CURRENT PERSPECTIVES IN HEALTH SCIENCES

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General Director: Berkan Balpetek
Cover and Page Design: Duvar Design
Printing : July-2026
Publisher Certificate No: 49837
E-ISBN:978-625-8936-31-5

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Chapter 1

Beyond HLA Matching in Transplantation Through Eplet Analysis, Molecular Matching, and Immunological Risk Assessment

Gözde ÖZTAN[1]

ABSTRACT

Conventional human leukocyte antigen (HLA) matching classifies donor-recipient compatibility according to the number of antigen- or locus-level mismatches; however, donor-recipient pairs with the same mismatch count may have markedly different alloimmune risks. This observation has prompted the development of molecular matching approaches that assess structural and functional disparities relevant to transplantation immunology. Eplet analysis estimates B-cell-associated immunogenicity by identifying small clusters of amino acids on donor HLA molecules that are accessible to antibodies. Amino-acid-level mismatch algorithms evaluate donor-recipient differences within a broader structural framework, whereas the Predicted Indirectly Recognizable HLA Epitopes (PIRCHE-II) approach estimates the likelihood that donor-derived HLA peptides will be presented by the recipient's HLA class II molecules and elicit indirect CD4+ T-cell help. In particular, HLA-DR and HLA-DQ molecular mismatch burdens have been associated with de novo donor-specific antibody development, antibody-mediated rejection, and graft loss in multicenter cohorts. Nevertheless, strong correlations among algorithms, the absence of universal thresholds, HLA typing or imputation errors, population diversity, the limited number of antibody-verified eplets, and the modifying effects of adherence to immunosuppressive therapy currently limit the routine clinical implementation of these approaches. This chapter reviews the concepts of epitopes, eplets, amino acid mismatches, and PIRCHE-II, together with the relevant computational tools, available clinical evidence, and laboratory requirements. It also discusses potential applications in organ allocation, donor selection, and post-transplant monitoring, as well as current standardization and ethical considerations.

Keywords: HLA, eplet, molecular mismatch, HLAMatchmaker, HLA-EMMA, PIRCHE-II, donor-specific antibody, antibody-mediated rejection, graft survival

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1. INTRODUCTION

Successful long-term graft survival depends on an accurate and comprehensive assessment of immunological compatibility between the donor and recipient. Traditionally, histocompatibility assessment has relied on counting HLA-A, HLA-B, and HLA-DR antigen mismatches. This approach remains important in transplantation practice, particularly in deceased-donor organ allocation, because it is rapid, readily interpretable, and supported by decades of clinical experience. Nevertheless, conventional antigen mismatch counts do not fully capture the extensive genetic and structural polymorphism of HLA molecules and implicitly treat different mismatches as having equivalent immunogenic effects. In reality, individual HLA mismatches may differ in their likelihood of recognition by the recipient immune system, the magnitude of the alloimmune response they induce, and their contribution to clinical outcomes [1, 2].

Under conventional matching systems, two donor-recipient pairs with the same number of HLA antigen mismatches may be considered to carry equivalent immunological risk. However, pairs with identical antigen mismatch counts can have substantially different alloimmune risk profiles because of differences in the three-dimensional HLA surface, the distribution of antibody-accessible amino acids, and the processing of donor-derived HLA peptides by the recipient's antigen-presentation system. Specific amino acid clusters on donor HLA molecules may be recognized by B-cell receptors and anti-HLA antibodies, whereas peptides derived from donor HLA proteins may be presented to CD4+ T cells by recipient HLA class II molecules. In addition, immune memory acquired through previous transplantation, pregnancy, or blood transfusion may cause the same molecular mismatch to produce different clinical consequences in different recipients [3-5].

These observations indicate that transplantation immunology must address more than the question, "How many HLA mismatches are present?" Contemporary histocompatibility assessment also considers which HLA loci are mismatched, which amino acids differ between donor and recipient molecules, whether these differences are exposed on the HLA surface and accessible to antibodies, and whether donor-derived peptides can stimulate recipient T-cell responses. HLA mismatch is therefore increasingly viewed not as a categorical variable defined solely at the antigen or locus level, but as a multidimensional biological characteristic encompassing both B-cell and T-cell alloreactivity [3-5].

Molecular HLA mismatch assessment seeks to transform conventional antigen-level matching into a more detailed and continuous measure of biological risk. The principal approaches include eplet mismatch load, amino acid mismatch counts, measures of electrostatic or hydrophobic disparity, and computational tools such as HLA-EMMA and PIRCHE-II. Eplet analysis identifies small polymorphic amino

acid configurations on the HLA surface that may contribute to antibody binding and quantifies eplets present in the donor but absent from the recipient. Amino-acid-based methods assess overall sequence differences or their distribution within selected structural regions. Electrostatic and hydrophobic mismatch analyses additionally consider the physicochemical properties of amino acid substitutions that may influence antigen-antibody interactions [5-8].

PIRCHE-II addresses a different dimension of molecular mismatch by estimating whether peptides derived from donor HLA molecules can bind to recipient HLA class II molecules and be presented to CD4+ T cells. Thus, eplet analysis primarily characterizes structural disparities relevant to B-cell and antibody recognition, whereas PIRCHE-II estimates the potential for indirect T-cell allorecognition. HLA-EMMA and related methods further characterize molecular disparity by mapping amino acid mismatches to antibody-accessible regions of HLA molecules. These approaches should therefore be regarded as complementary rather than interchangeable, because they represent distinct but interconnected components of the alloimmune response [5-8].

The strongest clinical evidence for molecular HLA mismatch assessment comes from kidney transplantation. Numerous observational studies have shown that a high molecular mismatch burden, particularly at HLA class II loci, is associated with primary alloimmunity. Eplet and amino acid mismatches at HLA-DR and especially HLA-DQ have been linked to the development of de novo donor-specific anti-HLA antibodies after transplantation. The emergence of de novo donor-specific antibodies (dnDSA) is, in turn, closely associated with microvascular inflammation, antibody-mediated rejection (ABMR), transplant glomerulopathy, and long-term graft dysfunction [9-13].

The clinical prominence of HLA-DQ mismatches is partly explained by the polymorphism of both the alpha and beta chains and by the numerous heterodimers that different chain combinations can form. This structural diversity may create clinically relevant molecular disparities that are not apparent in conventional antigen-level assessment. Consequently, donor-recipient pairs with the same number of HLA-DQ antigen mismatches may have markedly different eplet or amino acid mismatch burdens. The association of a higher HLA-DQ molecular mismatch burden with dnDSA, ABMR, and graft failure suggests that molecular matching may identify long-term immunological risk more precisely than conventional antigen mismatch counts [9-13].

The role of molecular HLA scores in clinical practice nevertheless requires cautious interpretation. Much of the available evidence is derived from retrospective or observational cohorts, and centers differ in HLA typing resolution, mismatch algorithms, software versions, and definitions of clinical outcomes. Moreover, the

assumption that every eplet or amino acid difference contributes equally to the total molecular mismatch burden has not been conclusively validated. Some motifs may elicit strong and reproducible antibody responses, whereas others may have limited immunogenic potential or become clinically relevant only in particular recipient HLA backgrounds [14, 15].

Interpretation of molecular mismatch scores must also account for the recipient's immunological history, pre-existing or de novo DSA profile, adherence to immunosuppressive therapy, transplant type, donor characteristics, and graft biopsy findings. Molecular matching should therefore not replace established clinical and laboratory assessments; instead, it should serve as a risk-stratification tool that complements HLA typing, anti-HLA antibody testing, virtual or physical crossmatch, graft function assessment, and histopathological examination. Universal thresholds and standardized algorithms are not yet available to support the use of molecular scores alone to accept or decline donor offers, allocate organs, adjust immunosuppression, or determine the need for biopsy [14, 15].

Integrating molecular HLA matching into organ allocation also raises ethical and logistical considerations. Selecting donors with a lower molecular mismatch burden may reduce dnDSA development and long-term graft loss, particularly in younger recipients. Conversely, rigid allocation based solely on optimal molecular matching could prolong waiting times for recipients with rare HLA genotypes and worsen inequities in organ access across ethnic or genetic groups. The potential clinical benefit of molecular matching must therefore be balanced against organ availability, waiting-list mortality, equitable access, and existing allocation priorities [14, 15].

This chapter aims to explain molecular mismatch concepts that extend beyond conventional HLA antigen matching; compare the biological foundations of eplet analysis, amino-acid-based assessment, HLA-EMMA, and PIRCHE-II; and evaluate the evidence supporting their use in predicting post-transplant alloimmune risk. It also discusses how molecular matching results are generated and interpreted in laboratory practice, the circumstances in which they may inform donor selection and long-term risk stratification, and the remaining challenges related to standardization and ethical implementation. The objective is to provide a balanced framework that recognizes the potential of molecular HLA assessment while acknowledging unresolved questions and the limitations of using these methods as stand-alone clinical decision tools.

2. LIMITATIONS OF CONVENTIONAL HLA MATCHING

Conventional HLA matching is based on serologically defined antigen groups or low-resolution HLA types. Although this approach captures broad and clinically relevant differences, it does not reveal amino acid diversity among alleles within the

same antigen group or the variation in structural immunogenicity among apparently equivalent antigen mismatches [1, 4]. Polymorphic residues within HLA molecules shape peptide binding, T-cell receptor contact surfaces, and external surfaces accessible to antibodies. Consequently, a single antigen mismatch may contain a variable number of amino acid motifs that are absent from the recipient's HLA repertoire. This molecular variability helps explain why donor-recipient pairs with the same number of locus-level mismatches may have different risks of dnDSA and rejection [3, 6, 9].

Conventional matching also captures locus-specific risk only incompletely. Because HLA-DQ is a heterodimer formed by polymorphic alpha and beta chains, DQA1 and DQB1 alleles should be evaluated together. The repeated association of HLA-DQ eplet mismatches with dnDSA and ABMR suggests that assessment based only on HLA-DR or broad antigen groups may be insufficient [9-12]. Conventional matching should not, however, be abandoned: antigen mismatch counts are readily applicable in organ allocation, transferable across laboratories, and supported by extensive historical data. The most rational strategy is to complement this established framework with a high-resolution, context-sensitive molecular risk layer rather than to replace it [14, 15].

3. IMMUNOLOGICAL BASIS OF EPITOPES AND EPLETS

3.1. Epitopes, eplets, and antibody accessibility

An epitope is the three-dimensional antigenic surface recognized by the paratope of an antibody. HLA epitopes are not necessarily linear peptide sequences; they may be formed by amino acid residues that become spatially adjacent after the molecule folds. An eplet is an operational concept used in the HLAMatchmaker framework to describe a small configuration of polymorphic amino acids located within approximately 3 Å of a central polymorphic residue involved in antibody contact [3, 16].

An eplet present on donor HLA molecules but absent from the recipient's HLA repertoire may theoretically constitute a foreign B-cell target. However, not every predicted eplet is equally immunogenic. Surface accessibility, electrostatic properties, neighboring residues, HLA expression, antigen abundance, the availability of T-cell help, and the recipient's immune history all influence whether an antibody response develops [16-18]. Antibody-verified eplets have gained experimental support from human monoclonal antibodies or detailed antibody-specificity patterns. Although such verification provides stronger biological evidence than theoretical geometry alone, currently verified eplets represent only a fraction of overall HLA diversity [17, 18].

3.2. Integrated evaluation of B- and T-cell responses

Recognition of a donor HLA eplet by a B cell generally requires cognate help from CD4+ T cells activated through indirect allorecognition to generate a high-affinity, class-switched antibody response. Recipient antigen-presenting cells process donor HLA proteins, present the resulting peptides on the recipient's HLA class II molecules, and activate the corresponding T-cell clones. This biological cooperation explains why eplet-based approaches that estimate B-cell targets and PIRCHE-II, which estimates T-cell presentation potential, may provide complementary information [7, 8, 19, 32].

Molecular mismatch models do not establish causality; they estimate potential antigenic disparity and peptide presentation. A high score does not mean that DSA will inevitably develop, and a low score does not imply zero risk. Immunosuppression intensity, drug exposure, treatment adherence, infection, and inflammation strongly modify the phenotypic expression of molecular risk, as illustrated in Figure 1 [10, 20, 21].

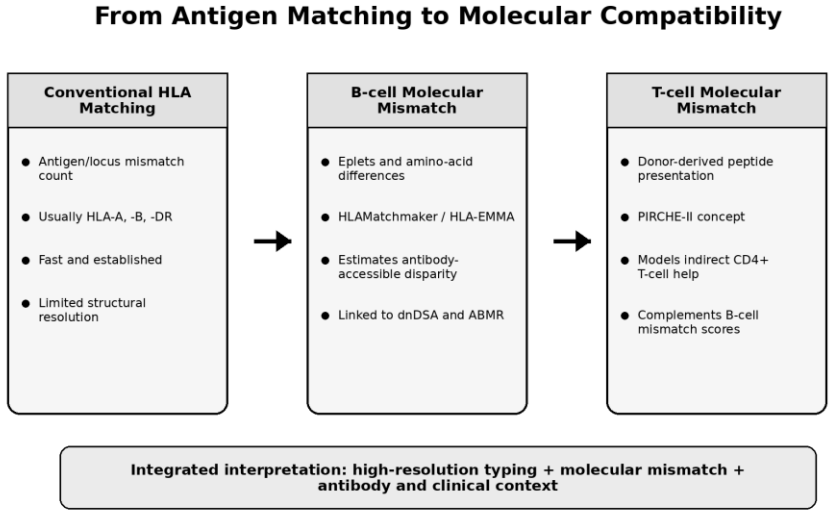

Figure 1. From antigen matching to molecular compatibility. The figure compares conventional antigen-level matching with B-cell-oriented molecular mismatch and T-cell-oriented indirect recognition models. Integrated interpretation requires high-resolution HLA typing and clinical context.

4. MOLECULAR MATCHING METHODS

4.1. HLAMatchmaker and eplet mismatch load

HLAMatchmaker identifies eplets present on donor HLA molecules but absent from the recipient's HLA repertoire. Results may be reported as the total number of eplet mismatches at the locus, chain, or single-molecule level and,

where appropriate, as the antibody-verified eplet mismatch load. The single-molecule approach evaluates the mismatch burden contributed by each donor HLA-DR or HLA-DQ molecule rather than relying only on the total class II load [9, 11, 16].

Multiple studies have reported a dose-response relationship between HLA-DR/DQ eplet mismatch load and dnDSA development. For HLA-DQ in particular, antibody-verified eplet mismatch load has been associated with dnDSA, T-cell-mediated rejection, ABMR, and graft loss [9, 10, 12]. However, several cohorts have not identified an absolute threshold below which risk is absent; instead, risk appears to increase continuously with mismatch load [9].

4.2. Amino acid-level mismatch and HLA-EMMA

HLA-EMMA is a user-friendly molecular mismatch tool that calculates solvent-exposed amino acid differences between donor and recipient HLA molecules from high-resolution typing data. It identifies polymorphic residues that are present in the donor but absent from the recipient and located on HLA surface regions potentially accessible to antibodies. Unlike eplet analysis, HLA-EMMA is not restricted to predefined geometric amino acid configurations and can therefore evaluate all accessible polymorphic residues. The tool supports comparisons of both HLA class I and class II molecules, including HLA-DR, HLA-DQ, and HLA-DP [6].

A higher amino acid mismatch burden suggests that the recipient immune system may recognize a greater number of molecular structures as foreign. Nevertheless, not every solvent-exposed amino acid difference is equally antigenic or immunogenic. The position and physicochemical properties of a residue, the three-dimensional configuration formed with neighboring residues, and the presence of structurally similar motifs within the recipient's HLA repertoire may all influence the likelihood of an antibody response [5, 22].

Amino acid mismatch, eplet mismatch, and electrostatic disparity scores are highly correlated in many cohorts because they describe overlapping structural differences using distinct mathematical and biological representations. However, algorithms differ in how they account for residues actually recognized by antibodies, the immunogenicity of motifs formed by multiple amino acids, and interactions between alpha and beta chains in heterodimeric molecules such as HLA-DQ. HLA-EMMA results should therefore be interpreted alongside eplet analysis and other molecular mismatch methods, with consideration of clinical and serological findings [5, 22].

4.3. PIRCHE-II: modeling indirect T-cell allorecognition

PIRCHE-II is a computational approach that estimates the likelihood that peptides derived from donor HLA proteins will bind to recipient HLA class II molecules and be presented to CD4+ T cells. Whereas eplet analysis focuses on structural disparities on the HLA surface that may be accessible to antibodies, PIRCHE-II evaluates helper T-cell epitopes that may be generated from donor HLA molecules internalized by B cells. It therefore models the indirect allorecognition component of the cooperation between B cells and T cells required for antibody development [7, 19].

Higher PIRCHE-II scores have been associated with dnDSA development, biopsy-proven rejection, and ABMR in several transplant cohorts. Multicenter data indicate that PIRCHE-II scores derived from HLA-DQB1 and HLA-DRB1 may provide prognostic information that is independent of or complementary to class II eplet mismatch load. These findings suggest that humoral alloimmune risk depends not only on antibody-accessible surface motifs but also on the capacity of donor HLA peptides to be presented to recipient CD4+ T cells [8, 13, 23, 32].

PIRCHE-II results may nevertheless vary according to the HLA-peptide binding prediction model, the resolution and accuracy of HLA typing, the donor HLA loci included, and the imputation methods used for missing alleles. The same total score may also arise from different peptide compositions. Laboratory reports should therefore specify the algorithm and version, the HLA loci analyzed, the typing resolution, and any imputations; the results should be interpreted together with eplet analysis, antibody findings, and clinical data, as summarized in Table 1 [14, 15].

Table 1. Comparison of major approaches to molecular HLA mismatch assessment

Approach	Primary biological focus	Input requirement	Typical output	Main limitation
Antigen mismatch	Broad locus-level disparity	Low- or intermediate-resolution typing	0-6 or locus-specific mismatch count	Treats distinct alleles as equivalent
Eplet mismatch	Antibody-accessible structural motifs	High-resolution HLA typing	Total, antibody-verified, or single-molecule eplet mismatch load	Not every predicted eplet is immunogenic

Approach	Primary biological focus	Input requirement	Typical output	Main limitation
HLA-EMMA / amino acid mismatch	Solvent-exposed polymorphic residues	High-resolution HLA typing	Amino acid mismatch count by locus	Limited direct functional weighting
PIRCHE-II	Indirect CD4+ T-cell recognition	High-resolution donor and recipient HLA typing	Predicted donor HLA-derived peptides	Predictions depend on model and version
Integrated model	Combined B-cell, T-cell, and clinical risk	Typing, antibody, treatment, and clinical data	Continuous or categorical risk estimate	Requires validation and governance

5. CLINICAL EVIDENCE

5.1. De novo donor-specific antibody development

The most consistent outcome associated with molecular mismatch is dnDSA development. Prospective and retrospective kidney transplant cohorts have shown that the probability of dnDSA development increases with HLA-DR/DQ eplet or amino acid mismatch burden, with the strongest associations generally observed for class II loci, particularly HLA-DQ [9-12]. Studies in multiethnic populations further show that molecular mismatch burden varies widely within the same antigen mismatch category, despite a strong overall correlation with conventional antigen mismatch. Molecular assessment may therefore capture individual risk differences that conventional matching does not explain [11, 25].

The development of dnDSA is not determined by HLA structure alone. Treatment nonadherence and inadequate tacrolimus exposure may interact with molecular mismatch burden and increase the risk of dnDSA development or acute rejection [20, 26]. Eplet scores should therefore not be interpreted as independent or immutable determinants of clinical outcome.

5.2. Rejection and graft survival

A high molecular mismatch burden at HLA class II loci has been associated not only with dnDSA development but also with ABMR and long-term graft failure. In an analysis of 5,159 kidney transplant recipients from four centers, class II eplet mismatches and PIRCHE-II scores derived from HLA-DQB1 and HLA-DRB1 were independently associated with ABMR. These findings indicate that humoral alloimmune risk reflects both antibody-accessible surface motifs and donor-derived peptides capable of supporting indirect T-cell allorecognition [13].

Antibody-verified HLA-DQ eplet mismatch load has shown a linear association with dnDSA development, T-cell-mediated rejection, ABMR, and graft loss. The absence of a clearly defined zero-risk threshold indicates that molecular mismatch should not be interpreted as a binary classification of "compatible" or "incompatible." Eplet mismatch load is more appropriately viewed as a continuous biological variable along which risk increases progressively [9]. Higher HLA-DR/DQ eplet mismatch burden has also been independently associated with transplant glomerulopathy, supporting a relationship between molecular mismatch and chronic allograft injury [24].

After dnDSA has developed, the prognostic value of the baseline molecular mismatch burden appears less consistent. At this stage, more proximal biological indicators, including antibody specificity, strength, persistence, MFI pattern, complement-binding capacity, microvascular inflammation, biopsy findings, and treatment response, may become more informative [27]. Molecular mismatch analysis may therefore have its greatest value in estimating risk before primary alloimmunity develops and in individualizing the intensity of post-transplant surveillance.

5.3. Pediatric transplantation and other transplant settings

Molecular matching is particularly relevant in pediatric kidney transplantation because recipients may require retransplantation during their lifetime and sensitization can have long-term consequences. Small pediatric cohorts have reported associations of HLA-EMMA and PIRCHE-II scores with HLA antibodies, rejection, or graft outcomes; however, the available sample sizes remain limited [28].

Research on molecular matching in heart, lung, and hematopoietic stem cell transplantation is expanding, but the evidence is more heterogeneous than in kidney transplantation. Organ-specific immunobiology, allocation time constraints, acceptable ischemia time, and disease urgency may alter the clinical relevance of molecular matching. Thresholds developed for one transplant type should therefore not be transferred directly to another [14, 15].

6. LABORATORY AND BIOINFORMATICS REQUIREMENTS

The principal prerequisite for molecular mismatch analysis is accurate high-resolution HLA typing with adequate locus coverage. For class II assessment, inclusion of HLA-DRB3/4/5, HLA-DQA1, HLA-DQB1, HLA-DPA1, and HLA-DPB1 in addition to HLA-DRB1 is important. In particular, both HLA-DQA1 and HLA-DQB1 are required to model the heterodimeric HLA-DQ molecule accurately [6, 11].

Allele imputation from low-resolution types may be useful in research, but it carries a risk of misclassification related to ancestry, haplotype frequencies, and rare alleles. Direct high-resolution genotyping should therefore be preferred for clinical decision-making. When imputation is used, the associated uncertainty and probability distribution should be reported. Analysis reports should specify the software and version, the version of the HLA reference database, the loci analyzed, total and locus-specific scores, whether antibody-verified eplets were used, whether a single-molecule or total-load approach was applied, and any missing data. Without these details, comparisons across centers are difficult [14, 15].

Antibody specificities determined by single-antigen bead assays may be interpreted alongside molecular analyses; however, MFI is not a quantitative measure of antibody concentration. Prozone effects, denatured antigens, differences in antigen density among beads, and laboratory protocols can all influence results. Molecular scores should not replace serological testing, crossmatch, biopsy findings, or clinical graft function data [29, 30].

7. CLINICAL APPLICATIONS

7.1. Living-donor selection

When a recipient has several medically suitable living donors, molecular mismatch burden may be considered an additional ranking criterion alongside donor age, kidney function, anatomical suitability, ABO compatibility, and donor safety [15, 32]. In younger recipients, minimizing class II molecular mismatch may be particularly relevant because of the long-term consequences of sensitization and the potential need for retransplantation [9, 12, 15].

Donor selection should not be reduced to choosing the lowest eplet mismatch count. Small score differences may have uncertain clinical significance, and a donor with a lower molecular mismatch burden may have greater surgical or medical risk. Decisions should therefore be made by a multidisciplinary team using a shared decision-making approach [14, 15].

7.2. Deceased-donor allocation and equity

Incorporating molecular matching into deceased-donor organ allocation may improve long-term histocompatibility, but this potential benefit must be balanced against waiting time, geographic distribution, pediatric priority, high sensitization, medical urgency, and ethnic equity. Strict eplet thresholds could reduce organ access for recipients with rare HLA haplotypes [31].

A fair allocation model could use molecular compatibility as a weighted benefit rather than an absolute exclusion criterion. Such an algorithm should not be introduced into clinical practice until its effects across ethnic and geographic

populations have been evaluated through simulation within a transparent governance framework [15, 31].

7.3. Post-transplant monitoring and personalized treatment

For recipients with a high molecular risk profile, more frequent DSA monitoring, enhanced support for medication adherence, and careful assessment of calcineurin inhibitor exposure may be considered. Immunosuppression minimization strategies may be investigated in low-risk recipients; however, randomized trials demonstrating the benefit of treatment modification based on molecular scores remain insufficient [20, 21].

Risk assessment should not remain fixed at the time of transplantation. Newly detected dnDSA, variability in drug exposure, infection, graft function, and biopsy findings should be dynamically interpreted in relation to the baseline molecular mismatch burden. The most informative clinical model is likely to integrate genomic mismatch with immunological and clinical data that evolve over time (Figure 2; Table 2) [13, 20, 23].

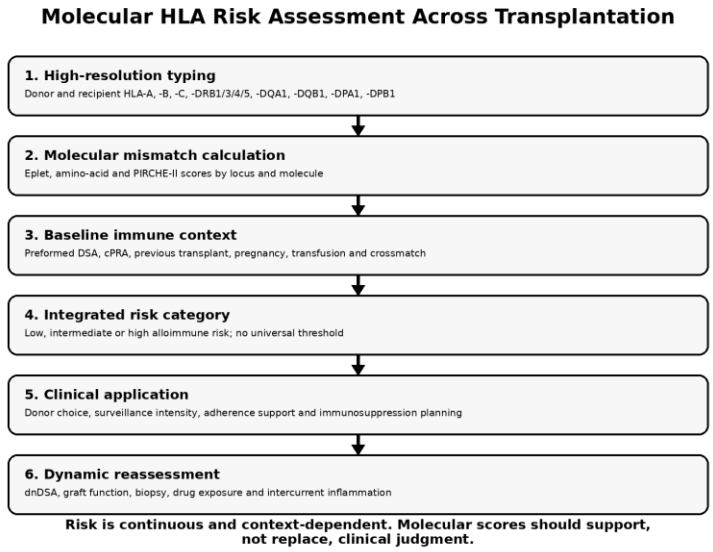

Figure 2. Molecular HLA risk assessment across the transplant pathway. The workflow emphasizes high-resolution typing, molecular mismatch calculation, baseline sensitization, integrated risk categorization, clinical application, and dynamic reassessment after transplantation.

Table 2. Potential clinical uses and safeguards for molecular HLA matching

Clinical setting	Potential use	Required safeguards	Current evidence level
Living-donor selection	Rank otherwise suitable donors	Do not override donor safety or major clinical factors	Moderate; strongest in kidney transplantation
Deceased-donor allocation	Include molecular compatibility as a weighted factor	Equity simulation, transparent governance, and population validation	Emerging
Post-transplant monitoring	Adjust the intensity of DSA and adherence surveillance	Interpret with drug exposure, graft function, and biopsy data	Moderate observational evidence
Immunosuppression personalization	Identify candidates for intensified or minimized therapy	Prospective interventional validation required	Insufficient for routine score-only decisions
Retransplantation	Avoid repeated immunogenic targets when feasible	Integrate historical antibodies and unacceptable antigens	Emerging; selected high-risk cases

8. LIMITATIONS AND STANDARDIZATION ISSUES

The first limitation is that an "eplet" is a biologically informative computational representation rather than a fully experimentally defined epitope. Although antibody-based validation has progressed, direct experimental evidence is still unavailable for most predicted eplets [17, 18].

The second limitation is that algorithms use different conceptual frameworks and assumptions. Total eplet mismatch load, antibody-verified eplet load, the number of solvent-accessible amino acid mismatches, and PIRCHE-II scores are correlated but do not measure the same dimension of risk. The optimal method or combination for a given clinical outcome has not been established across all populations [5, 13, 22].

The third limitation is that threshold values are cohort dependent. Differences in immunosuppression protocols, DSA testing frequency, laboratory methods, follow-up duration, population composition, and outcome definitions can alter the performance of the same cutoff. Thresholds defining "low" and "high" risk in a single center should therefore not be generalized without external validation [11, 14, 25].

The fourth limitation is clinical actionability. Randomized evidence remains insufficient to determine which immunosuppressive adjustment should follow a

high molecular score, how frequently DSA should be monitored, or whether an organ offer should be accepted or declined. Predictive accuracy and clinical benefit are not equivalent [14, 15].

The fifth limitation concerns data governance and accessibility. Version changes in commercial or closed algorithms may affect reproducibility and cost. Algorithms intended for clinical use must be evaluated for transparency, quality control, data security, and compliance with regulatory requirements.

9. FUTURE PERSPECTIVES

Future molecular HLA risk models are expected to consider not only total mismatch counts but also the antigenicity and immunogenicity of individual motifs. Human monoclonal antibodies, structural biology, peptide-binding assays, and T-cell assays may strengthen the biological validation of computational predictions [17, 18].

Multicenter prospective studies should evaluate the clinical utility of molecular scores using harmonized high-resolution typing and antibody-testing protocols. Pragmatic randomized trials of score-guided DSA monitoring or immunosuppression adjustment will be required to determine whether these predictive tools improve graft outcomes.

Machine-learning models may integrate eplet, amino acid, and PIRCHE-II scores with preformed DSA, drug exposure, treatment adherence, clinical laboratory data, and biopsy transcript profiles. However, biologically interpretable and externally validated models that perform equitably across populations should be preferred over opaque models with apparently high accuracy. In the near term, molecular matching is more likely to refine living-donor selection, reduce long-term sensitization in younger recipients, guide DSA surveillance, and explain risk heterogeneity not captured by conventional HLA matching than to serve as a stand-alone determinant of organ acceptance or rejection.

10. CONCLUSION

Eplet analysis and other molecular HLA mismatch methods have moved histocompatibility assessment beyond the simple counting of antigen mismatches toward a more detailed model that considers structural and functional differences between donor and recipient HLA molecules. In particular, higher molecular mismatch burdens at HLA-DR and HLA-DQ have been associated with dnDSA development, ABMR, transplant glomerulopathy, and graft loss across kidney transplant cohorts [9-13, 24].

Eplet analysis evaluates antibody-accessible disparities on the HLA surface, whereas amino-acid-based methods characterize sequence-level differences between donor and recipient. PIRCHE-II estimates the potential for peptides derived from donor HLA molecules to be presented by recipient HLA class II molecules. These methods should therefore be regarded as complementary tools that assess different components of B- and T-cell-mediated alloimmunity rather than as interchangeable tests [9-13].

Molecular mismatch scores are not absolute tests of donor-recipient compatibility. Their interpretation is influenced by HLA typing resolution and accuracy, the algorithm and database used, the extent of antibody validation, population and immunological characteristics, immunosuppressive therapy, and treatment adherence. In addition, not all eplets or amino acid differences are equally immunogenic [14, 15, 20].

Eplet, amino acid, and PIRCHE-II scores should therefore be interpreted together with DSA status, crossmatch results, graft function, histopathological findings, and the patient's clinical course. Current evidence does not support the use of these scores alone to accept or decline an organ, modify immunosuppression, or determine the need for biopsy. Safe clinical integration will require standardized analysis and reporting, external validation in diverse populations, and prospective intervention studies based on molecular risk [14, 15, 20].

In conclusion, molecular HLA matching complements rather than replaces conventional HLA compatibility assessment and may enable a more individualized definition of immunological risk. Integration of molecular data with serological, histopathological, and clinical indicators may improve donor selection and post-transplant monitoring. Ultimately, the clinical value of these technologies will depend not only on the level of detail in the scores they generate but also on whether the information can be applied in a manner that improves patient outcomes while preserving feasibility, equitable organ access, and sound clinical judgment.

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Chapter 2

Deep Learning in Pediatric Dentistry: Current Applications, Reported Performance and Clinical Limits

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Abstract

Deep learning has become the dominant artificial intelligence approach in paediatric dental imaging. Current models classify images, locate teeth or lesions, outline structures, stage dental development, and estimate age. This critical narrative review examines where these models have been used and how well they have performed, with emphasis on studies published from 2020 to 24 July 2026. The most consistent technical results have been reported for tooth detection, segmentation, and numbering in panoramic radiographs and digital impressions. Internal test F1 scores often approach or exceed 0.95 for these well-defined tasks. Dental age models have also reported mean absolute errors near 0.6 years in selected paediatric cohorts, although a broader meta-analysis found substantial variation and a pooled error of 1.75 years. Results for caries are less uniform. Performance changes with dentition, lesion depth, image type, annotation method, and metric. Models for pulp involvement, furcation lesions, periapical lesions, enamel defects, and eruption anomalies remain task specific and are supported mainly by retrospective, single-centre studies. High internal performance does not establish transportability, clinical benefit, or safety. Patient-level data separation, an independent external cohort, locked thresholds, clinically appropriate reference standards, subgroup analysis, and prospective evaluation are still uncommon. Deep learning is currently most defensible as a supervised aid for charting, second reading, and developmental assessment. It should not create an indication for imaging, replace the clinical examination, or make irreversible treatment decisions on its own.

Keywords: Deep learning; paediatric dentistry; convolutional neural networks; dental caries; tooth detection; dental age estimation; diagnostic imaging; external validation

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1. Introduction

Deep learning is a branch of machine learning in which layered neural networks learn patterns directly from examples. In paediatric dentistry, these models primarily analyse panoramic or bitewing radiographs, intraoral photographs, and digital impressions. Depending on the task, the output may be a class label, a bounding box, a segmentation mask, a developmental stage, or a numerical estimate such as dental age. These applications are clinically relevant because mixed dentition increases charting complexity and subtle early disease is not always interpreted consistently.

The literature has expanded rapidly. An umbrella review published in 2026 identified seven systematic reviews that contained 109 primary studies. Image-based models achieved pooled sensitivities and specificities near 80% to 83%, with areas under the receiver operating characteristic curve between 0.87 and 0.91. Most included reviews, however, were rated as low or critically low in methodological quality (Garg et al., 2026). A separate paediatric systematic review and meta-analysis reported higher pooled performance for radiographic caries detection, but also found marked heterogeneity and little external or prospective validation (Karamüftüoğlu et al., 2026).

These differing estimates are not necessarily contradictory. Deep learning performance in paediatric dentistry cannot be represented by a single measure. An F1 score for tooth numbering is not directly comparable with an area under the curve for caries detection or a mean absolute error for age estimation. Results also depend on the children included, the acquisition protocol, and the definition of the target condition. Performance may be overestimated when images from the same child cross data partitions or when the test cohort does not come from a genuinely independent setting.

Accordingly, this chapter addresses two linked questions: where deep learning is currently used in paediatric dentistry and what the reported performance indicates about readiness for clinical use. The purpose is not to rank architectures, but to identify tasks with reproducible value, explain the limitations of current studies, and define the evidence required before a model output influences care.

2. Scope and Review Approach

This chapter is a critical narrative review rather than a systematic review or meta-analysis. PubMed searches were updated through 24 July 2026. Search concepts combined paediatric populations or primary and mixed dentitions with deep learning, convolutional neural networks, transformers, YOLO, and U-Net. Clinical concepts included caries, plaque, pulp and periapical findings, tooth

detection and numbering, developmental anomalies, ectopic eruption, molar incisor hypomineralisation, dental development, and dental age.

Peer-reviewed studies with paediatric data were prioritised. Systematic and umbrella reviews were used to describe the wider evidence, while representative primary studies were used for exact sample sizes and performance measures. Reporting and evaluation guidelines were included when they directly informed interpretation. Studies without a clear paediatric population were not used to support paediatric performance claims.

No formal risk-of-bias instrument was applied. Each study was read in relation to its task, input, reference standard, data partition, validation setting, and reported metric. Results are presented as published. They should not be interpreted as a new pooled estimate or as a comparison of commercial products.

The review gives greater weight to recent work because model design and reporting have changed quickly. Older studies remain when they established a clinically relevant task or provide an important benchmark. Current guidance is used to frame image selection and evaluation. The American Academy of Pediatric Dentistry states that radiographs should be selected according to the child's history, examination, and individual need. They should not be used as indiscriminate screening tests (American Academy of Pediatric Dentistry, 2025).

3. Current Deep Learning Tasks and How Their Performance Is Read

Four task types account for most paediatric dental studies. Classification assigns a label to an image or region, such as caries present or absent. Object detection adds location, usually as a bounding box around a tooth or lesion. Segmentation outlines the pixels or surface that belong to the target. Regression produces a continuous value, such as estimated age.

The choice of architecture usually follows the task. ResNet, DenseNet, EfficientNet, and vision transformers are frequently used for classification. YOLO and related detectors are designed to find objects quickly. U-Net and its variants are common for segmentation. Multistage systems link these components. A model may first detect each developing tooth, then assign a stage, and finally convert the stages into a dental age.

Model names do not establish clinical quality. A newer YOLO version can perform poorly if the target is small, the labels are inconsistent, or the test set resembles the training data too closely. A simpler network may be adequate for a narrow task. The decisive questions are whether the model was tested on unseen children, whether the output answers the clinical question, and whether errors were measured at the point where a decision would be made. Performance measures should therefore be read as an interpretive sequence:

Classification. Sensitivity and specificity describe different errors; precision, negative predictive value, and F1 depend on the threshold and prevalence, while area under the curve summarizes ranking. Reports should include prevalence, thresholds, confusion matrices, confidence intervals, and results by age, dentition, and severity.

Detection and segmentation. Precision, recall, and mean average precision show whether an object was found and localized at a stated intersection-over-union threshold. Dice and intersection over union measure overlap, but small lesions are sensitive to boundary error. Match criteria, lesion size, annotation agreement, exclusions, and class-specific results are essential.

Staging and age estimation. Weighted kappa and macro-F1 describe agreement across ordered or imbalanced stages. Mean absolute error, root mean squared error, bias, and prediction intervals describe age-estimation error. Stage distribution, age range, calibration, outliers, and external validation must accompany these results.

Assistance and deployment. Reader comparisons should use the same cases and thresholds and distinguish assisted from unassisted decisions. Prospective evaluation should report failures, time, overrides, subgroup outcomes, downstream actions, and incidents; equality with one reader on one dataset does not establish clinical benefit.

No single measure can characterise model performance. Sensitivity is central when missed disease has important clinical consequences, whereas precision becomes more important when false alerts may prompt additional imaging or treatment. In segmentation, overlap quantifies localisation but does not show whether the finding changes management. For age estimation, the magnitude and distribution of error, together with any systematic bias, must be considered.

Current reporting guidance reflects these distinctions. CLAIM asks imaging studies to describe acquisition, independence of data partitions, reference standards, preprocessing, failures, and external testing (Tejani et al., 2024). STARD-AI applies when a model is evaluated as a diagnostic test (Sounderajah et al., 2025). TRIPOD+AI is relevant to models that estimate a future or continuous outcome (Collins et al., 2024). These checklists improve transparency, but they cannot correct a biased sample or an unsuitable reference standard.

4. Caries, Plaque, and Surface Assessment

4.1 Caries on panoramic radiographs

Caries is the most frequently studied disease target. Panoramic radiographs are readily available in retrospective archives, which makes them convenient for

model development. Convenience should not be confused with diagnostic suitability. A deep learning model does not make a panoramic image the preferred view for every caries question.

A U-Net model trained with 6,075 panoramic radiographs from children aged 4 to 14 years reported F1 scores of 0.882 in primary dentition, 0.819 in mixed dentition, and 0.868 in permanent dentition (Asci et al., 2024). The lower result in mixed dentition is clinically plausible because overlapping primary teeth, erupting permanent teeth, restorations, and variable root resorption create a more complex image.

Another study classified 6,028 teeth on paediatric panoramic radiographs. A tooth-type enhanced Swin transformer achieved an accuracy of 0.856, an F1 score of 0.857, and an area under the curve of 0.922. The model performed better than the authors' baseline networks and was more accurate than two attending dentists for selected primary molars (Zhou et al., 2023). This result supports the use of dental context in model design. It does not establish whole-mouth diagnostic superiority.

4.2 Bitewing radiographs and lesion severity

Bitewings are better suited to approximal caries, but the target remains difficult (American Academy of Pediatric Dentistry, 2025). Early enamel changes are small, and adjacent severity categories may not have a sharp boundary. A 2025 study used 1,023 bitewings from children aged 3 to 10 years to train five object detectors for primary molars. The best staging agreement was a weighted kappa of 0.713. Sensitivity was 0.509 for all lesions and 0.659 for dentine lesions considered to require operative care. Specificity and overall accuracy were high, showing why these measures must be read together rather than in isolation (Tan et al., 2025).

An early-access reader comparison published in July 2026 used 1,427 bitewings of primary teeth, including 247 test images. YOLOv8 achieved a recall of 0.51, precision of 0.41, F1 score of 0.44, and mAP of 0.41. The corresponding values for general dentists were 0.29, 0.31, 0.29, and 0.22. Both the model and dentists performed better for extensive lesions than for initial lesions. The model tended to underestimate lesion depth (Komtui et al., 2026). This standalone comparison does not show whether dentists make better decisions when assisted by the model.

Güçlü et al. (2025) used 1,000 primary-tooth and 1,000 permanent-tooth bitewings with 5,704 annotated interproximal lesions. In the primary-tooth test set, precision was 0.80, recall was 0.78, and F1 was 0.79. The permanent-tooth values were slightly lower. The single-centre dataset was enriched for positive

cases, contained no completely caries-free bitewings, and was annotated by one examiner. It was also split by radiograph rather than strictly by patient. These features limit independence and the applicability of the results to routine prevalence.

Progress in bitewing research should therefore be judged less by a single sensitivity estimate than by the shift from binary image labels towards lesion localisation and clinically meaningful severity thresholds. The next step is a locked, patient-level external test that includes restorations, overlapping contacts, non-diagnostic images, and a disease spectrum representative of routine practice.

4.3 Intraoral photographs and digital impressions

Photographs avoid ionising radiation and may support school screening or remote assessment. They are also sensitive to lighting, plaque, saliva, blur, angle, tooth visibility, and camera quality. A 2025 school-based study trained YOLOv8x on 3,221 intraoral photographs. Overall mAP was 45.8%, with a precision of 72.6% and recall of 41.1%. Results varied across ICDAS categories, although the system processed images faster than manual assessment (Fadilah et al., 2025). Speed is valuable only when poor-quality or incomplete views are recognised.

Three-dimensional intraoral scans provide another surface representation. Jones et al. (2025) trained a model with carious teeth from one cohort and tested it on an independent cohort of 119 teeth. Overall lesion detection reached 67% sensitivity and 73% precision. Extensive lesions were detected more reliably than early or moderate lesions, and performance declined slightly in the external cohort. This is a useful proof of concept because it includes independent data and reports where the model fails.

Deep learning has also been used to visualise plaque. A convolutional model trained with 886 photographs of primary teeth achieved a mean intersection over union near 0.73 in separate evaluations and performed similarly to an experienced paediatric dentist (You et al., 2020). Plaque segmentation may help education and repeated monitoring. It still depends on consistent photography and should not be presented as a complete caries-risk assessment.

Across modalities, input quality must be treated as part of model performance. A system that rejects a blurred or incomplete image and explains the reason is more clinically useful than one that processes it silently. Studies should report the proportion of unusable inputs and retain these cases in analyses intended to reflect clinical performance.

5. Tooth Detection, Numbering, and Digital Charting

Tooth detection is the most technically mature deep learning task in paediatric dentistry. The target is relatively large, its location is structured, and the output can be checked directly on the image. The task is still challenging in mixed dentition because primary and permanent teeth overlap and eruption changes the visible anatomy.

Beser et al. (2024) trained YOLOv5 models on 3,854 mixed-dentition panoramic radiographs. Internal testing produced an F1 score of 0.99 for detection and 0.98 for segmentation. A separate charting model trained on 4,821 paediatric panoramic radiographs reported F1 scores of 0.95 for primary teeth and 0.90 for permanent tooth germs. Performance was lower for restorations, root canal treatment, and supernumerary teeth (Kaya et al., 2024). High performance on common teeth therefore should not be extended to uncommon findings.

Digital impressions offer a different route to automated charting. A model evaluated on 716 impressions from 351 children in multiple source datasets achieved an F1 score of 0.996 for tooth detection, a Dice score of 0.969 for segmentation, and a macro-F1 of 0.989 for labelling. Processing took less than two seconds on average. Errors clustered around unusual conditions and ambiguous eruption patterns (van Nistelrooij et al., 2025).

Recent external testing clarifies what can happen when the image environment changes. Nishimura et al. (2026) trained and tested YOLOv8 and YOLOv10 across two paediatric panoramic datasets with different institutions and acquisition protocols. The mAP remained high, but fell from approximately 0.94–0.96 in one setting to about 0.90–0.91 under domain shift. Bite blocks were occasionally mistaken for a primary central incisor, and rare classes remained vulnerable.

Taken together, these studies support a practical near-term role in which the model prefills a chart and the clinician confirms every label. The interface should expose uncertain or missing teeth rather than forcing an apparently complete record. Any time saving should be measured after clinical corrections, not from model inference time alone.

6. Eruption Anomalies and Enamel Defects

6.1 Mesiodens and other developmental anomalies

Mesiodens detection has received sustained attention because the target is clinically important and usually located in a defined region. A two-stage system first estimated the maxillary anterior region and then classified mesiodens in 988 panoramic radiographs. Five-fold cross-validation produced an accuracy, precision, recall, F1 score, and area under the curve of 0.971 (Kim et al., 2022).

More recent work shows why a separate inference set matters. In a 2026 study of 480 paediatric panoramic radiographs, one YOLOv11 model reached a validation mAP of 99.2% but an inference F1 score of 84.3%. Another configuration had a more stable inference F1 score of 96.8% (Hartman et al., 2026). The lower result does not invalidate the model. It reveals the optimism that can arise when the validation set guides model selection.

Dens invaginatus is a less common target. YOLOv5 and YOLOv8 models were evaluated on 656 panoramic radiographs from patients aged 8 to 18 years. The best detection F1 score was 0.974 (Akgül & Gucyetmez Topal, 2026). Before clinical use, such a result needs confirmation in settings where prevalence is lower and subtle cases are mixed with other anterior anomalies.

The systematic evidence remains cautious. A review of six paediatric anomaly studies found average deep learning accuracy of 85.38% and sensitivity of 86.61%. Human readers achieved higher average values in the included comparisons, and the data were heterogeneous (Hartman et al., 2024).

6.2 Ectopic eruption

A multistage system developed from 1,576 panoramic radiographs of children aged 6 to 12 years combined tooth segmentation, developmental staging, and ectopic eruption diagnosis. Segmentation F1 was 0.979. Diagnostic accuracy was comparable with two of three dentists and exceeded the third on selected measures (Yu et al., 2025).

A 2026 model focused on ectopic canines and molars in mixed dentition. For canines, precision was 0.786, recall was 0.771, and F1 was 0.778. For molars, recall fell to 0.650 and F1 to 0.722 (Gülşen et al., 2026). These task-specific differences matter. A combined score would have concealed the weaker molar detection.

Deep learning may be useful as an alert on an already indicated panoramic radiograph. The final interpretation still requires the eruption path, available space, root development, adjacent structures, symptoms, and treatment timing. A box around an ectopic tooth is not a treatment plan.

6.3 Molar incisor hypomineralisation and similar appearances

Clinical photographs have been used to distinguish molar incisor hypomineralisation, caries, amelogenesis imperfecta, and fluorosis. In a dataset of 462 photographs, five pretrained convolutional networks achieved precision values from 83.98% to 92.86% (Alevizakos et al., 2022). The authors proposed training and educational use.

This remains an early application. A photograph may omit the distribution of defects, sensitivity, post-eruptive breakdown, and the child's history. Models also need images that represent coexisting conditions rather than one clean label per photograph. Current evidence supports assisted teaching and structured review more strongly than autonomous diagnosis.

7. Dental Development and Age Estimation

Dental development models often use a pipeline. Teeth are detected, segmented, assigned to developmental stages, and converted to an age. Each stage can introduce error. A model developed from 5,133 panoramic radiographs achieved a detection mAP of 0.995 and segmentation accuracy of 0.978. Stage-classification F1 scores, however, ranged from 0.692 for incisors to 0.908 for molars (Ong et al., 2024). Near-perfect detection did not guarantee equally accurate staging.

Kokomoto et al. (2024) used 8,023 panoramic radiographs for tooth-germ detection and more than 34,000 cropped tooth-germ images for stage classification. Detection mAP was 98.26%, while top-three stage accuracy exceeded 98% for single- and multi-rooted teeth. In 157 radiographs, the mean absolute difference between automated and manual dental-age calculations was lowest at 0.261 years with a weighted approach. This measures agreement with an expert-derived procedure rather than error against chronological age.

End-to-end models predict age directly from the full image. A Thai study of 2,491 panoramic radiographs reported a mean absolute error of 0.62 years in the 7- to 14-year group. Error increased to 1.41 years in participants aged 15 to 23 years (Sributsayakarn et al., 2025). A five-network ensemble in children aged 5 to 15 years reported a mean absolute error of 0.616 years and used heatmaps to show image regions associated with the estimate (Duru & Kaplan, 2026).

Another 2026 study used 3,367 paediatric panoramic radiographs and also collected 907 images from a separate clinical division. The internal end-to-end test produced a mean absolute error of 0.621 years. Manual review showed that orthodontic appliances could contribute to underestimation (Zeng et al., 2026). Error analysis of this kind is more informative than the average alone.

The wider literature is less uniform. A systematic review included 42 studies, but only 13 were considered at low risk of bias. In nine studies suitable for meta-analysis, the pooled mean absolute error was 1.75 years, with a 95% confidence interval from 0.96 to 2.55 years (Rokhshad et al., 2025). Differences in population, age range, reference method, and validation design explain part of the variation.

Dental age support may help developmental assessment when the model has been validated in a comparable population. It should not be treated as an exact biological clock. A model developed for clinical timing also should not be transferred directly to legal or forensic decisions, where the consequences and required uncertainty are different.

8. Pulpal, Furcation, and Periapical Findings

Deep learning is beginning to move from surface detection to findings that may influence pulp treatment. These tasks require particular caution because a radiograph does not show pulp histology. Current AAPD guidance bases pulp diagnosis on symptoms together with clinical and radiographic signs, and notes that no single method reliably determines vitality in deeply carious primary teeth (American Academy of Pediatric Dentistry, 2024).

A YOLOv8 classifier evaluated pulp involvement in 482 carious primary molars from 900 children. Top-one accuracy was 78.7% for maxillary primary molars and 87.8% for mandibular primary molars (Sohrabi et al., 2025). The different results by arch show why a single pooled value would be incomplete. The labels were derived from clinical charts, so consistency of the original diagnostic process also affects the model.

Furcation lesions have been linked to suggested treatment categories in a small retrospective study of 387 panoramic radiographs. The best model reached an mAP of 0.434 at an intersection-over-union threshold of 0.5, with precision of 0.440 and recall of 0.483 (Karamüftüoğlu et al., 2025). These values are not sufficient for autonomous treatment selection. Symptoms, restorability, resorption, successor development, and the child's overall treatment plan remain essential.

A 2026 internal validation study used 408 paediatric panoramic radiographs, including preprocessed image variants, to detect periapical lesions. YOLOv7 achieved sensitivity of 76.1%, specificity of 99.8%, and an F1 score of 86.4%, outperforming dental students in the same comparison (Shahmaleki et al., 2026). The study did not establish performance against specialists, on periapical radiographs, or in an independent institution.

At present, these models are better positioned as second readers or teaching aids than as decision-makers. Their outputs should be described as image findings rather than direct pulp diagnoses. Prospective evaluation should determine whether assistance improves the complete clinical decision, including cases in which radiographic and clinical information disagree. Table 1 compares representative studies together with their reported performance and the principal limitation of each evaluation.

Table 1. Representative paediatric deep learning studies and their reported performance

Clinical task	Study data	Model and output	Reported test result	Interpretation
Caries segmentation on panoramic radiographs	6,075 radiographs; ages 4–14 years (Asci et al., 2024)	U-Net; lesion mask	F1: 0.882 primary, 0.819 mixed, and 0.868 permanent dentition	Performance changed by dentition; no independent external cohort was reported.
Caries detection and staging on bitewings	1,023 radiographs; ages 3–10 years (Tan et al., 2025)	Five object detectors; lesion box and severity	Best weighted kappa 0.713; sensitivity 0.509 for all lesions and 0.659 for operative dentine lesions	High specificity did not remove the problem of missed lesions.
Caries detection compared with general dentists	1,427 primary-tooth bitewings; 247 test images (Komtui et al., 2026)	YOLOv8; lesion box and depth	Model versus dentists: recall 0.51 versus 0.29; F1 0.44 versus 0.29; mAP 0.41 versus 0.22	The model tended to underestimate lesion depth; assisted clinical decisions were not tested.
Interproximal caries segmentation	2,000 bitewings and 5,704 lesions (Güçlü et al., 2025)	YOLOv5x; lesion mask	Primary teeth: precision 0.80, recall 0.78, F1 0.79	Positive-case enrichment, one annotator, and radiograph-level splitting limit clinical transportability.
Caries detection on digital impressions	332 carious teeth plus 119 external teeth (Jones et al., 2025)	Attention U-Net; lesion mask	Overall sensitivity 67% and precision 73%	Independent testing was included; early and moderate lesions remained difficult.
Plaque segmentation on primary teeth	886 training photographs plus separate sets of 98 and 102 photographs (You et al., 2020)	Convolutional network; plaque mask	Mean intersection over union about 0.72–0.73	Results were similar to one experienced dentist in a controlled setting.
Tooth detection and segmentation	3,854 mixed-dentition panoramics (Beser et al., 2024)	YOLOv5; tooth labels and masks	F1 0.99 for detection and 0.98 for segmentation	Strong internal performance supports supervised chart prefilling.

Clinical task	Study data	Model and output	Reported test result	Interpretation
Tooth charting on digital impressions	716 scans from 351 children (van Nistelrooij et al., 2025)	Context and high-resolution network; tooth mask and number	Detection F1 0.996, Dice 0.969, macro-F1 0.989	Multiple source datasets were included; unusual eruption patterns caused errors.
Tooth detection under domain shift	200 internal and 192 external panoramics (Nishimura et al., 2026)	YOLOv8 and YOLOv10; tooth boxes	mAP fell from about 0.94–0.96 to about 0.90–0.91	External data exposed bite-block confusion and rare-class errors.
Ectopic eruption diagnosis	1,576 panoramics; ages 6–12 years (Yu et al., 2025)	Multistage network; tooth mask, stage, and diagnosis	Segmentation F1 0.979; diagnostic accuracy comparable with two of three dentists	The design is clinically relevant, but the evaluation was retrospective and single-centre.
Mesiodens detection	480 paediatric panoramics (Hartman et al., 2026)	YOLOv11; lesion detection	One model fell from 99.2% validation mAP to 84.3% inference F1; another reached 96.8% inference F1	Model selection should favour stable unseen-data performance, not the highest validation score.
MIH and similar defects	462 clinical photographs (Alevizakos et al., 2022)	Five convolutional classifiers; four-class label	Precision ranged from 83.98% to 92.86%	The evidence supports training use more clearly than standalone clinical diagnosis.
Dental development staging	5,133 panoramics (Ong et al., 2024)	YOLOv5, U-Net, and EfficientNet; tooth stage	Detection mAP 0.995; staging F1 0.692–0.908 by tooth group	The weakest component limits the reliability of the complete pipeline.
Dental age estimation	2,491 panoramics; ages 7–23 years (Sributsayakarn et al., 2025)	EfficientNetB0; age regression	Mean absolute error 0.62 years at ages 7–14 and 1.41 years at ages 15–23	Performance was age dependent and should not be averaged across the full range.

Clinical task	Study data	Model and output	Reported test result	Interpretation
Pulp involvement in primary molars	482 teeth from 900 children (Sohrabi et al., 2025)	YOLOv8 classifier; binary label	Top-one accuracy 78.7% for maxillary and 87.8% for mandibular molars	The model relies on radiographic appearance and cannot replace a complete pulp diagnosis.
Periapical lesion detection	408 paediatric panoramics (Shahmaleki et al., 2026)	YOLOv7; lesion detection	Sensitivity 76.1%, specificity 99.8%, and F1 86.4%	Internal comparison with students is encouraging but not external clinical validation.

Taken together, the reported results show that the most consistent technical performance appears in narrow, visually distinct tasks such as tooth localisation. Tasks with greater diagnostic or treatment consequences show lower sensitivity, less complete overlap, or wider subgroup variation. Because the studies occupy different stages of evaluation, an externally tested model with a lower headline score may provide stronger evidence than a model assessed only after a random internal split.

9. From Reported Performance to Clinical Use

9.1 The test set must represent the intended child population

Paediatric datasets should state age, dentition, disease spectrum, site, device, and image quality. Multiple images from one child must remain in the same partition. A test set should not be used for threshold choice, architecture selection, or repeated tuning. External testing requires a new data source that did not influence development.

Mixed dentition should be examined as a distinct domain rather than a small subgroup. The lower caries F1 in mixed dentition and the age-related differences in tooth numbering show that performance changes with development. Children with appliances, missing teeth, developmental conditions, or poor-quality images should not disappear from the analysis.

9.2 The reference standard must match the clinical claim

An expert's bounding box is an appropriate reference for localisation, but not automatically for disease truth. Caries severity may require more than one blinded examiner and a defined consensus process. Pulp treatment labels can reflect

symptoms, clinical findings, radiographs, and local preferences. Chronological age and manually estimated dental age answer different questions.

Reference uncertainty should be measured. Inter-examiner agreement and adjudication should be reported. If the target cannot be defined consistently, the model should express uncertainty rather than learn a false precision.

9.3 Thresholds should be chosen from consequences

The same probability threshold is not suitable for every use. A screening aid may prioritise sensitivity and send uncertain cases for review. A system that could influence operative treatment requires a high positive predictive value and explicit confirmation. Age estimation needs an interval and an error distribution, not only one decimal value.

The expected prevalence also changes predictive values. A balanced research dataset can produce an attractive accuracy while a low-prevalence clinic experiences many false positives. Local calibration and decision analysis should be completed before implementation.

9.4 Human comparison should test assistance, not competition

Several studies compare a model with one or more clinicians. These comparisons are useful only when readers evaluate the same cases under controlled conditions. More importantly, the relevant question is often whether a dentist using the model performs better than the dentist alone.

Prospective evaluation should begin with silent use, in which the model runs without changing care. Investigators can then measure image rejection, latency, record matching, failure modes, and subgroup performance. Early clinical studies should report how users interpret and override the output, following DECIDE-AI (Vasey et al., 2022).

9.5 Model output must remain subordinate to imaging indication and clinical examination

Deep learning should analyse only an image that is already justified for the child. It should not encourage additional radiographs merely to satisfy a model input. A lesion flag, age estimate, or eruption alert is only one component of the evidence; the dentist remains responsible for integrating the output with the history, examination, and treatment consequences. A child-specific pathway should define the age and dentition subgroup, confirm the radiographic indication, and document parent or guardian consent and developmentally appropriate child assent in accordance with local requirements. Current evidence can then be interpreted in three practical tiers:

Technically mature support tasks. Tooth detection, segmentation, and numbering have relatively strong technical evidence, including some external testing. Chart prefilling is a defensible supervised use, but prospective multicentre studies should measure correction errors and total charting time in routine mixed dentition.

Promising but heterogeneous applications. Radiographic caries detection, eruption anomalies, mesiodens, dental development, and age estimation can support second reading or supervised assessment. Transfer remains limited by view, dentition, lesion depth, prevalence, population, and uncommon anatomy; patient-level external tests and prespecified calibration are required.

Early or decision-sensitive applications. Photograph- or scan-based caries and plaque assessment, MIH, and pulpal, furcation, or periapical findings remain supported mainly by small or retrospective studies. Their present role is teaching, research, standardized screening, or supervised second reading; prospective full-mouth and multimodal studies must evaluate clinical decisions and outcomes.

10. Current Research Priorities

The next phase of research should focus less on new architecture names and more on reliable clinical evaluation. Multicentre datasets require locked external cohorts, patient-level separation, consistent annotations, and complete reporting of excluded or unusable inputs. Age, dentition, device, image quality, disease severity, and uncommon anatomy should be prespecified as subgroups.

Studies should report confidence intervals and denominators for every clinically important metric. Small lesions and rare anomalies require enough positive cases to estimate sensitivity. When data are insufficient, the correct conclusion is uncertainty, not equivalence.

Current approaches such as transformers, attention modules, lightweight networks, and multimodal models may improve performance. Their value should be tested against a clear baseline. A larger model is not automatically better. Lightweight systems may be preferable when they maintain performance and can run securely in the clinical environment.

Multimodal research is especially relevant to pulpal and treatment decisions. Images can be combined with symptoms, clinical findings, tooth restorability, and developmental information. The input collected at the intended decision point must be defined carefully to avoid leakage from later treatment labels.

Prospective reader-assistance studies are needed for the most mature tasks. They should compare unaided and aided clinicians, include an appropriate washout period, and record false actions, reading time, overrides, and uncertainty.

After that, comparative clinical studies can evaluate whether assistance reduces missed disease, unnecessary treatment, delays, or charting burden.

Evaluation should continue after deployment. A version change, new detector, new imaging device, or altered population can change performance. Clinics need a named owner, version records, incident review, rollback, and a route for clinicians to contest the output. A model that cannot be monitored or withdrawn is not ready for paediatric care.

11. Conclusion

Deep learning in paediatric dentistry has progressed beyond isolated demonstrations. Tooth detection, segmentation, and numbering now show high and increasingly well-tested technical performance, while dental development and age estimation can be accurate in selected cohorts. Results for caries, enamel defects, pulp involvement, furcation lesions, and periapical findings are potentially useful but remain less consistent.

The central limitation is no longer a lack of high internal scores, but the gap between technical performance and demonstrated clinical benefit. A reliable paediatric system requires patient-level data separation, a clinically appropriate reference standard, independent external validation, results stratified by age and dentition, explicit uncertainty, and prospective evaluation of assisted decisions.

The most appropriate current role is therefore supervised support. Deep learning may prefill a chart, highlight a region, organise developmental information, or provide a second estimate. The clinician must verify the output within the child's history, examination, imaging indication, and treatment context. This bounded role uses the technology's present strengths without extending the claims beyond current evidence.

Acknowledgements

The author has no acknowledgements to declare.

Conflict of Interest

The author declares no conflict of interest.

Funding

No external funding was received for this work.

Data Availability

No new data were generated or analysed for this narrative review. All information supporting this chapter is available in the cited literature.

Use of Artificial Intelligence

OpenAI Codex was used solely for language editing to improve the clarity, grammar, and academic style of the manuscript. The author independently reviewed and critically revised all suggested changes and approved the final manuscript. The author accepts full responsibility for the accuracy, originality, and integrity of the work. No confidential or identifiable patient data were provided to the system.

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Chapter 3

Molar–Incisor Hypomineralisation in Children: From Early Recognition to Restorative and Extraction-Orthodontic Decisions

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Abstract

Molar–incisor hypomineralisation (MIH) is a developmental enamel defect that can make first permanent molar eruption a period of breakdown, pain, difficult oral hygiene, and repeated treatment. This focused narrative review links early recognition in the primary dentition with treatment decisions in the developing permanent occlusion. The literature was reviewed through 23 July 2026, with priority given to the 2025 American Academy of Pediatric Dentistry best-practice document, European Academy of Paediatric Dentistry GRADE-based guidance, and recent systematic reviews and meta-analyses. Diagnosis should follow the clinical phenotype rather than a presumed cause. Hypomineralised second primary molars are an early risk marker, but heterogeneous evidence does not allow individual prediction. Management should integrate symptoms, post-eruptive breakdown, restorability, child-reported impact, eruption stage, and occlusion. Fluoride-based prevention and close review support caries control, whereas comparative evidence for desensitising and remineralising agents remains limited. Adhesive fissure sealants are suitable for fully erupted molars without breakdown. Localised defects can be restored with composite resin when isolation and margins in sound enamel are achievable. Glass ionomer materials are useful for interim stabilisation. Recent 2026 reviews report favourable short- and medium-term outcomes for full coronal coverage in extensively affected molars, but long-term comparative evidence remains limited. For a poor-prognosis first permanent molar, planned extraction may reduce cumulative treatment burden. Because spontaneous space closure is less predictable in the mandible, timing should be based on dental development, radiographic findings, and orthodontic assessment. The proposed pathway connects recognition, stabilisation, restoration, and extraction planning while keeping uncertainty explicit.

Keywords: Molar–incisor hypomineralisation; paediatric dentistry; dental hypersensitivity; restorative dentistry; first permanent molar

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1. Introduction

Molar–incisor hypomineralisation is a qualitative developmental enamel defect affecting at least one first permanent molar, with or without involvement of permanent incisors. Although affected enamel forms at normal thickness, it has reduced mineral content, increased porosity, and altered mechanical properties. Its clinical expression ranges from a small demarcated opacity to extensive post-eruptive breakdown (PEB), dentine exposure, hypersensitivity, atypical caries, and early tooth loss (American Academy of Pediatric Dentistry [AAPD], 2025; Lygidakis et al., 2022). These are not merely cosmetic variations. A child may avoid brushing or chewing, experience pain during routine examination, and undergo repeated repairs at an age when trust in dental care is still developing.

The first permanent molars erupt at a strategically important point in occlusal development. An early decision may influence tooth survival, treatment burden, arch development, and later orthodontic need. Because no single material or procedure suits every phenotype, management depends on prognosis. The central question is often whether a molar can be maintained predictably or whether planned extraction and molar substitution offer a lower treatment burden; chronological age alone cannot resolve this choice.

Hypomineralised second primary molars (HSPM) can alert the dental team before the first permanent molars erupt, while recent reviews clarify both the potential and uncertainty of treatment. Studies nevertheless use different diagnostic thresholds, severity classifications, outcomes, and follow-up periods (Gizani et al., 2026; Lopes et al., 2021).

This chapter follows the child from early recognition in the primary dentition to definitive decisions in the permanent dentition. It concentrates on diagnosis, sensitivity, preservation of tooth structure, posterior and anterior treatment, and extraction–orthodontic coordination. General caries management and pulp therapy are discussed only where they alter an MIH-specific decision.

2. Focused Narrative Review Method

This chapter is a focused narrative review, not a systematic review or meta-analysis. PubMed/MEDLINE and the reference lists of major professional guidance documents were searched through 23 July 2026. Search concepts combined *molar incisor hypomineralisation*, *molar incisor hypomineralization*, *molar hypomineralisation*, *hypomineralised second primary molar*, and *HSPM* with terms for prevalence, aetiology, diagnosis, differential diagnosis, hypersensitivity, oral health-related quality of life, prevention, sealants, restoration, anterior aesthetics, extraction, space closure, and orthodontics.

Priority was given to professional guidance from the AAPD and the European Academy of Paediatric Dentistry (EAPD), followed by systematic reviews, meta-analyses, and clinically relevant comparative or longitudinal studies. General websites, commercial product pages, and unreviewed educational material were not used as evidence. For feasibility, the review was limited to English-language sources. Records were not screened independently by two reviewers, and no independent risk-of-bias assessment was undertaken. Evidence certainty therefore reflects judgements in the included guidance and reviews, supplemented by appraisal of design, consistency, precision, and directness.

3. Terminology, Phenotype, and the HSPM–MIH Continuum

The EAPD definition remains clinically useful: MIH requires a demarcated hypomineralisation defect in at least one first permanent molar; incisor involvement is common but not mandatory (Lygidakis et al., 2022). "Molar hypomineralisation" is sometimes used as a broader term because similar defects may affect second primary molars, canines, premolars, or second permanent molars. Until a universally accepted broader definition replaces MIH, clinicians should record the exact teeth and surfaces involved rather than infer the phenotype from the label alone.

HSPM describes demarcated opacities, PEB, atypical restorations, or tooth loss attributable to hypomineralisation in one or more second primary molars. Its chief value is anticipatory. A 2026 systematic review and meta-analysis of 24 studies and 22,678 participants found that children with HSPM had substantially higher odds of MIH (pooled crude odds ratio [OR] 8.55, 95% confidence interval [CI] 4.72–15.50) (Tarrahi et al., 2026). The heterogeneity was extreme (I^2 96.97%), most studies were cross-sectional, and adjusted estimates were not consistently available. HSPM should therefore be described as a strong association and practical risk marker, not as a test that predicts which individual child will develop MIH.

The distinction matters in communication. Parents should not be told that an affected primary molar guarantees defective permanent teeth. Instead, HSPM justifies a planned eruption review, reinforcement of preventive care, and early access to a clinician able to assess newly erupted first permanent molars. Primary canines may also show hypomineralisation, but the evidence linking hypomineralised primary canines with MIH is based on very few data and is not ready for individual prediction (Tarrahi et al., 2026).

MIH enamel usually begins as a clearly demarcated white, cream, yellow, or brown opacity. The tooth surface may be intact at eruption, after which masticatory forces fracture porous enamel. Yellow-brown defects tend to be

deeper and more porous than white-cream opacities, but colour alone cannot determine treatment. PEB produces sharp, irregular margins and must be distinguished from primary enamel hypoplasia, in which deficient enamel is present before eruption and the defect margins are generally smooth (AAPD, 2025).

4. Epidemiology and Aetiology: What Can Be Said with Confidence

MIH is common, but prevalence estimates depend on examination age, calibration, case definition, and whether unerupted or already restored teeth can be classified. A 2025 systematic review and meta-analysis included 135 studies from 53 countries and estimated global MIH prevalence at 15.5% (95% CI 14.4–16.6), with individual estimates ranging from 0.6% to 46.6% (Ammar et al., 2025). The same analysis found no significant global increase across five-year intervals from 2000 to 2020. A separate meta-analysis likewise found no convincing temporal rise after accounting for study differences (Sluka et al., 2024). Increased clinical awareness and more consistent recording may therefore explain at least part of the impression that MIH is becoming more frequent.

The defect develops during enamel maturation, but no single prenatal, perinatal, childhood, genetic, or environmental exposure explains all cases. The EAPD's GRADE appraisal judged much of the observational evidence for systemic factors to be low or very low certainty, largely because parental recall and confounding make illness, fever, medication, prematurity, and social circumstances difficult to separate (Garot et al., 2022; Lygidakis et al., 2022).

Meta-analyses have reported associations with illness during pregnancy, low birth weight, early childhood illness, fever, and antibiotic exposure (Juárez-López et al., 2023). Such estimates should not be presented as causal. Antibiotic use, for example, may be a marker of the infection or fever for which the drug was prescribed. Recall bias, inconsistent exposure definitions, and residual confounding remain plausible. A 2026 review of early respiratory disease found that adjusted asthma estimates were imprecise and not statistically significant, while pneumonia was associated with MIH; certainty for all respiratory associations was rated very low (Brandão Osterno et al., 2026).

Genetic and epigenetic findings support susceptibility rather than a simple inherited disorder. Variants related to enamel formation and immune response have been investigated, and a gene–environment model is biologically plausible. Current evidence is insufficient for clinical genetic testing, individual risk scores, or assigning causation to a child's medical history. In practice, an aetiological interview can document relevant developmental history, but it should not delay treatment or imply parental responsibility. Because enamel already formed before

eruption cannot be “prevented” from becoming MIH enamel, the clinically actionable form of prevention is early recognition of the phenotype and prevention of its consequences.

5. Clinical Recognition and Differential Diagnosis

The preferred examination age for population recording has traditionally been around eight years, when the index teeth are often sufficiently erupted and severe defects have not all been obscured by restoration or extraction. Clinical care should begin earlier. Second primary molars should be inspected before exfoliation, and first permanent molars should be reviewed during eruption. Teeth should be cleaned and examined wet initially; prolonged air drying may provoke pain and is unnecessary for identifying a demarcated opacity.

The minimum record should identify each affected tooth and surface, opacity colour and extent, PEB, caries, atypical restoration, hypersensitivity, and whether any missing tooth is attributable to MIH. The EAPD recommends considering defects greater than 1 mm and offers short and long recording forms that combine MIH/HSPM features with the modified Developmental Defects of Enamel approach (Ghanim et al., 2015; Lygidakis et al., 2022). Photographs are useful for monitoring, provided lighting and scale are reasonably consistent.

Radiographs do not diagnose an intact demarcated opacity reliably. They are indicated when needed to assess caries depth, pulpal or periapical status, restorability, and the developing dentition. Before planned extraction, a panoramic image may be needed to assess the permanent second molar’s development and angulation, premolar development, hypodontia, and third molar presence. Imaging should answer a clinical question and follow local radiation-protection standards. The principal clinical features that distinguish MIH from other enamel defects are summarised in Table 1.

Table 1. Differential diagnosis of an MIH-like enamel appearance

Condition	Typical pattern	Surface at eruption	Main distinguishing clue
MIH	Sharply demarcated, asymmetric opacities affect at least one first permanent molar. Incisors may also be involved.	Enamel is initially of normal thickness. Post-eruptive breakdown may develop after the tooth enters function.	Yellow-brown colour, hypersensitivity, atypical restorations, or rapid breakdown support MIH.
Dental fluorosis	Diffuse, bilateral, and relatively symmetrical changes affect teeth formed during the same exposure period.	The enamel surface is usually intact at eruption. Severe fluorosis may include pitting.	Diffuse borders and a symmetrical distribution favour fluorosis. Fluorosis and MIH can coexist.
Enamel hypoplasia	A local or chronological disturbance reduces the quantity of enamel.	Pits, grooves, or missing enamel are already present when the tooth erupts.	Smooth margins around a pre-eruptive enamel defect favour hypoplasia. Irregular post-eruptive loss favours MIH.
Amelogenesis imperfecta	Many teeth are affected in a generalised or familial pattern, often across both dentitions.	Enamel quantity or quality is altered throughout the dentition.	Generalised involvement and a family history favour amelogenesis imperfecta. A negative family history does not exclude a new variant.
Local trauma or infection affecting a permanent successor	A single permanent tooth is usually affected in the region of an injured or infected primary predecessor.	The tooth may show a local opacity, hypoplasia, or altered crown form at eruption.	A tooth-specific history and distribution favour a local developmental defect rather than MIH.
Early caries or white-spot lesion	The lesion follows plaque-retentive cervical, proximal, or fissure sites rather than a developmental pattern.	The surface may lose lustre, become rough, and change with biofilm activity.	Plaque stagnation and active progression favour caries. Caries can also develop on an MIH-affected surface.

Distinguishing among these conditions requires pattern recognition supported by the clinical history. Coexisting defects are possible, particularly MIH with caries or fluorosis. A 2026 meta-analysis did not confirm a significant association between MIH and fluorosis after pooled analysis, but moderate heterogeneity and variation in diagnostic calibration support recording each defect separately rather than assigning all findings to a single diagnosis (Bahloul et al., 2026).

6. Severity, Hypersensitivity, and Child-Centred Burden

The EAPD's pragmatic mild/severe classification is useful at chairside. Mild MIH comprises demarcated opacities without breakdown, only provoked sensitivity, and limited aesthetic concern. Severe MIH includes breakdown or caries, spontaneous or persistent sensitivity affecting brushing or mastication, or a strong psychosocial effect (Lygidakis et al., 2022). The AAPD also describes a moderate category for opacities with limited PEB, atypical restoration, or limited caries without cuspal involvement (AAPD, 2025). The MIH Treatment Need Index (MIH-TNI) adds the presence of hypersensitivity and the extent of breakdown, making explicit that a small but painful defect may require more urgent care than its area suggests (Steffen et al., 2017).

No index should replace a tooth-by-tooth prognosis. Record at least four dimensions: structural loss, symptoms, restorability, and impact on the child. The most severe feature should drive immediate management. A molar without visible breakdown but with pain on brushing requires stabilisation; an asymptomatic but rapidly enlarging defect requires structural protection.

A meta-analysis of observational studies estimated that, among children with MIH, caries affected approximately 51% at the patient level, hypersensitivity 42%, and PEB 26%; heterogeneity exceeded 85% for most outcomes (Gevert et al., 2024). These figures describe study populations, not the probability for an individual child. Another meta-analysis found higher caries experience in children with MIH across 17,717 participants, while acknowledging the multifactorial nature of caries (Mazur et al., 2023).

MIH of any severity was not significantly associated with poorer oral health-related quality of life (OHRQoL) in one meta-analysis. Moderate or severe disease, however, was associated with poorer OHRQoL (OR 3.43, 95% CI 1.69–6.98) (Awwad et al., 2023). Hypersensitivity is more common in molars, larger defects, and teeth with structural breakdown, although estimates vary (Linner et al., 2021). Evidence linking MIH with dental fear remains inconsistent; nevertheless, repeated painful treatment is a plausible pathway (Jälevik et al., 2022). Ask the child about brushing, chewing, sleep, school, smiling, and previous care. Parent reports should not replace the child's account.

7. Prevention, Desensitisation, and Fissure Protection

7.1 Prevention starts at eruption

For a child with HSPM or a newly erupted MIH molar, the immediate objectives are to control pain, make cleaning possible, prevent caries, and protect the surface from PEB. Twice-daily brushing with age-appropriate fluoridated toothpaste, individual dietary counselling, and professional fluoride varnish are reasonable elements of a caries-prevention plan (AAPD, 2025; Lygidakis et al., 2022). Fluoride varnish should be described primarily as caries prevention. Evidence that it permanently remineralises the developmental defect or reliably controls MIH hypersensitivity is insufficient.

Recall interval should reflect severity, eruption stage, symptoms, caries activity, home care, and restoration status. Both AAPD and EAPD guidance support review every three to six months for at-risk or affected children, with the shorter interval used during eruption, active breakdown, uncontrolled sensitivity, or recent treatment (AAPD, 2025; Lygidakis et al., 2022).

7.2 Desensitisation

Options studied for sensitivity include fluoride preparations, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), related calcium-phosphate formulations, arginine-calcium carbonate, hydroxyapatite products, silver compounds, sealing, restorative coverage, and laser-based procedures. Confidence in comparative effectiveness remains limited. A 2024 meta-analysis found no significant advantage of CPP-ACP over fluoride for remineralisation. CPP-ACP reduced hypersensitivity compared with fluoride varnish, but heterogeneity was high (I^2 83%) and confidence intervals were wide (Cavalcante et al., 2024). CPP-ACP is derived from milk protein and should not be used in a child with relevant milk-protein allergy.

A 2025 systematic review suggested that resin or glass ionomer sealing can reduce mild hypersensitivity, while crown coverage produced the largest reductions in severe cases. The included studies were small and follow-up was mostly short. These findings support covering porous enamel but do not establish a product hierarchy (Hjertberg et al., 2025). At follow-up, use the same stimulus and a child-appropriate response scale. Improvement should include brushing and chewing, not only an immediate chairside score.

Silver diamine fluoride or related silver-fluoride protocols may control caries and sensitivity in selected posterior teeth. The child and caregiver must understand the likelihood of dark staining on demineralised or carious tissue. Evidence specific to non-carious MIH enamel remains less developed than

evidence for caries arrest, and silver products should not be presented as a universal remineralising treatment.

7.3 Sealants

For a fully erupted molar with an intact surface or minimal non-cavitated change, a resin-based fissure sealant placed with an adhesive is a reasonable first-line option. The EAPD graded this recommendation as strong on moderate-certainty evidence (Lygidakis et al., 2022). Moisture control and follow-up are essential because adhesion to hypomineralised enamel is less predictable.

The 2026 restorative systematic review found complete or partial retention above 80% at 12 months in one sealing study, while another trial reported substantially better retention for phosphoric-acid-etched resin sealant than for a giomer used with a self-etch primer (Gizani et al., 2026). These findings favour conventional etch-and-rinse resin protocols when isolation is achievable. A glass ionomer sealant is useful during incomplete eruption or poor moisture control, but it should be regarded as transitional and checked for loss. Table 2 translates the available evidence into phenotype-specific clinical goals and actions while stating the principal limitations.

Table 2. Evidence-informed intervention by clinical phenotype

Clinical finding	Immediate goal	Practical action	Evidence limitation
HSPM before first permanent molar eruption	Plan prevention and review before the first permanent molars erupt.	Record HSPM, reinforce daily fluoride-based prevention, and schedule a review during eruption.	HSPM is strongly associated with MIH, but high heterogeneity and mostly cross-sectional data prevent individual prediction.
Intact MIH opacity with no or mild sensitivity	Prevent caries and post-eruptive breakdown.	Use age-appropriate fluoridated toothpaste and risk-based varnish. Place an adhesive resin sealant when isolation is reliable.	Short follow-up and variable sealant retention limit certainty.

Clinical finding	Immediate goal	Practical action	Evidence limitation
Intact opacity with troublesome sensitivity	Make brushing, eating, and dental care comfortable.	Use a structured desensitising plan, cover porous enamel when needed, and reassess with the same pain scale.	No topical agent has established long-term superiority. Current evidence supports individualised treatment and regular reassessment.
Localised post-eruptive breakdown without cuspal loss	Stabilise the tooth and restore a cleanable form.	Use glass ionomer cement for short-term stabilisation when isolation is limited. Place an adhesive restoration once stable margins can be achieved.	Lesion definitions vary, and long-term comparative data remain limited.
Multisurface or cuspal breakdown	Protect the remaining crown and control pain.	Consider a preformed metal crown or another full-coverage restoration after assessing pulpal status and long-term tooth prognosis.	Recent reviews report favourable short- and medium-term outcomes, but the evidence comes from few heterogeneous studies.
Poor-prognosis first permanent molar	Reduce repeated treatment while protecting the developing occlusion.	Arrange paediatric dental and orthodontic assessment. Maintain the tooth temporarily or plan extraction according to disease urgency and dental development.	Most space-closure evidence is retrospective and of very low certainty, particularly for mandibular outcomes.
Aesthetic incisor opacity	Address the child's concern with the least invasive suitable treatment.	Begin with observation or a minimally invasive option matched to lesion depth. Use conservative composite masking when needed.	Long-term comparative trials are scarce, and colour response varies between lesions.

8. Restoring Posterior Teeth

8.1 Stabilisation and pain control

Hypersensitivity can make local anaesthesia, isolation, and cooperation difficult. Treatment should begin with explanation, adequate analgesia and anaesthesia, and the least traumatic procedure that makes the tooth comfortable and cleanable. If definitive isolation is not possible, high-viscosity glass ionomer cement (GIC) or resin-modified GIC can protect exposed dentine and reduce sensitivity. Its fluoride release and relative tolerance of moisture are useful during eruption. Conventional GIC is less suitable as a definitive material across load-bearing cusps because of its mechanical limitations (Lygidakis et al., 2022).

An interim restoration is an active stage of care, not abandonment. Record the intended review date and definitive plan. This is particularly important when the tooth is being maintained until the second permanent molar reaches a favourable developmental stage for an extraction decision.

8.2 Direct adhesive restoration

Composite resin is appropriate for a localised defect when the tooth is restorable, pain can be controlled, rubber-dam isolation is feasible, and margins can be placed in clinically sound enamel. The central challenge is not dentine bonding but the porous, protein-rich affected enamel and uncertainty about where defective enamel ends. The EAPD review supported composite restorations under rubber dam using an approach that removes sufficiently compromised enamel to reach stable margins. Evidence did not show a meaningful retention advantage for self-etch versus total-etch protocols or for sodium-hypochlorite deproteinisation (Lygidakis et al., 2022; Somani et al., 2022).

This does not justify indiscriminate removal of every discoloured area. The operator should remove unsupported and clearly friable enamel, test the remaining margin conservatively, and avoid extending the cavity solely to eliminate colour. A small repairable restoration may be preferable to aggressive preparation in an immature tooth, provided the family understands the need for surveillance.

The 2026 systematic review reported mean clinical success of approximately 84% at 12 months and 83% at 36 months across restorative interventions. Glass ionomer cement had the lowest 12-month mean, while fabricated ceramic restorations and preformed metal crowns had the highest values at selected follow-ups. Methodological differences prevented quantitative pooling, and risk of bias was often unclear. These descriptive figures do not establish a universal material hierarchy (Gizani et al., 2026).

8.3 Full coronal coverage and indirect restoration

A preformed metal crown is often a pragmatic option for a severely affected first permanent molar with multisurface or cuspal breakdown. It covers porous enamel, controls sensitivity, protects remaining structure, and restores contact and occlusion. The EAPD strongly recommends this approach for severe cases on moderate-certainty evidence (Lygidakis et al., 2022). A 2026 systematic review of five heterogeneous studies reported better short- and medium-term survival than multisurface direct restorations. Follow-up was generally limited to 12–24 months, so long-term certainty remains low (Joshi et al., 2026).

Clinical photographs and a detailed baseline record should be obtained before full coverage because the underlying enamel cannot be inspected without crown removal. Fit, occlusion, gingival health, cement integrity, and symptoms require review. Orthodontic separators may reduce the need for proximal reduction in selected children.

Indirect composite, metal, or ceramic restorations may be considered when cooperation, isolation, remaining structure, aesthetics, and cost permit. They protect cusps but demand preparation and chair time, and no indirect material is consistently superior. In a young child, preserving future treatment options is more important than prematurely committing to an extensive definitive restoration.

Pulpal assessment is part of restorability, but detailed pulp therapy lies outside this chapter. Spontaneous pain, deep caries, abscess, or periapical pathology changes the prognosis and may move the decision toward appropriate pulp treatment or extraction. A vital pulp procedure should not be chosen merely to postpone an unavoidable extraction without considering occlusal timing.

9. Management of Affected Incisors

Treatment of incisor opacities should be guided by the child's symptoms and preferences rather than appearance alone. First determine whether the child is concerned, whether there is sensitivity or breakdown, and whether the request reflects teasing, caregiver anxiety, or the child’s own preference. Conservative observation is appropriate when the child is unconcerned. Photographs and shade records help communicate that complete colour matching may not be achievable.

Treatment should match lesion depth and colour. Microabrasion removes a thin superficial enamel layer and is most suitable for shallow white-cream opacities. Resin infiltration changes light transmission through porous enamel and may mask selected deeper lesions. A 2025 systematic review found both approaches promising, but protocols and lesion definitions varied and long-term evidence remained limited (Nefzaoui et al., 2025). A separate meta-analysis

found an optical benefit from resin infiltration. Heterogeneity was extremely high, so the average effect should not be promised to an individual child (Hoan et al., 2024).

Yellow-brown or structurally defective lesions may require conservative composite masking, sometimes after limited enamel removal. Opaquing resin can reduce the amount of tissue removed. External bleaching raises age, sensitivity, consent, and jurisdiction-specific regulatory issues and is rarely a first procedure in a young child. Veneers and extensive preparations should generally be deferred until maturation unless exceptional functional and psychosocial circumstances justify them. Because colour, eruption, gingival position, and the child's priorities change, staged treatment is often preferable.

Treatment may improve quality of life, but certainty is low. A 2026 systematic review of five studies and 491 children found improvement in OHRQoL after MIH treatment, while rating the evidence low certainty because of risk of bias and study limitations (Hoogeveen et al., 2026). Patient-centred outcomes should therefore be assessed directly rather than inferred from technical colour change.

10. Severe First Permanent Molars: Restore or Plan Extraction?

10.1 Establish the prognosis before choosing the procedure

A poor-prognosis first permanent molar may expose a child to repeated restorations, pain, emergency attendance, general anaesthesia, and eventual extraction at an unfavourable stage. Planned extraction can reduce this burden and allow the second permanent molar to substitute, but the outcome is not guaranteed. The decision requires a shared assessment of tooth prognosis, the child's circumstances, the developing dentition, and access to continuing care.

Factors favouring maintenance include a restorable crown, controllable symptoms, reliable follow-up, hypodontia, a spaced arch, or a need to preserve the molar for orthodontic anchorage. Factors favouring extraction include progressive PEB, deep caries or pulpal/periapical disease, persistent pain, repeated restoration failure, poor ability to tolerate repeated treatment, and a developing dentition in which substitution is feasible (AAPD, 2025; Lygidakis et al., 2022). Financial or geographic barriers matter because a technically ideal restoration is not a durable solution if review and repair are inaccessible. These contextual factors should be discussed without blaming the family.

10.2 Dental development is more informative than a birthday

The frequently quoted "eight-to-ten-year window" is a useful prompt for assessment, not an automatic extraction rule. A panoramic radiograph should establish the second permanent molar's developmental stage and angulation,

presence and position of the third molar, premolar development, missing teeth, and the underlying malocclusion. Demirjian stage E of the second permanent molar, when bifurcation mineralisation has begun, has been associated with more favourable spontaneous space closure (Hamza et al., 2024). The radiographic stage, not chronological age by itself, should anchor timing.

In a 2024 systematic review and meta-analysis, spontaneous space closure occurred in an estimated 85.3% of maxillary sites and 48.1% of mandibular sites. Stage E was associated with greater odds of closure in both arches; in the mandible, age eight to ten years and the presence of a third molar were also associated with improved odds. Certainty was very low because 14 of 15 included studies were retrospective and methods varied (Hamza et al., 2024). A 2025 systematic review similarly identified age, second molar stage and inclination, and possible third molar influence, while emphasising continuing uncertainty (Alqanas et al., 2025).

These averages should be explained plainly. Maxillary substitution is usually more favourable, whereas mandibular second molars may tip, rotate, or leave residual spacing. Extraction after eruption of the second permanent molar is less likely to close spontaneously and more likely to require active orthodontics.

10.3 Orthodontic coordination

Orthodontic consultation is particularly important when there is Class II or Class III malocclusion, marked crowding or spacing, deep bite, open bite, transverse discrepancy, hypodontia, asymmetric planned extraction, or uncertain second molar angulation. The orthodontist should see the same clinical and radiographic information used to establish the restorative prognosis.

Routine balancing extraction of a sound contralateral first permanent molar is not recommended merely to preserve symmetry. Compensating extraction of an opposing sound maxillary molar after loss of a mandibular molar should also be individualised rather than automatic because the risk and consequence of overeruption vary (AAPD, 2025). If an affected molar must be removed before the preferred stage because of pain or infection, urgent health needs take priority; the family should then be counselled about the greater probability of later orthodontic intervention. Table 3 integrates the prognostic, developmental, occlusal, and contextual factors needed for a structured maintain-versus-extract discussion.

Table 3. Maintain-versus-extract assessment for a severely affected first permanent molar

Decision domain	Findings favouring maintenance	Findings favouring planned or urgent extraction
Tooth prognosis	Maintenance is favoured when the crown is restorable, symptoms are controlled, and no pulpal or periapical disease is present.	Extraction is favoured by progressive multisurface or cuspal breakdown, deep caries, pulpal or periapical disease, repeated failure, or persistent pain.
Child and treatment burden	Maintenance is more feasible when the child can tolerate care and a reliable review pathway is available.	Extraction may reduce burden when anaesthesia is difficult, emergency visits recur, or extensive repeated treatment is expected.
Developing dentition	Hypodontia, spacing, an anchorage need, or an unfavourable second molar position may favour maintenance.	Extraction planning is more favourable when successors are present and the second molar has a suitable stage and angulation. A developing third molar or crowding may support space use but does not guarantee closure.
Arch and occlusion	Maintenance is favoured when molar loss would create a new occlusal or orthodontic problem.	Extraction is more suitable when an orthodontic plan can use the space or guide molar substitution.
Timing	Maintenance is preferred when the second molar is too early or too advanced for favourable substitution and the affected tooth can be kept comfortable.	Extraction may be timed near a favourable second molar stage. Uncontrolled pain, infection, or non-restorability takes priority over ideal timing.
Care context and preferences	Maintenance remains appropriate when the family accepts repair and can access continuing review.	Extraction may be appropriate when the family prefers a lower cumulative treatment burden after balanced counselling and orthodontic follow-up is available.

No single factor in Table 3 determines the decision. Active infection, uncontrolled pain, or an unrestorable tooth can override an otherwise favourable orthodontic window. Conversely, an ideal developmental stage does not justify

extracting a restorable, asymptomatic tooth without a child-centred discussion of alternatives.

11. An Eruption-to-Occlusion Clinical Decision Pathway

The following pathway is an original synthesis of the reviewed evidence. It is intended as a communication and planning aid, not as a validated scoring system.

Step 1: Identify an early marker. Record HSPM or another convincing hypomineralisation phenotype in the primary dentition. Explain increased risk without deterministic language and arrange review around first permanent molar eruption.

Step 2: Confirm the phenotype. On eruption, examine all first permanent molars and incisors, document each surface, and distinguish MIH from fluorosis, hypoplasia, amelogenesis imperfecta, local developmental injury, and caries. Use radiographs only for caries, pulp, restorability, or developing-dentition questions.

Step 3: Characterise the treatment need. For each tooth, record PEB and caries, hypersensitivity and function, extent and location, ability to isolate, and the child's aesthetic or psychosocial concern. At patient level, record cooperation, previous treatment burden, caries activity, access to care, and preferences.

Step 4: Stabilise first. Make brushing and eating comfortable, apply an individual preventive plan, and cover exposed porous tissue. Use a temporary glass ionomer restoration when definitive treatment or a definitive extraction decision must wait.

Step 5: Choose the least burdensome durable branch.

Intact, low-symptom molar: Protect the fissures and monitor.

Localised breakdown with favourable isolation: Restore adhesively and review the margins.

Multisurface or cuspal breakdown with a maintainable prognosis: Use full coverage or a suitable indirect restoration.

Poor-prognosis molar: Obtain orthodontic and radiographic assessment, then either maintain the tooth to a planned developmental stage or extract when disease urgency and dental development indicate.

Incisor concern: Begin with observation or the least invasive phenotype-matched aesthetic option, and stage further care.

Step 6: Verify the outcome. Use a risk-based review interval. Reassess pain, brushing, function, PEB, sealant or restoration integrity, caries, child-reported impact, eruption, and occlusion. After extraction, monitor second molar eruption, angulation, residual space, opposing tooth position, and the need for active orthodontic guidance.

12. Follow-Up Across the Developing Dentition

Follow-up is integral to treatment because clinical needs change during eruption. At each three- to six-month review, document symptoms using the same measure together with plaque and caries activity, new PEB, sealant or restoration integrity, crown fit, gingival health, and the child's experience. Photographs help identify new breakdown.

An intact sealed molar may move to a longer interval once eruption, sensitivity, home care, and retention are stable. A tooth with a temporary restoration or severe involvement requires a clearly documented definitive plan. Clinically meaningful failure includes pain, caries progression, exposed dentine, cuspal fracture, loss of function, or unplanned retreatment, not every minor repair.

After extraction, follow-up should confirm the eruption path of the second permanent molar in both planes, contact formation, residual spacing, tipping or rotation, premolar position, and overeruption of an opposing tooth. A favourable early radiograph does not eliminate the need for observation through eruption. The minimum longitudinal dataset in Table 4 separates routine review measures from findings that require earlier reassessment or escalation.

Table 4. Minimum longitudinal review dataset for a child with MIH

Review domain	Record consistently	Earlier review or escalation trigger
Symptoms and child burden	Use the same child-appropriate measure for sensitivity or pain; record effects on brushing, chewing, sleep, school, and daily life.	Persistent or worsening pain, impaired hygiene or function, or increasing child-reported impact
Enamel and restoration integrity	New post-eruptive breakdown; sealant or restoration retention and margins; crown fit; exposed dentine and cuspal integrity	New or rapid breakdown, loss of coverage, exposed dentine, cuspal fracture, or repeated unplanned retreatment
Caries and cleanability	Plaque, caries activity, home care, and gingival health	Active or progressing caries, or inability to clean comfortably
Eruption and occlusion of a maintained tooth	Eruption stage, occlusion, restorability, and prognosis	Worsening prognosis or approach to an extraction-planning window requiring radiographic or orthodontic reassessment

Review domain	Record consistently	Earlier review or escalation trigger
Development after extraction	Second molar eruption in both planes, angulation, rotation, contact, residual space, premolar position, and opposing tooth position	Unfavourable eruption, residual space, tipping, rotation, or overeruption requiring orthodontic review
Plan and interval	Current prevention and desensitisation; temporary or definitive status; adherence, preferences, and the next risk-based review	A temporary restoration or severe involvement without a definitive plan, repeated emergencies, or accumulating treatment burden

13. Evidence Gaps and Research Priorities

Future treatment trials should use calibrated EAPD-compatible diagnosis, tooth-level severity and hypersensitivity, prespecified caries status, and common outcomes including pain, function, restoration survival, retreatment, OHRQoL, periodontal effects, and child acceptance. Follow-up beyond two or three years is especially important for full-coverage and indirect restorations.

HSPM studies need prospective cohorts and adjusted estimates that separate prediction from shared risk. Aetiology research requires longitudinal exposure data and control of confounding. Extraction studies need prospective multicentre designs with standard dental-development staging, arch-specific outcomes, and reporting of subsequent orthodontics. Until then, conditional language and shared decision-making remain essential.

14. Conclusion

MIH care is most successful when it begins before structural failure. Recognition of HSPM creates an opportunity to review first permanent molars as they erupt, manage sensitivity, establish preventive care, and protect vulnerable fissures. Once breakdown occurs, the restorative plan must account for compromised enamel, moisture control, symptoms, child cooperation, and cumulative treatment burden. Direct adhesive restorations, interim glass ionomer materials, and full coronal coverage each have a role, but comparative evidence remains heterogeneous.

For a severely affected first permanent molar, preservation and extraction are both active treatment strategies. Planned extraction can support molar substitution, especially in a favourable developmental and occlusal setting, but mandibular closure is uncertain and chronological age is an imperfect proxy. A

staged, child-centred pathway that connects early recognition with restorative prognosis and orthodontic planning offers a coherent strategy for reducing repeated unplanned care.

Acknowledgements

The author has no acknowledgements to declare.

Conflict of Interest

The author declares no conflict of interest.

Funding

No external funding was received for this work.

Ethics Statement

Ethics committee approval and informed consent were not applicable because this chapter is a focused narrative review and reports no new research involving humans, animals, or identifiable data.

Data Availability

No new data were generated or analysed for this narrative review. All information supporting this chapter is available in the cited literature.

Use of Artificial Intelligence

OpenAI Codex was used solely for language editing to improve the clarity, grammar, and academic style of the manuscript. All AI-assisted content was independently reviewed, critically revised, and approved by the author, who accepts full responsibility for the accuracy, originality, and integrity of the final work. No confidential or identifiable patient data were provided to the system.

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Chapter 4

Management of Medically Compromised Patients in Oral Surgery

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Introduction

The increasing prevalence of chronic systemic diseases and aging populations has significantly changed the clinical landscape of oral and maxillofacial surgery. Modern oral surgeons are increasingly required to manage patients with complex medical conditions including cardiovascular diseases, diabetes mellitus, anticoagulant therapy, osteoporosis-related medications, immunosuppression, renal disease, liver dysfunction, and hematological disorders [1].

Medically compromised patients present unique perioperative challenges because systemic conditions may directly influence surgical risk, wound healing, infection susceptibility, bleeding tendency, and pharmacological management [2]. Consequently, safe and effective oral surgical care requires comprehensive medical assessment, interdisciplinary collaboration, and individualized treatment planning.

Historically, many medically compromised patients were denied elective oral surgery because of concerns regarding systemic complications. However, advances in medicine, pharmacology, anesthesia, and perioperative monitoring have significantly improved the safety of surgical interventions in this population [3]. Contemporary management emphasizes risk stratification and modification rather than automatic treatment avoidance.

Among the most important clinical considerations are bleeding disorders and anticoagulant therapy. The widespread use of direct oral anticoagulants, antiplatelet agents, and vitamin K antagonists has increased the complexity of perioperative bleeding management [4]. Clinicians must carefully balance hemorrhagic risk against the potentially life-threatening consequences of thromboembolic events associated with unnecessary medication discontinuation.

Medication-related osteonecrosis of the jaw (MRONJ) has also become a major concern in oral surgery. Bisphosphonates, denosumab, and antiangiogenic

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medications may impair bone remodeling and increase the risk of jaw necrosis following dentoalveolar surgery [5]. Appropriate preventive strategies and minimally traumatic surgical techniques are therefore essential.

Diabetes mellitus represents another highly prevalent systemic condition influencing oral surgical outcomes. Hyperglycemia may impair neutrophil function, collagen synthesis, angiogenesis, and wound healing while increasing postoperative infection risk [6].

Cardiovascular diseases additionally require careful perioperative evaluation because stress, vasoconstrictors, and surgical anxiety may precipitate ischemic or arrhythmic events in susceptible patients [7]. Similarly, immunocompromised individuals are at increased risk of opportunistic infections and delayed healing.

The complexity of medically compromised patient management continues to increase because of polypharmacy and multimorbidity. Drug interactions, altered pharmacokinetics, and systemic instability frequently complicate oral surgical treatment planning [8].

This chapter reviews the principles of risk assessment and perioperative management in medically compromised patients undergoing oral surgical procedures, with particular focus on anticoagulant therapy, antiresorptive medications, diabetes mellitus, cardiovascular disease, and immunosuppression.

Preoperative Medical Assessment

Comprehensive preoperative assessment is the cornerstone of safe oral surgical management in medically compromised patients. Detailed evaluation allows identification of systemic risk factors, optimization of medical conditions, and modification of surgical strategies when necessary [9].

A thorough medical history should include systemic diagnoses, previous hospitalizations, allergies, current medications, smoking status, alcohol use, and prior surgical complications [10]. Particular attention should be paid to cardiovascular status, anticoagulant use, diabetic control, immunosuppressive therapy, and history of bleeding disorders.

Medication review is critically important because many commonly prescribed drugs may influence surgical outcomes. Anticoagulants, antiplatelet agents, corticosteroids, bisphosphonates, chemotherapeutic agents, and immunosuppressive medications require specific perioperative considerations [11].

Vital signs including blood pressure, heart rate, respiratory status, oxygen saturation, and blood glucose levels may provide important information regarding systemic stability [12]. Uncontrolled hypertension, severe hyperglycemia, or active infection may necessitate postponement of elective procedures.

Laboratory investigations should be individualized according to medical status and planned surgery. Commonly requested tests include complete blood count, coagulation profile, blood glucose measurements, glycated hemoglobin, renal function tests, and liver function analysis [13].

Risk stratification systems such as the American Society of Anesthesiologists (ASA) classification may help estimate perioperative risk and guide treatment planning [14]. ASA I and II patients generally tolerate routine office-based oral surgery well, whereas ASA III and IV patients may require hospital-based management or medical consultation.

Communication with the patient's physician is often necessary in medically complex cases. Interdisciplinary collaboration may help optimize systemic conditions and clarify medication management before surgery [15].

Psychological assessment is also important because medically compromised patients often experience significant treatment-related anxiety. Stress reduction protocols and effective communication may help minimize adverse cardiovascular and endocrine responses during surgery [16].

Ultimately, individualized treatment planning based on careful medical evaluation remains essential for minimizing complications and improving surgical outcomes in medically compromised populations.

Anticoagulant and Antiplatelet Therapy

Management of anticoagulated patients is one of the most common challenges in oral surgery. Increasing numbers of patients receive anticoagulant or antiplatelet therapy for prevention of thromboembolic events associated with atrial fibrillation, prosthetic heart valves, deep vein thrombosis, pulmonary embolism, and ischemic cardiovascular disease [17].

Traditionally, anticoagulant medications were frequently discontinued before oral surgery because of bleeding concerns. However, contemporary evidence demonstrates that interruption of anticoagulant therapy may significantly increase thromboembolic risk while most minor oral surgical procedures can be safely performed with appropriate local hemostatic measures [18].

Warfarin remains an important vitamin K antagonist used worldwide. Surgical management of warfarin-treated patients typically involves evaluation of the international normalized ratio (INR). Most simple dentoalveolar procedures may be safely performed when INR values are within therapeutic ranges, generally below 3.5 [19].

Direct oral anticoagulants (DOACs) including apixaban, rivaroxaban, dabigatran, and edoxaban are increasingly replacing warfarin because of more predictable pharmacokinetics and reduced monitoring requirements [20]. Nevertheless,

management protocols for DOAC-treated patients remain more variable because laboratory monitoring is less standardized.

Current guidelines generally recommend continuation of anticoagulant therapy during minor oral surgery combined with local hemostatic techniques such as suturing, oxidized cellulose, collagen sponges, gelatin foam, tranexamic acid mouthwash, and pressure application [21].

Antiplatelet agents including aspirin and clopidogrel are also frequently encountered in oral surgery practice. Dual antiplatelet therapy may substantially increase bleeding risk; however, interruption may precipitate catastrophic cardiovascular complications including stent thrombosis [22].

Several studies have demonstrated that postoperative bleeding associated with antiplatelet therapy is usually manageable with local measures and rarely life-threatening [23]. Consequently, continuation of therapy is often preferred for routine oral surgical procedures.

Local anesthesia techniques also require consideration in anticoagulated patients. Deep regional nerve blocks may carry increased hematoma risk, particularly in patients with severe coagulopathy [24]. Careful injection technique and aspiration are therefore essential.

Postoperative instructions should emphasize bleeding control measures and emergency contact information. Most postoperative bleeding episodes occur within the first 24–48 hours and can generally be controlled conservatively [25].

Bisphosphonates and Medication-Related Osteonecrosis of the Jaw

Medication-related osteonecrosis of the jaw represents one of the most significant complications associated with antiresorptive and antiangiogenic therapies. MRONJ is characterized by exposed necrotic bone or persistent bone exposure in patients receiving these medications without prior history of jaw radiation therapy [26].

Bisphosphonates are widely used in osteoporosis, Paget disease, metastatic bone disease, and multiple myeloma. These agents inhibit osteoclast-mediated bone resorption and significantly reduce skeletal complications [27]. However, suppression of bone remodeling may impair healing following dentoalveolar surgery.

Denosumab, a monoclonal antibody targeting RANKL, is also associated with MRONJ risk despite a mechanism different from bisphosphonates [28]. Antiangiogenic medications such as bevacizumab and sunitinib may additionally contribute to jaw osteonecrosis.

Tooth extraction is the most common precipitating factor for MRONJ development. Other contributing factors include periodontal disease, ill-fitting dentures, poor oral hygiene, smoking, diabetes mellitus, corticosteroid therapy, and prolonged medication exposure [29].

Risk assessment should consider medication type, route of administration, treatment duration, and underlying systemic disease. Intravenous antiresorptive therapy generally carries significantly greater MRONJ risk than oral osteoporosis therapy [30].

Preventive dental evaluation before initiation of antiresorptive therapy is critically important. Elimination of oral infection, extraction of hopeless teeth, and optimization of oral hygiene may significantly reduce future MRONJ risk [31].

When oral surgery is necessary in patients receiving antiresorptive medications, minimally traumatic techniques are recommended. Primary wound closure, antibiotic prophylaxis, chlorhexidine rinses, and atraumatic extraction methods may reduce complication rates [32].

Drug holidays remain controversial because evidence regarding their effectiveness is limited. Decisions regarding temporary medication discontinuation should be individualized and made collaboratively with the patient's physician [33].

Management of established MRONJ depends on disease stage and symptom severity. Conservative therapy including antimicrobial rinses, antibiotics, pain control, and limited debridement is often preferred in early stages, whereas advanced disease may require surgical resection [34].

Diabetes Mellitus and Oral Surgery

Diabetes mellitus is one of the most common systemic diseases encountered in oral surgery practice and represents a major factor influencing surgical outcomes. Both type 1 and type 2 diabetes are associated with impaired wound healing, increased infection susceptibility, microvascular dysfunction, and altered immune response [35].

Hyperglycemia negatively affects neutrophil chemotaxis, phagocytosis, collagen synthesis, fibroblast function, and angiogenesis [36]. Consequently, diabetic patients may experience delayed healing and increased postoperative complications following oral surgical procedures.

Periodontal disease and oral infections are also more prevalent in diabetic individuals, further complicating surgical management [37]. Chronic inflammation and bacterial burden may impair glycemic control, creating a bidirectional relationship between diabetes and oral disease.

Preoperative glycemic assessment is critically important before oral surgery. Glycated hemoglobin (HbA1c) levels provide valuable information regarding long-term glycemic control [38]. Poorly controlled diabetes is generally associated with higher complication rates and may necessitate postponement of elective surgery until metabolic stabilization is achieved.

Blood glucose monitoring on the day of surgery is additionally recommended, particularly for insulin-dependent patients. Severe hyperglycemia may impair healing, whereas hypoglycemia represents an acute medical emergency requiring immediate management [39].

Morning appointments are often preferred for diabetic patients because endogenous cortisol levels are higher and glycemic control is generally more stable earlier in the day [40]. Patients should usually maintain normal meals and antidiabetic medication schedules unless otherwise instructed by their physician.

Antibiotic prophylaxis may be considered in selected poorly controlled diabetic patients undergoing extensive surgery, although routine prophylactic use remains controversial [41]. Strict aseptic technique and infection control are particularly important.

Stress reduction protocols are also beneficial because surgical anxiety may increase catecholamine release and worsen glycemic instability [42]. Effective pain control further contributes to metabolic stability and improved recovery.

Studies evaluating implant therapy in diabetic patients have demonstrated generally favorable outcomes when glycemic control is adequate [43]. Nevertheless, poorly controlled diabetes may increase peri-implantitis risk and impair osseointegration.

Postoperative follow-up should include careful monitoring for delayed healing, infection, and wound dehiscence. Patient education regarding oral hygiene and glycemic management remains essential for long-term success.

Cardiovascular Diseases and Oral Surgery

Cardiovascular diseases represent one of the leading causes of morbidity and mortality worldwide and are highly prevalent among oral surgery patients. Hypertension, ischemic heart disease, arrhythmias, heart failure, and valvular disorders all require careful perioperative consideration [44].

Hypertension is among the most commonly encountered conditions in dental practice. Poorly controlled hypertension may increase the risk of intraoperative bleeding, myocardial ischemia, and cerebrovascular events [45]. Blood pressure measurement should therefore be performed routinely before oral surgical procedures.

Elective oral surgery is generally postponed in patients with severe uncontrolled hypertension until medical stabilization is achieved [46]. Stress reduction techniques, short appointments, and effective local anesthesia contribute significantly to cardiovascular safety.

Local anesthetics containing vasoconstrictors require special consideration in cardiovascular patients. Epinephrine-containing anesthetics improve hemostasis and

anesthetic duration; however, excessive vasoconstrictor administration may provoke tachycardia, arrhythmias, or hypertensive episodes [47].

Current evidence suggests that limited epinephrine doses are generally safe in stable cardiovascular patients when careful aspiration and injection techniques are used [48]. Nevertheless, intravascular injection must be strictly avoided.

Patients with ischemic heart disease may experience angina or myocardial infarction precipitated by stress and pain. Adequate anxiety control and profound anesthesia are therefore critically important [49]. Nitroglycerin and emergency equipment should be readily available when treating high-risk cardiac patients.

Infective endocarditis prophylaxis remains another important issue. Current guidelines recommend antibiotic prophylaxis only for selected high-risk patients undergoing procedures involving gingival manipulation or mucosal perforation [50]. Overuse of prophylactic antibiotics is discouraged because of increasing antimicrobial resistance concerns.

Heart failure patients may demonstrate reduced tolerance for lengthy procedures and supine positioning [51]. Short appointments and semi-supine positioning may improve patient comfort and cardiovascular stability.

Arrhythmias may additionally complicate oral surgery management, particularly in anxious patients or those receiving sympathomimetic drugs [52]. Careful monitoring and stress reduction remain essential.

Comprehensive understanding of cardiovascular pharmacology, emergency management, and perioperative risk assessment is therefore fundamental for safe oral surgical practice.

Immunocompromised Patients

Immunocompromised patients represent a particularly vulnerable population in oral surgery because of increased susceptibility to infection, impaired healing, and altered inflammatory response [53]. Causes of immunosuppression include HIV infection, malignancy, chemotherapy, organ transplantation, corticosteroid therapy, autoimmune disease treatment, and congenital immune disorders.

The degree of immunosuppression significantly influences surgical risk. Mild immunosuppression may have minimal clinical impact, whereas profound neutropenia or severe T-cell dysfunction may substantially increase postoperative complications [54].

Cancer patients receiving chemotherapy frequently develop oral mucositis, neutropenia, thrombocytopenia, and opportunistic infections [55]. Timing of oral surgery relative to chemotherapy cycles is therefore critically important.

Absolute neutrophil count and platelet count should often be evaluated before invasive procedures in oncology patients [56]. Severe neutropenia may necessitate postponement of elective surgery or implementation of antibiotic prophylaxis.

HIV-positive patients may safely undergo routine oral surgery when immune status is stable and viral load is controlled [57]. However, advanced immunosuppression may increase infection risk and delay wound healing.

Transplant recipients receiving immunosuppressive medications are additionally susceptible to opportunistic infections and medication-related complications [58]. Coordination with transplant physicians is frequently necessary before major procedures.

Long-term corticosteroid therapy may suppress adrenal function and impair inflammatory response. Historically, stress-dose corticosteroid supplementation was commonly recommended; however, current evidence suggests that many minor oral surgical procedures may be safely performed without additional supplementation in stable patients [59].

Strict infection control measures are critically important in immunocompromised populations. Elimination of oral infection sources and optimization of oral hygiene may significantly reduce systemic infectious complications [60].

Postoperative follow-up should be particularly meticulous because early signs of infection may be subtle in severely immunosuppressed individuals. Prompt intervention remains essential for preventing serious complications.

Polypharmacy and Drug Interactions

Polypharmacy has become increasingly common among medically compromised patients, particularly elderly individuals with multiple chronic diseases. Concurrent use of multiple medications may significantly complicate oral surgical management because of altered pharmacodynamics, pharmacokinetics, and drug interaction potential [61].

Commonly prescribed cardiovascular drugs, anticoagulants, antidepressants, corticosteroids, antidiabetic agents, and immunosuppressive medications may all interact with drugs used in oral surgery [62]. Careful medication review is therefore essential before prescribing analgesics, antibiotics, sedatives, or local anesthetics.

Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase bleeding risk in anticoagulated patients and may additionally impair renal function in susceptible individuals [63]. Alternative analgesics such as acetaminophen are often preferred in high-risk populations.

Macrolide antibiotics and azole antifungals may interfere with cytochrome P450 metabolism and significantly alter serum levels of anticoagulants, statins, and

immunosuppressants [64]. Recognition of such interactions is critically important for preventing serious adverse events.

Elderly patients may additionally demonstrate altered hepatic and renal clearance, increasing sensitivity to sedatives and opioids [65]. Conservative dosing strategies are therefore generally recommended.

Electronic prescribing systems and drug interaction databases may improve medication safety; however, clinical judgment remains essential because many patients present with highly individualized medical circumstances [66].

Interdisciplinary communication with physicians and pharmacists may help optimize perioperative medication management and reduce preventable complications.

Anxiety and Stress Management in Medically Compromised Patients

Psychological stress and dental anxiety may significantly influence systemic stability during oral surgical procedures. Anxiety-induced catecholamine release may increase blood pressure, heart rate, blood glucose levels, and myocardial oxygen demand [67].

Medically compromised patients often experience heightened fear because of concerns regarding systemic complications. Effective communication, reassurance, and careful explanation of procedures may substantially reduce anxiety levels [68].

Stress reduction protocols include short morning appointments, profound anesthesia, adequate pain control, and comfortable clinical environments [69]. Nitrous oxide sedation and oral anxiolytics may additionally benefit selected patients.

Monitoring of vital signs during surgery may improve safety in high-risk individuals. Emergency preparedness and staff training are also essential components of medically complex patient management [70].

Ultimately, successful oral surgical care in medically compromised populations requires not only technical surgical expertise but also comprehensive understanding of systemic disease, pharmacology, and patient-centered perioperative management.

Future Perspectives in the Management of Medically Compromised Patients

The management of medically compromised patients in oral surgery is expected to become increasingly sophisticated as advances in medicine, pharmacology, biotechnology, and digital healthcare continue to evolve. Aging populations and increasing prevalence of chronic systemic diseases will further expand the need for individualized and interdisciplinary surgical care [71].

One of the most important future developments involves precision medicine approaches. Genetic profiling, biomarker analysis, and individualized pharmacological assessment may allow clinicians to predict bleeding risk, infection

susceptibility, wound healing capacity, and medication response more accurately [72].

Artificial intelligence and digital health technologies are also expected to significantly influence perioperative risk assessment. Machine learning systems may assist clinicians in identifying high-risk patients, predicting complications, and optimizing treatment planning based on large clinical datasets [73].

Point-of-care diagnostic devices may further improve chairside management. Portable coagulation analyzers, glucose monitoring systems, inflammatory biomarker tests, and salivary diagnostics may facilitate rapid perioperative evaluation and decision-making [74].

Telemedicine and integrated electronic medical record systems may additionally enhance communication between oral surgeons and physicians managing systemic diseases [75]. Such interdisciplinary coordination is particularly important in complex patients receiving anticoagulants, immunosuppressive therapy, or cancer treatment.

Regenerative medicine and biologically driven surgical approaches may also improve outcomes in medically compromised populations. Growth factors, platelet concentrates, stem cell therapies, and tissue engineering strategies may enhance healing in diabetic, irradiated, or immunosuppressed patients [76].

Another emerging area involves development of safer pharmacological protocols with reduced systemic interactions and complication risks. Novel anticoagulants, targeted immunotherapies, and improved antimicrobial stewardship strategies may simplify future perioperative management [77].

Minimally invasive surgical techniques are expected to gain increasing importance because reduced surgical trauma may improve postoperative recovery and decrease systemic stress responses [78]. Technologies such as piezosurgery, guided surgery, laser-assisted surgery, and robotic-assisted procedures may therefore become increasingly valuable in medically fragile patients.

Educational advancements are also essential. Continuous professional development regarding systemic disease management, emergency medicine, pharmacology, and interdisciplinary care will remain critical for oral surgeons treating complex patient populations [79].

Despite ongoing technological progress, individualized patient-centered care and careful clinical judgment will continue to represent the foundation of safe oral surgical management in medically compromised individuals.

Conclusion

The growing prevalence of chronic systemic diseases has made the management of medically compromised patients an essential component of contemporary oral and

maxillofacial surgery. Successful treatment requires comprehensive understanding of systemic pathology, pharmacology, perioperative risk assessment, and interdisciplinary collaboration.

Conditions such as anticoagulant therapy, diabetes mellitus, cardiovascular disease, antiresorptive medication use, and immunosuppression significantly influence surgical planning and postoperative outcomes. Careful medical evaluation and individualized treatment modification are therefore fundamental for minimizing complications and optimizing patient safety.

Current evidence increasingly supports conservative and minimally disruptive approaches in medically compromised populations. For example, continuation of anticoagulant and antiplatelet therapy with appropriate local hemostatic measures is often safer than unnecessary medication interruption because of thromboembolic risk.

Medication-related osteonecrosis of the jaw remains a major concern in patients receiving antiresorptive and antiangiogenic therapies. Preventive dental care, atraumatic surgical techniques, and close interdisciplinary communication are essential for reducing MRONJ risk.

Diabetic patients may safely undergo oral surgery when glycemic control is optimized, while cardiovascular patients require careful stress reduction, hemodynamic monitoring, and appropriate vasoconstrictor management. Immunocompromised individuals additionally require meticulous infection control and postoperative monitoring.

Polypharmacy and drug interactions represent increasingly important challenges because many medically compromised patients receive multiple medications simultaneously. Thorough medication review and interdisciplinary collaboration are therefore essential components of modern oral surgical care.

Future advances involving artificial intelligence, precision medicine, salivary diagnostics, regenerative therapies, minimally invasive surgery, and integrated digital healthcare systems are expected to further improve perioperative safety and individualized treatment planning.

Ultimately, successful management of medically compromised patients depends on balancing surgical necessity with systemic risk while maintaining a patient-centered, evidence-based, and multidisciplinary approach.

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Chapter 5

Piezosurgery in Oral and Maxillofacial Procedures: Biological Advantages and Clinical Applications

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Introduction

Technological innovations have significantly transformed modern oral and maxillofacial surgery by promoting minimally invasive approaches, improved surgical precision, and enhanced biological outcomes. Among these advances, piezosurgery has emerged as one of the most important developments in bone surgery because of its ability to perform selective and micrometric osteotomies while minimizing soft tissue injury [1].

Piezosurgery is based on ultrasonic microvibrations generated through the piezoelectric effect. Unlike conventional rotary instruments and oscillating saws, piezoelectric devices cut mineralized tissues selectively while preserving adjacent soft tissues such as nerves, blood vessels, and mucosa [2]. This selective cutting property has made piezosurgery increasingly valuable in implantology, bone grafting, sinus floor elevation, orthognathic surgery, nerve lateralization, distraction osteogenesis, periodontal surgery, and maxillofacial trauma management.

The piezoelectric phenomenon was first described by Jacques and Pierre Curie in 1880. In piezosurgery systems, electrical energy is converted into ultrasonic mechanical vibrations through piezoelectric ceramic transducers [3]. These microvibrations typically operate within frequencies ranging from 25 to 35 kHz, allowing precise bone cutting with minimal macroscopic trauma.

One of the major advantages of piezosurgery involves improved surgical safety. Conventional rotary instruments may inadvertently damage adjacent soft tissues because of uncontrolled rotational movement and limited tactile sensitivity [4]. In contrast, piezoelectric devices generally do not cut nonmineralized tissues at operative frequencies, thereby significantly reducing the risk of nerve and vascular injury.

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Another important advantage involves improved biological response and bone healing. Experimental studies have demonstrated reduced osteocyte damage, decreased thermal injury, improved cell viability, and enhanced early bone regeneration following piezoelectric osteotomy compared with conventional rotary instrumentation [5]. Reduced surgical trauma may additionally improve postoperative pain, edema, and patient recovery.

Piezosurgery has become particularly important in anatomically delicate regions such as the maxillary sinus, inferior alveolar nerve canal, mental foramen, and orbital floor [6]. The enhanced precision and tactile control of piezoelectric devices facilitate safer osteotomies in these high-risk anatomical areas.

Despite these advantages, piezosurgery is associated with certain limitations including longer operative times, higher equipment costs, and a learning curve for inexperienced operators [7]. Nevertheless, continuous technological improvements and increasing clinical experience have substantially expanded its role in oral and maxillofacial surgery.

This chapter reviews the principles, biological mechanisms, surgical advantages, clinical applications, limitations, and future perspectives of piezosurgery in oral and maxillofacial procedures.

Principles and Mechanism of Piezosurgery

Piezosurgery is based on the piezoelectric effect, in which certain crystalline materials generate mechanical deformation when exposed to electrical current [8]. Piezoelectric surgical devices contain ceramic transducers that convert electrical energy into ultrasonic vibrations transmitted to specialized surgical tips.

These ultrasonic microvibrations generally range between 60 and 210 μm in amplitude and operate at frequencies optimized for mineralized tissue cutting [9]. Frequencies around 25–35 kHz are effective for bone cutting while minimizing effects on surrounding soft tissues.

Selective tissue cutting represents the most important characteristic of piezosurgery. Mineralized tissues such as cortical and cancellous bone are effectively cut because of their density and rigidity, whereas soft tissues require substantially higher vibration frequencies for incision [10]. Consequently, structures such as nerves, blood vessels, and mucosa are relatively protected during osteotomy procedures.

Cavitation effects generated by ultrasonic vibrations additionally contribute to improved surgical visibility. Irrigation fluid subjected to ultrasonic oscillation forms cavitation bubbles that collapse and create localized pressure changes [11]. This process helps maintain a relatively blood-free surgical field and improves visualization.

Continuous irrigation during piezosurgery also plays a major role in minimizing thermal injury. Excessive heat generation during bone cutting may impair osteocyte viability and delay bone healing [12]. Piezoelectric systems generally produce lower thermal damage compared with rotary instruments when adequate irrigation is maintained.

The micrometric cutting capability of piezosurgery allows highly controlled osteotomies with improved tactile sensitivity [13]. Surgeons may therefore perform more precise bone manipulations in anatomically complex regions.

Specialized piezosurgery tips are available for different surgical applications including osteotomy, osteoplasty, sinus membrane elevation, bone harvesting, periodontal surgery, and endodontic microsurgery [14]. Tip design significantly influences cutting efficiency, surgical precision, and access to difficult anatomical regions.

The effectiveness of piezosurgery depends on multiple factors including device power, tip design, irrigation efficiency, bone density, and operator technique [15]. Excessive pressure applied during surgery may reduce vibration efficiency and increase heat generation; therefore, gentle controlled movements are generally recommended.

Biological Advantages of Piezosurgery

One of the major reasons for the increasing popularity of piezosurgery is its favorable biological profile compared with conventional rotary instruments and oscillating saws. Numerous experimental and clinical studies have demonstrated improved tissue preservation and enhanced healing responses following piezoelectric osteotomy [16].

Reduced thermal injury is among the most important biological advantages. Conventional burs and saws may generate substantial heat during bone cutting, particularly under inadequate irrigation conditions [17]. Excessive temperatures above approximately 47°C may induce osteonecrosis and impair osseointegration.

Piezosurgery generally produces lower thermal damage because of micrometric vibrations, continuous irrigation, and reduced frictional heat generation [18]. Histological studies have demonstrated improved osteocyte survival and reduced bone necrosis following piezoelectric osteotomy.

Another major advantage involves preservation of soft tissues. Selective cutting properties significantly reduce the risk of accidental nerve, vascular, and mucosal injury [19]. This is particularly important in procedures performed near the inferior alveolar nerve, Schneiderian membrane, lingual nerve, or orbital contents.

Improved bone healing has additionally been reported following piezosurgery. Experimental studies have demonstrated earlier expression of bone morphogenetic proteins, increased osteoblastic activity, and enhanced angiogenesis after piezoelectric osteotomy [20]. Reduced inflammatory response and preservation of bone microarchitecture may contribute to accelerated regeneration.

Cavitation effects generated during surgery may also reduce bacterial contamination and improve surgical visibility [21]. Improved visibility facilitates more precise surgical manipulation and may reduce intraoperative complications.

Postoperative morbidity may additionally be reduced following piezosurgery. Several studies have reported decreased postoperative pain, swelling, and trismus compared with conventional rotary instrumentation [22]. Such improvements may significantly enhance patient comfort and recovery.

Bone harvesting procedures also benefit from improved cell viability. Autogenous bone chips collected during piezosurgery often demonstrate higher osteogenic potential and greater cellular vitality than bone harvested using rotary instruments [23]. This may improve graft integration and regenerative outcomes.

Despite these advantages, clinical outcomes remain influenced by surgical experience, device parameters, and procedure complexity. Proper surgical technique and adequate irrigation remain essential for achieving optimal biological results.

Piezosurgery in Dental Implantology

Implant dentistry represents one of the most important application areas of piezosurgery. Precise osteotomy preparation, preservation of anatomical structures, and minimization of surgical trauma are essential for successful implant placement and osseointegration [24].

Piezosurgery allows highly controlled implant site preparation with improved tactile sensitivity and reduced overheating risk [25]. Preservation of bone vitality may contribute positively to osseointegration and peri-implant healing.

One of the greatest advantages of piezosurgery in implantology is its safety near critical anatomical structures. Implant placement in the posterior mandible may involve close proximity to the inferior alveolar nerve canal [26]. Piezoelectric devices significantly reduce the risk of accidental nerve injury during osteotomy preparation and nerve lateralization procedures.

Immediate implant placement may also benefit from piezosurgical techniques because of reduced trauma and preservation of thin alveolar bone walls [27]. Atraumatic extraction and precise osteotomy preparation are particularly important in esthetically demanding areas.

Piezosurgery has become especially valuable in ridge splitting and ridge expansion procedures. Conventional rotary instruments may increase fracture risk during manipulation of narrow alveolar ridges [28]. Piezoelectric osteotomy allows controlled cortical expansion with improved precision and reduced trauma.

Bone grafting and guided bone regeneration procedures are additional important indications. Piezosurgery facilitates atraumatic harvesting of autogenous bone blocks and particulate grafts from intraoral donor sites such as the mandibular ramus, symphysis, and maxillary tuberosity [29].

Sinus floor elevation procedures have also benefited significantly from piezoelectric surgery because of reduced Schneiderian membrane perforation risk. The selective cutting ability allows safer lateral window preparation compared with rotary burs [30].

Although piezosurgery may increase operative time during implant site preparation, many clinicians consider the biological and safety advantages sufficient to justify its use, particularly in complex or high-risk procedures.

Piezosurgery in Maxillary Sinus Augmentation

Maxillary sinus floor elevation is one of the most frequently performed regenerative procedures in implant dentistry and oral surgery. Because of reduced posterior maxillary bone height resulting from alveolar resorption and sinus pneumatization, sinus augmentation is often necessary before implant placement [31].

One of the most common complications of lateral window sinus surgery is Schneiderian membrane perforation. Conventional rotary burs and saws may inadvertently damage the sinus membrane during osteotomy preparation, potentially compromising graft stability and increasing postoperative complications [32].

Piezosurgery has significantly improved the safety of sinus augmentation procedures because of its selective cutting properties. Piezoelectric devices effectively cut mineralized bone while minimizing injury to the Schneiderian membrane [33]. Multiple studies have demonstrated lower membrane perforation rates when piezosurgery is used for lateral window preparation compared with conventional rotary instrumentation.

Another major advantage involves improved surgical visibility. Cavitation effects generated during piezoelectric surgery help maintain a cleaner operative field with reduced bleeding [34]. Enhanced visualization facilitates safer membrane elevation and more precise manipulation of graft materials.

Reduced postoperative morbidity has additionally been reported in piezosurgery-assisted sinus augmentation. Patients may experience less swelling, pain, and discomfort compared with conventional approaches [35]. Reduced inflammatory response and minimized surgical trauma likely contribute to improved recovery.

Piezoelectric devices may also facilitate more conservative and precise bony window preparation. Smaller osteotomies and controlled bone removal may preserve more native bone and improve graft stability [36].

Bone particles collected during piezosurgical osteotomy additionally demonstrate favorable biological properties and may contribute to regenerative healing within the sinus cavity [37].

Although piezosurgery generally requires longer operative time than rotary instrumentation, many surgeons prefer its enhanced safety profile, especially in anatomically complex or high-risk sinus procedures.

Piezosurgery in Bone Grafting and Regenerative Surgery

Bone grafting procedures are fundamental components of oral and maxillofacial reconstruction and implant rehabilitation. Autogenous bone remains the gold standard grafting material because of its osteogenic, osteoinductive, and osteoconductive properties [38].

Piezosurgery has become increasingly important in bone harvesting procedures because of its ability to preserve cellular vitality and minimize donor site morbidity. Bone harvested with piezoelectric devices often demonstrates improved osteocyte survival and greater regenerative potential compared with bone harvested using rotary instruments [39].

Common intraoral donor sites include the mandibular ramus, symphysis, zygomatic buttress, and maxillary tuberosity. Piezoelectric osteotomy allows highly precise harvesting of cortical bone blocks while reducing the risk of adjacent nerve or soft tissue injury [40].

Reduced thermal damage during bone harvesting is particularly important because osteocyte viability significantly influences graft integration and remodeling [41]. Histological studies have shown less bone necrosis and more favorable healing following piezosurgical harvesting.

Guided bone regeneration procedures additionally benefit from piezoelectric osteotomy. Precise cortical perforations and decortication may enhance vascularization and cellular migration within grafted sites [42].

Alveolar ridge augmentation, sinus grafting, cleft reconstruction, and peri-implant defect management are among the most common regenerative

applications involving piezosurgery [43]. Improved graft adaptation and reduced surgical trauma may positively influence regenerative outcomes.

Another important application involves distraction osteogenesis. Piezoelectric osteotomy allows highly precise corticotomies while preserving periosteal vascular supply and minimizing soft tissue injury [44]. Preservation of biological integrity may contribute to improved bone formation during distraction phases.

Piezosurgery has also been investigated in periodontal regenerative surgery and root surface debridement because of its conservative tissue interaction and improved healing characteristics [45].

Although regenerative procedures using piezosurgery may require greater technical sensitivity and longer surgical duration, the biological benefits frequently justify its application in complex reconstructive cases.

Piezosurgery in Orthognathic Surgery

Orthognathic surgery requires highly precise osteotomies in anatomically sensitive regions involving major neurovascular structures. Conventional saws and burs may increase the risk of nerve injury, excessive bleeding, and unfavorable fractures during osteotomy procedures [46].

Piezosurgery has increasingly been integrated into orthognathic surgical protocols because of its micrometric precision and selective cutting ability. Le Fort I osteotomy, bilateral sagittal split osteotomy, genioplasty, and segmental osteotomies may all benefit from piezoelectric instrumentation [47].

One of the most important advantages involves reduced risk of inferior alveolar nerve injury during sagittal split osteotomy. Piezoelectric devices allow controlled corticotomy preparation with improved tactile sensitivity near the mandibular canal [48].

Reduced intraoperative bleeding is another important benefit. Improved surgical visibility may facilitate more precise osteotomies and reduce operative stress [49].

Some studies have additionally reported reduced postoperative neurosensory disturbances following piezosurgery-assisted orthognathic procedures [50]. Preservation of adjacent soft tissue structures likely contributes to improved neural outcomes.

Le Fort I osteotomy may also benefit from piezoelectric surgery because of improved safety near the descending palatine artery and nasal mucosa [51]. Controlled osteotomies may reduce accidental soft tissue injury and unfavorable fractures.

Despite these advantages, piezosurgery may prolong operative time in extensive orthognathic procedures because bone cutting speed is generally slower

than conventional saw systems [52]. Consequently, some surgeons use hybrid approaches combining piezosurgery in high-risk anatomical regions with conventional instruments in less delicate areas.

Piezosurgery in Maxillofacial Trauma Surgery

Management of maxillofacial fractures frequently requires osteotomy, reduction, fixation, and delicate manipulation near critical anatomical structures. Piezosurgery offers several advantages in trauma surgery because of its precision and soft tissue preservation properties [53].

Orbital fracture management represents one of the most important trauma-related applications. The orbital region contains delicate soft tissues including extraocular muscles, orbital fat, neurovascular structures, and the globe itself [54]. Piezoelectric devices allow safer osteotomy and reconstruction procedures with reduced soft tissue injury risk.

Zygomaticomaxillary complex fractures and orbital floor reconstruction may particularly benefit from precise piezoelectric osteotomies [55]. Improved visualization and controlled bone cutting facilitate accurate reduction and fixation.

Mandibular fracture management may also involve piezosurgical applications during osteotomy preparation, bone remodeling, and nerve decompression procedures [56]. Reduced risk of iatrogenic nerve injury is especially valuable in fractures involving the mandibular canal region.

Another important application involves removal of displaced fixation hardware and management of post-traumatic deformities. Precise bone cutting may improve reconstructive accuracy and minimize collateral damage [57].

Pediatric maxillofacial trauma surgery may additionally benefit from piezosurgery because preservation of developing anatomical structures is critically important in growing patients [58].

Although evidence regarding piezosurgery in trauma surgery continues to expand, many surgeons consider it particularly useful in anatomically delicate regions requiring maximal surgical precision.

Piezosurgery and Neurosensory Preservation

Preservation of neural structures remains one of the most important goals in oral and maxillofacial surgery. Inferior alveolar nerve, lingual nerve, mental nerve, and infraorbital nerve injuries may lead to long-term sensory deficits and reduced quality of life [59].

Piezosurgery has demonstrated substantial advantages in reducing iatrogenic nerve injury risk because of its selective cutting characteristics. Soft tissues

generally remain protected at operative ultrasonic frequencies, allowing safer manipulation near neural structures [60].

Inferior alveolar nerve lateralization procedures represent one of the most clinically important examples. Conventional rotary instruments may increase the risk of direct nerve trauma during cortical bone removal [61]. Piezoelectric surgery facilitates controlled bone removal around the nerve canal with improved safety.

Third molar surgery is another area where piezosurgery has demonstrated promising results. Impacted mandibular third molars located close to the mandibular canal present increased neurosensory risk [62]. Several studies have suggested reduced postoperative paresthesia rates when piezosurgery is used for bone removal.

Neurosensory preservation is also highly relevant in orthognathic surgery, implantology, cyst enucleation, and trauma reconstruction. Reduced mechanical trauma and improved precision may contribute to better neural outcomes [63].

Histological studies have demonstrated reduced inflammatory damage and improved neural preservation following piezoelectric osteotomy compared with rotary instrumentation [64]. Nevertheless, operator experience and careful surgical planning remain essential for minimizing nerve injury risk.

Limitations and Challenges of Piezosurgery

Despite its numerous biological and clinical advantages, piezosurgery is associated with several important limitations. One of the most frequently reported disadvantages is increased operative time. Piezoelectric osteotomy is generally slower than conventional rotary instruments or oscillating saws, particularly in dense cortical bone [65].

Longer surgical duration may contribute to operator fatigue and may limit efficiency in extensive reconstructive procedures [66]. Consequently, some clinicians selectively combine piezosurgery with conventional instruments depending on anatomical complexity.

High equipment cost represents another important limitation. Piezoelectric systems and specialized surgical tips may require substantial financial investment compared with traditional surgical instrumentation [67].

Learning curve and operator technique are also significant considerations. Excessive pressure applied during surgery may reduce cutting efficiency and increase heat generation [68]. Surgeons unfamiliar with piezoelectric instrumentation may initially experience reduced procedural efficiency.

Tip wear and maintenance additionally influence surgical performance. Repeated sterilization and prolonged use may reduce cutting efficiency over time [69].

Although soft tissue safety is a major advantage, inappropriate tip angulation or excessive force may still produce unintended tissue injury [70]. Continuous irrigation and careful surgical control therefore remain essential.

Another limitation involves restricted effectiveness in extremely dense cortical bone. In such situations, cutting speed may become significantly reduced compared with conventional rotary systems [71].

Despite these limitations, many clinicians consider the improved biological response, surgical precision, and safety profile sufficient to justify the use of piezosurgery in selected oral and maxillofacial procedures.

Future Perspectives of Piezosurgery

The future of piezosurgery in oral and maxillofacial surgery appears highly promising as technological innovations continue to improve surgical precision, biological safety, and clinical efficiency. Ongoing developments in ultrasonic technology, digital surgery, robotics, and regenerative medicine are expected to further expand the applications of piezoelectric surgery [72].

One of the most important future directions involves integration of piezosurgery with computer-assisted surgical navigation and robotic systems. Real-time navigation technologies combined with piezoelectric osteotomy may significantly improve surgical accuracy and reduce intraoperative complications in anatomically complex regions [73].

Artificial intelligence-assisted surgical planning may additionally optimize osteotomy design, tip selection, and cutting pathways according to patient-specific anatomical characteristics [74]. Such technologies may improve procedural predictability and reduce operator dependency.

Another important area of development involves improved piezoelectric tip design. Advances in material engineering and ultrasonic modulation may increase cutting efficiency while preserving the biological advantages of selective osteotomy [75]. More efficient cutting systems may help overcome one of the primary limitations of current piezosurgery devices, namely prolonged operative time.

Regenerative medicine applications are also expected to expand substantially. Because piezosurgery preserves osteocyte viability and enhances early bone healing, it may become increasingly integrated with tissue engineering, growth factor delivery systems, stem cell therapies, and platelet concentrate applications [76].

Piezoelectric surgery may additionally gain importance in minimally invasive and flapless surgical approaches. Reduced tissue trauma and enhanced precision are highly compatible with contemporary trends toward minimally invasive oral surgery and rapid patient recovery [77].

Another emerging field involves integration of piezosurgery with dynamic surgical navigation and augmented reality systems. Such technologies may allow surgeons to visualize anatomical structures and osteotomy pathways more precisely during surgery [78].

Educational applications are also likely to evolve. Virtual simulation platforms combined with piezosurgery training modules may improve surgical learning curves and enhance resident education [79].

Although additional high-quality randomized clinical studies remain necessary to establish standardized protocols and long-term evidence, piezosurgery is expected to become an increasingly central component of precision-based oral and maxillofacial surgery.

Conclusion

Piezosurgery represents one of the most important technological advances in contemporary oral and maxillofacial surgery. Through ultrasonic microvibrations and selective cutting properties, piezoelectric devices allow precise osteotomies while preserving adjacent soft tissues such as nerves, blood vessels, and mucosa.

Compared with conventional rotary instruments and oscillating saws, piezosurgery offers numerous biological advantages including reduced thermal injury, improved osteocyte viability, enhanced bone healing, superior soft tissue preservation, and reduced postoperative morbidity. These characteristics have contributed significantly to its growing popularity across a wide range of surgical procedures.

Piezosurgery has demonstrated valuable clinical applications in implantology, sinus floor elevation, bone grafting, orthognathic surgery, trauma reconstruction, nerve lateralization, periodontal surgery, and regenerative procedures. Its safety profile is particularly advantageous in anatomically delicate regions involving major neurovascular structures.

Among the most important clinical benefits are improved surgical precision, enhanced visibility through cavitation effects, reduced risk of membrane perforation during sinus surgery, and improved neurosensory preservation. Experimental and clinical studies additionally suggest more favorable biological healing responses following piezoelectric osteotomy.

Nevertheless, important limitations remain, including increased operative time, higher equipment costs, and technical sensitivity. Further improvements in

device efficiency, tip design, and digital integration are expected to address many of these challenges in the future.

Emerging technologies involving artificial intelligence, robotic surgery, navigation systems, augmented reality, and regenerative medicine may further expand the role of piezosurgery in oral and maxillofacial surgery. As minimally invasive and biologically driven surgical concepts continue to evolve, piezosurgery is likely to become an increasingly important component of modern precision surgery.

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Chapter 6

Bronchiectasis: Contemporary Medical, Interventional, And Surgical Management

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ABSTRACT

Bronchiectasis is a chronic respiratory disorder characterized by irreversible bronchial dilatation, impaired mucociliary clearance, persistent airway inflammation, and susceptibility to recurrent infection. Common clinical manifestations include chronic productive cough, recurrent respiratory exacerbations, and hemoptysis, all of which may substantially impair quality of life and contribute to increased morbidity and mortality. Management requires an individualized, multidisciplinary approach and is primarily based on airway clearance techniques, culture-directed antimicrobial therapy, and treatment of the underlying etiology. Bronchial artery embolization represents the preferred first-line intervention for selected patients with significant or recurrent hemoptysis. Surgical resection should be considered in carefully selected patients with localized disease, persistent symptoms despite optimized medical therapy, recurrent infection, significant or life-threatening hemoptysis, or irreversibly destroyed lung parenchyma. When supported by comprehensive preoperative evaluation and appropriate patient selection, complete anatomical resection may provide durable symptom control, reduce infectious exacerbations, preserve pulmonary function, and improve quality of life.

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1. INTRODUCTION

Bronchiectasis is a heterogeneous chronic respiratory disorder characterized by permanent bronchial dilatation secondary to structural damage of the airway wall. Its etiology is multifactorial and includes post-infectious, genetic, obstructive, immunological, and inflammatory conditions. Recurrent or severe lower respiratory tract infections, primary ciliary dyskinesia, cystic fibrosis, immunodeficiency disorders, and selected autoimmune diseases are among the recognized underlying causes. Kartagener syndrome represents a clinical phenotype of primary ciliary dyskinesia rather than a separate etiological category. Localized bronchiectasis may also develop as a consequence of bronchial obstruction caused by an aspirated foreign body, an endobronchial neoplasm, bronchial stenosis, or another lesion compromising airway patency. Establishing the underlying cause is essential because etiological classification influences disease-specific treatment, clinical surveillance, and the selection of appropriate medical, interventional, or surgical management strategies (1).

The feasibility of pulmonary resection in patients with bronchiectasis depends on the anatomical extent of disease and the predicted functional capacity of the remaining lung. Candidates for surgery should therefore have sufficient cardiopulmonary reserve to tolerate the planned resection. In cystic fibrosis, bronchiectatic changes are commonly bilateral and diffuse, which generally limits the role of anatomical resections such as segmentectomy, lobectomy, or pneumonectomy. Nevertheless, pulmonary resection may be considered in exceptional, carefully selected patients with severe localized disease or complications arising predominantly from one lung. For patients with advanced diffuse disease and progressive respiratory failure, lung transplantation may represent the definitive surgical option when established eligibility criteria are fulfilled (2).

Bronchiectasis may develop at any stage of life, although its prevalence rises substantially with advancing age. Epidemiological studies also indicate a predominance of women among adults with the disease (3). In children, the etiological spectrum differs from that observed in older populations and is more strongly associated with previous respiratory infections and inherited disorders. A systematic diagnostic assessment should also consider primary immunodeficiency, congenital abnormalities of the airways, and occult foreign-body aspiration, particularly when the disease is localized or the clinical presentation is atypical (4).

2. PATHOPHYSIOLOGY AND MORPHOLOGY

The pathogenesis of bronchiectasis is driven by a self-perpetuating interaction among impaired mucociliary clearance, persistent airway infection, dysregulated inflammation, and progressive structural damage to the bronchial wall. Failure to eliminate airway secretions facilitates microbial persistence, which promotes neutrophil-dominant inflammation and further compromises mucociliary function. The resulting tissue injury and bronchial distortion subsequently increase susceptibility to recurrent infection and continued disease progression. This interdependent process was traditionally described by Cole as a "vicious cycle" and is increasingly conceptualized as a "vicious vortex," emphasizing that its pathological components interact simultaneously rather than through a strictly linear sequence (5).

According to the conventional morphological classification, bronchiectasis is categorized as cylindrical (tubular), varicose, or cystic (saccular) on the basis of the configuration and extent of bronchial dilatation. Cylindrical bronchiectasis, the most frequently encountered pattern, is characterized by relatively uniform airway enlargement with failure of normal peripheral tapering. Varicose bronchiectasis displays irregular bronchial contours with alternating areas of dilatation and narrowing, whereas the cystic form consists of markedly dilated, sac-like airways that may extend toward the pleural surface. Although these patterns broadly reflect increasing structural distortion, radiological morphology alone does not reliably determine symptom burden, exacerbation frequency, functional impairment, or prognosis. Clinical severity should therefore be evaluated by integrating morphological findings with the anatomical extent of disease, underlying etiology, microbiological profile, and overall clinical course (6).

The anatomical distribution of bronchiectasis varies according to its underlying etiology. Although any pulmonary lobe may be affected, lower-lobe involvement is common, particularly in the left lower lobe, while the right middle lobe is another frequently involved site. This distribution may be explained by regional bronchial anatomy, gravity-dependent retention of secretions, and impaired drainage associated with defective mucociliary clearance (7). Conversely, upper-lobe-predominant disease is more frequently encountered in patients with cystic fibrosis and in those with post-tuberculous structural lung damage. Recognition of the extent and lobar distribution of bronchiectasis is clinically relevant because these patterns may provide etiological clues, guide further diagnostic evaluation, and contribute to individualized treatment planning (8,9).

3. DIAGNOSTIC EVALUATION

3.1 High-Resolution Computed Tomography

Thin-section high-resolution computed tomography (HRCT) is the imaging modality of choice for confirming the diagnosis of bronchiectasis and evaluating its anatomical extent, morphological pattern, and regional distribution. Although abnormalities may be visible on chest radiography, particularly in advanced disease, radiographic findings are neither sufficiently sensitive nor specific to establish the diagnosis. Conventional chest computed tomography (CT) may demonstrate bronchial dilatation; however, thin-section imaging provides more detailed assessment of the peripheral airways and associated pulmonary abnormalities. The principal CT features of bronchiectasis include an increased bronchoarterial ratio, failure of normal bronchial tapering, and visualization of airways abnormally close to the pleural surface. The “signet-ring sign” refers to a dilated bronchus seen in cross-section adjacent to a comparatively smaller pulmonary artery, whereas the “tram-track sign” describes the parallel linear appearance of thickened, dilated bronchial walls viewed longitudinally. Peripheral bronchial visibility, particularly within approximately 1 cm of the costal pleura or in direct contact with the mediastinal pleura, provides additional evidence of pathological airway dilatation (10).

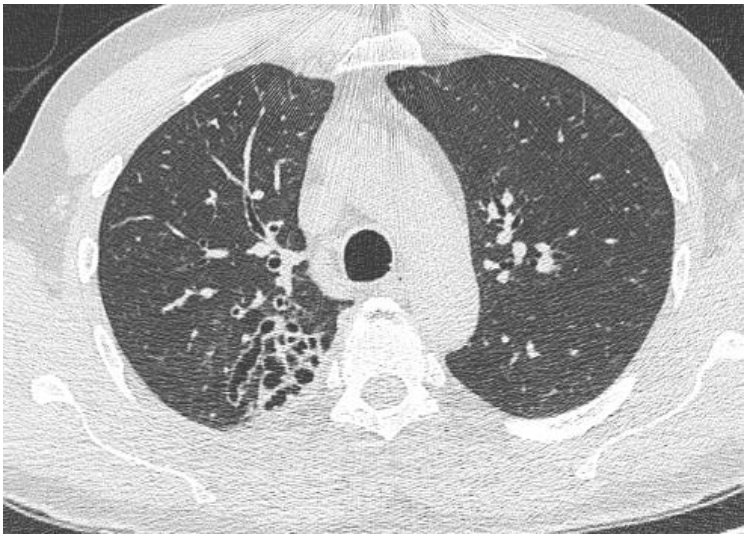

Figure 1. Axial thin-section chest CT image demonstrating localized cystic bronchiectasis in the right lung.

3.2 Bronchoscopy

Bronchoscopy is not routinely required for every patient with bronchiectasis but is particularly valuable in individuals with localized disease, unexplained clinical deterioration, or suspected airway obstruction. It enables direct assessment of the bronchial lumen and may identify an aspirated foreign body, endobronchial neoplasm, bronchial stenosis, or another obstructive lesion. Bronchoscopic sampling may also provide microbiological information when sputum cannot be obtained or when routine sputum cultures are non-diagnostic, particularly in patients with persistent or atypical infection (11,12).

3.3 Preoperative Functional Assessment

A comprehensive preoperative assessment is essential for patients being considered for pulmonary resection. Pulmonary function testing, including measurement of forced expiratory volume in one second (FEV_1), provides an initial estimate of the patient's ability to tolerate the proposed loss of functioning lung parenchyma. Diffusing capacity of the lung for carbon monoxide (DLCO) should also be evaluated when clinically indicated, particularly before major anatomical resection or in patients with underlying parenchymal lung disease. Predicted postoperative FEV_1 and DLCO should be calculated according to the planned extent of resection. In patients whose functional reserve remains uncertain or appears borderline, cardiopulmonary exercise testing may provide additional objective assessment of operative risk and assist in determining the safest extent of resection (13).

4. CLINICAL AND MICROBIOLOGICAL ASSESSMENT

4.1 Clinical Assessment

The clinical presentation of bronchiectasis is heterogeneous and commonly includes chronic cough, sputum production, recurrent respiratory infections or exacerbations, and hemoptysis of variable severity. Digital clubbing may be observed in patients with advanced or longstanding suppurative disease, although it is not specific to bronchiectasis. Exacerbation frequency is an important indicator of disease activity; patients experiencing three or more episodes annually are generally considered to have a frequent-exacerbator phenotype. This pattern is associated with impaired quality of life, progressive loss of pulmonary function, and increased healthcare utilization and should therefore prompt reassessment of the patient's treatment strategy. Changes in sputum volume, consistency, color, odor, or purulence may indicate an acute exacerbation, particularly when accompanied by worsening cough, dyspnea, fatigue, or hemoptysis. Careful symptom assessment, early recognition of exacerbations,

and timely initiation of appropriate treatment are essential. In patients with anatomically localized disease, persistent symptoms, recurrent exacerbations, or clinically significant hemoptysis despite optimized medical therapy, multidisciplinary evaluation for surgical treatment may be appropriate (14).

4.2 Microbiological Assessment

Sputum microbiological analysis is an essential component of both initial assessment and longitudinal management because it enables antimicrobial therapy to be tailored to the identified pathogen and its susceptibility profile. Frequently isolated bacterial pathogens include *Haemophilus influenzae, Pseudomonas aeruginosa, Moraxella catarrhalis, Streptococcus pneumoniae,* and *Staphylococcus aureus*. Enterobacterales, including *Klebsiella pneumoniae* and *Escherichia coli*, may also be detected in selected patients. Investigation for nontuberculous mycobacteria and *Aspergillus* species should be performed when clinically indicated, and their isolation should be interpreted in conjunction with clinical and radiological findings. Persistent *P. aeruginosa* infection is particularly important because it influences eradication strategies, long-term antimicrobial management, and the potential use of inhaled antibiotic therapy (15).

5. MEDICAL MANAGEMENT

5.1 Airway Clearance and Mucoactive Therapy

Medical management constitutes the foundation of bronchiectasis care and should be individualized according to symptom burden, exacerbation frequency, microbiological findings, underlying etiology, and associated comorbidities. Airway clearance techniques are central to long-term care and should ideally be selected and taught by a respiratory physiotherapist. Postural drainage and oscillatory positive expiratory pressure devices may facilitate the mobilization and expectoration of retained secretions by combining positive expiratory pressure with airway oscillation. Mucoactive therapies, including nebulized hypertonic saline, may be considered in selected patients with difficult sputum expectoration, whereas the benefit of agents such as N-acetylcysteine should be assessed individually.

5.2 Antimicrobial Therapy

Antimicrobial treatment should be guided by clinical severity, previous microbiological results, and current culture and susceptibility findings whenever available. Acute exacerbations may require oral or intravenous antibiotics, depending on disease severity and the identified or suspected pathogen. Long-

term macrolide therapy may be considered for patients with recurrent exacerbations despite optimized airway clearance and management of underlying causes, after appropriate assessment of potential contraindications and exclusion of nontuberculous mycobacterial infection. Inhaled antibiotics represent an important treatment option for selected patients with chronic *Pseudomonas aeruginosa* infection and recurrent exacerbations (16,17).

6. HEMOPTYSIS

6.1 Initial Assessment and Stabilization

Hemoptysis in patients with bronchiectasis ranges from minor blood-streaked sputum to life-threatening airway bleeding. Clinical severity should not be determined solely by the estimated volume of expectorated blood, which is often inaccurate, but should also incorporate the rate and persistence of bleeding, the patient's respiratory and hemodynamic status, gas-exchange impairment, and ability to maintain airway patency. In life-threatening hemoptysis, the immediate priorities are airway protection, preservation of ventilation and oxygenation, and hemodynamic stabilization. Airway obstruction and contamination of the unaffected lung may result in asphyxia and are more immediate threats than the degree of blood loss itself.

6.2 Initial Medical Management

Minor, self-limited hemoptysis may be managed conservatively with clinical observation and treatment directed at the underlying infection or other precipitating cause. Tranexamic acid may be considered as an adjunctive therapy in appropriately selected patients, although the optimal route, dose, and patient-selection criteria remain incompletely defined (18). Persistent, recurrent, or life-threatening bleeding requires urgent multidisciplinary management. Depending on the patient's clinical condition and the suspected source of hemorrhage, subsequent interventions may include bronchoscopy, computed tomography angiography, bronchial artery embolization, and surgical resection in carefully selected cases.

6.3 Airway Management

In patients with life-threatening hemoptysis, positioning the suspected bleeding lung in the dependent position may help limit spillage of blood into the contralateral lung. Definitive airway management should prioritize rapid placement of a large-bore single-lumen endotracheal tube, which facilitates effective suctioning, flexible bronchoscopy, and deployment of a bronchial blocker when lung isolation is required. Routine use of a double-lumen

endotracheal tube is generally discouraged in the emergency setting because its narrower lumens may impede evacuation of blood and clot, while placement can be technically difficult and prone to malposition in a contaminated airway. Flexible bronchoscopy can assist in localizing the bleeding source, clearing secretions and smaller clots, and positioning a bronchial blocker. Rigid bronchoscopy may provide superior airway control and permit removal of larger clots when appropriate expertise and equipment are available. Temporary endobronchial measures, including balloon tamponade or cautious administration of topical vasoconstrictive agents, may be used as bridging interventions while definitive hemostatic treatment is arranged (19).

6.4 Definitive Management

In bronchiectasis, clinically significant hemoptysis most commonly arises from hypertrophied bronchial arteries and, less frequently, from non-bronchial systemic or pulmonary arterial vessels. Chronic airway inflammation promotes vascular remodeling, enlargement of the bronchial circulation, and development of fragile systemic collaterals that are susceptible to rupture. In hemodynamically stable patients, computed tomography angiography can help localize the likely bleeding site, delineate bronchial and non-bronchial systemic arterial anatomy, and guide subsequent embolization or operative planning. Bronchial artery embolization is generally the preferred first-line definitive intervention for significant, recurrent, or life-threatening hemoptysis. Surgical resection should be reserved for carefully selected patients with anatomically localized disease, persistent or recurrent bleeding despite embolization, or a resectable underlying lesion requiring definitive treatment. Whenever possible, surgery should be performed after stabilization and precise localization of the bleeding source rather than under uncontrolled emergency conditions (20).

7. BRONCHIAL ARTERY EMBOLIZATION

7.1 Indications and Clinical Role

Bronchial artery embolization is a minimally invasive endovascular treatment and is generally considered the preferred first-line intervention for significant, recurrent, or life-threatening hemoptysis arising from bronchiectasis. It is particularly valuable in patients with bilateral or extensive disease, limited cardiopulmonary reserve, substantial comorbidity, or other factors that increase the risk of pulmonary resection. Embolization may provide definitive control of bleeding or serve as a temporizing measure before elective surgery in patients with localized resectable disease (21).

7.2 Angiographic Evaluation and Technique

The procedure is performed by interventional radiologists through arterial access, most commonly via the femoral or radial artery. Selective angiography is used to identify abnormal bronchial and non-bronchial systemic vessels supplying the suspected bleeding region. Angiographic findings may include arterial hypertrophy and tortuosity, abnormal parenchymal vascularity, systemic-to-pulmonary shunting, aneurysmal change, or active contrast extravasation. In bronchiectasis, chronic airway inflammation promotes angiogenesis and remodeling of the bronchial circulation, resulting in enlarged and fragile systemic vessels. Active contrast extravasation is a specific sign of ongoing hemorrhage but is detected in only a minority of procedures; therefore, its absence does not exclude the responsible vascular territory or preclude embolization (22).

7.3 Prevention of Procedure-Related Complications

Non-target embolization is the principal mechanism underlying serious complications of bronchial artery embolization. Particular attention should be paid to spinal arterial branches arising from bronchial or intercostobronchial arteries, including branches that may contribute to the anterior spinal circulation (23). The artery of Adamkiewicz is a major anterior radiculomedullary artery that reinforces the anterior spinal artery and may demonstrate a characteristic hairpin configuration on angiography (24). Unrecognized passage of embolic material into the spinal circulation can result in spinal cord ischemia, paraparesis, or paraplegia. Careful angiographic evaluation and superselective microcatheterization of the pathological vessel beyond any spinal arterial origin, whenever technically feasible, are therefore essential for reducing the risk of non-target embolization (25). More common and usually self-limited adverse effects include transient chest or back pain and dysphagia (26).

7.4 Embolic Materials

The selection of an embolic agent should be individualized according to vascular anatomy, the caliber and configuration of the target vessel, the presence of systemic-to-pulmonary shunting, and the operator's experience. Commonly used materials include polyvinyl alcohol particles, calibrated microspheres, and liquid embolic agents; coils are reserved for selected indications. The objective is to achieve distal occlusion of the pathological vascular bed while preserving normal arterial territories and avoiding passage of embolic material into spinal or pulmonary circulations.

Particle size is an important determinant of both procedural efficacy and safety. Particles smaller than 300 μm may penetrate excessively distal vessels and

increase the risk of non-target embolization, including entry into spinal arterial branches. Consequently, particles measuring 300–500 μm or larger are commonly preferred, with the final choice tailored to the angiographic findings and the presence of potentially hazardous anastomoses. Coils are not routinely used as the primary embolic material for diffuse bronchial arterial hypervascularity because they produce proximal vessel occlusion without necessarily treating the distal pathological bed. Proximal coil placement may also hinder future superselective access if recurrent hemoptysis requires repeat embolization. Nevertheless, coils may be appropriate in selected circumstances, such as the treatment of a focal aneurysm or pseudoaneurysm (27).

7.5 Outcomes and Recurrence

Bronchial artery embolization achieves effective initial control of hemoptysis in most patients; however, recurrent bleeding remains possible. Early recurrence may result from incomplete embolization, failure to identify all culprit vessels, or involvement of non-bronchial systemic or pulmonary arterial sources. Late recurrence may reflect recanalization of previously embolized vessels, development of new systemic collaterals, or progression of the underlying pulmonary disease. Repeat embolization is technically feasible and may provide renewed control of bleeding, provided that the vascular anatomy and potential sources of recurrence are reassessed carefully (28).

8. SURGICAL MANAGEMENT

8.1 Indications for Surgery

Surgical treatment should be considered in selected patients with localized bronchiectasis who remain symptomatic despite optimized medical therapy. Common indications include recurrent pulmonary infections, persistent productive cough with impaired quality of life, recurrent or clinically significant hemoptysis, localized destroyed lobe or lung, irreversible bronchial obstruction, and suspicion of an underlying malignancy or other localized pathological lesion. Careful patient selection through multidisciplinary evaluation is essential to ensure that the anticipated benefits of surgery outweigh the associated operative risks (29).

The decision to proceed with surgery should be based on a comprehensive multidisciplinary evaluation, balancing disease localization, symptom severity, underlying etiology, cardiopulmonary reserve, and the anticipated functional benefit of resection.

8.2 Principles of Surgical Management

Once the decision to proceed with surgery has been made, the operative strategy should be individualized according to the anatomical distribution of disease, symptom severity, underlying etiology, cardiopulmonary reserve, and anticipated function of the remaining lung. The extent of resection may range from segmentectomy or lobectomy to bilobectomy or, in carefully selected patients with unilateral extensive destruction, pneumonectomy. Anatomical resection is generally preferred because bronchiectatic changes often extend beyond macroscopically apparent abnormalities. The operative objective is complete removal of irreversibly diseased and symptomatic parenchyma whenever this can be achieved without compromising postoperative pulmonary function. Incomplete resection may be unavoidable in patients with bilateral or multifocal disease but is associated with a higher likelihood of persistent or recurrent symptoms (29,30).

8.3 Preoperative Optimization and Surgical Approaches

Elective surgery should ideally be undertaken after control of acute infection, reduction of airway secretions, and optimization of the patient's respiratory and nutritional status. Culture-directed antimicrobial treatment, airway clearance therapy, and pulmonary rehabilitation may facilitate operative preparation. Surgical access may involve video-assisted thoracoscopic surgery (VATS), robot-assisted thoracic surgery (RATS), or open thoracotomy. Minimally invasive resection can be considered in patients with favorable anatomy and manageable pleural adhesions and may reduce postoperative pain, length of hospitalization, and recovery time. Open thoracotomy remains appropriate when extensive adhesions, calcified lymph nodes, distorted hilar anatomy, major vascular involvement, or the need for complex resection makes minimally invasive dissection unsafe or impractical (31).

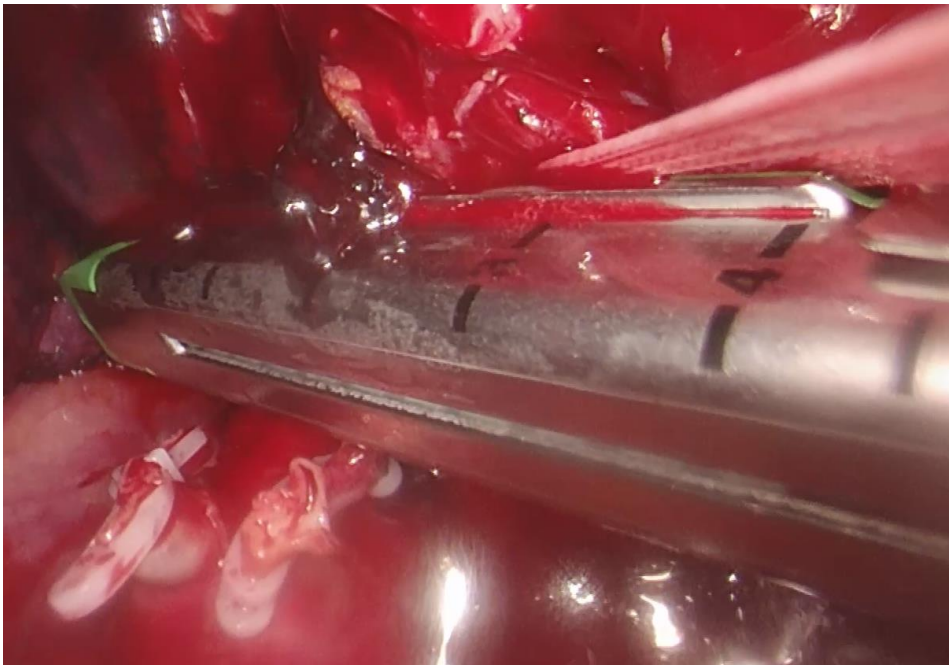

Figure 2. VATS left upper lobectomy for localized bronchiectasis demonstrating endoscopic stapler division of the pulmonary fissure.

8.4 Intraoperative Challenges and Postoperative Complications

Dense pleural and hilar adhesions resulting from recurrent infection and chronic inflammation are among the principal technical challenges encountered during surgical treatment of bronchiectasis. Adhesiolysis may obscure anatomical planes, prolong operative time, and increase the risk of vascular injury. Extensive adhesions, severely distorted hilar anatomy, or uncontrolled intraoperative bleeding may necessitate conversion from VATS to open thoracotomy. Such conversion should be regarded as a safety measure rather than a surgical failure. In carefully selected patients with a unilaterally destroyed lung, including those with extensive post-tuberculous structural damage, pneumonectomy may be required when lesser resection cannot achieve adequate disease control. Potential postoperative complications include atrial arrhythmias, pneumonia, atelectasis, prolonged air leakage, hemorrhage, empyema, respiratory failure, and bronchopleural fistula (32).

8.5 Lung Transplantation

Lung transplantation may be considered in selected patients with advanced bilateral and diffuse bronchiectasis who develop progressive respiratory failure, severe functional limitation, or recurrent life-threatening complications despite

optimized multidisciplinary treatment. Referral to a transplantation center should be undertaken before the development of irreversible extrapulmonary organ dysfunction, and candidacy should be determined according to established transplantation criteria (33).

9. CONCLUSION

The management of bronchiectasis requires an individualized, multidisciplinary, and evidence-based approach that integrates the underlying etiology, anatomical distribution of disease, symptom burden, exacerbation frequency, microbiological profile, cardiopulmonary reserve, and overall clinical condition. High-resolution computed tomography remains the cornerstone of diagnosis, while microbiological evaluation and functional assessment are essential for guiding both medical and surgical decision-making.

Optimized medical therapy, including airway clearance techniques and culture-directed antimicrobial treatment, forms the foundation of long-term management. Bronchial artery embolization is the preferred first-line intervention for significant or recurrent hemoptysis, whereas surgical resection should be considered in carefully selected patients with localized disease, persistent symptoms despite optimized medical therapy, recurrent infection, significant hemoptysis, or irreversibly destroyed lung parenchyma. When surgery is indicated, complete anatomical resection should be pursued whenever physiologically feasible while preserving the maximum amount of functional lung tissue.

For patients with advanced bilateral disease and progressive respiratory failure despite optimal multidisciplinary management, lung transplantation may represent the final therapeutic option. Ultimately, successful long-term outcomes depend on appropriate patient selection, careful timing of intervention, and close collaboration among pulmonologists, thoracic surgeons, interventional radiologists, anesthesiologists, infectious disease specialists, physiotherapists, and lung transplantation teams.

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Chapter 7

Beyond the Alveolar Cleft: Sinonasal Findings on CBCT and Their Clinical Relevance in Patients with Cleft Lip and Palate

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INTRODUCTION

Cleft lip and palate (CLP) is a complex craniofacial condition involving structures beyond the obvious cleft of the lip, alveolus, and palate. Failure of the normal fusion of the facial processes during embryonic development can influence the growth and spatial relationships of the maxilla, nasal floor, nasal septum, turbinates, and paranasal sinuses. Moreover, surgical repair, altered midfacial growth, and functional changes that develop throughout childhood can further alter the anatomy of the nasomaxillary complex. Therefore, radiographic assessment of patients with CLP should not be limited to the alveolar defect and dental structures.

Cone-beam computed tomography (CBCT) is frequently used in patients with cleft lip and palate (CLP) for clinically justified purposes, such as preoperative assessment before secondary alveolar bone grafting, localization of unerupted or displaced teeth, assessment of dentofacial deformities, and planning of orthodontic or orthognathic treatment. Although the main indication may be dentoalveolar, medium- and large-field CBCT scans often include the nasal cavity, maxillary sinuses, osteomeatal complex, upper airway, and parts of the remaining paranasal sinuses. This broader field of view provides an opportunity and a professional obligation to systematically evaluate all structures that are included.

The relevance of this broader approach is corroborated by the high frequency of incidental findings reported in patients with CLP. Santos et al. found incidental CBCT findings in most of the evaluated patients, often involving more than one anatomical region. After dental and maxillary findings, the paranasal sinuses were among the most affected areas, with inflammatory-type opacification being a prominent finding. In this population, these findings indicate that CBCT

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interpretation should go beyond the region directly related to orthodontic or surgical planning (Santos et al., 2020).

Recent CBCT studies show that CLP patients may have reduced maxillary sinus volume, increased mucosal changes, nasal septal deviation, and certain variations of the osteomeatal complex. However, these changes do not appear to affect all patients or all sinonasal structures in the same way. Some findings are more consistent than others, and results vary depending on cleft type, age, treatment history, measurement method, and anatomical region studied. For example, reduced maxillary sinus volume has been reported in both unilateral and bilateral CLP, but the relationship between sinus size, cleft side, and mucosal involvement is complex (Kula et al., 2016; Altındağ et al., 2024; Vogiatzi et al., 2026).

Turbinate and osteomeatal complex changes also showed more selective and varied distribution, but nasal septal deviation appears to be a relatively consistent finding. While many other variations such as concha bullosa, Haller cells, Agger nasi cells, and several variations of the uncinate process did not differ significantly from controls, Göksel and Özcan reported higher frequencies of deviated nasal septum, paradoxical middle turbinate, and bifid middle turbinate in patients with CLP (Göksel and Özcan, 2023). While there was no discernible change in the total nasal cavity airway volume, Cebeci and Polat Akmansoy discovered more recently that nasal septal deviation and mucosal thickening were more common in the CLP group (Cebeci and Polat Akmansoy, 2026).

These observations demonstrate an important principle in interpretation: regional anatomic deformity does not necessarily correspond to a proportional change in the entire sinonasal system. A patient may have marked septal deviation or focal osteomeatal changes and yet have a nasal cavity volume similar to that of a noncleft individual. Conversely, reduced sinus aeration may be due not only to developmental hypoplasia but also to mucosal involvement that reduces the remaining air-filled space.

This chapter provides an overview of the CBCT findings of the maxillary sinus, nasal septum, turbinates, osteomeatal complex, sphenoid sinus, and nasal airway in patients with CLP. Special attention is paid to the clinical significance of these findings and to the limitations of the interpretation of structural changes in isolation. Radiographic mucosal thickening or opacification of the sinus should not be equated with clinically diagnosed rhinosinusitis. Imaging findings should be correlated with symptoms, clinical examination, dental status, treatment history, and, if necessary, otorhinolaryngological assessment.

Developmental and Anatomical Background

CLP is the result of a disturbance in the synchronized growth and fusion of the facial processes during embryogenesis. The cleft may involve the lip, the alveolar process, the hard and soft palates, and the nasal floor depending on its extent and laterality. The defects are not limited to the margins of the defect since the maxillary and medial nasal processes contribute to the formation of the anterior maxilla and adjacent nasal structures. Altered growth may affect the transverse, vertical, and anteroposterior dimensions of the nasomaxillary complex.

During fetal development, the maxillary sinus arises from the nasal cavity and gradually grows larger throughout childhood and adolescence. Its ultimate form is a result of craniofacial growth, dental development, bone remodeling of adjacent structures, and aeration. The sinus is irregularly shaped and located near the nasal cavity, alveolar process, orbital floor, and posterior maxilla. Therefore, disorders affecting maxillary growth can also impact the size and internal structure of the sinus.

This developmental relationship is especially important in unilateral CLP. The anterior part of the maxilla is directly related to the structures involved in the cleft, and recent volumetric evidence suggests that the anterior part of the maxillary sinus may be more affected than the posterior part. Vogiatzi et al. reported a smaller total sinus volume on the cleft side in children with unilateral CLP, with the difference mainly related to the anterior sinus compartment. On the other hand, conventional linear measurements did not show the same degree of asymmetry. This finding shows why volumetric assessment may provide information that cannot be reliably obtained from maximum width, height, or length alone (Vogiatzi et al., 2026).

Maxillary sinus changes in CLP are not merely due to congenital hypoplasia. Postnatal factors may also play a role. Maxillary growth may be influenced by surgical repair and scarring, and other factors that influence sinus development and aeration include altered nasal airflow, velopharyngeal dysfunction, recurrent upper respiratory infections, and mucociliary dysfunction. The relative contribution of each of the mechanisms is unknown, and most of the existing CBCT studies are cross-sectional. Thus, developmental and acquired influences cannot always be disentangled.

Kula et al. give an important example of such interaction. The bony maxillary sinus volume and the residual air space volume were less in children with unilateral CLP than in matched controls, whereas the volume and percentage of mucosal thickening were greater. This suggests that the reduced aerated sinus volume may be due to the combined effects of altered skeletal development and

mucosal involvement. The lack of significant difference between the cleft and non-cleft sides further suggests that the changes in the sinonasal region may not be caused solely by the local cleft defect.

The nasal septum is another important component of the altered nasomaxillary anatomy. Septal deviation can result from asymmetric growth, displacement of the nasal base, or complex interactions between cartilage and surrounding facial bones. Studies consistently report a higher frequency of septal deviation in patients with CLP, especially in unilateral cases. Dedeoğlu et al. found anterior septal deviation to be more common in unilateral CLP, while later studies confirmed that septal deformity remains one of the most reproducible sinonasal differences between cleft and non-cleft groups (Dedeoğlu et al., 2016; Göksel and Özcan, 2023; Cebeci and Polat Akmansoy, 2026).

The clinical significance of septal deviation cannot be established from the morphology alone, as the functional significance of septal deviation depends on the location and extent, contact with the turbinates, involvement of the nasal valve, condition of the mucosa, and the presence of compensatory changes in the contralateral nasal cavity. This may explain why a higher prevalence of septal deviation does not always correlate with a measurable reduction in total nasal cavity volume.

Drainage and ventilation of the maxillary, frontal, and anterior ethmoid sinuses are primarily dependent on the osteomeatal complex. The osteomeatal complex is an anatomically narrow area comprising the maxillary sinus ostium, ethmoid infundibulum, hiatus semilunaris, ethmoid bulla, middle turbinate, and the frontal recess. Variations such as paradoxical middle turbinate, concha bullosa, Haller's cells, enlarged ethmoid bulla, or altered morphology of the uncinate process may restrict drainage pathways in some situations. However, the presence of an anatomical variation alone is not a sign of obstruction or disease. Its importance depends on size, orientation, mucosal contact, and the anatomy surrounding it.

This selective interpretation is confirmed by research in patients with CLP. Although paradoxical and bifid middle turbinates have been more frequently described in some CLP cohorts, many other osteomeatal complex variants are found equally frequently in cleft and control populations. Hence, CLP should not be seen as a cause of a generalized increase in all sinonasal anatomical variations. Rather, the available evidence supports a pattern of specific regional alterations superimposed on the broad anatomical variability observed in the general population.

The sphenoid sinus, a more remote component of the paranasal sinus system, develops over a prolonged period extending into adolescence. Its pneumatization

can encompass the sphenoid body, clivus, lesser wing, greater wing, anterior clinoid process, and pterygoid processes. Morphological assessment is of particular significance prior to transsphenoidal and craniofacial procedures, given the sinus's close proximity to the optic nerve, internal carotid artery, cavernous sinus, pituitary gland, and cranial base. Studies in CLP populations have revealed partially contradictory findings, suggesting that the developmental effects of clefting on the sphenoid sinus are less uniform than those observed in the anterior nasomaxillary region (Yalcin, 2020; Tepe et al., 2025; Gringo et al., 2026).

In conclusion, sinonasal anatomy in CLP should be understood as the result of interacting developmental, functional, and treatment-related influences. The most visible cleft may be anteriorly located, but its anatomical context extends throughout the nasal cavity and paranasal sinuses. At the same time, not every radiographic difference is necessarily caused by the cleft, clinically symptomatic or relevant to treatment. Meaningful interpretation requires attention to age, cleft type, side, previous surgery, orthodontic intervention, imaging indication, and the clinical question addressed.

Maxillary Sinus Morphology and Volume

The maxillary sinus is one of the sinonasal structures most closely associated with the disturbed nasomaxillary development seen in cleft lip and palate patients. As it occupies a large portion of the maxillary body and develops simultaneously with the surrounding craniofacial structures, alterations in maxillary growth may be reflected in sinus size, shape, and aeration. However, the relationship is not entirely predictable. Maxillary sinus morphology is influenced not only by the original cleft anatomy but also by age, dental development, surgical repair, orthodontic treatment, nasal airflow, and mucosal condition.

3D volumetric assessment is particularly useful in this context. The maxillary sinus has an irregular shape that cannot be reliably represented by a single linear measurement. Maximum height, width, or anteroposterior length may be similar when the overall configuration of the sinus differs. Therefore, volumetric segmentation provides a more complete estimate of sinus size and allows regional changes to be identified.

Recent data in children with unilateral cleft lip and palate illustrate this distinction. Vogiatzi et al. reported a smaller maxillary sinus volume on the cleft side but no corresponding differences with conventional linear measurements. The reduction was most evident in the anterior portion of the sinus, while the posterior compartment was relatively preserved. This regional pattern is

anatomically plausible because the anterior maxilla is more directly involved in cleft formation and associated growth disturbance and further suggests that cleft-related sinus change may involve shape redistribution rather than uniform reduction in all dimensions (Vogiatzi et al., 2026).

This finding has a major clinical implication: two maxillary sinuses may seem similar when evaluated by maximum dimensions but differ greatly in their internal volume and anteroposterior distribution. Therefore, volumetric analysis may offer more information than isolated linear measurements in the evaluation of sinus morphology in patients with CLP. However, the small sample size of many available studies and the inclusion of specific age groups limit the generalizability of these patterns.

Evidence for a reduction in maxillary sinus volume is also present in bilateral cleft lip and palate. Altındağ et al. found the overall mean sinus volume in patients with bilateral CLP was lower than that of age- and sex-matched controls. The mean volumes were reported to be around 8.01 cm^3 in the bilateral CLP group and 11.09 cm^3 in the control group. Since bilateral clefts involve both sides of the anterior maxilla, the lower volume may reflect a more generalized alteration in maxillary development rather than a side-specific asymmetry (Altındağ et al., 2024).

However, a decreased volume should not be automatically interpreted as a congenital maxillary sinus hypoplasia. Volumetric studies may measure different anatomical components. Some measure the entire bony sinus cavity, whereas others measure only the remaining air-filled space. These values are not interchangeable. A sinus may have a relatively small bony boundary, reduced aeration due to mucosal thickening, or a combination of both.

Kula et al. addressed the distinction and separately studied bony sinus volume, aerated space, and mucosal thickening in children with unilateral CLP. Patients with UCLP had smaller bony sinus volumes and smaller airspace volumes with greater absolute and proportional mucosal thickening than matched controls. These findings suggest that a single mechanism is not responsible for the reduced aerated volume in CLP. Developmental differences in sinus morphology and mucosal involvement may contribute simultaneously (Kula et al., 2016).

The lack of significant difference between the cleft and non-cleft sides in some unilateral CLP studies also makes a purely local explanation questionable. Although the structural deficit is unilateral, the nasomaxillary complex functions as an integrated anatomical system. Changes in airflow, septal deviation, mucociliary dysfunction, recurrent inflammation, and treatment-related alterations can affect both sinuses. Therefore, the non-cleft side should not be automatically considered as a totally unaffected internal control.

Age may also contribute to the differences noted among studies. The maxillary sinus continues to enlarge in size during childhood and adolescence, but the transverse and vertical growth rates are not necessarily the same at the various ages of development. Any volumetric difference identified before alveolar bone grafting may not be as striking, or may not have the same clinical significance, in an adult who has completed facial growth and undergone multiple surgical or orthodontic procedures. Cross-sectional studies with wide age ranges may thus be pooling patients at very different stages of sinus and midfacial development.

Another reason for the inconsistent results is the variation in methodology. Studies vary in voxel size, field of view, segmentation software, slice thickness, definitions of sinus boundaries, and whether mucosal tissue is included or excluded from the volume measured. There may also be differences between manual and semiautomatic segmentation—particularly near the ostium, alveolar recess, and irregular anterior sinus wall. Therefore, the numerical values obtained from different investigations should be compared with respect to how the sinus was defined and measured.

From a clinical standpoint, awareness of diminished or regionally altered sinus volume may be important prior to orthognathic surgery, sinus surgery, implant placement, and orthodontic movement of posterior maxillary teeth. A smaller anterior compartment or irregularity of the sinus floor may alter the spatial relationship between the sinus, dentition, and alveolar process. However, the volume of the sinuses does not necessarily indicate that they are not functioning properly, inflamed, or in need of treatment.

In summary, there is evidence in the literature to suggest the presence of morphological and volumetric differences in the maxillary sinuses of at least some CLP patients. These differences can be regional or generalized, unilateral or bilateral, depending upon developmental stage and cleft type. The most balanced interpretation is that reduced sinus volume is evidence of a combination of altered craniofacial development and superimposed functional or mucosal influences rather than a uniform pattern of isolated congenital hypoplasia. This distinction is particularly relevant in light of the mucosal changes and drainage pathways as described in the next section.

Mucosal Changes and Sinus Drainage

The lining of the maxillary sinus is respiratory mucosa, which, through coordinated mucociliary activity, moves secretions towards the natural ostium. Adequate sinus ventilation and drainage depend on the patency of the ostium, the anatomy of the osteomeatal complex, mucosal function, and pressure

relationships between the sinus and nasal cavity. Interference at any of these levels may reduce aeration and promote retention of secretions. In patients with cleft lip and palate, altered nasomaxillary anatomy, septal deformity, previous surgery, recurrent respiratory disease, and changes in nasal airflow may interfere with this drainage system. The relative contribution of each factor cannot usually be determined from CBCT alone.

Radiographic mucosal changes may include linear thickening along the sinus wall, dome-shaped or polypoid opacities, partial opacification, or complete loss of aeration. These findings are often incidental and not specific to a single disease. Mucosal thickening may be associated with upper respiratory infection, allergy, local inflammation, odontogenic disease, or transient mucosal responses. Therefore, mucosal thickening on CBCT should be described as an imaging finding, rather than automatically labeled as sinusitis.

The correlation between mucosal involvement and sinus aeration is especially important during the analysis of sinus volume. Kula et al. independently quantified the bony sinus cavity, the remaining airspace, and volume of mucosal thickening in children with unilateral CLP. The CLP group had smaller bony sinus and airspace volumes than controls but larger absolute and proportional mucosal thickening. Therefore, the smaller air-filled space was caused not only by reduced bony boundaries but also by increased soft-tissue occupation within the sinus (Kula et al., 2016).

This distinction has methodological and clinical relevance. Decreased aerated volume should not be equated automatically with developmental hypoplasia, and, on a threshold-based segmentation, an apparently small sinus may in part reflect mucosal disease rather than decreased skeletal dimensions. Studies that measure only the air-filled compartment may therefore report lower volumes than studies that segment the entire bony sinus cavity. Clear identification of the segmented compartment is vital in comparing results between investigations.

Kula et al. also found no significant difference between the cleft and noncleft sides prior to pooling the bilateral measurements. This indicates that mucosal involvement may not be limited to the side of the visible cleft. The sinonasal system works as a connected unit, and septal deviation, altered airflow, mucociliary dysfunction, or recurrent inflammatory exposure may influence both maxillary sinuses. Hence, the non-cleft side should be interpreted with caution when used as an internal control in unilateral cases (Kula et al., 2016).

More recent pediatric evidence supports a higher frequency of selected mucosal findings but not a uniform increase in all sinus abnormalities. Çelik et al. categorized maxillary sinus findings as mucosal thickening greater than 3 mm, polypoid thickening, partial opacification, or complete opacification. The number

of sinuses with mucosal thickening exceeding 3 mm was significantly higher in the CLP group, while the other categories did not show significant differences from controls. The distribution of abnormalities was also not consistently associated with cleft type or cleft side (Çelik et al., 2025).

The findings indicate that CLP may be associated with a greater tendency for some mucosal changes without necessarily causing a global increase in all maxillary sinus pathologies. The fact that cleft laterality did not reliably predict the side of the sinus finding also supports a multifactorial rather than purely local explanation. In a similar way, Cebeci and Polat Akmansoy found a greater frequency of mucosal thickening in patients with CLP, although the total nasal cavity volume was similar between groups. Regional mucosal or drainage-related changes may therefore occur even when global nasal cavity dimensions are not significantly changed (Cebeci and Polat Akmansoy, 2026).

The natural maxillary sinus ostium drains into the middle meatus via the osteomeatal complex. As the ostium is located superiorly on the medial sinus wall, drainage is largely dependent on active mucociliary transport rather than gravity. Local narrowing due to mucosal edema or unfavorable anatomical relationships may hinder ventilation and clearance of secretions. However, an anatomical variation seen on CBCT does not prove that the drainage pathway is functionally blocked. Static imaging does not have the capacity to directly measure mucociliary transport, nasal resistance, pressure changes, or dynamic airflow.

This distinction is particularly pertinent to the discussion of osteomeatal variations. Structures such as a paradoxical middle turbinate, Haller cell, concha bullosa, enlarged ethmoid bulla, or altered uncinate process may narrow the middle meatus in an individual patient, but the clinical effect of these structures is dependent on size, orientation, associated mucosal contact, and symptom status. Some variants are common to both cleft and non-cleft populations. Therefore, the presence of these variants alone should not be considered evidence of impaired drainage or chronic rhinosinusitis.

The high prevalence of incidental sinonasal findings emphasizes the need for systematic review of the entire CBCT volume. Santos et al. found paranasal sinus findings in almost half of the evaluated patients with CLP, most commonly inflammatory-type opacification. These observations may justify clinical questioning or referral in selected cases but should not lead to treatment solely on the basis of imaging (Santos et al., 2020).

In the clinical interpretation, therefore, assessment of the patient for nasal obstruction, facial pressure, purulent discharge, altered smell, recurrent respiratory symptoms, dental infection, or prior sinonasal treatment is

appropriate. When significant mucosal thickening, ostial obstruction, air-fluid levels, or extensive opacification is demonstrated, correlation with dental findings and otorhinolaryngological assessment where indicated is appropriate. In the asymptomatic patient, limited mucosal thickening may be an incidental or transient finding.

Furthermore, studies should be compared with caution, as there is no universally accepted CBCT threshold for clinically relevant mucosal thickening. Different investigations have used different cut-off values and classification systems. Seasonal variation, allergic status, recent infection, dental disease, and the timing of imaging could further influence the observed prevalence. Çelik et al. specifically commented that differences in radiographic classification and the lack of consensus regarding mucosal thickness may limit comparisons across studies.

In conclusion, the present evidence indicates that children and adolescents with CLP may have more frequent or extensive mucosal changes in the maxillary sinus than non-cleft controls. However, these findings are not consistently related to the side or type of cleft, and they do not constitute a clinical diagnosis of sinusitis. The most likely interpretation is that altered development, mucosal involvement, and drainage-related anatomy might act together to cause the reduced aeration observed in some patients. CBCT provides valuable morphological information, but the functional significance of these findings requires clinical correlation.

Nasal Septum, Turbinates, and Osteomeatal Complex

The nasal septum, turbinates, and osteomeatal complex constitute an anatomic and functional unit. The septum separates and shapes the nasal passages. The turbinates regulate airflow, humidification, and mucosal contact. The osteomeatal complex is the main drainage and ventilation route of the maxillary, frontal, and anterior ethmoid sinuses, and it is located on the lateral nasal wall. Changes in one part can affect the spatial relationships of the others, but structural variation does not necessarily imply functional impairment.

Among the sinonasal findings associated with cleft lip and palate, nasal septal deviation seems to be one of the most constant. The deviation may be due to asymmetric development of the nasal floor, displacement of the maxillary and medial nasal processes, altered support of the septal cartilage, or postoperative growth changes. In unilateral CLP, these effects often produce a complex deformity rather than a simple displacement of an otherwise straight septum.

Dedeoğlu et al. reported a higher frequency of anterior nasal septal deviation in patients with unilateral CLP as compared to non-cleft controls. This anterior

predominance makes clinical sense, because the cartilaginous–bony junction and the anterior nasal base lie near the cleft area. Septal deviation has also been described as one of the more reproducible anatomical differences between cleft and control groups in later CBCT studies (Dedeoğlu et al., 2016; Göksel and Özcan, 2023; Cebeci and Polat Akmansoy, 2026).

Cleft laterality may be related to septal deviation direction. In the study of Cebeci and Polat Akmansoy, the deviation was mostly to the cleft side in unilateral cases. This finding is consistent with the idea that asymmetric nasomaxillary growth may displace the septum toward the affected side structurally. Individual patterns, however, remain variable, especially in the context of surgical repair and continuing facial growth. Septal direction should therefore be documented and not inferred from the side of the cleft.

The mere presence of septal deviation does not permit evaluation of its clinical effect. An X-ray may show a deviation that causes few symptoms, while a smaller deformity near the nasal valve or in contact with a turbinate may be more functionally relevant. The degree of narrowing, site of deviation, condition of mucosa, compensatory changes, and the patient's perception of nasal obstruction should be considered.

There is volumetric evidence to support this distinction. Cebeci and Polat Akmansoy found a significantly greater nasal septal deviation in CLP patients, but no significant difference in total nasal cavity airway volume compared to controls. Hence, a visible regional deformity does not necessarily lead to a proportional decrease of the total nasal cavity volume. Morphology and global volume are related but separate aspects of nasal anatomy (Cebeci and Polat Akmansoy, 2026).

Turbinate Changes

The turbinates may differ in size, orientation, number, or internal pneumatization. These are concha bullosa, paradoxical middle turbinate, bifid middle turbinate, secondary middle turbinate, and turbinate hypertrophy. Some of these variants may influence the width of the middle meatus, but many are also seen frequently in noncleft individuals.

The CLP group had a higher frequency of paradoxical and bifid middle turbinates (Göksel and Özcan). Concha bullosa was very common in both groups, and there was no significant difference. This pattern implies that CLP does not correlate with a global increase in all turbinate variants. Instead, some changes in the morphology of the middle turbinate may be more prevalent in the setting of a background of wide normal anatomical variability (Göksel and Özcan, 2023).

A paradoxical middle turbinate is one where the convex surface is lateral rather than medial. Depending on its size and orientation, it may decrease the space of the middle meatus or change the relationship with the uncinate process. Likewise, a bifid middle turbinate is made of two bony lamellae and may also change the local anatomy. But the presence of either variation should not be taken as pathological alone.

Cebeci and Polat Akmansoy also noted that paradoxical middle turbinate was more common in the CLP group, while turbinate hypertrophy was common in both groups without a corresponding difference in total nasal cavity volume. This supports the hypothesis that turbinate enlargement may be a local or a compensatory response and not a good marker for generalized nasal airway reduction (Cebeci and Polat Akmansoy, 2026).

It is also relevant to distinguish the structures under evaluation. Studies on paradoxical, bifid or pneumatized middle turbinates do not directly assess the same variable as studies on the size of inferior turbinates. Thus, apparent discrepancies between reports may reflect different anatomical targets, rather than conflicting findings.

Osteomeatal Complex Variations

The osteomeatal complex is made up of the maxillary sinus ostium, ethmoid infundibulum, hiatus semilunaris, ethmoid bulla, middle turbinate, uncinate process, and frontal recess. Its narrow and anatomically variable configuration is important in sinus ventilation, drainage, and endoscopic surgical planning.

This region can be observed with several variations, including Agger nasi cells, Haller cells, enlarged ethmoid bulla, concha bullosa, paradoxical turbinate, pneumatized uncinate process, and bifid or atelectatic uncinate processes. If they are large enough, or in the wrong location, these structures can constrict a drainage path. However, their size, orientation, associated mucosal contact, and anatomy of the middle meatus as a whole determine their functional effect.

The existing CLP studies did not support the hypothesis that all osteomeatal complex variants are more prevalent in this population. Göksel and Özcan reported a higher prevalence of paradoxical middle turbinate, bifid middle turbinate, and septal deviation, whereas Agger nasi cells, Haller cells, concha bullosa, enlarged ethmoid bulla, and most uncinate process variations showed no significant differences between groups (Göksel and Özcan, 2023).

In a similar way, Cebeci and Polat Akmansoy found a different, but selective, distribution of OMC findings. Patients with CLP had a higher incidence of paradoxical middle turbinate, septal deviation, and mucosal thickening, whereas controls had a higher incidence of Haller cells and nasal septal pneumatization.

These findings suggest that the osteomeatal complex is not uniformly involved in cleft-related changes in all its components (Cebeci and Polat Akmansoy, 2026).

Dedeoğlu et al. investigated a broad range of nasal and paranasal variations in unilateral CLP, such as conchal variations, accessory maxillary ostia, sinus septa, ethmoidal cells, and sphenoid extensions. Many common sinonasal variants were not consistently increased in the cleft group, except anterior septal deviation and selected findings in the sphenoid. This previous evidence supports the more recent interpretation that CLP causes regional anatomical changes rather than a generalized increase in sinonasal variation (Dedeoğlu et al., 2016).

Clinical Interpretation

OMC variation on CBCT should not be considered equivalent to impaired drainage or chronic rhinosinusitis. CBCT depicts bony anatomy and some mucosal changes but does not depict mucociliary activity, nasal resistance, airflow, or duration of symptoms. However, a Haller cell, concha bullosa, or paradoxical turbinate may be clinically irrelevant in one patient and may contribute to narrowing in a different patient.

A systematic assessment of CBCT should describe the following:

- Location and direction of septal deviation
- complex deformities or prominent septal spurs,
- orientation and pneumatization of the middle turbinal,
- turbinate hypertrophy, if any,
- large ethmoidal cells.
- morphology of the uncinate process,
- the apparently patent maxillary ostium and infundibular area,
- and related mucosal changes.

Reporting should be confined to findings that change local relationships, block a drainage pathway, or have possible surgical relevance. Small common variants that do not affect adjacent structures may be reported without implying disease.

Preoperative three-dimensional evaluation is especially important before functional endoscopic sinus surgery and other procedures involving the lateral nasal wall. A deviated septum, altered turbinate anatomy, unusual ethmoidal cells, or uncinate process variations may change surgical orientation and increase the risk of injury when the anatomy is taken for granted. Both Göksel and Özcan and Cebeci and Polat Akmansoy emphasized the importance of CBCT-based anatomical assessment in patients with CLP, particularly when sinonasal surgery is planned (Göksel and Özcan, 2023; Cebeci and Polat Akmansoy, 2026).

In summary, the current data suggest that a deviated nasal septum is a fairly constant finding in CLP, while turbinate and osteomeatal complex variations are more selective and heterogeneous. This pattern underlines the need for patient-based interpretation. The radiologist should not consider these structures as incidental nor assume that each variation is functionally significant. The significance of these structures is dependent upon the combination of morphology, mucosal findings, symptoms, and the planned clinical or surgical approach.

Sphenoid Sinus and Upper Airway

The sphenoid sinus is centrally located in the skull base adjacent to the pituitary gland, optic nerves, internal carotid arteries, cavernous sinuses, and numerous cranial nerves. The pneumatization of the sphenoid sinus develops in childhood and adolescence and may extend into the body of the sphenoid, the clivus, the lesser and greater wings, and the anterior clinoid and pterygoid processes. Although cleft lip and palate predominantly affects the anterior nasomaxillary complex, several CBCT studies have investigated the extent of its developmental effect on the sphenoid sinus.

The sphenoid sinus is most commonly classified as conchal, presellar, sellar, or postsellar based on the position of its posterior wall relative to the sella turcica. Other types include lateral, clival, anterior, lesser-wing, pterygoid, and conjoined extensions. These anatomic variations are of clinical importance because large or asymmetric pneumatization may alter the bony confines of important neurovascular structures.

The available findings in patients with CLP are not entirely consistent. Yalcin reported a higher prevalence of the presellar type and lower frequencies of postsellar and clival extensions in the CLP group, suggesting that posterior pneumatization was relatively limited compared with controls (Yalcin, 2020). Earlier findings by Dedeoğlu et al. were generally compatible with this interpretation, as pterygoid process pneumatization, greater-wing pneumatization, and overall sphenoid overpneumatization were less frequent in patients with unilateral CLP (Dedeoğlu et al., 2016).

However, more recent studies suggest a more selective relationship. Tepe et al. failed to find significant differences between the main conchal, presellar, sellar, and postsellar types in unilateral CLP, bilateral CLP, and control groups. Anterior pneumatization was more common in both cleft groups, and lesser-wing pneumatization was more frequent in bilateral CLP. The absence of side-related differences also suggested that sphenoid morphology is not purely determined by the local side of the cleft (Tepe et al., 2025).

Similarly, Gringo et al. reported no significant differences in the major sphenoid sinus types between bilateral CLP patients and controls. Paknahad and Agharokh reported similar distribution of sphenoid and frontal sinus pneumatization between cleft and non-cleft groups. Collectively, these results indicate that CLP does not produce a uniform pattern of sphenoid sinus alteration (Gringo et al., 2026; Paknahad and Agharokh, 2025).

Age is a significant source of variability. Tepe et al. showed a less frequent occurrence of lesser-wing, lateral, and combined pneumatization in younger subjects in both CLP and control groups. Therefore, some observed differences between groups may be related to developmental stage and not solely to cleft status. Age, cleft type, classification method, and prior treatment should be taken into account before assigning a sphenoid sinus pattern directly to CLP.

The clinical importance of evaluating the sphenoid sinus is mainly surgical. Patients with CLP may eventually need orthognathic, craniofacial, sinonasal, or transsphenoidal surgery. Therefore, when the sphenoid sinus is included in the CBCT field of view, its pneumatization pattern, septations, and extensions toward the clivus, wings, or pterygoid processes should be evaluated, especially if these findings may affect surgical access or the relationship with adjacent neurovascular structures.

Assessment of the upper airway is more difficult in CLP. The shape of the airway may be affected by septal deviation, turbinate morphology, palatal anatomy, maxillary deficiency, and previous surgical repair. However, structural deformity does not necessarily correlate with a proportional reduction in airway volume. Cebeci and Polat Akmansoy noted that the overall volume of the nasal cavity airway was similar in patients with CLP and controls, despite more frequent septal deviation and specific regional osteomeatal changes in the cleft group. This suggests that localized narrowing may be compensated by enlargement elsewhere in the nasal cavity (Cebeci and Polat Akmansoy, 2026).

CBCT provides a static image of anatomy and does not directly assess nasal resistance, respiratory function, mucosal cycling, sleep-related airway collapse, or dynamic airflow. Airway volume should therefore not be used as an isolated indicator of functional obstruction. Imaging findings should be interpreted in conjunction with symptoms such as nasal obstruction, mouth breathing, snoring, recurrent respiratory problems, and, if relevant, otorhinolaryngologic or sleep-related assessment.

Sphenoid sinus and airway findings usually expand the scope of CBCT interpretation beyond the anterior cleft region. Evidence to date suggests that changes in sphenoid pneumatization are selective rather than universal and that regional nasal deformity can occur without a significant change in total airway

volume. Their main use is to assess anatomy on a patient-specific basis and for multidisciplinary treatment planning.

Clinical Interpretation and CBCT Reporting

CBCT examinations in patients with cleft lip and palate are often required for planning alveolar bone grafts, evaluation of dental anomalies, orthodontic treatment, or evaluation of craniofacial morphology. But the diagnostic responsibility for the entire imaged volume remains. Examinations of medium and large fields can also include the nasal cavity, paranasal sinuses, airway, temporomandibular joints, cranial base, and cervical structures. Incidental findings are especially common in this population and may affect multiple anatomic regions within the same patient. The interpretation of the alveolar cleft and associated teeth should not be stopped here (Santos et al., 2020).

A practical approach to assessment of the sinonasal region should start with the maxillary sinuses, considering their overall development, symmetry, aeration, wall integrity, and relation to the dentition. Volumetric asymmetry or apparent hypoplasia should be considered along with mucosal occupation, as a decreased airspace does not necessarily equate with a proportionally smaller bony sinus. Morphology and extent of linear mucosal thickening, polypoid changes, and partial or complete opacification should be described. The report should also comment on possible odontogenic sources when periapical, periodontal, or postoperative changes are adjacent to the sinus floor.

Examination of the nasal septum should include direction, location, and severity of deviation and prominent spurs or contact with the turbinates. Variations of the turbinate and osteomeatal complex should be recorded when they significantly alter local anatomy, constrict a drainage pathway, or may be relevant to planned surgery. They should not be held as evidence of obstruction simply because they are there. Similarly, for the sphenoid sinus, prominent pneumatization, septations, and extensions toward the clivus, pterygoid processes, or sphenoid wings may be noted, as appropriate for craniofacial or sinonasal surgical planning.

The report’s language is medically important. Terms such as "mucosal thickening," "sinus opacification," or "radiographic inflammatory change" are usually more appropriate than a definitive diagnosis of sinusitis. Clinical rhinosinusitis needs to be correlated with the symptoms, examination findings, and duration of disease. Static CBCT images do not evaluate mucociliary clearance, dynamic airflow, nasal resistance, or inflammatory process activity. Hence, a minor incidental mucosal finding in an asymptomatic patient has a

different significance than extensive bilateral opacification with nasal obstruction, discharge, facial pressure, or recurrent infection.

Referral should be considered for sinonasal findings that are extensive, obstruct the drainage region, are associated with suspected odontogenic disease, or may impact planned surgical treatment. Otorhinolaryngological evaluation is also indicated in patients with persistent sinonasal symptoms or significant anatomic narrowing. The role of the radiologist is not to assign clinical significance to every variation but rather to identify findings that may change diagnosis, treatment planning, or the need for further evaluation.

Methodological Limitations and Future Directions

Published literature on CBCT of sinonasal structures in patients with CLP is heterogeneous. The majority of studies are retrospective, single-center studies with relatively small or highly selected samples. Patients are frequently grouped into broad age bands despite the fact that the maxillary and sphenoid sinuses continue to develop throughout childhood and adolescence. Differences in cleft type, laterality, surgical history, orthodontic treatment, and timing of imaging further complicate comparisons.

A further important limitation is variability in the imaging and measurement methods. Studies use different CBCT devices, voxel sizes, fields of view, reconstruction settings, and segmentation software, as well as anatomical boundaries. Some measure the entire bony sinus cavity; others measure only the aerated compartment. Mucosal tissue may be included, excluded, or analyzed separately. Thus, numerical volume values from different studies may not refer to the same anatomic quantity. This distinction is especially relevant as smaller bony sinus volume and larger mucosal occupation may coexist in patients with CLP (Kula et al., 2016).

Definitions of mucosal abnormalities and anatomical variants are also not consistent. Clinically relevant mucosal thickening has been defined using several thresholds. Seasonal infection, allergy, dental disease, and recent respiratory illness are rarely adequately controlled. On the other hand, the non-cleft side in unilateral CLP is often used as an internal control, although both sides can be influenced by bilateral functional and developmental influences. “Several studies have found no side-specific differences, suggesting that this assumption should be used cautiously.

Future studies should include age-stratified and cleft-specific cohorts, standardized segmentation protocols, well-defined anatomical boundaries, and reproducibility analyses with multiple observers. Datasets from multiple centers would allow assessing the stability of findings across devices, populations, and

treatment protocols. Longitudinal studies before and after critical stages of cleft care may further clarify whether sinonasal differences are primarily due to congenital development, subsequent growth, surgical intervention, or chronic mucosal changes.

Equally important is the integration of imaging with clinical and functional information. Future studies should correlate CBCT findings with sinonasal symptoms, endoscopic evaluation, nasal airflow measurements, allergy status, dental infection, and treatment history. Automated segmentation and quantitative image analysis may provide efficiency gains; however, these methods require external validation and should maintain clinically meaningful anatomic boundaries. The question should not be about more differences, but about which imaging findings predict symptoms, alter treatment, or require intervention.

CONCLUSION

Sinonasal evaluation in patients with cleft lip and palate is far more than the obvious alveolar defect. CBCT studies of some patients show decreased or regionally altered maxillary sinus volume, increased mucosal involvement, nasal septal deviation, and selected turbinate or osteomeatal complex variations. However, these findings are not uniform, and their relation to cleft type or side is often inconsistent. Again, Sphenoid sinus morphology seems to be heterogenous as well, with no one pattern characterizing all those with CLP.

Context matters for the clinical relevance of these findings. Reduced aeration may be caused by developmental morphology, mucosal occupation, or both; anatomical variation does not necessarily imply functional obstruction; and radiographic mucosal change does not equate to a clinical diagnosis of sinusitis. CBCT, therefore, should be interpreted in a systematic way based on the entire field of view corresponding to symptoms, dental findings, previous treatment, and planned procedures.

A careful, patient-specific approach allows CBCT to contribute not only to evaluation of the cleft and dentition but also to recognition of sinonasal findings that may impact multidisciplinary care. The value of imaging is mainly to separate clinically significant changes from common anatomic variation and to avoid underreporting and overdiagnosis.

References