicenter case-control study was conducted on 52 patients with BMS and 51 healthy controls matched for age and sex. Sociodemographic data, educational level, and body mass index (BMI) were recorded. Frailty and related domains were assessed using validated instruments: Sunfrail, Short Physical Performance Battery, Morisky Medication Adherence Scale, Prevención con Dieta Mediterránea, Mini Nutritional Assessment, General Practitioner Assessment of Cognition, Quick Mild Cognitive Impairment, Geriatric Depression Scale, Social Provisions Scale and 12-Item Short Form Survey. Statistical analysis included descriptive statistics, Mann-Whitney U test, Pearson's chi-squared test and Student's t test.

Results: compared with controls, BMS patients showed significantly lower educational attainment, reduced mobility, higher medication burden with poorer adherence and greater healthcare utilization. They also presented significantly higher BMI and worse physical performance. Cognitive impairment was more pronounced in the BMS group with poorer results in most neurocognitive tasks. Psychological and social domains were markedly compromised, with higher levels of distress and loneliness. Quality of life was significantly lower in both physical and mental health components.

Conclusions: patients with BMS exhibit a greater multidimensional frailty burden than healthy controls, involving physical, cognitive, psychological, and social decline. These findings support the need for personalized, multidisciplinary strategies to improve clinical management and quality of life in this vulnerable population.

ARTIFICIAL INTELLIGENCE FOR IMAGE-LEVEL DETECTION OF HIGH-RISK ORAL LICHEN PLANUS: A MULTICENTER STARD-AI PILOT STUDY

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Aim: recognizing atrophic-erosive oral lichen planus (OLP-AE) could represent a clinical challenge, often leading to misdiagnosis and diagnostic delay. This study aimed to develop a deep learning (DL) model to support clinicians in detecting and isolating the elusive OLP-AE using clinical photographs.

Materials and methods: in adherence to STARD-AI guidelines, a multicenter retrospective convenience dataset was created by collecting clinical photographs of histologically confirmed OLP lesions from the University Hospital of Palermo (Italy) and the University of Granada (Spain). SentiSight.AI was used for labeling, segmentation, and training. 352 photos were split at the patient-level into training (n = 282) and validation (n = 70) sets. Performance was assessed via image-level classifi-

cation from segmentation masks, using a multi-class single-label logic based on the highest-confidence prediction.

Results: for the reticular (OLP-R) class, the model achieved 84.3% accuracy (95% CI: 73.6-91.9%), 85.3% precision, 82.9% sensitivity, and an 84.1% F1-score. For high-risk OLP-AE, accuracy was 87.1% (95% CI: 77.0-93.9%), precision 100%, sensitivity 74.3%, specificity 100%, and F1-score 85.3%.

Conclusions: the DL model demonstrated promising performance in classifying OLP subtypes, with high precision and specificity in differentiating erosive variants from the surrounding mucosa, where their subtle presentation may lead to under recognition. Further validation on larger, multicenter datasets is needed to improve sensitivity and ensure generalizability in clinical practice.

NANOTECHNOLOGY AND ORAL MEDICINE: ROLE OF THE PERSONALIZED PROTEIN CORONA IN ORAL LESION DIAGNOSIS AND MANAGEMENT

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Objective: early diagnosis and monitoring of oral squamous cell carcinoma (OSCC) and potentially malignant epithelial lesions (PMEL) remain challenging with conventional biopsy-based methods. Nanotechnology approaches based on protein corona analysis may offer minimally invasive and reproducible tools.

Materials and methods: we evaluated a diagnostic strategy based on personalized protein corona formed on graphene oxide nanosheets incubated with plasma from 24 subjects: 8 OSCC, 8 PMEL, and 8 non-oncological (NOP). Samples were collected at baseline (t0), 3 months (t1), and 6 months (t2). Protein corona fingerprints were analyzed by SDS-PAGE, quantifying integral areas in the 23-25 kDa and 40-60 kDa regions. Linear discriminant analysis (LDA) was applied to distinguish OSCC and PMEL.

Results: differences among groups were observed in both regions, with higher variability and increased signals in OSCC patients. LDA enabled distinction between OSCC and PMEL at all time points, with accuracies of 69% (t0), 63% (t1), and 75% (t2). The highest discrimination performance was observed at t2, suggesting improved separation between the two groups during follow-up.

Conclusions: these preliminary results indicate that personalized protein corona profiling combined with multivariate analysis can discriminate OSCC from PMEL patients and may support longitudinal monitoring after treatment. Although classification accuracy is moderate, the observed improvement at later time points highlights the potential of this minimally invasive approach. Validation in larger cohorts is warranted to confirm its clinical applicability for diagnosis and follow-up of oral lesions.

CLINICOPATHOLOGICAL FEATURES AND MALIGNANT TRANSFORMATION OF ORAL LICHEN PLANUS: A PROSPECTIVE FIVE-YEAR FOLLOW-UP STUDY OF 212 PATIENTS

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Aim: Oral lichen planus (OLP) is a chronic inflammatory disease characterized by T-cell-mediated immune dysfunction targeting oral epithelial cells. Systematic reviews have established OLP as a potential premalignant condition of the oral cavity. The objective of this study was to investigate the clinicopathological features of OLP and the prevalence of malignant transformation in this setting.

Methods: a prospective cohort study of patients with histopathologically confirmed oral lichen planus was conducted. Age, sex, underlying diseases, smoking, and coexisting conditions were recorded. All patients included in the study were evaluated for a period of at least five years.

Results: a study group of 212 patients (143 female and 69 males; mean age 61.2 years). At the time of diagnosis, 61 pa-

tients had hypertension and 21 patients had diabetes mellitus. Thirty-eight patients had Hashimoto's thyroiditis and were being treated with levothyroxine. Forty-eight patients were current smokers, and 14 patients were former smokers. Regarding clinical characteristics, 141 patients had keratotic lichen planus, and 71 patients had erosive atrophic lichen planus. During the follow-up period, five patients (2.3% of the sample) developed squamous cell carcinoma. The erosive atrophic subtype was the factor most strongly associated with the risk of OSCC, with an odds ratio of 5.2.

Conclusions: preliminary data from this study confirm a cancerization rate of 2.3%. Patients with erosive atrophic forms of disease affecting the tongue or palate should be enrolled in a rigorous follow-up program.

AI-ASSISTED EARLY DETECTION OF ORAL CANCER: A MULTIMODAL CLINICAL DECISION SUPPORT SYSTEM FOR ORAL LESION ASSESSMENT

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Aim: to develop an artificial intelligence (AI) system for early detection of oral cancer, designed to support dentists in identifying suspicious lesions and improving clinical decision-making.

Methods: a dataset of 1,271 intraoral images, including oral cancer lesions and healthy mucosa, was collected and manually annotated by clinicians. The proposed system follows a multi-stage pipeline integrating three components: (i) YOLOv11 for lesion detection and localization, (ii) Grad-CAM for visual explanation of model predictions, and (iii) a Large Language Model (DistilGPT-2) for automatic generation of clinical reports. This framework enables identification of abnormal areas, visualization of diagnostically relevant regions, and translation of visual outputs into clinically interpretable text.

The generated reports were evaluated by expert clinicians to assess clarity, coherence, and clinical relevance.

Results: the YOLOv11 model showed good lesion detection performance, with high precision (0.82) and reliable localization. Grad-CAM heatmaps were consistent with clinically relevant mucosal regions. LLM-generated reports achieved high clinical coherence and clarity, with an accuracy of 94% based on expert evaluation, supporting effective interpretation of AI outputs.

Conclusions: this multimodal AI system integrates detection, explainability, and language-based reporting into a unified framework. Such an approach may support early detection of oral cancer, reduce diagnostic variability, and improve management of oral potentially malignant disorders.

GROWTH FACTOR ERV1-LIKE (GFER)/AUGMENTER OF LIVER REGENERATION (ALR) REGULATION IN ORAL SQUAMOUS CELL CARCINOMA (OSCC) STROMA, AND ITS SULFHYDRYL OXIDASE ACTIVITY ON STAT3 AS AN INDEPENDENT MECHANISTIC INSIGHT

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Aim: Oral squamous cell carcinoma (OSCC) progression is strongly influenced by the tumor microenvironment, particularly associated cancer-associated fibroblasts (CAFs).

Methods: in this study, we investigated the role of the Augmenter of Liver Regeneration (ALR), also known as growth factor erv1-like (Gfer) gene, in modulating redox homeostasis, apoptosis, and exosomal biomarker expression in CAFs derived from OSCC tissues. Additionally, we investigated whether Gfer can utilize Signal Transducers and Activators of Transcription-3 (STAT3) monomers as substrates for disulfide bond formation and to determine whether its sulfhydryl oxidase activity is sufficient to catalyze STAT3 dimerization. Furthermore, we validated the expression of exosomal markers CD63, Alix, and

HSP70 in CAFs/OSCC-derived vesicles, supporting their diagnostic relevance.

Results: our results demonstrate that Gfer knockdown in OSCC-associated CAFs significantly increases reactive oxygen species (ROS) levels and induces a pro-apoptotic shift, characterized by reduced Bcl-2 expression, elevated Bax levels, and activation of caspase-9 and caspase-3.

Conclusions: our findings highlight a crucial role for Gfer in regulating redox balance, apoptosis, and mitochondrial integrity in OSCC-associated CAFs. Additionally, exosomal markers CD63, Alix, and HSP70 were confirmed, reinforcing their potential as OSCC biomarkers. Overall, targeting stromal components such as Gfer may offer novel strategies for OSCC diagnosis and therapy.

SELECTIVE MODULATION OF THE CELL SECRETOME BY DOXORUBICIN AND COLD PLASMA TREATED WATER SOLUTION IN HEAD AND NECK CANCER CELL MODELS

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Aim: cold atmospheric plasma-treated water solutions (PTWS) are reservoir of reactive species able to modulate cellular responses. This study examined whether PTWS combined with doxorubicin (DOXO) alters secretome profiles in HaCaT and FaDu cells under DOXO, DOXO+Air, and DOXO+O₂ conditions.

Methods: cells were exposed to DOXO alone or in combination with PTWS (Air or O₂). Supernatants were analyzed by DDA proteomics, filtered (Unused >1.3), and normalized by removing control proteins. Functional analysis was performed using GO enrichment and semantic clustering.

Results: in HaCaT cells, although many proteins were initially identified (up to n = 219), treatment-specific genes were limited, with the highest number in DOXO+PTWS O₂ (n = 14), followed by DOXO+Air (n = 12) and DOXO (n = 9). In FaDu cells, a

similar number of proteins was identified (up to n = 207), but treatment-specific genes were more abundant, again highest in DOXO+PTWS O₂ (n = 30), followed by DOXO+PTWS Air (n = 12) and DOXO (n = 7). GO enrichment analysis indicated predominantly homeostatic processes in HaCaT cells (coagulation, ECM organization, inflammation, migration), whereas FaDu cells showed enrichment in immune, apoptotic, cytoskeletal, phosphorylation, and remodeling pathways. These signatures are consistent with stress- and tumor-associated activation, particularly under plasma conditions.

Conclusions: DOXO+PTWS alters the secretome depending on the formulation of PTWS used. HaCaT responses are limited, whereas FaDu shows broader activation, especially after exposure to PTWSO₂, indicating greater tumor cell sensitivity to plasma-based treatment.

ORAL LICHEN PLANUS IN CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW OF CLINICAL FEATURES, MANAGEMENT, AND OUTCOMES, WITH AN ILLUSTRATIVE CASE SERIES

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Aim: to assess clinical presentation, associated conditions, management, and outcomes of pediatric oral lichen planus (OLP), including a case series of six patients from a tertiary Oral Medicine center.

Methods: a systematic review was conducted according to PRISMA guidelines and registered in PROSPERO. Four databases (MEDLINE, Scopus, Embase, Web of Science) were searched up to February 2026. Studies on OLP in patients aged 0-18 years were included. Data on demographics, clinical features, treatment, and outcomes were extracted, and risk of bias was assessed using a JBI-informed approach. Six pediatric cases from our institution were also descriptively analyzed.

Results: forty-six studies, including 158 patients, were analyzed (mean age 11.9 years). The reticular form was most common

(60.8%), followed by erosive (21.5%) and plaque-like lesions (12.0%). Buccal mucosa (64.6%) and tongue (56.3%) were the most involved sites; 55.6% of patients were symptomatic. Extraoral involvement occurred in 35.8% and comorbidities in 29.1%. Topical corticosteroids were the main treatment (63.1%), while 21.5% required no therapy. The six additional cases showed similar patterns, with prevalent plaque/reticular forms, frequent tongue involvement, and a generally favorable course.

Conclusions: pediatric OLP is a rare but clinically relevant condition with heterogeneous presentation and frequent extraoral involvement. Although prognosis appears favorable, limited evidence and short follow-up warrant caution. The integration of our case series supports the need for standardized long-term prospective studies.

ANTIBIOTIC FUNCTIONALIZATION OF HYBRID BIOMATERIALS FOR APPLICATIONS IN ORAL SURGERY. AN *IN VITRO* STUDY

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Aim: complex clinical conditions in oral medicine are often associated with impaired healing and persistent local infection. In these settings, the efficacy of systemic antibiotics may be limited by poor tissue penetration and bacterial biofilm. Antibiotic-functionalized hybrid biomaterials may represent a promising strategy, combining local antimicrobial delivery with bioactive support for bone tissue regeneration.

Methods: a hybrid scaffold (HS), synthesized through a biomineralization process of Type I collagen with magnesium-doped hydroxyapatite, was used for its ability to support bone healing and provide localized antibiotic delivery. Commercial metronidazole (MDZ), commonly used in dentistry, was selected for this study. Drug-loaded HS were incubated in water-based solution at 37°C. The antibiotic release profile was evaluated by UV-Vis

test at different time points over 1 week.

Results: the MDZ loading approach was optimized for clinical adaptability. The MDZ concentration was selected to obtain a sustained drug release, in a clinically relevant dose.

Conclusions: the results support the potential application in several clinical settings, including medication-related osteonecrosis of the jaw, osteoradionecrosis, and tooth extraction procedures in patients at risk of developing these conditions. HS regenerative efficacy is already well documented, together with promising preliminary data on local antibiotic release. Further studies are currently underway to evaluate the combined release with amoxicillin and antibacterial efficacy, in order to confirm its translational potential in the clinical setting.

ANTIFUNGAL ACTIVITY OF OZONATED OLIVE OIL AGAINST MDR CANDIDA ALBICANS: AN *IN VITRO* STUDY ON PMMA-BASED PROSTHODONTIC RESIN

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Aim: sub-prosthetic candidiasis is a common oral infection around the world that is caused by different types of *Candida*. The rise of antifungal resistance, along with the challenges of administering these medications to certain patient populations and the associated risk of candidemia, has prompted researchers to seek new therapeutic options, including products based on ozonated olive oil. This study aims to assess the *in vitro* antifungal efficacy of an acrylic resin denture disinfectant that contains ozonated olive oil.

Methods: a series of PMMA cylinders (10 x 5 mm) were immersed in a liquid medium containing 5% human saliva. After 48 hours of incubation at 37°C, samples were exposed to: (i)

0.20% chlorhexidine (Curasept, Milan, Italy), or (ii) ozonated olive oil (Ialozon Clean Spray, Gemavip, Cagliari, Italy), or (iii) distilled water as a control. After 10 minutes, the residual biofilm was assessed using the spectrophotometric crystal violet method as outlined in the protocols established by Montana State University.

Results: cylinders exposed to ozonated oil base product showed a greater biofilm decrease (90%) compared with Chlorhexidine.

Conclusions: an ozonated olive oil-based spray can be considered effective and safe option for PMMA resin material to decontaminate prosthetic devices.

EVALUATION OF A SALIVARY BIOMARKER FOR EARLY IDENTIFICATION OF RAS

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Introduction: Recurrent aphthous stomatitis (RAS) is the most common ulcerative condition of the oral cavity, although its etiology remains unclear. A recent pilot study from our research unit identified CST1 as a potential salivary biomarker, showing significantly reduced expression during the acute phase compared to healthy subjects. However, intra-individual CST1 trends across different clinical phases have not yet been investigated. This study aims to compare salivary CST1 levels in the same patients during acute and remission phases of RAS.

Materials and methods: five RAS patients were recruited at the Oral Pathology Unit of CIR Dental School according to specific inclusion and exclusion criteria. Unstimulated whole saliva samples were collected from each subject during both acute and remission phases using passive drooling and stored at -80°C until analysis. CST1 expression was assessed by Western blot.

Results: saliva samples collected during remission showed consistently high CST1 expression. In contrast, samples from the acute phase exhibited markedly reduced or undetectable CST1 levels.

Discussion: CST1 is a salivary cystatin with inhibitory activity against cysteine proteases. Its reduction during the acute phase suggests a dysregulation of the protease/inhibitor balance, potentially increasing local proteolytic activity. This may contribute to tissue damage and delayed healing, especially with microbial co-infections.

Conclusions: despite the small sample size, these preliminary findings suggest CST1 as a promising salivary biomarker for early RAS detection, with potential diagnostic and prognostic relevance. Larger studies are needed to confirm these results.

ROLE OF LONG NON-CODING RNA TUG1 IN ORAL SQUAMOUS CELL CARCINOMA (OSCC): POTENTIAL AS A PROGNOSTIC AND THERAPEUTIC BIOMARKER

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Aim: Oral squamous cell carcinoma (OSCC) accounts for over 377,700 new cases diagnosed annually worldwide. Taurine Upregulated Gene 1 (TUG1) is a long non-coding RNAs (lncRNAs) potentially involved in cancer cell biology and chemoresistance. The study evaluated the role of TUG1 in OSCC samples and its effects on chemotherapy sensitivity in OSCC cell lines.

Methods: the study included 54 OSCC samples treated at the University of Foggia (2010-2022). TUG1 expression was analysed by In Situ Hybridization on tissue microarrays and by pathological analysis. The HSC-3 OSCC cell line underwent TUG1 knockdown and was analysed by Real-Time PCR. Cell viability and chemosensitivity to cisplatin (CDDP) and 5-fluorouracil (5-FU) were evaluated using the MTT assay.

Results: TUG1 expression was higher in OSCC samples compared with controls (2341.8 ± 1124.1 vs 717 ± 314.9 ; $p=0.006$). Tumours with moderately/poorly differentiation and tongue localization showed higher TUG1 levels compared to well-differentiated OSCCs and to tumours of other subsites. TUG1 knockdown in HSC-3 cells resulted in a reduction in gene expression (0.474 ± 0.062 and 0.473 ± 0.003 vs 1 ± 0.087 ; $p \leq 0.001$) and decrease in cell viability at 72 h ($p \leq 0.01$). Moreover, TUG1 downregulation increased cellular sensitivity to CD-DP and 5-FU treatment ($p \leq 0.01$).

Conclusions: these data demonstrate TUG1 overexpression in OSCC samples and suggest its involvement in cellular proliferation and chemosensitivity, indicating its potential role as biomarker and therapeutic target in OSCC.

OREGANO ESSENTIAL OIL AS A NEW PHOTSENSITIZER IN PDT AGAINST MDR CANDIDA SPP.: *IN VITRO* STUDY

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Aim: fungal infections of the oral cavity, particularly those caused by multi-drug resistant (MDR) *Candida albicans* represents an increasingly common clinical challenge. This necessitates the exploration of alternative, safe, and biocompatible therapeutic strategies. The aim of this study was to evaluate the antifungal activity of oregano essential oil alone and in combination with polarised light against MDR *Candida* spp.

Materials and methods: the antifungal activity of the oil (OEO; Zane Hellas®, Greece) was assessed by the Kirby-Bauer method and with determination of the minimum inhibitory concentration (MIC). Four wells were created in each 90 mm Petri dish previously infected with *C. albicans* MDR. Group 1: one well was filled with 50 µL of sterile distilled water as a neg-

ative control, while the others received 50 µL of OEO; Group 2: three wells with 50 µL of OEO and one well with sterile distilled water, irradiated with a Bioptron® device (Bioptron AG, Switzerland), wavelength: 480–3400 nm, power density of ~40 mW/cm², for 5 minutes at a distance of 5–10 cm from the agar surface. Following treatment, all plates were incubated at 37°C for 48 hours.

Results: in the *in vitro* tests, oregano essential oil resulted in complete inhibition of fungal growth, with a halo of inhibition greater in group 2 and an MIC 10 times lower in group 2.

Conclusions: the results suggest that oregano essential oil possesses marked *in vitro* antifungal potential alone and in association with polarised light.

CARDIOVASCULAR AND PROTHROMBOTIC RISK IN AN ORAL LICHEN PLANUS COHORT: A CROSS-SECTIONAL STUDY

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Aim: to evaluate the cardiovascular and prothrombotic risk in a cohort of patients with Oral Lichen Planus (OLP), and to identify the most relevant markers for vascular risk.

Methods: consecutive patients with a diagnosis of OLP under follow-up at the Oral Medicine Department of Policlinico Gemelli were enrolled. All participants underwent thrombophilic screening and cardiovascular risk assessment through standardized hematological and laboratory tests. Data were analyzed using SPSS v.25.0.

Results: the cohort comprised 55 patients (76.4% female, mean age 63 years). The most frequent subtype was reticular (80%). Buccal mucosa (81.8%) and gingiva (60%) were mostly affected. Most patients had at least one comorbidity (76.4%), including cardiovascular disease (34.5%), hypercholesterolemia (>200 mg/

dL) (45.5%), hyperhomocysteinemia (>15 µmol/L) (90.9%). Markers of endothelial activation and inflammation, mostly factor VIII (58.2%), vWF ristocetin cofactor activity (38.2%) and vWF antigen (21.8%) were increased. Lupus Anticoagulant positivity was detected in 21.8% of the patients and antiphospholipid antibodies (IgG/IgM) were rare. Standard coagulation parameters (PT, INR, aPTT) were within normal limits.

Conclusions: cardiovascular and prothrombotic risk in OLP patients appears to be driven by acquired inflammatory mechanisms rather than hereditary thrombophilic factors. Hyperhomocysteinemia, Factor VIII and vWF support a systemic pro-thrombotic and endothelial activation state. These findings emphasize the need for cardiovascular monitoring in OLP management.

FUNCTIONAL META-ANALYSIS OF ORAL AND GUT MICROBIOME REVEALS DIVERSITY BETWEEN HYPERTENSIVE AND NON-HYPERTENSIVE CONTROLS

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Aim: this study maps the taxonomic and functional landscape of oral and gut microbiota in hypertensive (HTN, exposed) vs non-HTN (non-exposed) adults. We aim to identify microbial signatures of blood pressure dysregulation and evaluate if oral-gut functional coupling mediates the association between the microbiome and systemic hypertension.

Methods: 16S (V3-V4) and shotgun data from oral (saliva/bio-film) and fecal samples were analyzed. ASVs were generated via DADA2 on 16s, while shotgun were treated using MetaPhlan4. Alpha and beta diversity measures were obtained by linear mixed-effects and PERMANOVA respectively. MaAsLin2 pipeline was adopted for investigating differential abundance between exposure. Cross-niche ecological coupling was as-

sessed via Picrust2, Mantel tests, and SourceTracker for oral-to-fecal microbial contribution.

Results: alpha diversity was similar between groups, while beta diversity showed clear segmentation in HTN. Functional analysis revealed significantly reduced Kegg Orthology (KOs) in HTN for the nitrate-nitrite-NO and putrescine/spermidine transport. Taxonomic analysis linked these functions to *Neisseria* and *Haemophilus* (nitrate reducers), which were more abundant in non-HTN controls.

Conclusions: HTN is linked to oral dysbiosis and, intriguingly, with reduced NO synthesis and polyamine transport potential. These findings highlight the oral-gut axis as a key regulator of cardiovascular homeostasis and suggest nitrate-reducing taxa as potential therapeutic targets.

SYSTEMIC HEALTH STATUS AND INFLAMMATORY BIOMARKER PROFILE IN EARLY-ONSET ORAL SQUAMOUS CELL CARCINOMA: A CROSS-SECTIONAL STUDY

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Aim: dysregulated inflammation and immune deficiency have been proposed as potential risk factors in the development of oral squamous cell carcinoma (OSCC) in young patients without common risk factors (smoke and alcohol use). This study examines systemic condition, pharmacological therapies and peripheral biochemical parameters related to immune dysregulation in young-onset OSCC, compared with late-onset OSCC and age-matched healthy controls.

Methods: the study population included four groups: 20 early-onset OSCC (mean age: 39.8), 40 late-onset OSCC (mean age: 72.7) and 20 young (mean age: 39.1) and 20 elderly (average age: 70.8) healthy controls. Medical history, ongoing therapies and preoperative peripheral biochemical parameters were analyzed in all groups. Clinical, histological and

prognostic data were collected for the tumor groups.

Results: early-onset OSCC showed a higher prevalence of autoimmune diseases respect to elderly (30% vs 10%). One-way ANOVA showed between group differences in circulating lymphocytes ($p = 0.03$), monocytes ($p < 0.01$), lymphocytes-to-monocyte ratio (LMR) ($p = 0.01$) with a trend for platelet-to-lymphocyte ratio (PLR) ($p = 0.06$). Specifically, early-onset oral cancer cases exhibited lower lymphocyte and monocyte counts, and higher value of LMR and PLR.

Conclusions: these preliminary findings suggest a distinct immune profile in patients with early-onset OSCC based on peripheral blood parameters. Further studies are warranted to validate these results through the analysis of immune-related biomarkers in tumor tissue specimens.

PERIODONTITIS IN ITALIAN PATIENTS WITH ESTABLISHED ORAL LICHEN PLANUS: A CROSS-SECTIONAL STUDY

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Aim: Oral lichen planus (OLP) is a chronic inflammatory disease characterized by T-cell-mediated immune dysfunction targeting oral epithelial cells. The results of various studies have shown that periodontal parameters were higher in the case group compared with the control group. The objective of this study was to assess the prevalence and severity of periodontitis (P) among Italian patients affected by oral lichen planus (OLP).

Methods: a prospective cohort study of patients with histopathologically confirmed OLP. A full-mouth periodontal examination was performed. All patients were staged according to the 2017 AAP/EFP classification of periodontal diseases.

Results: this cross-sectional study included 212 subjects (143 females and 69 males; mean age 61.2 years). At the time of di-

agnosis, 38 patients had Hashimoto's thyroiditis and were being treated with levothyroxine. Regarding clinical characteristics, 141 patients had keratotic lichen planus and 71 patients had erosive atrophic lichen planus. 141 patients (66.5% of the sample) had periodontal disease. Specifically, there were 23 patients with stage I disease, 63 patients with stage II disease, 39 patients with stage III disease and 15 patients with stage IV disease. Periodontal disease was significantly associated with lichen type and subjective symptoms.

Conclusions: higher prevalence and increased severity of periodontal disease were observed among patients affected by oral lichen planus. OLP clinical severity was strongly correlated with periodontal clinical parameters.

10-YEAR CARDIOVASCULAR RISK (PREVENT SCORE) IN RELATION TO PERIODONTAL CLINICAL PROFILE: A CROSS-SECTIONAL ANALYSIS OF THE NHANES POPULATION

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Aim: the link between periodontitis and cardiovascular disease (CVD) is well-documented. The 2023 AHA PREVENT score represents the current state-of-the-art in predictive modeling, integrating renal function (eGFR) into 10-year risk estimation. This study examines the association between periodontal status and CVD risk using this novel algorithm.

Methods: this cross-sectional study analyzed NHANES 2009–2014 data from adults aged 30–79 years with full-mouth periodontal examination. Periodontitis was defined using CDC/AAP criteria and dichotomized as healthy (Non-exposed) vs moderate/severe (Exposed). PREVENT scores were derived from clinical and biochemical data, including CKD-EPI eGFR. Associations were evaluated using unweighted and survey-weighted linear regression models. Continuous periodontal meas-

ures (mean CAL and PPD) were also analyzed in relation to PREVENT risk, adjusting for age, sex, smoking, and diabetes.

Results: the periodontitis group demonstrated significantly higher PREVENT risk compared to healthy individuals (15.7% vs 14.4%; $p < 0.001$). Multivariable modeling identified periodontitis as an independent risk predictor (Estimate: +1.24%; $p < 0.05$). A linear dose-response relationship was observed for mean CAL and PPD. Stratified analysis showed peak risk (39.6%) in exposed elderly males.

Conclusions: periodontitis is independently associated with increased 10-year CVD risk. These findings emphasize the clinical relevance of incorporating oral health indicators into systemic risk stratification to refine primary prevention strategies.

ORAL CARE IN INTENSIVE CARE: A CROSS-SECTIONAL STUDY

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Aim: oral hygiene procedures are an essential preventive strategy to reduce systemic infections and ventilator-associated pneumonia (VAP) in Intensive Care Unit (ICU) patients. In this cross-sectional study, the oral health of ICU patients was assessed to evaluate the oral hygiene status and to promote the integration of dental hygienists into the multidisciplinary team.

Methods: from April 2024 to July 2025, patients referring to ICU at San Paolo Hospital of Milan were enrolled. Clinical evaluation included the recording of medical history, consciousness levels, the Bedside Oral Exam (BOE) across 8 parameters, plaque and tongue coating indices, edentulism, and tooth mobility. Conscious patients completed questionnaires regarding previous habits, satisfaction, and the perceived utility of an oral health professional in the ICU preventive team.

Results: 44 patients were enrolled (excluding minors, severe dis-

abilities, or facial masks). The sample (30 males, 14 females; mean age 65.8) included patients with spontaneous respiration (n = 19), tracheostomy (n = 19), endotracheal tubes (n = 3). The BOE revealed moderate dysfunction in 20 patients and severe in 18; 70% of them showed impairments in saliva. Diagnoses included 19 oral lesions (e.g., 4 suspected candidiasis, 4 pressure ulcers, traumatic fibromas). Tongue coating exceeding 50% of the tongue surface in 20 cases. Limited time, poor lighting, involuntary clenching hinder the correct oral hygiene procedures in ICU patients. Patient satisfaction was low (2.4-2.7/5), while the perceived utility of a dental hygienist in the preventive ICU team was very high (4.8/5).

Conclusions: this study confirms the importance of oral care in ICU patients and suggests the need for specialized protocols managed by ICU nurses and dental professionals, in a multidisciplinary approach.

CLINICAL EVALUATION OF THE BEVIGILANT™ DEVICE IN ORAL CANCER SCREENING

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Aim: to evaluate the diagnostic performance of the BeVigilant™ device in oral cancer screening by assessing sensitivity, specificity, and predictive values.

Methods: patients presenting with clinically evident oral lesions were enrolled. An oral swab was collected and analyzed using the BeVigilant™ device, which assesses p16 and EGFR biomarkers through a standardized digital system. Results were categorized as “monitor” or “investigate.” Patients with non-evaluable samples (n = 2) were excluded. Only patients undergoing biopsy were included in the diagnostic performance analysis, considered the gold standard.

Results: a total of patients with histopathological diagnosis were included in the analysis. The BeVigilant™ device showed

a sensitivity of 100% and a specificity of 70%, with a positive predictive value of 25% and a negative predictive value of 100%. The device demonstrated high reliability in ruling out malignant lesions, with no false-negative results observed. Eleven patients without clinical indication for biopsy were excluded from the diagnostic accuracy analysis.

Conclusions: the BeVigilant™ device represents a promising non-invasive adjunct in oral cancer screening, particularly as a rule-out test due to its high sensitivity and negative predictive value. Its use may support clinical decision-making and reduce unnecessary biopsies.

Further studies on larger cohorts are needed to confirm these findings.

ORAL MANIFESTATIONS OF MULTISITE HPV INFECTION IN HIV-POSITIVE AND HIV-NEGATIVE PATIENTS: OBSERVATIONAL CLINICAL STUDY

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Aim: to investigate the correlation between oral and extra-oral lesions across different anatomical sites and their association with HPV infection.

Methods: an observational clinical study was conducted on 48 patients with multisite HPV infection involving oral and extra-oral sites (oropharyngeal, cutaneous, vaginal, urethral, and anal), previously sampled and HPV-genotyped. Extra-oral lesions were present in 91.7% of cases, 31/48 patients were HIV-positive. All patients underwent systematic oral screening, careful medical history collection, clinical evaluation, and standardized photographic documentation. Lesions were excised using a 940 nm diode laser and analyzed histopatholog-

ically. Clinical variables were recorded to assess topographical correlations.

Results: oral lesions were identified in 17 of 48 patients and showed a significant association with extra-oral involvement, supporting a multisite infection pattern. Histopathology revealed 35.3% papillomatous lesions, 5.9% focal epithelial hyperplasia (Heck's disease), and 11.8% verrucous lesions.

Conclusions: HPV infection frequently presents as a multisite disease involving multiple anatomical regions. Most lesions were HPV-related, confirming its etiological role. Oral screening is essential for lesion detection. These findings underline the importance of a multidisciplinary approach. The study is ongoing.

KNOWLEDGE, ATTITUDE, AND PERCEPTION (KAP) OF PATIENTS TOWARDS MEDICATION-RELATED OSTEONECROSIS OF THE JAW (MRONJ): A PILOT STUDY

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Aim: this study aimed to evaluate the level of Knowledge (K), Attitude (A) and Perception (P) of Medication-Related Osteonecrosis of the Jaw (MRONJ) among patients candidate to or undergoing anti-resorptive and/or anti-angiogenic therapy.

Methods: a pilot study was conducted on 39 patients stratified in three groups: pre-treatment (pre-TP), in-treatment (TP), and with MRONJ diagnosis. All completed a self-administered KAP questionnaire. Oral health-related quality of life was assessed with Oral Health Impact Profile (OHIP-14).

Results: the preliminary analyses showed good internal consistency (Cronbach's α : K = 0.839, AP = 0.710). MRONJ patients showed higher levels of K ($p = 0.017^*$), with a positive correlation between education and K ($p = 0.036^*$; $p = 0.360$). Overall K was limited: pre-TP and TP correctly answered only

25% of questions. Patients adhered poorly to preventive measures: 35% had no dental evaluation before therapy. Attendance to check-ups (46.16%) and oral hygiene sessions (76.3%) was limited, mainly due to lack of medical indication (TP: 60%; MRONJ: 100%). 61% of patients judged information received not adequate, while 20% believed that both dentists and prescribing physicians had insufficient knowledge. All participants emphasized the need for better collaboration between healthcare professionals. MRONJ patients reported significantly worst results in OHIP-14 ($p < 0.001^{**}$).

Conclusions: the findings highlight a substantial gap in patients' knowledge of MRONJ and the need to improve education and interdisciplinary collaboration, to optimize prevention, early diagnosis, and MRONJ outcomes.

MONOCYTES MITIGATE PLASMA-TREATED WATER-INDUCED CYTOTOXICITY IN HEAD AND NECK CANCER CELLS

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Aim: Plasma-treated water solutions (PTWS), enriched with long-lived reactive oxygen and nitrogen species (RONS), represent a tumor-selective therapeutic strategy. This study evaluated PTWS cytotoxicity in head and neck cancer (HNC) cells and the modulatory role of monocytes in the tumor microenvironment.

Methods: FaDu and SAS HNC cells and HaCaT epithelial cells were treated with PTWS oxy 20' or air 20' for 24 h. Cell death, ROS, and lipid peroxidation were assessed. SAS and FaDu cells were co-cultured with CD14⁺ monocytes and exposed to PTWS.

Results: SAS cells were most sensitive (~65% death; ~35% late apoptotic, ~30% non-apoptotic), with 2-fold ROS increase and lipid peroxidation of ~27% (air) and ~56% (oxy).

FaDu cells showed intermediate sensitivity (~20% air, ~50% oxy), modest ROS increase, and <10% lipid peroxidation. HaCaT cells displayed low cytotoxicity (<30%) with minimal ROS and no lipid peroxidation. Monocytes alone showed 18% (air) and 59% (oxy) death. In co-culture, monocyte mortality reached ~99%, reducing SAS cell death by ~50% via apoptosis attenuation and abolishing lipid peroxidation. In FaDu cells, co-culture slightly reduced death, induced early apoptotic arrest, and decreased lipid peroxidation to ~1%.

Conclusions: monocytes act as key modulators of PTWS response, protecting HNC cells while undergoing extensive death, highlighting a TME-dependent limitation of PTWS efficacy.

TRENDS IN STAGE AND AGE AT DIAGNOSIS OF ORAL SQUAMOUS CELL CARCINOMA OVER TIME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Aim: to assess whether age at diagnosis of oral squamous cell carcinoma (OSCC) has changed over time and whether stage at presentation has varied across decades.

Methods: a PRISMA-based systematic review (PROSPERO: CRD420251048070) was conducted. MEDLINE, Scopus, and Web of Science were searched. Studies reporting age and/or stage across calendar periods were included. Pooled mean age at diagnosis was calculated in studies eligible for meta-analysis, and subgroup analyses were performed by decade of publication. Heterogeneity was assessed using I².

Results: 29 studies (15,911 OSCC cases) were included. OSCC remained mainly a midlife malignancy. In meta-analysis (10 studies), pooled mean age was 55.92 years (95% CI: 53.00-58.84), with substantial heterogeneity (I² = 99.17%).

Decade-stratified analysis suggested a modest age reduction in recent cohorts. Staging data were inconsistent and showed no clear shift toward earlier stages. Among studies with complete stage I-IV data (n = 6,950), early-stage (I-II) accounted for 54.2% and advanced-stage (III-IV) for 45.8%. Variability in staging systems (AJCC/UICC) limited comparisons.

Conclusions: evidence does not support a global shift toward early-onset OSCC but suggests a modest, population-dependent trend toward younger age at diagnosis. Lack of consistent reduction in stage at presentation indicates earlier detection alone does not explain this pattern. More standardized data reporting in large studies is needed to clarify whether young-onset OSCC reflects changing of exposure to risk factors, distinct tumor biology, or both.

REGENERATIVE EFFECTS OF ZINC L-CARNOSINE IN RADIATION-INDUCED ORAL MUCOSITIS (RIOM): A META-ANALYSIS OF THE LITERATURE AND CASE SERIES

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Aim: to evaluate the regenerative and protective effects of zinc L-carnosine (ZnC) in radiation-induced oral mucositis (RIOM) through a systematic review with meta-analysis and a clinical case series.

Methods: a systematic review following PRISMA guidelines included 8 clinical studies (n = 544) assessing ZnC in oral mucosal injury. Meta-analyses were performed on the incidence of moderate (≥ 2) and severe (≥ 3) mucositis. Additionally, a case series of three patients with RIOM treated with ZnC mouthwash combined with Nd:YAG photobiomodulation was analyzed, evaluating pain (VAS/NRS) and lesion size reduction.

Results: meta-analysis showed a significant reduction in severe mucositis under the common-effect model (OR 0.48;

95% CI 0.32-0.72) and in moderate mucositis (OR 0.56; 95% CI 0.33-0.95), although significance was not maintained in random-effects models.

In this series of cases, a rapid reduction in pain was observed as early as the first 2 days (a decrease of >80% on the VAS scale), with complete healing of the mucosa achieved within 7 - 21 days. The lesion resolved completely, with no adverse events reported.

Conclusions: ZnC appears to support both prevention and regeneration of oral mucosa in RIOM. The combined approach with photobiomodulation may enhance clinical outcomes, particularly in pain control and healing time. However, evidence is limited by heterogeneity and small sample size, warranting further controlled studies.

DIAGNOSTIC CHALLENGES IN UNICYSTIC AMELOBLASTOMAS: A CRITICAL REVIEW OF LITERATURE AND A CASE REPORT

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Aim: this study aims to review published cases of mural unicystic ameloblastoma and their characteristics, and to report a diagnostically challenging case mimicking a simple bone cyst.

Methods: a keyword based literature review was conducted through PUBMED/Medline using the entry terms “mural”, “intra-mural”, “unicystic ameloblastoma” with the boolean operator “AND”.

Results: a total of 30 cases were identified. Of these, 18 (60%) occurred in males, and only 4 did not report swelling as the main clinical feature. In 28 cases (93%), the lesion was located in the mandible. Additionally, 10 cases did not include ameloblastoma among the initial diagnostic hypotheses. The present case involves a 38-year-old male with a

unilocular radiolucent lesion between teeth 45 and 46, both vital. Initial hypotheses included simple bone cyst, lateral periodontal cyst, and benign odontogenic tumor. The first surgery revealed an empty cavity, suggesting a simple bone cyst. After 10 months, lesion growth was observed, requiring reintervention. Histopathology showed epithelial cords in a plexiform pattern with basal palisading and reverse polarization, consistent with unicystic ameloblastoma with intramural proliferation. The patient remains under follow-up for four years with complete healing of lesion and no recurrence.

Conclusions: follow-up and histopathological analysis are essential for accurate diagnosis and proper management, especially when initial and conclusive diagnoses differ.

ORAL MICROBIOME CHANGES DURING MECHANICAL VENTILATION: DYSBIOSIS AND CLINICAL IMPLICATIONS

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Aim: this systematic review assessed how mechanical ventilation affects oral microbiome composition, ecological balance and clinical implications in critically ill patients.

Methods: a PRISMA-based review was conducted using PubMed/MEDLINE, Scopus and Web of Science (2015–2025). Included studies were randomised controlled trials and prospective cohorts analysing oral microbiota in mechanically ventilated adults. Variables included sampling timing, microbiome composition, oral health interventions and infection outcomes. The search followed the PICO model.

Results: studies showed rapid oral microbiome dysbiosis during mechanical ventilation, with reduced commensal bacteria (*Streptococcus*, *Neisseria*, *Veillonella*) and increased oppor-

tunistic respiratory pathogens. Early Intensive Care Unit (ICU) microbial profiles predicted pneumonia risk. *Pseudomonas aeruginosa* emerged as a potential biomarker. Antibiotics, ventilation duration and baseline status influenced microbial changes. Oral hygiene interventions reduced pathogens and dysbiosis severity, but links with Ventilator-Associated Pneumonia (VAP) outcomes were inconsistent.

Conclusions: mechanical ventilation disrupts oral microbiome balance, promoting pathogens and reducing diversity. Oral hygiene lowers microbial load but has limited direct impact on infections. The oral cavity remains a key modifiable reservoir affecting respiratory health, highlighting the need for standardised longitudinal studies and improved oral care in ICU settings.

THE RELATIONSHIP BETWEEN PERI-IMPLANTITIS AND OSCC: A REVIEW OF CASE REPORTS AND CLINICAL RISK FACTORS

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Aim: to determine whether dental implants associated with peri-implantitis act as an independent causal factor for OSCC - Oral Squamous Cell Carcinoma - or whether its development is associated with a predisposed oral environment in which the implant acts as a cofactor, contributing to clinical risk stratification.

Methods: a literature review was conducted using PubMed/MEDLINE and Google Scholar. Case reports published between 1996 and 2025 with histologically confirmed peri-implant OSCC were included, while cases lacking adequate clinical history or documentation of risk factors were excluded. Application of these criteria resulted in a final sample of 66 patients.

Results: the majority of cases (65.2%) had preexisting risk factors. Specifically, 30.3% reported both a history of OSCC/

OPMD and risk habits (tobacco/alcohol), 18.2% had a history of OSCC/OPMD alone, and 16.7% presented only risk habits. Conversely, 35.0% of cases had no known risk factors.

Conclusions: current evidence does not support a direct oncogenic role of dental implants in healthy populations. However, peri-implantitis may act as a cofactor in mucosae predisposed by prior medical history or lifestyle-related risk factors (oral field cancerization), potentially accelerating malignant transformation. Although the limited number of cases prevents definitive conclusions, the severity of the condition needs rigorous follow-up in high-risk patients and a prompt differential diagnosis, essential to prevent diagnostic delays in recognizing OSCC, which would significantly worsen the prognosis.

DIAGNOSTIC CHALLENGES IN PEDIATRIC SJÖGREN'S SYNDROME: THE CENTRAL ROLE OF MINOR SALIVARY GLAND BIOPSY

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Aim: to investigate the diagnostic pathway of pediatric Sjögren's syndrome and to determine the clinical relevance of minor salivary gland biopsy in the absence of validated pediatric-specific classification criteria.

Methods: a systematic review was conducted according to PRISMA guidelines. PubMed, Scopus, and Web of Science were searched up to November 2025. Observational, retrospective, cohort, cross-sectional studies, case series, and case reports investigating the diagnostic role of minor salivary gland biopsy in pSS were included. Risk of bias was assessed using the Joanna Briggs Checklist. Data were qualitatively synthesized due to clinical and methodological heterogeneity.

Results: 39 studies were included. Recurrent or persistent parotitis emerged as the most frequent glandular manifesta-

tion, while joint involvement and lymphadenopathy were the predominant extra-glandular features. Anti-SSA antibodies were detected in approximately 64% of patients and anti-SSB in 51%, with ANA and rheumatoid factor positivity reported in 69% and 53% of cases. Minor salivary gland biopsy showed positive findings in nearly 70% of patients, demonstrating focal lymphocytic sialadenitis. Functional and imaging tests provided supportive but less consistent diagnostic contributions.

Conclusions: minor salivary gland biopsy represents a key component of the diagnostic work-up in pediatric Sjögren's syndrome. When integrated with clinical and serological findings, it may facilitate earlier and more accurate diagnosis, particularly in the absence of standardized pediatric classification criteria.

ORAL AND CONJUNCTIVAL MANIFESTATIONS OF HIGH-RISK ONCOGENIC HPV INFECTIONS: A NARRATIVE REVIEW

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Aim: Human Papillomavirus (HPV) infection represents a crucial etiological factor in the development of neoplastic lesions. This narrative review aims to analyze the spectrum of oral and conjunctival clinical manifestations associated with high-risk HPV (HR-HPV) strains, with a specific focus on genotypes 16 and 18, evaluating the pathogenetic and clinical analogies between these two anatomical sites.

Methods: a comprehensive literature search was conducted across major databases (PubMed, Scopus, Google Scholar), including studies published over the last 15 years. Selection criteria focused on original articles, systematic reviews, and case reports investigating the correlation between HR-HPV and the onset of dysplasia, oral squamous cell carcinoma (OSCC), and ocular surface squamous neoplasia (OSSN).

Results: the analysis highlights a strong association between

HR-HPV and the development of oropharyngeal carcinoma, with an increasing prevalence of the HPV-16 strain. Regarding the conjunctiva, although the role of HPV is less systematically defined compared to the genital tract, data suggest a significant correlation between HR-HPV and precancerous lesions (inverted papillomas and dysplasia) or invasive carcinomas. Both sites exhibit prolonged clinical latency and often present with non-specific morphology during early stages.

Conclusions: this review confirms the necessity of a multidisciplinary approach involving dentists and ophthalmologists for the early diagnosis of suspicious lesions. Recognizing viral biomarkers in extra-genital sites is fundamental for implementing targeted screening strategies and promoting the efficacy of universal vaccination in reducing the incidence of these pathologies.

BEYOND CLINICAL INSPECTION: A REVIEW OF MACHINE AND DEEP LEARNING-DRIVEN IMAGE CLASSIFICATION AND SEGMENTATION MODELS FOR ORAL LESIONS

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Aim: Oral cancer (OC) cases are increasing globally, with lesions that may arise de novo or secondary to potentially malignant disorders (OPMDs). Early detection of these lesions is vital for patient survival rates; however, this remains a clinical challenge for untrained clinicians. Deep learning (DL) and Machine learning (ML)-driven image classification and segmentation models hold promise as referral adjuncts for the detection of oral lesions and may reduce diagnostic delay. This review aims to provide research insights for future prospective studies on the use of AI for image classification and segmentation of oral lesions.

Methods: a narrative review was conducted across PubMed, Scopus, and Web of Science. The inclusion criteria were restricted to experimental studies evaluating the diagnostic performance of ML/DL models using Convolutional Neural Networks (CNNs) and Vision Transformers (VTs). This review ana-

lyzed the application of these models, either individually or in ensemble configurations, to assess their performance in the classification and segmentation of intraoral images.

Results: 37 articles were selected, including retrospective and experimental studies. The models analyzed were predominantly based on DL, of which 26 (70.3%) utilized CNNs, 3 (8.1%) used VTs, and 4 (10.8%) a combination of both. These studies evaluated the classification and segmentation of oral lesions, including OC (n = 14, 37.7%), OPMDs (n = 6, 13.3%), a combination of both (n = 17, 45.9%) with most of them (n = 30, 81.1%) incorporating control groups.

Conclusions: AI-driven models may represent innovative adjuncts for the early detection of OPMDs and OC supporting first-line healthcare providers without expertise in oral medicine and oncology. Future prospective studies are needed to validate these AI tools for real-world applicability.

PROGNOSTIC IMPACT OF MIR-34A IN HEAD AND NECK SQUAMOUS CELL CARCINOMA: A META-ANALYSIS, WITH TRIAL SEQUENTIAL ANALYSIS

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Aim: to assess whether miR-34a expression predicts survival in head and neck squamous cell carcinoma (HNSCC), we performed a systematic review, meta-analysis, and trial sequential analysis (TSA).

Methods: following a PROSPERO-registered protocol (CRD420251238772), we searched databases and grey literature for studies reporting overall survival (OS) or disease-free survival (DFS) by miR-34a expression in HNSCC. Hazard ratios (HRs) were extracted directly or reconstructed from Kaplan-Meier curves using the Tierney method and a Python tool (KM2HR).

Results: four retrospective studies (seven cohorts; 318 patients) were included. For OS, low *versus* high miR-34a expression was associated with worse survival in the fixed-effects model (HR 2.25, 95% CI 1.48-3.41), but not in the ran-

dom-effects model (HR 1.32, 95% CI 0.32-5.54; $I^2 = 77\%$). For DFS, fixed-effects analysis suggested poorer outcomes with low miR-34a (HR 2.92, 95% CI 1.24-6.88), whereas random-effects analysis was highly imprecise (HR 0.19, 95% CI 0.00-129.34; $I^2 = 91\%$). TSA for OS showed a tentative signal, crossing the monitoring boundary without reaching the required information size. TCGA exploration (n = 522) showed a non-significant trend toward worse OS with low miR-34a and was not pooled.

Conclusions: low miR-34a may be associated with poorer OS in HNSCC, but evidence is limited by retrospective design, small samples, and marked heterogeneity. Larger prospective, site-specific studies with standardized assays, predefined cut-offs, and adjustment for HPV status and clinical covariates are needed before clinical use.

ORAL MICROBIOTA IN THE MALIGNANT TRANSFORMATION OF ORAL LEUKOPLAKIA: A SCOPING REVIEW

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Aim: to map the available evidence on the composition of the oral microbiota in oral leukoplakia (OL) and its role in malignant transformation.

Methods: a scoping review was conducted following JBI methodology. Searches were performed in PubMed, Scopus, Embase, Web of Science, and Cochrane Library. After duplicate removal, titles/abstracts and full texts were screened. Studies including OL patients and assessing microbial composition through sequencing or molecular methods were included; animal and *in vitro* studies were excluded. Data extraction was performed using a standardized charting form by two independent reviewers.

Results: a total of 327 records were identified, 71 full-text articles were assessed, and 22 studies were included. Most were cross-sectional and used 16S rRNA sequencing on saliva,

swabs, or biopsies. Dysbiosis was consistently reported, with increased *Fusobacterium*, *Prevotella*, and *Porphyromonas* and reduced commensal taxa such as *Streptococcus*. Periodontopathogens were more prevalent in dysplastic and high-risk lesions. Some studies reported *Candida* species in association with epithelial dysplasia, although evidence remains limited and heterogeneous. Alterations in microbial diversity and community structure suggested ecological shifts associated with progression to OSCC. However, heterogeneity limited comparability.

Conclusions: oral microbiota may contribute to OL progression and malignant transformation. Despite recurrent dysbiotic patterns, no validated microbial biomarkers are available. Further standardized longitudinal studies are needed to clarify causal mechanisms and improve clinical applicability.

PROGNOSTIC ROLE OF WORST PATTERN OF INVASION IN ORAL SQUAMOUS CELL CARCINOMA

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Aim: the pattern of invasion (POI) describes the arrangement of neoplastic cells at the tumor-host interface and reflects how cancer infiltrates surrounding tissue. Accumulating evidence suggests that the Worst Pattern of Invasion (WPOI) is an independent prognostic factor in oral squamous cell carcinoma (OSCC). However, it is still considered a minor criterion and is currently recommended only as an optional reporting component in the College of American Pathologists (CAP) guidelines.

Methods: this study provides an extensive review of the literature regarding the prognostic role of WPOI in OSCC. A comprehensive search of databases — including PubMed, Web of Science, and Scopus — was performed for relevant English-language studies published between 1984 and 2025.

Results: WPOI emerged as an independent prognostic factor for locoregional recurrence, lymph node metastasis (LNM), overall survival, disease-specific survival, and bone infiltration, regardless of the oral subsite or pathological stage. Notably, WPOI-5 is the most significant predictor of occult LNM in early-stage OSCC. Consequently, evaluating WPOI has been suggested to guide postoperative management and identify occult LNM in early-stage cases.

Conclusions: the prognostic relevance of WPOI in OSCC highlights the importance of its evaluation in routine pathological practice. However, further multicentre prospective studies and accuracy analyses are required to standardize assessment methods and establish the most reliable WPOI scores and cut-off points.

PSYCHOLOGICAL IMPACT OF INVASIVE DENTAL PROCEDURES IN ONCOLOGICAL PATIENTS UNDERGOING ANTIRESORPTIVE THERAPY FOR BONE METASTASES FROM BREAST CANCER (PIDEOPAT): PRELIMINARY RESULTS

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Aim: in patients with metastatic breast cancer with bone involvement, antiresorptive drugs (AR) are associated with the risk of medication-related osteonecrosis of the jaw (MRONJ), particularly after invasive dento-alveolar procedures. At the University Hospital of Parma, eligible patients are enrolled in a Diagnostic-Therapeutic Care Pathway including preventive dental assessment and follow-up. This study evaluates the psychological impact of invasive dental treatments, considering masticatory function, aesthetics, and subsequent prosthetic rehabilitation.

Methods: this is an ongoing prospective observational study with a 48-month follow-up. At the first dental evaluation, patients completed two questionnaires: the OHIP-14 and the

Distress Thermometer. Patients are then divided into three groups: A (need for invasive treatment), B (no need), and C (refusal). Groups A and B undergo follow-up with questionnaires every 4 months; group A also answers specific questions on discomfort related to invasive dental procedures.

Results: preliminary data from 33 patients show oral and emotional discomfort, with over half reporting moderate-to-severe stress. Challenges with eating, oral discomfort, the use of prosthetics, and anxiety about potential complications all contribute to a considerable psychological burden.

Conclusions: findings highlight the need for structured psychological support and continuous multidisciplinary dental management.

ARTIFICIAL INTELLIGENCE-ASSISTED PERSONALIZATION OF POST-OPERATIVE ANALGESIA IN ORAL SURGERY IN MEDICALLY VULNERABLE PATIENTS: A CLINICAL FRAMEWORK FOR IBUPROFEN-PARACETAMOL COMBINATION THERAPY

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Aim: post-operative pain management in oral surgery may be challenging in medically vulnerable patients due to systemic diseases, chronic therapies and potential drug interactions. The aim of this study was to evaluate the role of an artificial intelligence-based clinical decision support system in guiding post-operative analgesic strategies, focusing on ibuprofen-paracetamol combination therapy.

Methods: clinical data from patients undergoing oral surgery were collected. For each patient, systemic conditions, ongoing pharmacological therapies, type and invasiveness of the surgical procedure, peri-operative medications and post-operative pain intensity assessed using a visual analogue scale (VAS) were recorded. These variables were integrated into an artificial intelligence-based system designed to generate personalized analgesic suggestions and support clinical deci-

sion-making, evaluating the appropriateness of ibuprofen-paracetamol combination therapy according to individual patient profiles.

Results: preliminary observations suggest that the AI-assisted approach may facilitate identification of appropriate analgesic strategies in medically vulnerable patients. By integrating clinical and pharmacological variables, the system may support clinicians in optimizing ibuprofen-paracetamol use while considering patient-specific conditions and potential risks.

Conclusions: artificial intelligence-based decision support may improve post-operative pain management in oral surgery by enabling more personalized and safer analgesic prescriptions. Its integration into clinical practice could support more informed decision-making in medically vulnerable patients.

IDENTIFICATION OF NEOPLASTIC METABOLIC SIGNATURES IN ORAL CANCER USING NON-INVASIVE CHEMILUMINESCENT CELL PHENOTYPING

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Aim: Oral squamous cell carcinoma (OSCC) represents the most common histological subtype of oral cancer and continues to show an increasing global incidence. Despite advances in oncological management, prognosis remains poor in advanced stages. This study aims to evaluate a non-invasive diagnostic strategy for the early detection and monitoring of OSCC, overcoming the limitations of surgical biopsy through molecular biomarker analysis.

Methods: cyto-salivary samples were collected using a cytobrush from tumor lesions and adjacent clinically healthy mucosa in patients with histologically confirmed OSCC. Samples were analyzed using the Stark Oral Screening[®] assay combined with the FemtoHunter[®] device. Six biomarkers (EGFR, p53, Ki67, B7-H6, PD-L1, HLA-E) were measured

through a chemiluminescent ELISA-based method.

Results: all biomarkers showed significant overexpression in tumor tissue compared to healthy mucosa. FemtoHunter[®] analysis demonstrated high diagnostic accuracy, enabling clear discrimination between malignant and normal tissues. The inclusion of immune-related biomarkers enhanced diagnostic performance by capturing both tumor proliferation and immune evasion mechanisms.

Conclusions: cytobrush-based multimarker analysis represents a promising, non-invasive approach for OSCC diagnosis and follow-up, showing diagnostic performance and potential for integration into clinical workflows for early detection and longitudinal monitoring.

IL-10 SUPPLEMENTATION IN THE MANAGEMENT OF RECURRENT APHTHOUS STOMATITIS: A PILOT STUDY

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Aim: Recurrent aphthous stomatitis (RAS) is a condition characterized by recurrent inflammatory ulcerative lesions (3-4 episodes per year) of the oral mucosa, that may impair nutrition and quality of life. The aim of this pilot study is to evaluate the use of oral drops containing IL-10 (GUNA IL-10) for the control of aphthous recurrences.

Methods: patients were instructed to take 20 sublingual drops twice daily for 3 months, according to the manufacturer's recommendations. Follow-up interviews assessed the occurrence of new ulcers.

Results: all 11 patients showed a marked reduction in canker sores at 3 and 6 months (3 months post-treatment), with improvement already evident after the first month of IL-10 supplementation. The mean number of aphthae decreased

from 2.86 at baseline (T0) to 1.0 after 3 months of IL-10 supplementation.

A clinical improvement was observed in 9 out of 11 patients, with complete resolution in several cases.

One patient showed no change, while one patient exhibited a slight increase in lesion number.

Conclusions: IL-10 supplementation was associated with a clinically meaningful improvement in aphthous lesions, evident from the first month and progressively increasing up to 3 months, with several cases of complete or near-complete remission. Clinical benefits were maintained even after treatment discontinuation. These findings support the potential role of IL-10 supplementation as a valuable therapeutic option for recurrent aphthous stomatitis, with a positive impact on patients' quality of life.

KI67 AND P53 AS PREDICTORS OF RECURRENCE AND MALIGNANT TRANSFORMATION IN DYSPLASTIC ORAL POTENTIALLY MALIGNANT DISORDERS: A PRELIMINARY LONGITUDINAL STUDY

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Aim: the management of Oral Potentially Malignant Disorders (OPMDs) with dysplasia requires balancing the invasiveness of surgery for a pre-malignant lesion with the need to prevent recurrence or malignant transformation. The study evaluated the prognostic role of ki67 and p53 in pre-operative biopsies of dysplastic OPMDs.

Methods: twenty-five patients undergoing surgical excision of OPMDs after diagnostic incisional biopsy showing high-grade dysplasia were enrolled. Inclusion criteria required immunohistochemical analysis of ki67 and p53 in the pre-operative biopsy, no evidence of carcinoma in the final surgical specimen and clear margins without cytological alterations. Altered expression of Ki67 and P53 was defined as staining in mature keratinocytes with >20% of positive cells. One-way ANOVA and Kaplan-Meier analysis evaluated the correlation between bio-

marker expression and the risk of recurrence or malignant transformation.

Results: mean post-surgical follow-up was 49.7 months. OPMD recurrence occurred in 12/25 patients, 7 OMPD progressed into carcinoma. Higher Ki67 and p53 were found in patients with recurrence ($p = 0.03$ and $p = 0.008$, respectively) and malignant transformation ($p = 0.02$ and $p = 0.0001$). Altered expression of Ki67 predicted recurrence ($p = 0.03$). Combination of Ki67 and p53 overexpression was found in 8 patients, 5 of whom developed oral cancer.

Conclusions: increased expression of ki67 and p53 in the pre-operative biopsy may indicate a more aggressive behavior of OPMDs. If confirmed in larger studies, this could enable a personalized therapeutic approach.

PRELIMINARY EVALUATION OF THE EFFICACY OF A $ZnCl_2$ BASED PROTOCOL IN THE MANAGEMENT OF SYMPTOMATIC GEOGRAPHIC TONGUE: PILOT STUDY

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Aim: geographic tongue is a benign inflammatory condition characterized by erythematous depapillated areas, often associated with a burning sensation. Currently, no standardized treatment is available. The aim of this pilot study is to evaluate the efficacy of a home-based protocol using products (Toothpaste and mouthwash) containing $ZnCl_2$ in reducing symptoms.

Materials and methods: 12 patients with a clinical diagnosis of symptomatic geographic tongue were enrolled. Patients were provided with a 60-day home-care protocol consisting of

a toothpaste and a mouthwash containing $ZnCl_2$. Clinical and symptomatic assessments were performed at baseline and at 3 months.

Discussion: preliminary findings suggest a potential beneficial role of $ZnCl_2$. However, the small sample size and the absence of a control group limit the significance of these results.

Conclusions: the tested protocol appears to represent a valid therapeutic option. Further studies with larger sample sizes and a controlled design are needed to confirm these findings.

ORAL MICROBIOTA IN OLP LESIONS: CORRELATION BETWEEN PERIODONTAL BACTERIA, ORAL HYGIENE AND COMORBIDITIES

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Aim: to investigate the presence and potential contribution of periodontal microorganisms in the pathogenesis of Oral Lichen Planus (OLP), a chronic immune-mediated inflammatory disease of unclear etiology, focusing on bacterial species from the red and orange complexes described by Socransky. Additionally, the study aimed to evaluate the presence of systemic comorbidities in OLP patients and their possible association with the disease.

Methods: ten patients with clinically and histologically confirmed OLP were enrolled. Microbiological samples were collected using a microbrush applied directly to lesion surfaces. Analyses were performed at the Molecular Biology Laboratory of San Giovanni di Dio Hospital in Cagliari. Periodontal pathogens were identified and quantified, including *Porphyromonas gingivalis*, *Tannerella forsythia*, *Prevotella intermedia*, and *Aggregatibacter actinomycetemcomitans*.

Results: high levels of *Fusobacterium nucleatum* were detected in all patients. Notably, *Treponema denticola* was absent in every case, a finding not previously reported. The most commonly affected sites were buccal and gingival mucosa. The mean age was 58 years, with a slight female predominance, consistent with known epidemiological data. Clinical manifestations were often symptomatic, potentially impacting patients' quality of life.

Conclusions: the results support a possible role of periodontal microorganisms in triggering or maintaining the immune response in OLP. The consistent presence of specific bacteria and the absence of others may indicate a distinct microbial profile. Larger studies are required to confirm these findings and to clarify interactions between microbial, local, and systemic factors, with potential implications for targeted therapeutic approaches.

A NOVEL OCT-BASED MORPHOLOGICAL HEALING SCORE FOR QUANTITATIVE ASSESSMENT OF TREATMENT RESPONSE IN ORAL LICHEN PLANUS

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Aim: to develop and validate a quantitative Optical Coherence Tomography-based score (OCT-MHS) for assessing treatment-induced morphological changes and comparing the efficacy of mucoadhesive clobetasol patches versus conventional topical clobetasol in oral lichen planus (OLP).

Methods: fourteen patients with clinically and histologically confirmed OLP were randomly assigned to mucoadhesive clobetasol patches (n = 7) or conventional topical clobetasol (n = 7).

The OCT-MHS was designed for standardized evaluation of mucosal architecture, incorporating four OCT-detectable features (keratin layer, epithelial layer, basement membrane, lamina propria), assessed for thickness, reflectivity, continuity, and

organization. Each feature was graded 0-2, yielding a total score (0-8). Lesions were evaluated at baseline (T0) and after 30 days (T1). Efficacy was defined as Δ OCT-MHS (T0-T1).

Results: OCT-MHS allowed quantitative, reproducible assessment of treatment response.

Mean scores decreased from 6.38 to 1.75 (Δ = 4.63) in the conventional group and from 4.43 to 0.71 (Δ = 3.72) in the patches group. Both treatments were effective, with patches achieving values closer to normal mucosal architecture.

Conclusions: OCT-MHS is a reliable quantitative tool for monitoring morphological changes and enables objective comparison of treatment efficacy in OLP, supporting its use in clinical and research settings.

EVALUATION OF SERUM CYFRA 21-1 AND C-REACTIVE PROTEIN LEVELS IN PATIENTS WITH ORAL POTENTIALLY MALIGNANT DISORDERS AND ORAL SQUAMOUS CELL CARCINOMA: A PILOT STUDY

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Aim: early diagnosis of oral squamous cell carcinoma (OSCC) and monitoring of oral potentially malignant disorders (OPMDs) require non-invasive and easily applicable biomarkers. This pilot study aimed to evaluate serum levels of cytokeratin 19 fragment (CYFRA 21-1) and C-Reactive Protein (CRP) in patients attending the Oral Medicine Department of the Policlinico Paolo Giaccone of Palermo.

Methods: blood samples were collected from 19 patients presenting with various oral lesions. Serum levels of CYFRA 21-1 and CRP were measured and correlated with the corresponding clinicopathological diagnoses, using literature-based cut-off values (2.37 ng/ml and 5 mg/l, respectively).

Results: CYFRA 21-1 positivity was observed in 3 patients (in-

cluding cases of leukoplakia, high-grade dysplasia and OSCC), while CRP positivity was detected in 2 patients (including cases of oral lichen planus and OSCC). One patient with a confirmed diagnosis of OSCC showed simultaneous positivity for both markers. The remaining patients were negative for both biomarkers.

Conclusions: preliminary findings suggest that the combined assessment of CYFRA 21-1 and CRP may reflect the pathogenetic profile of oral lesions, potentially distinguishing inflammatory conditions from dysplastic/neoplastic ones. A combined serological panel may represent a useful tool for preliminary screening and diagnostic support; however, studies with larger cohorts are needed to validate these findings.

INTRAORAL CAPILLAROSCOPY IN THE ASSESSMENT OF ORAL PIGMENTED LESIONS: A PILOT EXPLORATORY STUDY

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Aim: pigmented lesions of the oral mucosa represent a heterogeneous group of conditions with diverse aetiologies, including traumatic, melanocytic, neoplastic, and exogenous causes. While most oral pigmented lesions are benign and can be clinically monitored, biopsy with histopathological examination remains the gold standard for the diagnosis of lesions with suspicious features.

We hypothesize that intraoral capillaroscopy may provide additional diagnostic information by enabling *in vivo* assessment of the microvascular component underlying lesion pigmentation.

Methods: four patients (aged 12-52 years) with oral pigmented lesions of different aetiologies were evaluated. All underwent clinical examinations and intraoral capillaroscopy of both

the lesion and contralateral healthy mucosa. Microvascular parameters, including vessel density, diameter, and morphology, were also assessed.

Results: capillaroscopy (200×) improved visualization of lesion architecture and colour. Lesion colour reflected the interaction between pigment type, amount, depth, distribution, and vascular contribution. Capillaroscopy allowed discrimination of vascular involvement, facilitating differentiation between melanocytic and vascular/inflammatory lesions.

Conclusions: intraoral capillaroscopy is a promising non-invasive adjunct for evaluating oral pigmented lesions, enhancing diagnostic accuracy and supporting clinical decision-making. Further studies are needed to validate its utility.

ORAL CYTOBIOPSY: VALIDATION OF A NON-INVASIVE DIAGNOSTIC PROTOCOL FOR ORAL CANCER AND POTENTIALLY MALIGNANT DISORDERS

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Aim: the diagnostic landscape of Oral Squamous Cell Carcinoma (OSCC) remains burdened by late-stage detection and the limitations of incisional biopsy, which is prone to sampling errors in heterogeneous lesions or Potentially Malignant Disorders (OPMDs). Precision oncology necessitates shifting the diagnostic window toward the pre-phenotypic phase, identifying molecular aberrations before overt architectural distortion occurs.

Methods: this study validated an innovative hybrid cyto-salivary sampling method (cytobrush biopsy) in 15 treatment-naïve OSCC patients (Stages I-IV). To overcome the analyte dilution typical of whole saliva, samples were processed using the automated Femtohunter chemiluminescent ELISA platform (detection threshold: 20 fg/μL). The interrogation involved a dual-cluster panel: a metabolic-proliferative cluster (EGFR, p53, Ki67) and an immunological cluster (PD-L1, HLA-E, B7-H6).

Results: significant molecular discrimination was observed, with the tumor core yielding a bioluminescent signal 213% higher than the contralateral healthy mucosa. Simultaneous overexpression of all six biomarkers occurred in 86.7% of neoplastic cases, with zero positivity in healthy controls (Wilcoxon Test: $p < 0.001$). Critically, molecular intensity proved independent of TNM staging; Stage I tumors exhibited expression profiles comparable to Stage IV, confirming the protocol's high sensitivity in early-stage disease.

Conclusions: the Cytobrush-Femtohunter platform enables “dynamic functional phenotyping” of oral lesions, bypassing the limitations of traditional liquid biopsy. This non-invasive tool represents a paradigm shift for outpatient triage and serial theranostic immunomonitoring, facilitating the interceptive management of oral malignancy.

VALIDATION OF A NEW MAXILLARY NERVE BLOCK TECHNIQUE: THE “BACCI-CERRATO-ZANETTE” APPROACH

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Aim: to validate a new maxillary nerve block technique, the “Bacci-Cerrato-Zanette” (BCZ) approach.

Methods: BCZ technique was compared with the established “High Tuberosity” (HT) technique. A total of 50 healthy adult patients scheduled for bilateral dental procedures involving the maxillary molars were enrolled in this randomized split-mouth clinical trial. Each patient underwent both techniques randomized in two separate sessions (one week apart). For each block a vial (1.8 mL) of 4% Articaine with epinephrine 5 mcg was administered using a 27-gauge, 38 mm needle. Pain perceived during needle insertion and anesthetic injection was assessed using a Visual Analog Scale for pain. Pulpal anesthesia was evaluated by using an electric pulp test, while soft tissue anesthesia was assessed using the pin-prick test. Post-injection complications were recorded.

Results: both techniques were successful in achieving pulpal anesthesia (80%-95%) for first and second molars and approximately efficacy for second premolars (80%). Neither technique provided profound pulpal anesthesia for anterior teeth and first premolars. Soft tissue anesthesia was effective up to the premolar region.

Conclusions: maxillary nerve block anesthesia enables the performance of extensive surgical procedures involving the entire maxilla. The HT technique, lacking specific anatomical landmarks, is technically demanding and remains limited to a small number of specialists, unlike mandibular nerve blocks which are widely practiced. In contrast, the BCZ technique is simple, reproducible, and facilitated by the presence of clear anatomical landmarks. Its only limitation appears to be posterior maxillary edentulism.

THE NEXT DIMENSION: EVALUATING ULTRASONOGRAPHIC RADIOMICS IN ORAL CANCER

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Aims: this study aimed to evaluate the role of ultra-high frequency ultrasonography (UHFUS) in characterizing key radiomic features of oral squamous cell carcinoma (OSCC), including depth of invasion (DOI), echogenicity, pattern of invasion, and vascularization.

Methods: consecutive patients with OSCC underwent intraoral UHFUS (48 MHz) prior to surgery. DOI was measured from the basement membrane to the deepest tumor point. Tumor echogenicity and the continuity of the invasion front were assessed to predict the worst pattern of invasion (WPOI). Vascular parameters, including Resistive Index (RI), Pulsatility Index (PI), Peak Systolic Velocity (PSV), and Time Averaged Peak Velocity (TAPV), were evaluated using Color Doppler. Histological analysis served as the reference standard.

Results: UHFUS demonstrated high accuracy in DOI assessment, particularly for lesions <4 mm (75% accuracy), outperforming MRI in this subgroup. A discontinuous invasion front on ultrasonography correlated with non-cohesive WPOI (Types 4-5) in 82.6% of cases. Vascular analysis revealed significantly elevated PSV and TAPV in infiltrating tumors, while RI and PI were significantly reduced, reflecting disorganized, low-resistance angiogenesis in aggressive lesions

Conclusions: UHFUS provides a reliable, non-invasive tool for preoperative OSCC characterization. It accurately assesses DOI, predicts invasive growth patterns, and quantifies tumor vascularity, offering valuable radiomic insights that complement traditional imaging and support personalized treatment planning.

MINOR SALIVARY GLANDS ULTRASONOGRAPHY IMPROVES LYMPHOMA DETECTION IN HIGH-RISK SJÖGREN DISEASE PATIENTS

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Aims: the most severe complication of Sjögren's disease (SD) is the development of non-Hodgkin lymphoma. Infiltrate characterization through minor salivary glands biopsy constitutes a prognostic factor, and a Focus Score (FS) ≥ 3 is the threshold for risk estimation. The aim of this study was to assess the potential benefit of minor salivary glands ultra-high frequency ultrasonography (UHFUS) in SD patients risk stratification and prognostic assessment, and the correlation with histology and serology.

Methods: patients with suspected SD underwent complete rheumatological evaluation and serological analysis. Minor salivary glands UHFUS assessed structural homogeneity. Color-Doppler was employed to quantify glandular vascularization. Minor salivary glands biopsy was performed in all patients for FS estimation.

Results: a total of 288 patients were included. Diagnosis of lymphoma was confirmed in 29 patients, with a mean development after 3.24 ± 1.72 years. FS ≥ 3 corresponded to an UHFUS pattern characterized by markedly hypoechoic lesions showing posterior enhancement, hyperechoic strands or septa and intense vascularization, with an increase in all Doppler parameters ($p < 0.05$). Cryoglobulinemia and low C4 on serology were noted in 60% and 75% of lymphoma patients respectively, compared with 4% and 8% found in SD patients.

Conclusions: UHFUS assessment of minor salivary glands may support the identification of patients at higher risk of lymphoma development, in conjunction with histology and serology.

PREDICTIVE ROLE OF IMMUNOHISTOCHEMICAL MARKERS IN ORAL POTENTIALLY MALIGNANT DISORDERS WITHOUT HIGH-GRADE DYSPLASIA

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Aim: this longitudinal study evaluated the predictive role of individual and combined immunohistochemical biomarkers (ki67, p53 and Podoplanin) in a study population of OPMDs without high-grade dysplasia.

Methods: a prospective cohort of 130 OPMDs without high-grade dysplasia, diagnosed between 2012 and 2025 and regularly followed, was included. Altered Ki-67 and p53 expressions were defined as staining in mature keratinocytes with >20% positive cells; p53 null expression was also considered altered. Podoplanin pattern >2 (Kawaguchi classification) was considered positive. A composite immunohistochemical score was calculated based on the number of positive markers and classified into four different risk-scores (0-1-2-3). Clinical and histological variables were also recorded.

Results: malignant transformation occurred in 13/130 patients (10%) after a mean follow-up of 43.96 ± 29.06 months. Univariate analysis identified mild dysplasia ($p = 0.005$), p53 overexpression ($p = 0.003$), podoplanin pattern >2 ($p = 0.04$), and a high combined score ($p = 0.002$) as significantly associated with increased risk of transformation. At multivariate analysis, only the combined score remained significantly associated.

Conclusions: in the present study, individual and combined immunohistochemical markers appear to be associated with malignant transformation of OPMDs without high-grade dysplasia. Further studies are warranted to standardize their expression and assessment and to develop a validated risk scoring system capable of appropriately weighting their potential prognostic value.

A LONGITUDINAL STUDY OF THE ORAL MICROBIOTA IN PATIENTS UNDERGOING ANTIRESORPTIVE THERAPY

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Aim: to assess whether bisphosphonate-based antiresorptive therapy affects microbiota of saliva, dental plaque and gingival crevicular fluid (GCF) in periodontally healthy patients; to explore oral microbiota profiling as a non-invasive monitoring tool.

Materials and methods: this observational study enrolled six polymorbid adults starting bisphosphonate therapy. Inclusion criteria required preserved salivary flow and periodontal stability, with Plaque Index and Bleeding on Probing <25%. Saliva, plaque and GCF samples were collected at baseline and after 30 days. Bacterial communities were analyzed by 16S rRNA gene sequencing. Bioinformatic analysis was performed using QIIME2 and DADA2, with taxonomic assignment using the SILVA v138 database. Alpha diversity was evaluated using observed genera and beta diversity using Bray-Curtis dissimilarity, PCoA, PERMANOVA.

Results: no significant microbiota changes were observed after 30 days of therapy in any oral niche. Streptococcus predominated in saliva and GCF, while plaque showed a heterogeneous community enriched in anaerobic genera Prevotella, Fusobacterium and Veillonella. Alpha diversity was highest in saliva, intermediate in plaque, lowest in GCF. Beta diversity was mainly related to oral niche rather than treatment timepoint.

Conclusions: in the present cohort early bisphosphonate therapy did not induce detectable oral dysbiosis within 30 days. Niche-specific microbial profiles were preserved. These findings support longitudinal oral microbiota monitoring; however larger cohorts and longer follow-up are needed to assess whether delayed microbiome changes predict complications such as MRONJ.

LONG-TERM CARE OF OLP PATIENTS: A RETROSPECTIVE STUDY FROM A SINGLE HOSPITAL OUTPATIENT CLINIC

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Aim: to characterize the natural history of oral lichen planus in a single-center cohort, documenting the longitudinal evolution of the disease over time, the therapeutic strategies employed, and the proportion of patients achieving a clinical response *versus* those refractory to treatment.

Methods: a retrospective cohort study was conducted including OLP patients followed from 2007 to 2024 at the Policlinico Universitario Agostino Gemelli. Demographic, clinical, microbiological, therapeutic, and histopathological data were collected. Logistic regression analyses were used to identify predictors of dysplasia and malignant transformation.

Results: a total of 246 patients were included (70.3% female;

mean age 63.2 years) with a mean follow-up of 55.5 months. *Candida* spp. colonization was more frequent in red-type OLP. During follow-up, 17.1% developed epithelial dysplasia, associated with older age, red phenotype and higher biopsy number. Malignant transformation to OSCC occurred in 3.25% of patients after a mean of 28 months. The only independent predictor of malignancy was prior dysplasia at the same site.

Conclusions: OLP shows a dynamic clinical course with frequent progression to dysplasia and occasional malignant transformation. Dysplasia represents the key step toward carcinoma, supporting the need for risk-adapted follow-up and early biopsy of suspicious lesions.

EFFICACY AND SAFETY OF RITUXIMAB IN ORAL *PEMPHIGUS VULGARIS* AFTER FAILURE OF CONVENTIONAL IMMUNOSUPPRESSIVE THERAPY

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Aim: oral lesions in pemphigus vulgaris (PV) are reported to respond less effectively to conventional immunosuppressive therapy (CIST). Rituximab (RTX), an anti-CD20 monoclonal antibody, is approved for refractory PV; however, studies evaluating its use in patients with predominantly oral involvement are limited. This study aimed to retrospectively assess RTX efficacy and safety in patients with oral PV.

Methods: 22 patients with oral PV and a follow-up of ≥ 6 months were included. Two groups were analyzed: 10 treated with CIST and 12 who received RTX (1000 mg 2 infusions 14 days apart) after CIST failure. The primary outcome was the achievement of complete clinical remission on minimal therapy (CROM) within 6 months. Secondary outcomes included CROM duration, cumu-

lative steroid dose at 6 months, and adverse events (AEs).

Results: in the RTX group, a statistically significant higher number of patients achieved CROM within 6 months compared to the CIST group (7/12 58% vs 1/10 10%, $p = 0.03$). The duration of CROM was superimposable between groups. AEs were observed in 7/10 patients in CIST group compared to 1/12 in RTX group ($p = 0.006$). The cumulative prednisone dose at 6 months was 2686.68 ± 1642.49 mg in the CIST group *versus* 1449.32 ± 999.80 mg in the RTX group ($p = 0.03$).

Conclusions: RTX was effective and safe as a rescue therapy in patients with oral PV after CIST failure. These findings suggest that RTX may be a suitable first-line treatment option also for patients with predominantly oral PV.

HPV-RELATED ORAL LEUKOPLAKIA: A CASE REPORT OF A DISTINCT SUBTYPE OF OPMD

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Aim: to report a case of HPV-related oral leukoplakia, highlighting the diagnostic role of histopathology and viral molecular mechanisms.

Methods: a 53-year-old male with tobacco and alcohol use presented with a non-homogeneous hyperkeratotic lesion of the ventral tongue and floor of the mouth, clinically consistent with leukoplakia. An incisional biopsy was performed.

Results: histology showed altered epithelial architecture with koilocytosis, apoptotic and karyorrhectic cells, and ballooning degeneration, suggestive of viral cytopathic effect. These features, typical of HPV-associated oral epithelial dysplasia (HPV-OED), differ from conventional OED and require further testing.

Molecular analysis confirmed high-risk HPV (types 18/45). HPV-OED is now recognized by WHO as a distinct entity, with basaloid morphology, expansion of the proliferative compartment, and frequent p16 overexpression. HPV-driven carcinogenesis, mediated by E6 and E7 targeting p53 and pRb, represents an alternative to the multistep model. The patient underwent surgical excision.

Conclusions: HPV-related oral leukoplakia may be clinically indistinguishable from typical forms. However, histological features such as koilocytosis and apoptosis should prompt mandatory HPV testing. Recognition of HPV-OED is essential to improve diagnostic accuracy and risk stratification, avoiding misclassification as conventional leukoplakia.

CLINICOPATHOLOGICAL PROFILE AND RISK FACTORS OF ORAL SQUAMOUS CELL CARCINOMA: A RETROSPECTIVE STUDY

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Aim: to investigate associations among demographic, behavioral, clinical and histopathological variables in order to better define the risk profile of oral squamous cell carcinoma (OSCC) patients.

Methods: a retrospective study was conducted on patients referred to the department between 2015 and 2024. Inclusion criteria comprised patients aged ≥ 18 years with confirmed diagnosis of OSCC. Extracted variables included age, gender, tobacco and alcohol exposure, HPV history, systemic diseases, presence of oral potentially malignant disorders (OPMDs) history, tumor site, and histological grading. Statistical analysis was performed to identify associations between variables.

Results: a total of 48 OSCC patients, most of them were older than 60 years. The tobacco exposure was frequently reported,

often exceeding 20 pack-years, while alcohol consumption and HPV history were less common. The tongue was the most frequently affected site and moderate histological differentiation (G2) represented the predominant histological grade. OPMDs, particularly oral lichenoid lesions, were present in a relevant proportion of patients. Patients without OPMDs tended to show higher histological grading, suggesting potentially more aggressive tumor behavior.

Conclusions: OSCC presents a heterogeneous risk profile characterized by advanced age, tobacco exposure, tongue involvement and moderate histological differentiation. The lower histological differentiation in OPMDs patients might be due to the increased clinical monitoring, highlighting the importance of regular follow-up for early detection.

IMPACT OF BOTULINUM TOXIN TYPE A ON QUALITY OF LIFE AND FUNCTIONAL RECOVERY IN PATIENTS WITH REFRACTORY OROFACIAL PAIN

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Aim: the study evaluates the efficacy and safety of Botulinum neurotoxin type A (BoNT-A) in improving oral health-related quality of life and reducing pain interference in daily activities in patients with refractory orofacial pain.

Materials and methods: a retrospective study was conducted at the University of Trieste Dental Clinic on patients with Persistent Idiopathic Dentoalveolar Pain. The protocol involved BoNT-A injections (30-70U) in extraoral or intraoral sites for patients with pain intensity NRS>3 (Numerical Rating Scale). The following outcomes were assessed at T0 (baseline) and after monthly intervals (T1, T2 and T3): pain intensity on NRS, Oral Health Impact Profile-14 (OHIP-14), Graded Chronic Pain Scale (GCPS), Quality of Mastication (QM) questionnaires, and a two-colour chewing-gum test.

Results: seven patients were enrolled. Treatment led to significant improvements: mean NRS decreased from 5.4 ± 2.1 (T0) to 3.0 ± 3.0 at T3 ($p < 0.05$). OHIP-14 scores dropped from 27.5 ± 10.9 to 6.5 ± 1.5 , indicating restored social and psychological well-being. GCPS scores showed a reduction in pain-related disability from 3.1 ± 1.0 to 1.0 ± 0.0 . QM scores improved from 14.5 to 4.5, enhancing nutritional and social confidence. No serious adverse events occurred; only one patient reported transient localized muscle hypotonia.

Conclusions: BoNT-A significantly reduces orofacial pain intensity and restores long-term functional capacity and quality of life. The decrease in OHIP-14 and GCPS scores confirms BoNT-A as a valid, safe therapeutic tool for the rehabilitation of refractory patients.

CUMULATIVE TOBACCO AND ALCOHOL EXPOSURE AS PREDICTORS OF AGGRESSIVE DISEASE PHENOTYPES AND SURVIVAL IN ORAL SQUAMOUS CELL CARCINOMA: A MULTICENTER RETROSPECTIVE STUDY

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Aim: to evaluate the association between cumulative tobacco and alcohol exposure and aggressive disease features and survival in patients with oral squamous cell carcinoma (OSCC).

Methods: this multicenter retrospective study included patients with OSCC from Spain, Italy, and Greece using a shared database. Patients were stratified by cumulative exposure: 0 (none), 1 (tobacco or alcohol), and 2 (both). Clinical and pathological variables included surgical treatment, recurrence, pathological stage, depth of invasion (DOI), and survival status. An aggressive phenotype was defined as ≥ 1 of the following: DOI ≥ 10 mm, pT3-T4 stage, recurrence, or disease-specific death. Outcomes were compared across exposure groups using descriptive analyses.

Results: a total of 613 patients were included, of whom 437 underwent surgery. Combined exposure (score 2) was ob-

served in 45.8% of patients. Recurrence occurred in 183 patients overall (29.9%) and in 129/437 (29.5%) surgically treated patients. A dose-response relationship was observed, with median DOI increasing from 6 mm (score 0) to 11 mm (score 2). Advanced stage (pT3-T4) was more frequent in patients with combined exposure (43.0% vs 23.5%), as was disease-specific death (43.2% vs 35.3%).

Conclusions: a higher cumulative exposure burden was associated with more aggressive disease features and worse outcomes. Patients with combined exposure and poorer oral health showed the highest prevalence of aggressive phenotypes, suggesting a potential synergistic effect. Tobacco exposure was associated with earlier recurrence in the subset with available data.

CLINICAL FEATURES OF OPMDs AND RISK OF MALIGNANT TRANSFORMATION: A 10-YEAR RETROSPECTIVE STUDY

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Aim: to assess the malignant transformation risk (MT) in patients with oral potentially malignant disorders (OPMDs) in relation to clinical presentation and lesion site.

Methods: a retrospective study was conducted on patients referred between 2014 and 2024. The department database was searched to identify patients aged ≥ 18 years with a confirmed diagnosis of OPMDs. Collected data included anamnestic information, tobacco and alcohol use, and lesion characteristics, including morphology and anatomical site, and presence of dysplasia and/or MT. All data were recorded on an Excel sheet. Patients were categorized based on the presence of dysplasia and clinical presentation (white vs red lesions). All variables were subsequently analyzed.

Results: a total of 143 OPMDs patients (87 females, 56 males; mean age 61.4 years) were included. A significantly

higher risk of MT was observed in patients with red lesions ($p = 0.042$) and dysplasia ($p = 0.011$), particularly in erosive-atrophic forms, smokers ($p = 0.037$), and those with concomitant diseases ($p = 0.015$). Among white lesions, verrucous form (55.8%) appeared associated with MT. Patients with red lesions showed a greater number of clinical features ($p = 0.001$) and involved sites ($p = 0.008$). The buccal mucosa and gingiva were the most affected sites in both red and white lesions, while the tongue was the most affected site in cases of MT.

Conclusions: this study shows that OPMDs patients — particularly smokers with red, dysplastic lesions and comorbidities — have a higher risk of MT, underscoring the need for close monitoring and early intervention.

TONGUE SUBSITE DRIVES AGGRESSIVE BEHAVIOR IN ORAL SQUAMOUS CELL CARCINOMA

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Aim: this study investigates the association between the anatomical site of oral squamous cell carcinoma (OSCC) and adverse histopathological features, aiming to determine whether tumor location can serve as a predictor of tumor aggressiveness.

Methods: this retrospective multicenter Italian study included 99 patients with histologically confirmed oral squamous cell carcinoma (OSCC). Tumors were classified as tongue ($n = 44$, 44%) and non-tongue ($n = 55$, 56%). Primary outcomes were lymph node metastasis (pN+), lymphovascular invasion (LVI), and perineural invasion (PNI). Secondary outcomes included local, regional, and distant metastasis. Associations were assessed using descriptive analyses and logistic regression models.

Results: tongue tumors showed a higher prevalence of ag-

gressive features, including lymph node metastasis (61% vs 40%, $p = 0.03$), LVI (34% vs 22%), and PNI (41% vs 27%). In multivariable analysis, tongue location remained independently associated with lymph node metastasis (OR 2.3; 95% CI, 1.1-5.0) and showed a trend toward increased PNI. Regional recurrence and distant metastasis were more frequent in tongue tumors, while local recurrence rates were similar between groups.

Conclusions: tumors arising in the tongue are associated with increased nodal involvement and a higher risk of regional and distant progression. These findings support anatomical site as a clinically relevant factor in OSCC risk stratification. Incorporating tumor location into prognostic assessment may improve individualized management and inform treatment planning.

A RETROSPECTIVE ANALYSIS OF RADIOLOGICAL FINDINGS OF MRONJ IN PATIENTS WITH COMPROMISED TEETH

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Aim: to evaluate the radiological findings of MRONJ in patients receiving bone-modifying agents (BMAs) who underwent dental extractions.

Materials and methods: patients were enrolled at the Oral Medicine Unit (University Hospital P. Giaccone of Palermo) and underwent clinical-radiological evaluation (E. C. #1/2022).

In the presence of teeth with poor prognosis, a standardized medical-surgical protocol was applied, associated with alveolar bone biopsies. In patients with a histological diagnosis of MRONJ, the radiological preoperative images were retrospectively analyzed.

Results: ten patients were included, of whom 5 were assuming high-dose BMAs (HD-BMAs) and 5 low-dose BMAs (LD-BMAs). The mean duration of therapy with HD-BMAs was 14.4 ± 4.8 months, and with LD-BMAs was 124.8 ± 170 months.

Ten teeth were extracted, 8 for periodontal disease and 2 for decay. Periodontal space widening was observed in all orthopantomography; on CBCT, the most common radiological finding was periodontal space widening (100%), followed by cortical erosion (80%), focal bone marrow sclerosis (50%), and diffuse bone marrow sclerosis (30%). No bone exposure was observed. Based on clinical-radiological features, MRONJ cases were classified into stage 1 and stage 2 in 7 and 3 cases, respectively.

Conclusions: the present study shows that MRONJ was already present at the time of dental extraction and suggests that the surgical act does not turn out to be responsible for the pathology. Additionally, in the presence of compromised teeth, radiological findings should be evaluated to diagnose early stages of MRONJ.

RADIOLOGICAL FEATURES OF STAGE II MRONJ: A COMPARATIVE STUDY OF HIGH-DOSE BISPHOSPHONATE- AND DENOSUMAB-RELATED CASES

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Aim: Medication-related osteonecrosis of the jaw (MRONJ) is a drug-related adverse reaction that requires radiological imaging for diagnosis and staging. Recent studies suggest agent-specific radiographic patterns in MRONJ. This study aimed to compare radiological findings in patients treated with high-dose bisphosphonate (HD-BP) *versus* high-dose denosumab (HD-DMB) to identify potential drug-related jawbone differences and improve MRONJ management.

Methods: patients with stage II of MRONJ were enrolled at the Unit of Oral Medicine and Dentistry for Frail Patients (A.O.U.P. P. Giaccone, Palermo), over the last three years. MRONJ staging followed SIPMO-SICMF clinical-radiological recommendations. Maxillofacial CT and CBCT scans were independently and blindly evaluated by two radiologists, each with > 5 years of experience, with excellent interobserver agreement ($\kappa > 0.90$).

Results: twenty patients were evaluated, 10 in the HD-BP group (5 females, 5 males; mean age 76.2 ± 5.2 years) and 10 in the HD-DMB group (8 females, 2 males; mean age 69.5 ± 12.1 years). Median therapy duration before MRONJ onset was 23 months in the HD-BP group and 21 months in the HD-DMB group. Among the SIPMO-SICMF radiological signs assessed, cortical erosion (80% in HD-BP vs 20% in HD-DMB; $\chi^2 p = 0.011$) and sequestrum formation (70% vs 10%; $\chi^2 p = 0.009$) were significantly more frequent in HD-BP patients.

Conclusions: these preliminary findings suggest possible distinctive radiological differences between HD-BP and HD-DMB-related MRONJ. Future research on larger cohorts, potentially supported by artificial intelligence, could aim to confirm drug-specific radiological patterns, identify additional differences in radiological signs and improve early diagnosis.

TOWARDS AI-ASSISTED ORAL CANCER SCREENING: MULTI-CLASS CLASSIFICATION OF ORAL MUCOSAL LESIONS USING EXPLAINABLE FINE-TUNED DEEP CONVOLUTIONAL NEURAL NETWORKS ON INTRAORAL PHOTOGRAPHS

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Aim: Oral potentially malignant disorders (OPMDs) are commonly encountered during routine examination, but delayed referral worsens patient prognosis. This study aimed to develop an explainable deep learning system for multi-class classification of oral mucosal lesions from intraoral photographs, providing dental clinicians with an AI-assisted triage tool to distinguish between benign and potentially malignant lesions.

Methods: a dataset of 734 expert-annotated intraoral photographs across 10 diagnostic categories (leukoplakia, erythro-leukoplakia, OLP, ulcers, candidiasis, fibroma, epulis, geographic tongue, linea alba, healthy mucosa) was preprocessed with Reinhard normalization at 224×224. Four pre-trained architectures (ResNet-50, EfficientNet-B0, ConvNeXt-Tiny, ViT-B/16) were fine-tuned with class-balanced augmentation and MixUp, using 5-fold cross-validation.

Clinical utility was further evaluated on a 3-level triage task (Green: no referral; Yellow: other referral; Red: biopsy referral) and on binary biopsy-referral detection. Explainability was provided by Grad-CAM and Attention Rollout.

Results: ConvNeXt-Tiny achieved the best performance across all tasks: 10-class classification (accuracy 70%, macro-F1 0.72, AUC 0.94), 3-level triage (accuracy 89%, macro-F1 0.86, macro-AUC 0.97), and binary biopsy-referral detection (sensitivity 92.5%, specificity 87.6%, AUC-ROC 0.96). Saliency maps confirmed lesion-focused attention.

Conclusions: deep learning on intraoral photographs provides clinically meaningful support for biopsy-referral decisions across a broad spectrum of oral conditions. Dataset expansion and integration with intraoral scanning systems represent the next steps toward clinical translation.

MEDICATION-RELATED OSTEONECROSIS OF THE JAW: EXPERIENCE FROM THE DENTAL CLINIC AT THE MODENA HOSPITAL

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Aim: this study aimed to collect and analyze clinical data on MRONJ in cancer patients treated with antiresorptive or antiangiogenic drugs in the Modena area. Data were collected from January 2020 to September 2024 at the PDTA outpatient clinic of the Dental Clinic of the University Hospital of Modena, to assess the impact of current diagnostic and therapeutic approaches on patients' quality of life.

Methods: a retrospective database was created using Microsoft Excel, ensuring anonymity through alphanumeric codes. Inclusion criteria were cancer patients of any age and sex diagnosed with MRONJ during the study period, associated with high-dose therapies. Exclusion criteria included non-drug-related osteonecrosis, prior MRONJ diagnosis, low-dose therapies, previous head and neck radiotherapy, and in-

complete documentation. Patients underwent clinical and radiographic evaluation.

Results: 60 patients were evaluated; 10 were excluded, leaving 50 patients with 69 MRONJ sites. Surgery was indicated in 42 sites (60.87%), with 37 treated during the study period. Total resection (30 cases, 81%) showed a high healing rate (29/30). Partial resection (7 cases) resulted in 5 healed and 1 stable site, only one recurrence was observed. All surgical patients received adjunctive medical therapy. Among 27 non-surgical sites, 12 remained stable, 1 worsened, 2 were lost to follow-up, and for 13 cases patients died before outcome assessment.

Conclusions: both approaches appear effective when individualized. Less invasive strategies may offer a balance between treatment efficacy and quality of life.

PREVALENCE AND RISK FACTORS OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW IN BREAST AND PROSTATE CANCER PATIENTS WITH CANCER TREATMENT-INDUCED BONE LOSS

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Aim: the study aims to evaluate the incidence of Medication Related Osteonecrosis of the Jaw (MRONJ) in breast (BC) and prostatic (PC) patients received low dose bone modifying agents (BMAs), such as Bisphosphonate (BP) and Denosumab (DN).

Methods: the retrospective study included 51 BC and 30 PC patients, diagnosed with MRONJ on the Department of Surgical and Special Dentistry, Marche General Hospital, Italy, between 2010-2024. Clinic-pathological data and staging were collected according to SIPMO-SICFM criteria.

Results: 62% of MRONJ occurred in BP patients, about 44.0 ± 36.5 months from the beginning of therapy. In BP patients, the cumulative dose was significantly higher in BC respect to PC group (2886.8 ± 7177.6 vs 514.3 ± 1697.3). Compared to BP groups, the onset of MRONJ was significantly early in DN pa-

tients (18.6 ± 14.8 months), both in BC (45.7 ± 39.3 vs 23.3 ± 20.2) and PC patients (40.4 ± 30.6 vs 14.4 ± 8.3). In both groups, posterior mandible (56.8%) was the most involved site, complaining with pain and abscess/fistula (74%). In BC, stage 1 cases were significantly higher than PC (22 vs 8). Periodontal disease was the most frequent local risk factor. Chemotherapy, smoker and hypertension were the mostly systemic comorbidities. Relapses occurred in 26% of cases after 18.0 ± 19.2 months, without significant differences between the two groups.

Conclusions: based on the SIPMO- SIOMMS guidelines, specific strategies for MRONJ prevention in BC and PC patients should be adopted. Moreover, personalized approaches should be considered when patients develop bone metastases and are switched to high dose BMAs.

OSTEONECROSIS OF THE JAW IN ACUTE MYELOID LEUKEMIA: REPORT OF TWO ATYPICAL AND RARE CASES

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Aim: the aim was to report two cases of Osteonecrosis of the Jaws (ONJ) in patients affected by Acute Myeloid Leukaemia (AML) underwent chemotherapeutic treatment before receiving Hematological Stem Cell Transplantation (HSCT).

Methods: two female patients (47 and 23 yo) with AML treated with induction therapy (cytarabine and daunorubicin regimen) developed oral complications which, according to clinical, haematological and radiological (CT) evaluation, were consistent with maxillary osteonecrosis.

Results: case 1 presented gingival mucosal hyperemia, ulceration, mobility of teeth 1.1-1.2, and bone exposure in the right premaxilla. Case 2 presented left maxilla tumefaction associated with failed root canal treatment of teeth 2.5-2.6, and a bone sequestrum with sinus empyema. Neither patient

had a history of treatment with bone modifying agent or anti-angiogenic agent. Both were treated with antibiotics and antiseptics, followed by the surgical marginal resection of the necrotic bone. At 1 month follow-up, the patients showed good healing. Thus, the patients resume induction chemotherapy before HSCT.

Conclusions: chemotherapy is a critical factor in the development of ONJ: its cytotoxic effect is part of ONJ multifactorial pathogenesis in which a compromised immune system and tissue hypoxia create an extremely vulnerable microenvironment. This observation suggests that ONJ should be considered a broader pathological entity in medically complex patients even without classical MRONJ pharmacological triggers.

PLAQUE-TYPE ORAL LICHEN PLANUS AND PROLIFERATIVE VERRUCOUS LEUKOPLAKIA: A CASE SERIES AND RETROSPECTIVE ANALYSIS OF CLINICO-PATHOLOGICAL FEATURES

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Aim: the relationship between plaque-type oral lichen planus (OLP) and proliferative verrucous leukoplakia (PVL) remains unclear. This retrospective case series evaluated the clinical and histopathological evolution of patients initially diagnosed with plaque-type OLP and possible progression to PVL.

Methods: clinical records of patients diagnosed with plaque-type OLP between 2008 and 2025 were reviewed, excluding other forms. Patients were divided into two groups: Group 1 remained clinically stable, while Group 2 developed PVL lesions on an OLP background. Demographic, clinical, and histopathological data were collected.

Results: fifteen patients were included: Group 1 (n = 6) comprised 4 females and 2 males, mean age 55.6 years; Group 2 (n = 9) included 7 females and 2 males, mean age 72.6 years.

One patient in Group 2 developed malignant transformation. Clinically, Group 1 showed bilateral, symmetrical lesions, whereas Group 2 presented an asymmetrical, multifocal pattern. Histopathologically, Group 1 mainly showed typical OLP features, while Group 2 more often exhibited nonspecific findings, such as squamous hyperplasia with lichenoid infiltrate.

Conclusions: the potential relationship between plaque-type OLP and PVL remains uncertain. These findings highlight the importance of long-term clinical and histopathological follow-up. As a future clinical application, follow-up strategies could be tailored according to initial clinical and histopathological features. Further studies are warranted to better investigate the correlation between these entities and clarify their biological behavior and evolution.

PERI-IMPLANTITIS INDUCED MEDICATION-RELATED OSTEONECROSIS OF THE JAW: CLINICAL, RADIOLOGIC, HISTOPATHOLOGICAL AND TREATMENT FEATURES OF 59 CASES

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Aim: the aim of the present study is to report a case series of patients with peri-implantitis induced medication-related osteonecrosis of the jaw (MRONJ), describing the clinical and radiologic features of the condition and the surgical treatment outcome.

Methods: fifty-nine consecutive patients with clinical diagnosis of peri-implantitis associated with MRONJ were retrospectively included in the study. Surgical treatment was performed with a standardized operative protocol, involving implant removal, sequestrectomy, debridement of soft tissue, and bone curettage. Follow-up evaluating surgical outcome was performed at 12 months after surgery.

Results: patients were almost equally distributed in terms of underlying diseases in osteoporotic and oncologic patients. All

MRONJ lesions were symptomatic, and in 15 patients bone exposure was detected. In total, 163 implants were evaluated, with MRONJ being present around 95 implants. Thirty-two patients were diagnosed with Stage III MRONJ, and twenty patients with Stage II MRONJ. Surgical treatment led to complete healing in 83.1% of cases, with 100% success for maxillary MRONJ.

Conclusions: the clinical signs of peri-implantitis may reveal the presence of an underlying MRONJ diagnosis in patients under pharmacological treatment with anti-resorptive/antiangiogenic drugs. Surgical treatment seems to have a positive impact on MRONJ treatment in cases of peri-implant involvement.

ORAL SQUAMOUS CELL CARCINOMA IN PATIENTS WITHOUT TRADITIONAL RISK FACTORS: A CASE SERIES

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Aim: to describe oral squamous cell carcinoma (OSCC) cases in patients without traditional risk factors and highlight a possible shift in its epidemiological pattern.

Methods: patients attending the Oral Medicine Unit V. Margiotta, University Hospital P. Giaccone (Palermo), from January 2025 to January 2026 with a diagnosis of OSCC and no conventional risk factors (tobacco or alcohol) were included (Ethical Committee #11/2020). All patients provided written informed consent. Demographic and clinical data, including tumor location, were collected. MRI and incisional biopsy were performed. Patients were referred to Plastic Surgery and Oncology Units for management.

Results: a total of 12 patients were included (6 males/6 females). Mean age was 69.3 ± 18.1 years, with females older

than males (76.3 vs 62.3 years). A gender-related difference in tumor distribution was observed. In males, lesions mainly involved the lateral tongue (66.7%). In females, tumor sites were more heterogeneous, with the lateral tongue most frequently affected (33.5%), followed by lower gingival mucosa, palate, anterior floor of the mouth, and buccal mucosa. All patients lacked conventional risk factors. These findings may suggest distinct pathogenic pathways, possibly involving age-related, inflammatory, or viral mechanisms.

Conclusions: these findings suggest a changing pattern of OSCC, with increasing occurrence in patients without traditional risk factors and variable anatomical distribution. Further studies are needed to clarify underlying mechanisms and support early diagnosis regardless of risk profile.

THE ROLE OF THE DENTIST IN THE EARLY DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE: A CASE SERIES

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Aim: Inflammatory bowel diseases (IBDs), particularly Crohn's disease (CD), are chronic inflammatory disorders of gastrointestinal tract that may involve extra-intestinal sites, including the oral cavity. Oral lesions may represent an early sign of these diseases and precede the intestinal symptoms. The exact etiology of CD is still unclear, it might be an interaction between genetic predisposition, immune dysregulation, alterations of the intestinal microbiota and environmental factors. This case series aimed to present three cases in which oral manifestation led to an early diagnosis of IBDs.

Methods: three patients were referred to the department for presence of erythematous lesions with heterogeneous clinical aspects. Incisional biopsies were performed using two different surgical approaches: combined laser-scalpel technique, and conventional scalpel technique.

Results: from the patients' anamnestic data and histopathological findings, the patients were referred for further gastrointestinal assessment. In all three cases, the dentist played a crucial role in the suspicion of the presence of underlying IBDs and to initiate the diagnostic pathway. The multidisciplinary approach led to the definitive diagnosis through the histopathological examination of the oral lesions and the gastrointestinal investigations.

Conclusions: this case series highlights the key role of the dentist in the diagnosis of IBDs, particularly CD. Careful oral examination, well-timed biopsy, and appropriate referral may significantly contribute to an early diagnosis and improved multidisciplinary management.

COMPARISON OF KERATINOCYTE FOOTPRINT ASSAY AND BIOCHIP MOSAIC ASSAY FOR DETECTING ANTI-LAMININ-332 AUTOANTIBODIES IN MUCOUS MEMBRANE PEMPHIGOID

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Aim: to compare the performance of keratinocyte footprint assay and biochip assay for the detection of anti-laminin-332 autoantibodies in patients with mucous membrane pemphigoid (MMP).

Methods: six patients with MMP and primary oral mucosal involvement were evaluated by histological examination, direct immunofluorescence (DIF), salt-split skin indirect immunofluorescence (IIF), and ELISA for BP180/BP230 antibodies. Sera from the same patients were then tested using the Euroimmun Anti-Laminin 332 (LAM332) IIFT biochip assay and a native laminin-332 keratinocyte footprint assay.

Results: all 6 patients showed linear IgG deposition along the basement membrane zone on DIF, associated with additional

immunoreactants. Salt-split skin indirect immunofluorescence, available for five patients, showed roof binding in all evaluable sera. ELISA was positive in 50% of cases. None of the sera showed reactivity in the biochip assay, whereas 1/6 showed clear reactivity in the footprint assay.

Conclusions: in this preliminary cohort, the keratinocyte footprint assay showed a higher detection rate than the biochip assay. Although limited by the small sample size and the absence of a larger anti-laminin-332-positive series, these findings are consistent with previous reports and support further evaluation of both assays in larger, well-characterized cohorts, with potential implications for earlier serological identification of patients requiring malignancy screening.