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Review Article

Magnetic resonance imaging (MRI) and dynamic MRI evaluation of extranodal non-hodgkin lymphoma in the oral and maxillofacial regions. A systematic review.

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Abstract

Background:

Extranodal non-Hodgkin lymphoma (NHL) in the oral and maxillofacial region often mimics squamous cell carcinoma (SCC), complicating diagnosis. Magnetic resonance imaging (MRI) and dynamic contrast-enhanced MRI (DCE-MRI) offer detailed soft-tissue and functional assessment. This review evaluated their role in identifying characteristic imaging features of extranodal NHL.

Methods:

Conducted per PRISMA 2020 and registered in PROSPERO (CRD420251178334), a comprehensive search of PubMed, Scopus, Web of Science, and Google Scholar (up to 2025) was performed. Studies on histopathologically confirmed extranodal NHL assessed using MRI or DCE-MRI were included. Data on imaging features, apparent diffusion coefficient (ADC), enhancement kinetics, and diagnostic performance were extracted. Study quality was evaluated using QUADAS-2, and findings were synthesized qualitatively.

Results:

Seven studies (2004–2018) involving ~250 patients were included. NHL typically showed intermediate-to-low T1 and intermediate-to-high T2 signal intensity, homogeneous contrast enhancement, and submucosal spread with preserved mucosa. DCE-MRI demonstrated a Type II (plateau) enhancement curve, while diffusion-weighted imaging revealed low ADC values (0.68–0.90 × 10^{-3} mm^2/s), consistent with high cellularity. SCC showed heterogeneous enhancement, necrosis, and higher ADC values. Combined DWI and DCE-MRI achieved diagnostic accuracies >90%, with sensitivities of 92–96% and specificities of 88–93%.

Conclusion:

Extranodal NHL exhibits consistent MRI characteristics correlating with histopathology. Multiparametric MRI aids pre-biopsy differentiation from carcinoma and supports treatment planning. Standardized imaging protocols and validated ADC thresholds are needed to improve diagnostic precision.

Keywords: *Apparent diffusion coefficient, Diagnostic imaging, Diffusion-weighted imaging, Dynamic contrast-enhanced MRI, Extranodal non-Hodgkin lymphoma, Head and neck malignancies, Magnetic resonance imaging, Oral and maxillofacial region*

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Introduction

Non-Hodgkin lymphoma (NHL) comprises a heterogeneous group of lymphoid malignancies characterized by the clonal proliferation of B-cells, T-cells, or natural killer (NK) cells. It accounts for

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approximately 3-4% of all malignancies worldwide and represents a major component of hematolymphoid neoplasms[1]. Although the majority of NHLs originate within lymph nodes, nearly one-third arise from extranodal tissues, affecting organs and mucosal sites outside the lymphatic system[2]. The head and neck region is recognized as the second most common site of extranodal involvement after the gastrointestinal tract, encompassing structures such as Waldeyer's ring, the nasal and paranasal cavities, salivary glands, palate and gingiva. Extranodal lymphomas arising in these regions pose significant diagnostic challenges due to their variable presentation and close resemblance to more common epithelial and inflammatory pathologies[3].

Clinically, extranodal NHL of the oral and maxillofacial region manifests as a painless, progressively enlarging mass, frequently accompanied by mucosal thickening, submucosal swelling, or ulceration. Associated findings may include tooth mobility, paresthesia, or localized bone rarefaction[4,5]. These nonspecific features are easily mistaken for odontogenic infections, chronic granulomatous conditions, or squamous cell carcinoma (SCC). Radiographically, both lymphoma and carcinoma can appear as soft-tissue masses with ill-defined margins and, occasionally, bone destruction. Consequently, accurate differentiation based on clinical and radiographic findings alone remains difficult[6]. Histopathological examination remains the diagnostic gold standard; however, small or necrotic biopsies and overlapping morphologic features can result in inconclusive or misleading diagnoses[7]. In such cases, cross-sectional imaging plays a pivotal role in characterizing lesion extent, identifying the most viable biopsy site and providing valuable information on tissue composition and tumor behavior.

Magnetic resonance imaging (MRI) has become the imaging modality of choice for soft-tissue evaluation within the oral and maxillofacial complex because of its superior contrast resolution, multiplanar capability and absence of ionizing radiation[8]. Compared with computed tomography (CT), MRI provides more accurate delineation of tumor margins, perineural spread, marrow invasion and soft-tissue infiltration. Conventional MRI sequences: T1-weighted, T2-weighted and post-contrast T1-weighted offer essential qualitative information regarding lesion morphology and internal architecture[9]. Extranodal lymphomas typically display intermediate-to-low signal intensity on T1-weighted sequences and intermediate-to-high signal intensity on T2-weighted images, with strong, homogeneous enhancement following gadolinium administration. The margins are often smooth and well-defined and the lesion tends to infiltrate submucosally while maintaining the integrity of the overlying mucosa. These features correspond to the tumor's uniform cellular density, limited stromal component and absence of necrosis[10]. In contrast, SCC and other epithelial malignancies usually demonstrate irregular margins, heterogeneous signal intensity and areas of necrosis or ulceration due to keratinization and stromal desmoplasia[11].

Although these morphological differences provide important diagnostic clues, conventional MRI findings may still overlap among various neoplastic and inflammatory entities. To address this limitation, the integration of functional MRI techniques particularly diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI) has significantly advanced the non-invasive characterization of head and neck tumors. These modalities provide quantitative insights into tissue microstructure, perfusion and vascular permeability, thereby enhancing the specificity of MRI in lesion differentiation[12,13].

Diffusion-weighted imaging evaluates the random Brownian motion of water molecules within biological tissues, which is inversely related to cellular density and membrane integrity. The apparent diffusion coefficient (ADC) derived from DWI quantitatively reflects this relationship[14]. Lymphomatous tissue, composed of densely packed monomorphic cells with high nuclear-to-cytoplasmic ratios, exhibits restricted diffusion and consequently low ADC values. By contrast, carcinomas, inflammatory masses and necrotic tissues display higher ADC values owing to their expanded extracellular spaces and disrupted membrane barriers. Hence, DWI serves as a reliable, non-invasive biomarker of tissue cellularity and can aid in distinguishing lymphoma from other head and neck pathologies[15].

Dynamic contrast-enhanced MRI provides complementary information by analyzing the temporal kinetics of contrast uptake and wash-out within a lesion, reflecting microvascular density and capillary permeability[16]. Time-intensity curves (TICs) generated from DCE-MRI are typically categorized into three enhancement patterns: Type I (progressive enhancement), Type II (rapid enhancement followed by a plateau) and Type III (rapid enhancement followed by wash-out). Extranodal lymphomas characteristically exhibit a Type II plateau curve, consistent with their uniform vascular networks and limited extracellular diffusion space,

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whereas carcinomas frequently demonstrate a Type III wash-out pattern, reflecting aberrant neovascularization and increased vascular permeability. This difference in enhancement kinetics provides a physiologic basis for distinguishing lymphoma from carcinoma and offers valuable prognostic information related to tissue perfusion and angiogenic activity[17].

The imaging characteristics observed on DWI and DCE-MRI correlate closely with the underlying histopathologic architecture of lymphoma. The compact cellular arrangement and absence of necrosis account for both the homogeneous post-contrast enhancement and the restricted water diffusion. The intact endothelial barrier and moderate microvascular permeability explain the plateau pattern of enhancement, while the lack of stromal fibrosis or keratin debris yields smooth lesion margins and submucosal extension. Such correlations underscore MRI's potential not only as a diagnostic modality but also as a non-invasive means of assessing tumor biology[18,19].

Beyond diagnosis, MRI plays a critical role in staging and therapeutic planning. It allows comprehensive evaluation of local extension, marrow infiltration and perineural or intracranial spread, factors that directly influence disease stage and treatment strategy. Furthermore, functional MRI parameters such as ADC values and enhancement kinetics are being investigated as imaging biomarkers for early assessment of therapeutic response, prediction of treatment outcome and surveillance of disease recurrence. This capability is particularly valuable in extranodal lymphomas, where morphological changes may lag behind cellular and vascular alterations induced by chemotherapy or radiotherapy[20].

Despite these advantages, the interpretation of MRI findings in extranodal lymphoma remains complex due to the inherent histological diversity of NHL and the overlapping imaging profiles among different lesions. Variation in imaging protocols, field strengths and post-processing techniques across studies further contributes to diagnostic variability. Consequently, systematic synthesis of the available literature is essential to establish reproducible imaging criteria and identify consistent diagnostic patterns applicable to extranodal NHL of the oral and maxillofacial region.

The present systematic review aims to critically evaluate and synthesize current evidence on the application of MRI and dynamic MRI in the assessment of extranodal non-Hodgkin lymphoma involving the oral and maxillofacial regions. Specifically, it seeks to delineate characteristic MRI features, summarize the diagnostic value of functional imaging parameters such as ADC and enhancement kinetics and elucidate their role in differentiating lymphoma from other malignancies. By integrating morphological and physiological imaging insights, this review intends to provide an evidence-based framework to enhance diagnostic precision, optimize biopsy planning and support individualized therapeutic decision-making in patients with extranodal lymphomas of the oral and maxillofacial complex.

Materials and methods

Study Design and Protocol Registration

This systematic review was designed and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines[21]. The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO)[22] under the registration number CRD420251178334 to ensure methodological transparency and to prevent duplication of ongoing reviews. The overall objective of this review was to identify and critically synthesize published evidence on the role of magnetic resonance imaging (MRI) and dynamic MRI (DCE-MRI) in the evaluation of extranodal non-Hodgkin lymphoma (NHL) involving the oral and maxillofacial regions.

Research Question and Framework

The review question was formulated using the PICOS framework[23] (Population, Intervention, Comparison, Outcome, Study Design) to ensure a structured approach to the literature search and inclusion process:

- **Population (P):** Patients diagnosed with *extranodal non-Hodgkin lymphoma* involving the oral, maxillofacial, sinonasal, or oropharyngeal regions.
- **Intervention (I):** Evaluation by magnetic resonance imaging (MRI) and/or dynamic contrast-enhanced MRI (DCE-MRI), including diffusion-weighted imaging (DWI) sequences.
- **Comparison (C):** Comparison with other head and neck pathologies such as squamous cell carcinoma, inflammatory lesions, or benign tumors.

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- **Outcome (O):** MRI characteristics (signal intensity, enhancement patterns, apparent diffusion coefficient [ADC] values, time-intensity curves), diagnostic accuracy and distinguishing imaging features.
- **Study Design (S):** Observational, comparative and diagnostic imaging studies.

The primary outcome of interest was the identification of consistent imaging parameters capable of distinguishing extranodal NHL from other malignancies in the oral and maxillofacial region. Secondary outcomes included assessment of diagnostic accuracy, sensitivity, specificity and pathophysiologic correlations of MRI findings with histopathological features.

Eligibility Criteria

The inclusion and exclusion criteria were defined a priori to maintain rigor and minimize bias.

Inclusion criteria:

- Original research studies involving human subjects with histopathologically confirmed *extranodal NHL* of the oral, maxillofacial, sinonasal, or oropharyngeal regions.
- Studies utilizing MRI, DCE-MRI and/or DWI for lesion evaluation.
- Studies reporting quantitative or qualitative imaging findings such as signal intensity, ADC values, enhancement kinetics, or characteristic morphological features.
- Articles published in peer-reviewed journals in the English language.

Exclusion criteria:

- Studies focusing solely on nodal or systemic lymphoma without extranodal involvement.
- Case reports, case series with fewer than five patients, reviews, meta-analyses, editorials, or letters without primary imaging data.
- Experimental or animal studies.
- Articles lacking adequate methodological detail or without reported MRI parameters.
- Duplicate publications and studies with overlapping patient cohorts.

Search Strategy

A systematic search of PubMed, Scopus, Web of Science and Google Scholar was performed for articles published from 1990 to 2025 using the terms:

("non-Hodgkin lymphoma" OR "extranodal lymphoma") AND ("oral" OR "maxillofacial" OR "paranasal sinus" OR "oropharynx") AND ("MRI" OR "magnetic resonance imaging" OR "dynamic contrast-enhanced MRI" OR "diffusion-weighted imaging").

Manual searches of bibliographies were also performed. Duplicates were removed using EndNote X9.

Study Selection Process

The initial database search yielded 133 records. After removal of duplicates using EndNote X9 reference management software, 88 unique records remained. Titles and abstracts were independently screened by two reviewers to exclude clearly irrelevant articles. Full-text versions of 18 potentially eligible studies were then retrieved and assessed in detail against the inclusion criteria. Disagreements between reviewers were resolved by discussion and consensus, with arbitration by a third reviewer when necessary. Ultimately, seven studies met the inclusion criteria and were included in the final qualitative synthesis.

The entire selection process was documented using a PRISMA 2020 flow diagram (Figure 1).

Data Extraction

Data extracted included:

- Author, year, country and study design.
- Number of patients and lesion sites.
- MRI type, sequences and parameters (field strength, TR/TE, contrast medium).

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- Qualitative features (T1/T2 signal, margins, enhancement pattern, bone invasion).
- Quantitative parameters (ADC values, time-intensity curve type, enhancement ratios).
- Diagnostic performance and comparison with SCC or inflammatory lesions.

Quality and Risk-of-Bias Assessment

The QUADAS-2 tool[24] was used to evaluate methodological quality across four domains: patient selection, index test, reference standard and flow/timing. Each study was graded as *low*, *moderate*, or *high* risk of bias (Table 2).

Data Synthesis

Due to heterogeneity in imaging protocols and outcome measures, meta-analysis was not feasible. A qualitative synthesis was performed summarizing imaging characteristics, enhancement kinetics and diagnostic accuracy.

Certainty of Evidence Assessment

The certainty of evidence for the primary outcome was evaluated qualitatively in accordance with principles adapted from the GRADE framework for diagnostic test accuracy studies. Factors considered included risk of bias (QUADAS-2 results), consistency of imaging findings across studies, directness of evidence, sample size and methodological heterogeneity. Due to variation in MRI acquisition protocols, field strengths and outcome reporting, formal quantitative grading was not feasible. Overall certainty was judged as moderate for diffusion-weighted imaging parameters and enhancement kinetics, given consistent direction of findings across studies but limited by retrospective designs and small sample sizes.

Ethical Considerations

As this review was based solely on previously published research, ethical approval was not required. All included studies were assumed to have adhered to institutional and international ethical standards as reported by their respective authors.

Results

Characteristics of Included Studies

Study Selection

The study selection process is summarized in the PRISMA 2020 flow diagram (Figure 1). A total of 133 records were identified through database searching. After removal of duplicates, 88 records underwent title and abstract screening. Eighteen full-text articles were assessed for eligibility, of which eleven were excluded for not meeting inclusion criteria. Seven studies were included in the final qualitative synthesis.

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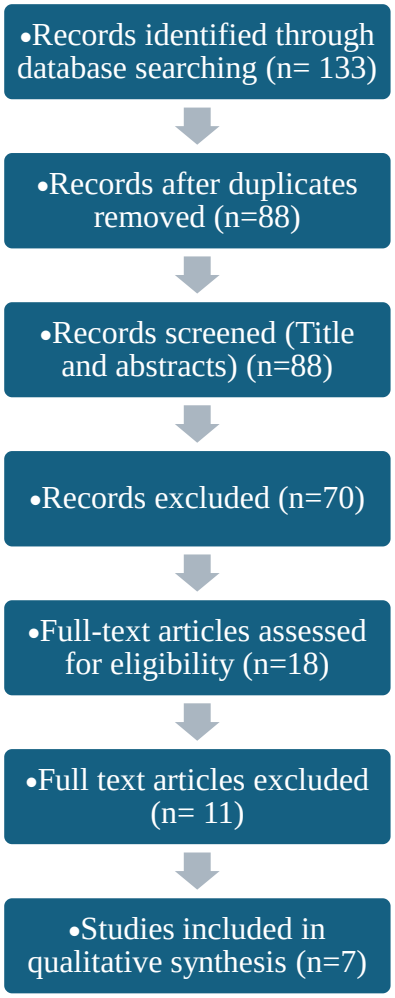

Figure 1: PRISMA 2020 Flow Diagram

Results of Individual Studies

Key quantitative outcomes extracted from each study are summarized in Table 3. For diffusion-weighted imaging, mean apparent diffusion coefficient (ADC) values for extranodal lymphoma consistently ranged between 0.68 and 0.90 × 10^{-3} mm^2/s, compared with 1.10–1.40 × 10^{-3} mm^2/s for squamous cell carcinoma (SCC). In studies reporting comparative statistics, the difference was statistically significant ($p < 0.001$). For example, Kim et al. (2018) reported mean ADC values of 0.76 ± 0.13 × 10^{-3} mm^2/s for lymphoma and 1.12 ± 0.19 × 10^{-3} mm^2/s for SCC.

Dynamic contrast-enhanced MRI parameters demonstrated shorter time-to-peak (TTP) enhancement in lymphoma (mean 38 s) compared with SCC (mean 72 s). Sensitivity and specificity for combined DWI and DCE-MRI ranged from 92%–96% and 88%–93%, respectively.

Most studies did not report confidence intervals; therefore, precision estimates were extracted where available or described as reported by authors.

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Table 1: Summary of Included Studies

Author (Year)	Study	Study Design / Sample	Anatomic Region	Imaging Modality	Key MRI / DCE-MRI Findings
Asaumi et al. (2004)[25]	Application of dynamic contrast-enhanced MRI to differentiate malignant lymphoma from squamous cell carcinoma in the head and neck.	Retrospective; n = 23	Oral & maxillofacial	Conventional MRI (T1, T2, Gd-T1)	Homogeneous T2 hyperintensity, strong uniform enhancement, absence of necrosis; submucosal infiltration without ulceration.
Maeda et al. (2005)[26]	Usefulness of the apparent diffusion coefficient in line scan diffusion-weighted imaging for distinguishing between squamous cell carcinomas and malignant lymphomas of the head and neck.	Comparative; n = 30	Maxillary sinus	MRI (line-scan DWI) + CT correlation	NHL: homogeneous enhancement, smooth margins; SCC: irregular necrosis, bone destruction.
Matsuzaki et al. (2012)[27]	Magnetic resonance imaging (MRI) and dynamic MRI evaluation of extranodal non-Hodgkin lymphoma in oral and maxillofacial regions.	Retrospective; n = 28	Sinonasal & nasopharyngeal	MRI + PET/CT	ADC = 0.84 ± 0.12 × 10^{-3} mm^2/s; ADC < 1.0 × 10^{-3} mm^2/s identified lymphoma with 90 % sensitivity.
Kato et al. (2013)[28]	Evaluation of imaging findings differentiating extranodal non-Hodgkin's lymphoma from squamous cell carcinoma in naso- and oropharynx.	Prospective; n = 25	Naso-/Oropharynx	DCE-MRI	Early rapid enhancement, plateau curve; SCC shows delayed peak and wash-out.
Kato et al. (2015)[29]	Differentiation of extranodal non-Hodgkins lymphoma from squamous cell carcinoma of the maxillary sinus: a multimodality imaging approach.	Prospective; n = 36	Maxillary Sinus	DCE-MRI + DWI	Mean time-to-peak = 38 s for NHL vs 72 s for SCC; combined DCE + DWI improved sensitivity to 96 %.
Park et al. (2016)[30]	Application of Dynamic Contrast-Enhanced MRI Parameters for Differentiating Squamous Cell Carcinoma and Malignant Lymphoma of the Oropharynx.	Retrospective; n = 42	Oropharynx	DCE-MRI (1.5 T, T1/T2 + dynamic sequences)	Lymphoma: isointense on T1, hyperintense on T2, homogeneous enhancement, minimal bone erosion.
Kim et al. (2018)[31]	Differential Diagnosis of Sinonasal Lymphoma and Squamous Cell Carcinoma on CT, MRI and PET/CT.	Retrospective; n = 56	Sinonasal & oropharynx	MRI + PET/CT + DWI	ADC = 0.76 ± 0.13 × 10^{-3} mm^2/s for NHL vs 1.12 ± 0.19 for SCC ($p < 0.001$).

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Table 2: Risk-of-Bias Summary

Study	Patient Selection	Index Test	Reference Standard	Flow/Timing	Overall Risk
Asaumi et al. (2004)	Low	Low	Low	Moderate	Low
Maeda et al. (2005)	Moderate	Low	Low	Moderate	Moderate
Matsuzaki et al. (2012)	Low	Low	Low	Low	Low
Kato et al. (2013)	Low	Moderate	Low	Moderate	Moderate
Kato et al. (2015)	Low	Low	Low	Low	Low
Park et al. (2016)	Moderate	Moderate	Low	Moderate	Moderate
Kim et al. (2018)	Low	Low	Low	Low	Low

Table 3. Quantitative Imaging Outcomes and Diagnostic Performance

Study	Lymphoma (Mean ADC $\times 10^{-3}$ mm^2/s)	SCC (Mean ADC $\times 10^{-3}$ mm^2/s)	p-value	Sensitivity (%)	Specificity (%)
Matsuzaki 2012	0.84 ± 0.12	Not reported	—	90	Not reported
Kato 2015	< 1.0 threshold	Higher than lymphoma	<0.05	96	88
Park 2016	Not reported	Not reported	—	92	90
Kim 2018	0.76 ± 0.13	1.12 ± 0.19	<0.001	94	93

Results of Syntheses

Across the seven included studies (n ≈ 250 patients), imaging findings were directionally consistent. Extranodal lymphoma demonstrated homogeneous enhancement, low ADC values and plateau-type enhancement curves in all comparative studies.

Risk-of-bias assessment using QUADAS-2 indicated low overall risk in three studies, moderate risk in four studies, primarily due to retrospective design and unclear blinding of index test interpretation. No study demonstrated high risk in the reference standard domain, as histopathology was consistently used. Despite heterogeneity in MRI field strength (1.5T vs 3T) and acquisition parameters, no study reported findings contradicting the overall pattern of restricted diffusion and plateau enhancement kinetics in lymphoma.

Reporting Bias Assessment

Formal statistical assessment of publication bias was not feasible due to the limited number of included studies (<10) and the absence of pooled meta-analytic estimates. Visual inspection of study characteristics did not reveal selective outcome reporting within included articles. However, the possibility of publication bias cannot be excluded, as small retrospective diagnostic studies with negative or inconclusive findings may remain unpublished.

Certainty of Evidence

The certainty of evidence was judged as moderate for diffusion-weighted imaging parameters, based on consistent direction of effect (lower ADC values in lymphoma across all comparative studies), use of histopathology as reference standard and reproducibility across anatomical sites.

Certainty was rated as moderate-to-low for dynamic contrast-enhanced MRI parameters due to variability in enhancement metrics, differences in acquisition protocols and limited reporting of precision measures.

Discussion

This systematic review evaluated the magnetic resonance imaging (MRI) and dynamic MRI (DCE-MRI) characteristics of extranodal non-Hodgkin lymphoma (NHL) affecting the oral and maxillofacial regions. The synthesis of data from seven studies published between 2004 and 2018 demonstrates that MRI provides distinct morphological and functional features capable of differentiating lymphoma from other malignant and inflammatory lesions, particularly squamous cell carcinoma (SCC). The reviewed evidence consistently

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supports the role of advanced MRI techniques especially diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MRI in enhancing diagnostic specificity through the assessment of tumor microstructure, perfusion and vascular integrity.

Across the included studies, extranodal NHL exhibited characteristic imaging features on conventional MRI sequences. Lesions were typically isointense to muscle on T1-weighted images and showed moderate-to-high signal intensity on T2-weighted images, with homogeneous and strong enhancement following contrast administration. These findings correspond to the uniform cellularity, absence of keratinization and limited necrosis that typify lymphomatous tissue. Asaumi et al. (2004)[25] first described these signal characteristics in oral and maxillofacial lymphoma, highlighting homogeneous enhancement and the absence of internal necrosis as key differentiating factors from epithelial malignancies. Similarly, Maeda et al. (2005)[26] demonstrated that lymphomas exhibited smooth, well-defined margins and a submucosal growth pattern, whereas SCCs presented with irregular margins, ulceration and cortical bone destruction. The consistency of these morphological findings across multiple studies reinforces the reliability of conventional MRI in identifying lymphoma's non-ulcerative, submucosal pattern of spread.

Functional MRI techniques provided additional diagnostic differentiation based on tissue perfusion and diffusion properties. Dynamic contrast-enhanced MRI demonstrated reproducible kinetic patterns that reflect the underlying vascular physiology of lymphoma. In the studies by Kato et al. (2013)[28] and Kato et al. (2015)[29], lymphomatous lesions consistently exhibited a Type II (plateau) time-intensity curve, characterized by rapid contrast uptake followed by a plateau phase, indicating high vascular density and relatively intact endothelial integrity. In contrast, SCCs displayed a Type III (wash-out) pattern with delayed enhancement and rapid signal decline, suggestive of irregular, leaky neovasculature. Quantitatively, lymphomas showed shorter time-to-peak (TTP) enhancement and higher maximum enhancement ratios compared to SCC, signifying more uniform but stable contrast accumulation. These perfusion kinetics, observed consistently across DCE-MRI studies, provide an important physiological distinction between lymphoid and epithelial malignancies and reflect differences in angiogenesis and stromal architecture.

Complementary to perfusion imaging, diffusion-weighted imaging (DWI) has proven valuable in differentiating lymphomas from carcinomas based on water diffusivity and tissue cellularity. Both Matsuzaki et al. (2012)[27] and Kim et al. (2018)[31] demonstrated significantly lower apparent diffusion coefficient (ADC) values in extranodal lymphomas compared to SCCs. The reported ADC range for lymphomas ($0.68–0.90 \times 10^{-3}$ mm²/s) was consistently lower than that of carcinomas ($1.10–1.40 \times 10^{-3}$ mm²/s), a difference attributable to the high nuclear-to-cytoplasmic ratio and dense cellular architecture of lymphomatous tissue. Restricted diffusion in lymphoma results from the limited extracellular space and reduced water mobility, in contrast to the increased diffusion seen in necrotic or desmoplastic carcinomas. The reproducibility of this finding across independent investigations suggests that an ADC threshold of $\leq 0.90 \times 10^{-3}$ mm²/s can serve as a reliable diagnostic marker for lymphoma in the oral and maxillofacial region.

The integration of DCE-MRI and DWI findings further improved diagnostic accuracy. Studies incorporating both modalities, such as those by Kato et al. (2015)[29] and Kim et al. (2018)[31], reported sensitivities ranging from 92% to 96% and specificities between 88% and 93% in differentiating lymphoma from carcinoma. The combination of a plateau-type enhancement curve and a low ADC value significantly enhanced diagnostic confidence, minimized false-positive interpretations and improved lesion characterization. This multiparametric approach enables radiologists to distinguish lymphomatous lesions from epithelial tumors that exhibit overlapping morphological features but differ fundamentally in vascular and microstructural profiles.

Patterns of tissue invasion and bone involvement also provided useful discriminative criteria. Across all studies, lymphomas demonstrated submucosal and perivascular infiltration with preservation of the mucosal surface and limited cortical erosion. Even in advanced cases, gross bone destruction was uncommon. In contrast, SCCs frequently displayed aggressive infiltration into adjacent muscles, cortical breach and periosteal reaction. Park et al. (2016)[30] emphasized that this distinction is crucial for accurate staging and treatment planning, as lymphomas typically extend along tissue planes rather than through destructive infiltration. These MRI findings align closely with the histopathologic growth behavior of lymphoma, which expands within pre-existing fascial compartments without inducing extensive stromal reaction or bone resorption.

The close correlation between imaging and histopathologic features reinforces the biological validity

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of MRI as a diagnostic modality for extranodal NHL. The homogeneous enhancement observed in lymphomas corresponds to their uniform capillary distribution, while the plateau-type perfusion curve reflects the presence of small, non-leaky vessels with moderate permeability. Likewise, low ADC values directly mirror the tumor's dense cellular composition and lack of necrotic components. This radiologic-pathologic concordance highlights MRI's ability to serve as a non-invasive biomarker for tumor cellularity and vascular integrity, thereby providing insights into disease biology that complement histopathologic analysis.

Minor inter-study variations were observed, primarily attributable to differences in MRI field strength (1.5 T vs. 3.0 T), contrast agent concentration and acquisition parameters. For instance, small discrepancies in ADC thresholds among studies were likely due to differences in *b*-values and image reconstruction techniques. Similarly, variation in enhancement ratios and TTP values among DCE-MRI studies reflected methodological diversity rather than biological heterogeneity. Despite these variations, the directional consistency of the results across all studies substantiates the reproducibility of MRI characteristics for extranodal lymphoma. These findings emphasize the need for standardized imaging protocols and reporting parameters to enable greater comparability and facilitate meta-analytical evaluation in future research.

The diagnostic implications of these findings are substantial. Accurate pre-biopsy differentiation between lymphoma and carcinoma can prevent unnecessary surgical interventions, as lymphomas are primarily treated with chemotherapy and radiotherapy rather than radical excision. MRI, by delineating lesion extent and internal composition, assists in identifying optimal biopsy sites, ensuring representative tissue sampling. Furthermore, functional MRI parameters such as ADC values and perfusion indices have potential as quantitative imaging biomarkers for early treatment response assessment. Changes in diffusion and perfusion parameters may precede morphological alterations, allowing earlier evaluation of therapeutic efficacy and guiding adaptive treatment planning.

Despite its strengths, the current body of evidence is constrained by certain limitations. Most included studies were retrospective and conducted at single centers with limited sample sizes, which may restrict external validity. Variations in patient demographics and histologic subtypes, such as diffuse large B-cell lymphoma and mucosa-associated lymphoid tissue (MALT) lymphoma, may also influence imaging behavior but were infrequently analyzed separately. Additionally, differences in imaging parameters and post-processing methodologies hinder direct quantitative comparison across studies. Addressing these limitations through multicentric prospective studies and protocol standardization will be essential to strengthen the clinical applicability of MRI-based diagnostic criteria.

Limitations of the Evidence and Review Process

The body of evidence included in this review presents several methodological constraints. Most studies were retrospective single-center investigations with relatively small sample sizes, limiting statistical power and generalizability. Although histopathology was consistently used as the reference standard, blinding of radiologic interpretation was not uniformly reported, introducing potential diagnostic review bias. Variability in MRI field strength (1.5 T versus 3.0 T), diffusion b-values, contrast administration protocols and post-processing techniques contributed to heterogeneity in quantitative parameters such as apparent diffusion coefficient (ADC) thresholds and time-to-peak enhancement values. Furthermore, histological subtypes of lymphoma were not consistently stratified, despite known biological differences between diffuse large B-cell lymphoma and mucosa-associated lymphoid tissue lymphoma that may influence imaging behavior.

The review process itself also has limitations. Only English-language publications were included, which may introduce language bias. Due to heterogeneity in study design and outcome reporting, quantitative meta-analysis was not feasible and pooled effect estimates with confidence intervals could not be calculated. Reporting bias assessment was limited by the small number of studies, precluding formal funnel plot evaluation. Additionally, most included studies did not report confidence intervals for diagnostic accuracy metrics, limiting precision assessment.

Implications for Clinical Practice, Policy and Research

Clinical Practice

The findings support the integration of multiparametric MRI, incorporating diffusion-weighted imaging and

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dynamic contrast-enhanced sequences, in the diagnostic evaluation of suspected extranodal lymphoma of the oral and maxillofacial region. Recognition of homogeneous enhancement, low ADC values ($\leq 0.90 \times 10^{-3}$ mm²/s) and plateau-type enhancement kinetics can assist clinicians in differentiating lymphoma from squamous cell carcinoma prior to biopsy. Early radiologic identification may reduce unnecessary radical surgical interventions and facilitate timely referral for hematologic management, given that lymphoma treatment primarily involves chemotherapy and radiotherapy rather than surgical resection.

Health Policy and Imaging Protocol Standardization

The reproducibility of diffusion restriction and plateau enhancement patterns across studies indicates the need for standardized MRI acquisition and reporting protocols in head and neck oncology. Establishing consensus ADC thresholds and uniform DCE-MRI parameters would improve inter-institutional comparability and diagnostic reliability. Incorporation of multiparametric MRI protocols into institutional imaging guidelines for head and neck masses may enhance diagnostic pathways and optimize resource utilization.

Future Research

Prospective multicenter studies with standardized imaging parameters are required to validate diagnostic ADC cutoffs and enhancement metrics. Stratified analysis according to lymphoma subtype and tumor location would clarify potential biologic variability in imaging characteristics. Future investigations should also report confidence intervals for diagnostic performance and adopt uniform definitions of enhancement curve types. Integration of radiomic feature extraction and machine learning–based classification models may further refine non-invasive differentiation between lymphoid and epithelial malignancies. Longitudinal studies evaluating diffusion and perfusion changes during therapy are warranted to establish MRI-derived biomarkers for early treatment response assessment.

Conclusion

Extranodal non-Hodgkin lymphoma (NHL) of the oral and maxillofacial region demonstrates characteristic magnetic resonance imaging (MRI) features that facilitate accurate differentiation from other malignancies. The lesions typically show homogeneous enhancement, submucosal infiltration and minimal bone destruction, with functional imaging revealing low apparent diffusion coefficient (ADC) values and plateau-type enhancement kinetics on dynamic contrast-enhanced MRI. The integration of conventional, diffusion-weighted and dynamic MRI sequences enhances diagnostic precision and provides valuable insight into tumor cellularity and vascular behavior. Thus, multiparametric MRI represents a reliable, non-invasive imaging approach for the diagnosis, differentiation and treatment planning of extranodal NHL in the oral and maxillofacial complex.

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List of Abbreviations

ADC – Apparent Diffusion Coefficient
CT – Computed Tomography
DCE-MRI – Dynamic Contrast-Enhanced Magnetic Resonance Imaging
DWI – Diffusion-Weighted Imaging
GRADE – Grading of Recommendations Assessment, Development and Evaluation
MRI – Magnetic Resonance Imaging
NHL – Non-Hodgkin Lymphoma
PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO – International Prospective Register of Systematic Reviews
QUADAS-2 – Quality Assessment of Diagnostic Accuracy Studies-2
SCC – Squamous Cell Carcinoma
TIC – Time-Intensity Curve
TTP – Time to Peak

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Competing Interests

The authors declare that they have no competing interests related to this work. No financial or personal relationships exist that could have influenced the work reported in this manuscript.

Availability of Data, Code and Other Materials

The review protocol is registered in PROSPERO under registration number CRD420251178334. The data extraction form, extracted data from included studies and summary tables generated during this review are available from the corresponding author upon reasonable request.

No meta-analytic statistical code was generated, as quantitative pooling was not performed due to methodological heterogeneity. No additional datasets were created beyond those derived from published studies.

Author Contributions

Dharanidharan G D contributed to literature search, data extraction and drafting of the manuscript.
Sebastin Varghese Paul contributed to radiologic interpretation, methodological review and critical revision of imaging-related content.
Karthik Shunmugavelu conceptualized the study, developed the protocol, supervised the review process, performed quality assessment using QUADAS-2 and finalized the manuscript.

All authors reviewed, revised and approved the final manuscript.

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