Application of diffusion-weighted magnetic resonance imaging in the diagnosis of odontogenic lesions: a systematic review

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Objectives. This systematic literature review addresses the use of diffusion-weighted magnetic resonance imaging (DWI) and apparent diffusion coefficient (ADC) for the evaluation of benign maxillomandibular odontogenic lesions.

Study Design. Databases were searched, and original research studies or case report manuscripts up to April 2019 were included, using the keyword "diffusion," combined with the keywords "maxillofacial pathology," "oral pathology," "odontogenic tumors," "dental tissue neoplasms," "odontogenic cysts," and the histologic denomination of benign odontogenic lesions, according to the World Health Organization classification. Only English language articles and studies pertaining to DWI were selected.

Results. Fifteen investigations (11 original articles and 4 case reports) of distinct benign odontogenic lesions were included. Most studies did not include exclusively odontogenic lesions in their samples.

Conclusions. It is too early to reach a conclusion that DWI and ADC can provide useful information in the differentiation of the histologic type of some benign odontogenic lesions on the basis of available data in the literature. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130:85−100)

Maxillomandibular lesions comprise a wide range of different histopathologic types, including odontogenic and nonodontogenic cysts, neoplasms, and inflammatory lesions. Often, the initial observation of these abnormalities is made with panoramic radiography, which is a common radiographic examination modality available in many dental clinics.

Panoramic radiographs revealing these lesions are usually complemented by 3-dimensional examinations, such as computed tomography (CT). This occurs mainly when a surgical approach is necessary. CT allows for evaluation of structures in multiple planes, which is essential for the characterization of the features of the lesion, evaluation of the involvement of adjacent structures, elaboration of diagnostic hypotheses, and surgical procedure planning. However, imaging examinations complement, but do not replace, histopathologic diagnosis.

Currently, magnetic resonance imaging (MRI) is not the imaging examination of choice for maxillomandibular lesions, particularly intraosseous lesions such as odontogenic neoplasms, although MRI has been applied to the assessment of salivary gland[1] and maxillary sinus disease.[2,3] However, CT and conventional MRI can be applied in the morphologic assessment of maxillofacial disease, with limited value in evaluating the prognostic features of lesions.[4]

Diffusion-weighted imaging (DWI), based on MRI data, has been recognized as a noninvasive biomarker that can predict treatment responses,[5] and has the ability to differentiate between benign and malignant lesions.[6,7] DWI reflects tissue microanatomy through the random movement of water molecules, also known as *Brownian movement*, in the intercellular medium.[4] The random motion of water molecules varies qualitatively, according to tissue features or intercellular conditions.[1] This variation can be expressed as a coefficient, known as the *apparent diffusion coefficient* (ADC),[8] which translates water molecule movement into numeric values.[1]

The ADC values from a specific region of interest (ROI) are calculated by assessing the difference in signal intensity on DWI[8] by using axial slices, which represent water diffusibility in the intercellular medium of a specific tissue.[1] Therefore, the lower the diffusibility, the lower are the ADC values.[1]

The application of DWI and ADC values in the study of maxillofacial lesions has been investigated recently. Thus, the objective of the present study was to review

Statement of Clinical Relevance

Diffusion-weighted magnetic resonance imaging provides information about tissue cellularity and describes tissues' physiologic processes. Because of its innovative application in the diagnosis of maxillomandibular lesions, only a few investigations are available in the literature.

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the literature regarding the application of DWI and ADC values in the evaluation of maxillofacial lesions, with emphasis on odontogenic cysts and tumors. The following questions were addressed:

1. "What has been investigated regarding the application of DWI in maxillofacial benign lesions, particularly odontogenic cysts and odontogenic neoplasms?"
2. "What were the main results?"
3. "What is the potential application of DWI in evaluating diagnoses of maxillofacial lesions?"

MATERIALS AND METHODS

Protocol and registration

This systematic review is registered at the National Institute for Health Research International Prospective Register of Systematic Reviews (PROSPERO) (No. CRD42019116888). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was followed.[9]

Data selection

The selection of studies potentially eligible for inclusion in this systematic review was performed by using PubMed Central (United States National Institutes of Health's National Library of Medicine), Embase (Excerpta Medica Database), Scopus (Elsevier), Cochrane Central Register of Controlled Trials, Web of Science (Institute of Scientific Information−Clarivate Analytics), and Google Scholar (Google) databases. These databases were searched without language restrictions, and we included articles published as recently as September 2018. The Boolean operator "AND" was used to combine the searches. Itemized search strategies were established for each database on the basis of the following search keywords: "odontogenic tumors AND diffusion," "dental tissue neoplasms AND diffusion," "odontogenic cysts AND diffusion," "maxillofacial pathology AND diffusion," "oral pathology AND diffusion," "ameloblastoma AND diffusion," "squamous odontogenic tumor AND diffusion," "calcifying epithelial odontogenic tumor AND diffusion," "adenomatoid odontogenic tumor AND diffusion," "ameloblastic fibroma AND diffusion," "primordial odontogenic tumor AND diffusion." "odontoma AND diffusion," "dentinogenic ghost cell tumor AND diffusion," "odontogenic fibroma AND diffusion," "odontogenic myxoma AND diffusion," "cementoblastoma AND diffusion," "cemento-ossifying fibroma AND diffusion," "radicular cyst AND diffusion," "inflammatory collateral cyst AND diffusion," "odontogenic keratocystic tumor AND diffusion," "odontogenic keratocyst AND diffusion," "dentigerous cyst AND diffusion," "lateral periodontal cyst AND diffusion," "botryoid odontogenic cyst AND diffusion," "glandular odontogenic cyst AND diffusion," "calcifying odontogenic cyst AND diffusion," "orthokeratinized odontogenic cyst AND diffusion," and "gingival cyst AND diffusion."

As odontogenic keratocyst was previously named "keratocystic odontogenic tumor," the keywords "keratocystic odontogenic tumor" AND "diffusion" were also considered in the search.

Eligibility criteria

Types of studies. Original studies and case reports were considered for inclusion. Abstracts, oral presentations, and literature reviews were excluded. Original investigations and case reports of studies that used MRI but did not consider DWI and/or ADC were not eligible. Articles exclusively related to software evaluations were excluded. Additionally, non-English language and nonhuman studies were excluded. The present review did not consider other imaging techniques, such as intravoxel incoherent motion, diffusional kurtosis imaging, or diffusion tensor imaging MRI.

Participant groups. Studies and case reports involving groups or cases of odontogenic maxillofacial lesions with DWI examinations were included in the data selection.

Data extraction

Data extraction was executed by 2 independent reviewers, who initially screened the titles and abstracts and then evaluated the full text of each selected investigation to choose eligible studies. A third reviewer checked each study previously considered eligible. Disagreements between the reviewers were resolved through discussion, and when an agreement could not be reached, 2 other collaborators were consulted. A DWI expert reviewed the selected studies to verify the MRI methodology. The authors or coauthors of the selected articles were contacted when additional data were required. All articles published until April 2019 were included.

Data analysis—risk of bias

The data search keywords and results are summarized in a flow chart (Figure 1). For brevity, the searches for specific lesions were combined on the basis of their World Health Organization (WHO) histologic classification (e.g., searches for ameloblastoma, squamous odontogenic tumor, calcifying epithelial odontogenic tumor, and adenomatoid odontogenic tumor are represented in Figure 1 under the heading "Benign epithelial odontogenic tumor AND diffusion"). A supplementary

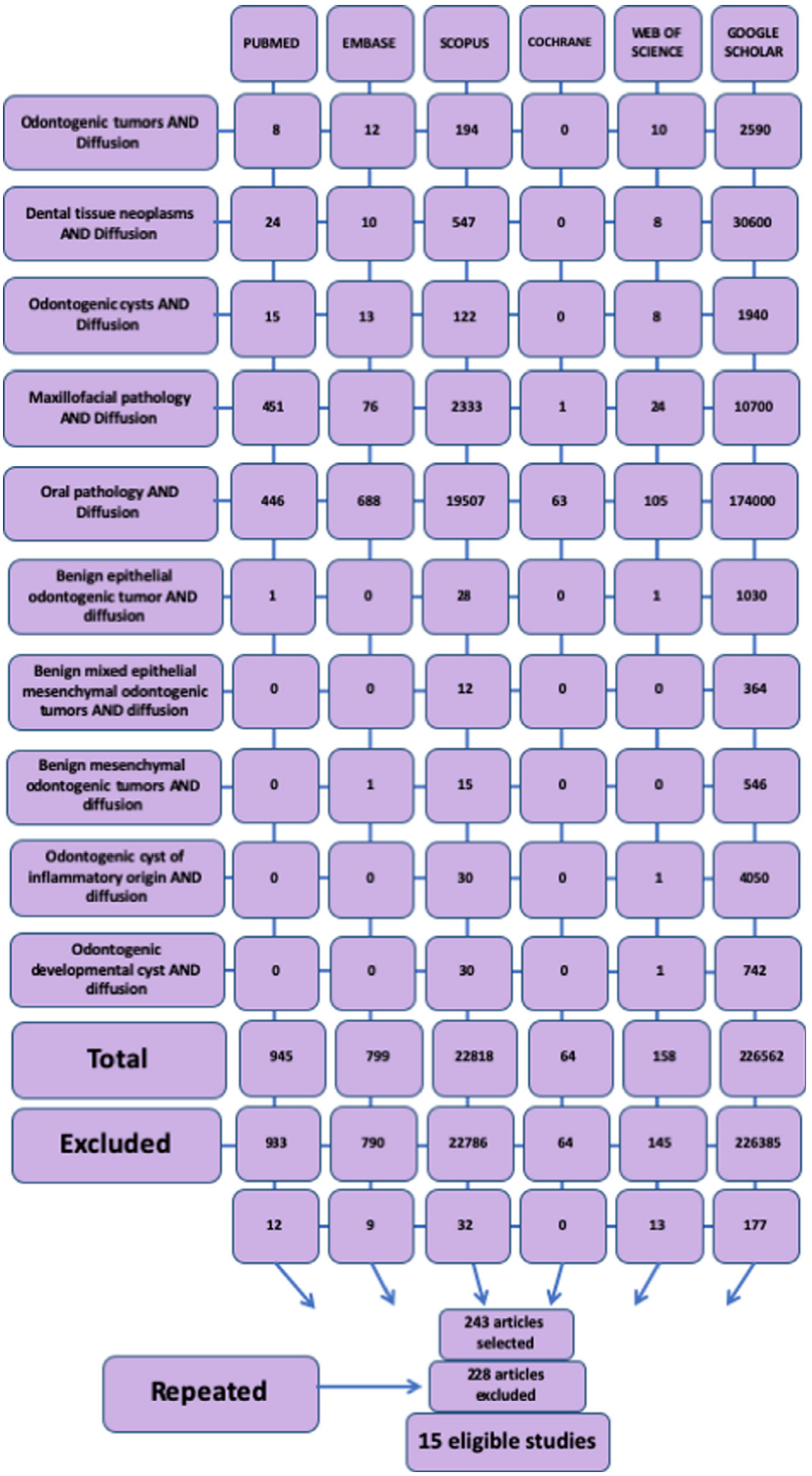

Fig. 1. Flow chart illustrating the literature review. Note: For flow chart presentation, lesion names are grouped according to World Health Organization histologic classifications. Benign epithelial odontogenic tumors included ameloblastoma, squamous odontogenic tumor, calcifying epithelial odontogenic tumor, and adenomatoid odontogenic tumor. Benign mixed epithelial mesenchymal odontogenic tumors included ameloblastic fibroma, primordial odontogenic tumor, odontoma, and dentinogenic ghost cell tumor. Benign mesenchymal odontogenic tumors included odontogenic fibroma, odontogenic myxoma, cementoblastoma, and cemento-ossifying fibroma. Odontogenic cysts of inflammatory origin included radicular cyst and inflammatory collateral cyst. Odontogenic developmental cysts included odontogenic keratocystic tumor, odontogenic keratocyst, dentigerous cyst, lateral periodontal cyst, botryoid odontogenic cyst, glandular odontogenic cyst, calcifying odontogenic cyst, orthokeratinized odontogenic cyst, gingival cyst, and keratocystic odontogenic tumor.

figure (Supplemental Figure S1; available at [URL/link]) containing a detailed data search for each specific lesion is available at. The main literature search findings are summarized in Figure 2. In Tables I to V, general and DWI-related data are shown for benign odontogenic lesions and nonodontogenic or malignant lesions that were compared with the benign odontogenic lesions in the included studies.

The ADC values were not compared directly because ADC values may be subject to several sources of variability,[10-12] such as equipment strength, differences in acquisition protocols, and ROI positioning.[1]

RESULTS

A total of 277,861 studies were initially found in the databases with the use of all keywords. After applying

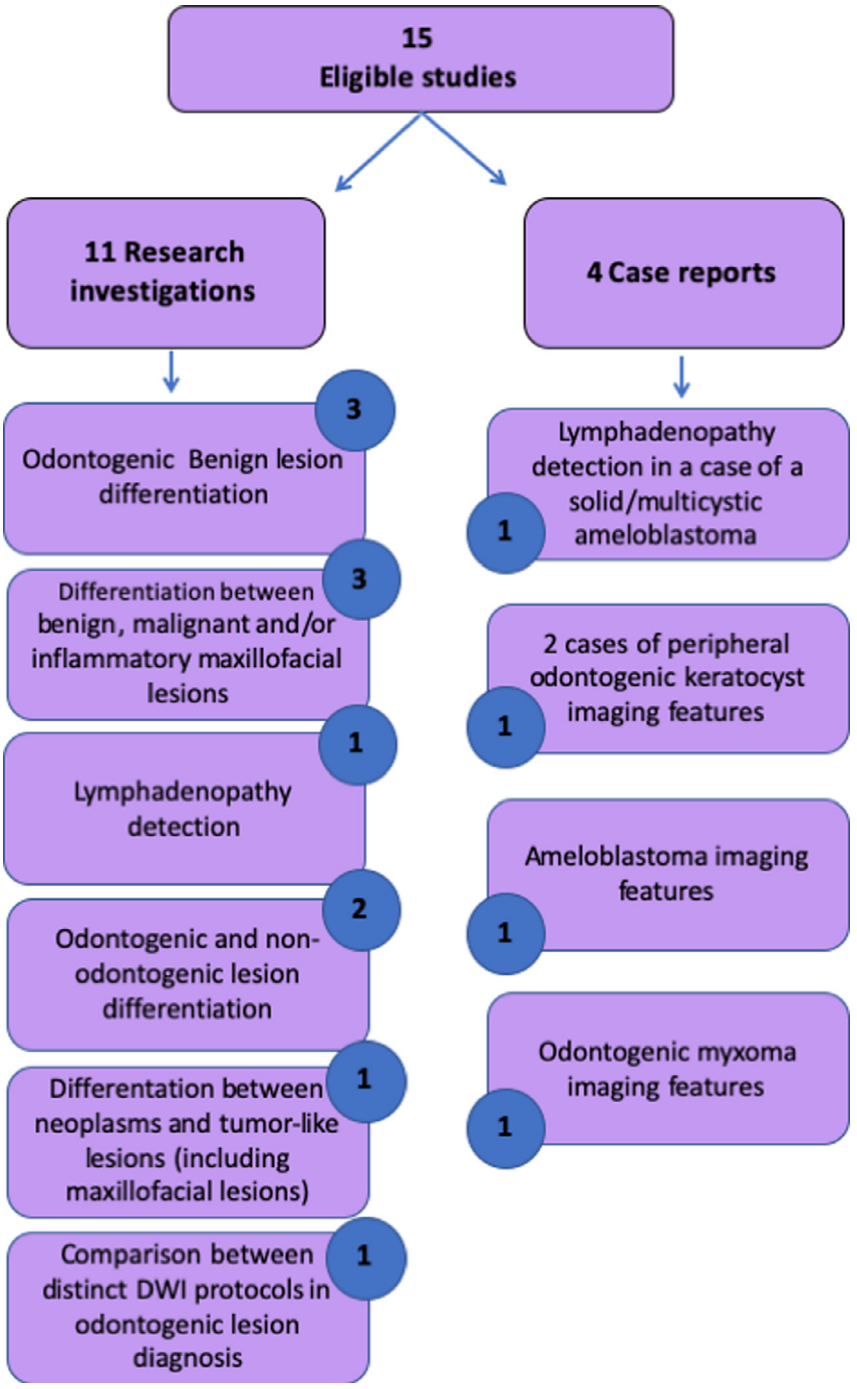

Fig. 2. Summary of the main literature findings.
DWI: Diffusion-weighted magnetic resonance imaging.

Table I. Summary of the investigations selected according to year of publication, location of the research, number of patients assessed, magnet strength in Tesla (T) and type of article published

Authors	Year	Location	No. of patients	Magnet strength	Type of article
Sumi et al.[13]	2008	Japan	16	1.5 T	Research article
Wang et al.[14]	2010	China	78	1.5 T	Research article
Cassetta et al.[15]	2012	Italy	10	3.0 T	Research article
Eida et al. [16]	2012	Japan	27	1.5 T	Research article
Neubauer et al.[17]	2012	Germany	44*(11)†	1.5 T and 3.0 T	Research article
Srinivasan et al.[18]	2012	India	20	1.5 T	Research article
Cassetta et al.[19]	2014	Italy	1	3.0 T	Case report
Zhu et al.[20]	2014	China	2	1.5 T	Case report
Seno et al.[21]	2015	Japan	1	1.5 T	Case report
Oda et al.[5]	2017	Japan	57	1.5 T	Research article
Han et al.[22]	2018	China	40	1.5 T	Research article
Peters et al.[23]	2018	Switzerland	72*(46)†	1.5 T	Research article
Salodiya et al.[24]	2018	India	1	Not reported	Case report
Panyarak et al.[25]	2019	Japan	141 *(139)†	3.0 T	Research article
Ogura et al.[26]	2019	Japan	16	1.5 T	Research article

ADC, Apparent diffusion coefficient.
*No. of patients evaluated in the study.
†No. of patients with lesions in the head area.

the inclusion and exclusion criteria and removing duplicate studies, 277,846 studies were excluded. A final of 15 studies[5,13-26] on the use of DWI in the study of odontogenic lesions were included. A flow diagram illustrating the literature search results is demonstrated in Figure 1. A supplementary figure (Figure S1) containing data search results for each specific lesion is available at [URL/link*]. In Figure 2, a summarized representation of the main results is shown. The following data were extracted and recorded: author information; publication year; location where the study was performed; number of participants evaluated; magnet strength (1.5 Tesla [T],[5,13,14,16,18,20-23,26] 3 T,[15,19,25] or both[17]); and type of article (see Table I). Eleven original research studies[5,13-18,22,23,25,26] and 4 case reports[19-21,24] were selected. The oldest study was from 2008,[13] the most recent from 2019.[26] The number of participants or lesions analyzed in the studies ranged from 10 people[15] to 141 people.[25]

The types of lesions and the specific odontogenic and nonodontogenic lesions included in the sample were also extracted (see Table II). Some investigations included only odontogenic lesions,[13,15,18,22] and some included nonodontogenic lesions.[5,14,16,23,25,26] Not all investigations were confined exclusively to the maxillofacial area, although all of the studies included maxillofacial lesions.[17,25]

The study objectives, samples studied, and the main results and conclusions pertaining to DWI of odontogenic cysts and benign neoplasms are listed in Table III. Only 3 original articles included only benign odontogenic neoplasms and cysts,[13,18,22] and 4 research investigations compared odontogenic lesions with nonodontogenic lesions in the jaws.[5,14,16,26] Two selected studies used DWI to investigate affected lymph nodes associated with the odontogenic neoplasm (ameloblastoma).[15,19]

ADC values for odontogenic cysts and benign odontogenic neoplasms and the statistical significance of the differences in ADC between lesions are presented in Table IV. Distinct comparisons were performed between odontogenic neoplasms and odontogenic cysts,[5,13,16,18,22] as well as between odontogenic lesions and nonodontogenic lesions.[5,14,22,26] Statistical comparisons were not performed in 3 research articles, although ADC data were presented.[18,22,26]

The numbers of benign neoplasms or tumor-like lesions, malignant neoplasms, and inflammatory lesions are listed for each study in Table V, which shows not only the odontogenic lesions but also all the lesions in the investigators' samples to give an overview of the abnormalities studied.

DWI and ADC maps of an odontogenic keratocyst from our collection were added to illustrate this review (Figures 3 and 4). In the case of a 22-year-old male with a keratocyst in the left posterior area of the mandible, the lesion can be observed as diffusion-weighted images in axial slices (see Figure 3) using 2 distinct b values (see Figures 3A [b = 0]; Figure 3B [b = 800]). ADC maps of the same slices are presented in black and white (see Figure 4A) and colored (see Figure 4B) formats. In the ADC colored map image, the blue areas show highly restricted water molecules diffusion, the green areas show restricted diffusion, the yellow areas show facilitated diffusion, and the red areas show highly facilitated diffusion. To illustrate the MRI

Table II. Types of lesions, specific odontogenic lesions included in the sample, and nonodontogenic lesions included in the sample (limited to the head)

Authors	Types of lesions	Odontogenic lesions included in the sample	Nonodontogenic lesions included in the sample*
Sumi et al.[13]	Ameloblastomas Odontogenic keratocysts	Ameloblastoma Odontogenic keratocyst	None
Wang et al.[14]	Solid lesions affecting masticatory space	Ameloblastoma Malignant ameloblastoma	Schwannoma Neurofibroma Fibrous dysplasia Pleomorphic adenoma Leiomyoma Eosinophilic lymphogranuloma Synovial chondromatosis Giant cell granuloma Desmoplastic fibroma Nodular fasciitis Inflammatory diseases Squamous cell carcinoma Adenoid cystic carcinoma Adenocarcinoma Lymphoepithelial carcinoma Rhabdomyosarcoma Osteosarcoma Malignant fibrous histiocytoma Synovial sarcoma Ewing sarcoma Plasmacytoma Angiosarcoma Myxofibrosarcoma Undifferentiated sarcoma
Casseta et al.[15]	Intraosseous lesions of the jaws†	Dentigerous cyst Ameloblastoma	None
Eida et al.[16]	Mandible cystic lesions	Ameloblastoma Dentigerous cyst Radicular cyst Odontogenic keratocyst	Simple bone cyst
Neubauer et al.[17]	Musculoskeletal tumors and tumor-like lesions in pediatric patients	Ameloblastic fibro-odontoma	Although authors declared 11 lesions in the head area, nonodontogenic lesions were not specified according to their location
Srinivasan et al.[18]	Odontogenic cysts Odontogenic neoplasms	Ameloblastoma Odontogenic keratocyst Odontogenic myxoma Dentigerous cyst	None
Cassetta et al.[19]	Ameloblastoma single case report†	Ameloblastoma	None
Zhu et al.[20]	Report of 2 cases of peripheral odontogenic keratocyst	Odontogenic keratocyst	None
Seno et al.[21]	PET-CT findings, ameloblastoma single case report	Ameloblastoma	None
Oda et al.[5]	Oral and maxillofacial lesions	Nasopalatine duct cyst Odontogenic keratocyst	Ranula Hemangioma Squamous cell carcinoma Basal cell carcinoma Pleomorphic adenoma Osteoradionecrosis of the jaw Medication-related osteonecrosis Malignant melanoma Odontogenic abscess
Han et al.[22]	Unicystic ameloblastomas Odontogenic keratocysts	Unicystic ameloblastoma Multicystic ameloblastoma Odontogenic keratocyst Dentigerous cyst	None

(*continued*)

Table II. Continued

Authors	Types of lesions	Odontogenic lesions included in the sample	Nonodontogenic lesions included in the sample*
Peters et al.[23]	Differentiation of neoplasms Inflammatory lesions in head and neck	Myxoma	Hemangioma Warthin tumor (Fibro)lipoma Schwannoma Meningioma Glomus tumor Adenoma Lymphangioma Lymphoepithelial cyst Carcinoma Lymphoma Wegener disease Sarcoidosis Rosai-Dorfman disease Myositis Inflammatory pseudotumor Focal parotitis Post-therapeutic inflammation
Salodiya et al.[24]	Single neoplasm case report	Odontogenic myxoma	None
Panyarak et al.[25]	Image quality and ADC assessment in head and neck neoplasms, using 2 distinct parameters	Ameloblastic carcinoma Odontogenic keratocyst Ameloblastoma Myxofibroma	Adenoid cystic carcinoma Mucoepidermoid carcinoma Osteosarcoma Pleomorphic carcinoma Spindle cell carcinoma Pleomorphic adenoma Hemangioma Lipoma Central ossifying fibroma Fibroma Neurofibroma Basal cell adenoma Lymphoplasmacytic lesion Spindle cell or pleomorphic lipoma Spindle cell tumor Warthin tumor
Ogura et al.[26]	Odontogenic keratocyst	Odontogenic keratocyst Nasopalatine duct cyst Radicular cyst Dentigerous cyst	Simple bone cyst

CT, computed tomography; *PET,* positron emission tomography.
*Considering only lesions in the head region.
†Investigations applied the use of diffusion-weighted magnetic resonance imaging in the detection of lymphadenopathy in odontogenic lesion patients.

features of this case, short tau inversion recovery (STIR), T1-weighted, and contrast-enhanced T1-weighted images in axial and coronal slices are presented in Figures 5 and 6, respectively.

DISCUSSION

Currently, DWI and ADC are applied in the detection, characterization, and differentiation of a number of neoplastic and nonneoplastic diseases in many organs and systems.[27] The assessment of odontogenic lesions using DWI has been studied only in a limited number of maxillofacial imaging investigations because it is an innovative technique in dentistry. DWI has the ability to reveal microscopic details about tissue lesion architecture[5] by evaluating water molecule motion, which is an advantage not found in other imaging techniques. Moreover, DWI examinations can be performed without additional time required during an MRI examination or the use of contrast agents[28] and can provide useful information about structures adjacent to the lesions.[29]

In this systematic review, we found that distinct odontogenic lesions (and some nonodontogenic lesions) could be differentiated from each other by

Table III. Study objectives, samples studied, and main results and conclusions pertaining to diffusion weighted magnetic resonance imaging of odontogenic cysts and benign neoplasms

Authors	Objective	Samples studied	Main results and conclusions
Sumi et al.[13]	DWI and ADC in the differentiation of ameloblastomas and odontogenic keratocysts, considering enhancing and nonenhancing features	9 patients with ameloblastoma and 7 patients with odontogenic keratocyst	The ADC values of nonenhancing ameloblastomas were significantly higher than ADC values of nonenhancing odontogenic keratocysts. ADC of the nonenhancing lesions may be useful for differentiation of ameloblastomas from odontogenic keratocysts
Wang et al. [14]	DWI and ADC in the differentiation of masticatory space solid lesions	78 patients divided into 3 groups. Group 1: Benign tumors and tumor-like lesions (23 cases, including 2 cases of ameloblastoma) Group 2: Inflammatory diseases (14 cases) Group 3: Malignant tumors (41 cases).	ADC values were significantly different among the 3 groups. DWI could be useful in the differentiation of solid benign tumors and tumor-like conditions from malignant neoplasms. ADC values have a limited diagnostic value in the differentiation of malignant neoplasms from inflammatory diseases in the masticatory space.
Cassetta et al. (2012)[15]	DWI in the detection of lymphadenopathy	Presence of lymphadenopathy in 10 patients with dentigerous cyst (8 cases) and ameloblastoma (2 cases)	DWI showed 3 patients with ipsilateral lymphadenopathy with a hypointense signal
Eida et al.[16]	Evaluation of the use of ADC values in the diagnosis of mandibular cystic lesions (emphasizing lesions with fluid-filled areas)	27 patients with odontogenic and nonodontogenic cystic mandibular lesions containing a large fluid-filled area: Ameloblastoma (5 cases), odontogenic keratocyst (5 cases), and dentigerous cyst (5 cases)	ADC values were similar between ameloblastomas and dentigerous cysts and between ameloblastomas and odontogenic keratocysts The ADC cutoff value of 2.29×10^{-3} mm^2/second was the most effective for differentiation of dentigerous cysts from ameloblastomas The threshold was $\times$ 1.19 10^{-3} mm^2/second was the most effective in differentiating dentigerous cysts from radicular cysts and odontogenic keratocysts ADC values were not effective for differentiation of some types of cystic lesions of the mandible
Neubauer et al.[17]	Analyzed if DWI can differentiate between benign and malignant musculoskeletal tumorous and tumor-like lesions in pediatric patients Compared DWI with standard MRI	44 patients divided into 2 groups: Group 1: 10 patients with malignant neoplasms Group 2: 34 patients with benign tumors or tumor-like lesions; Ameloblastic fibro-odontoma (1 case) included in this group	Mean ADC value of $\leq 1.03 \times 10^{-3}$ mm^2/second is a strong indicator of malignancy Investigators reported the ADC value of a single case of ameloblastic fibro-odontoma in the mandibular ramus, which was 1.68×10^{-3} mm^2/second
Srinivasan et al.[18]	Assessment of DWI and ADC in the differential diagnosis of odontogenic cysts and neoplasms	20 patients with odontogenic cysts or neoplasms (10 ameloblastomas, 5 odontogenic keratocysts, 3 odontogenic myxomas and 2 dentigerous cysts).	Ameloblastoma cystic areas showed free diffusion, hypointense in T1-weighted images and hyperintense in T2-weighted images Ameloblastoma solid areas showed restricted diffusion, hypointense T1-weighted images and intermediate-high signal on T2-weighted images Odontogenic keratocysts showed hypointense T1-weighted images, hyperintense T2-weighted images and restricted diffusion A significant difference was found between ADC values of odontogenic keratocyst and cystic ameloblastoma When ADC value of 2.0131×10^{-3} mm^2/second was applied as a cutoff value, 100% specificity and sensitivity was achieved in the differentiation between the two groups
Cassetta et al. (2014)[19]	Detection of lymphadenopathy in a case of solid/multicystic ameloblastoma	A 48-year-old man with deep pain on the left side of the mandible and a suppurating fluid leakage from the gingival margin of the second molar	Metastatic nodes present reduction of diffusibility, which is associated with hypercellularity (increased nuclear-to-cytoplasmic ratio) and hyperintensity in DWI images Inflammatory lymph nodes present as hypointense on DWI, with high diffusibility

(*continued*)

Table III. Continued

Authors	Objective	Samples studied	Main results and conclusions
Zhu et al. [20]	Imaging features of 2 peripheral odontogenic keratocyst cases	2 patients with peripheral odontogenic keratocysts	Mean ADC value was 1.29×10^{-3} mm^2/second
Seno et al.[21]	Imaging features of a case of ameloblastoma	A 78-year-old male patient with ameloblastoma who also had a PET-CT examination	DWI presented restricted diffusion with heterogeneous enhancement, which suggested a malignant neoplasm, resulting in patients undergoing further examination with PET-CT
Oda et al.[5]	The utility of DWI and ADC in the differential diagnosis of oral and maxillofacial lesions	Odontogenic keratocysts (3 cases) and nasopalatine duct cysts (2 cases) were compared	ADC values that presented significant differences: ranula versus odontogenic keratocyst; nasopalatine duct cyst versus odontogenic keratocyst; odontogenic abscess versus nasopalatine duct cyst DWI and ADC can be useful to differentiate oral and maxillofacial lesions
Han et al. [22]	The use of DWI and ADC for differentiation of unicystic/multicystic ameloblastoma, odontogenic keratocyst, and dentigerous cyst	40 patients with: unicystic ameloblastoma (11 cases); multicystic ameloblastoma (11 cases); odontogenic keratocyst (15 cases); and dentigerous cyst (3 cases)	Unicystic ameloblastoma showed free diffusion on DWI Odontogenic keratocyst showed restricted diffusion on DWI The ADC values of unicystic ameloblastomas were significantly higher than those of odontogenic keratocysts Dentigerous cysts showed restricted diffusion on DWI and similar ADC values compared with odontogenic keratocysts DWI and ADC can be used to differentiate between unicystic ameloblastomas and odontogenic keratocysts
Peters et al.[23]	The use of DWI and ADC in the differentiation between malignant neoplasms and benign lesions in the head and neck	72 patients divided into benign lesions (neoplasms and inflammatory lesions) and malignant neoplasms One case of myxoma was included	Benign lesions had higher ADC values than malignant lesions DWI can differentiate benign lesions from malignant neoplasms
Salodiya et al.[24]	Case report of an odontogenic myxoma in the mandible	37-year-old male with swelling in mandible	The neoplasm showed no restriction on DWI and a high ADC value ADC value for the lesion was not reported
Panyarak et al.[25]	Comparison of the distortion ratio, signal-to-noise ratio, and contrast-to-noise ratio between turbo spin-echo DWI and echo-planar imaging DWI of the orofacial region for the differential diagnosis of orofacial lesions	After applying exclusion criteria, 38 orofacial lesions (2 cases of ameloblastoma and 1 case of odontogenic keratocyst)	Benign lesions (cysts and benign neoplasms) and malignant neoplasms did not have significantly different ADC values When the ADC values of cysts and benign neoplasms were compared, a statistically significant difference was observed Benign neoplasms also presented ADC values significantly different compared with cysts and malignant neoplasms ADC values obtained with turbo-spin-echo DWI can be useful for the differential diagnosis of orofacial lesions
Ogura et al.[26]	The use of DWI and ADC in the differentiation between odontogenic keratocyst and other cystic lesions of the jaws and normal structures	16 patients with cystic lesions in the jaw, including 5 odontogenic keratocysts, 3 nasopalatine duct cysts and 4 dentigerous cysts	The mean ADC value of the odontogenic keratocysts was lower than the nasopalatine duct cysts, the radicular cysts, and the dentigerous cysts DWI and ADC can be used in the assessment of odontogenic keratocysts

ADC, apparent diffusion coefficient; *PET,* positron emission tomography; *CT,* computed tomography; *DWI,* diffusion-weighted magnetic resonance imaging.

Table IV. ADC data pertaining to odontogenic cysts and odontogenic benign neoplasms with respective *P* values when comparisons between odontogenic lesions were performed

Authors	Lesion	Sample mean ADC	P value
Sumi et al.[13]	Ameloblastomas (nonenhancing lesions)	2.8×10^{-3} mm^2/second	< .001
	Odontogenic keratocysts (nonenhancing lesions)	1.13×10^{-3} mm^2/second	
	Ameloblastomas (solid lesions)	1.30×10^{-3} mm^2/second	
	Odontogenic keratocysts (solid lesions)	Not obtained	
Wang et al.[14]	Benign neoplasms and tumor-like lesions	1.53×10^{-3} mm^2/second	< .0001
	Inflammatory diseases	1.01×10^{-3} mm^2/second	
	Malignant tumors	1.11×10^{-3} mm^2/second	
	Ameloblastomas (included in benign neoplasms and tumor-like lesions group)	1.59×10^{-3} mm^2/second	
Cassetta et al.[15]	Lymph nodes adjacent to odontogenic benign neoplasms	Not reported	Not performed
Eida et al.[16]	Ameloblastomas (fluid areas)	2.45×10^{-3} mm^2/second	
	Radicular cysts	0.90×10^{-3} mm^2/second	.04
	Ameloblastomas (fluid areas)		
	Odontogenic keratocysts	0.87×10^{-3} mm^2/second	.03
	Ameloblastomas (fluid areas)		
	Dentigerous cysts	0.49×10^{-3} mm^2/second	.02
Neubauer et al.[17]	Ameloblastic fibro-odontoma	1.68×10^{-3} mm^2/second	Single neoplasm in the benign lesion group
Srinivasan et al.[18]	Ameloblastomas (cystic areas)	2.19×10^{-3} mm^2/second	< .01
	Odontogenic keratocysts	1.01×10^{-3} mm^2/second	Other comparisons were not performed
	Ameloblastomas (solid areas)	1.04×10^{-3} mm^2/second	
	Odontogenic myxoma	2.09×10^{-3} mm^2/second	
	Dentigerous cysts	1.23×10^{-3} mm^2/second	
Cassetta et al.[19]	Lymph nodes adjacent to a multicystic ameloblastoma	Not reported	Not applicable (case report)
Zhu et al.[20]	Peripheral odontogenic keratocysts	1.29×10^{-3} mm^2/second	Not applicable (case report)
Seno et al.[21]	Ameloblastoma	Not reported	Not applicable (case report)
Oda et al.[5]	Ranula	2.69×10^{-3} mm^2/second	
	Odontogenic keratocyst	0.85×10^{-3} mm^2/second	< .001
	Nasopalatine duct cyst	2.34×10^{-3} mm^2/second	
	Hemangioma	1.45×10^{-3} mm^2/second	.007
	Nasopalatine duct cyst		
	Squamous cell carcinoma	1.30×10^{-3} mm^2/second	< .001
	Nasopalatine duct cyst		
	Pleomorphic adenoma	1.21×10^{-3} mm^2/second	.001
	Nasopalatine duct cyst		
	Odontogenic keratocyst	0.85×10^{-3} mm^2/second	.001
	Nasopalatine duct cyst		
	Odontogenic abscess	0.67×10^{-3} mm^2/second	< .001
Han et al.[22]	Unicystic ameloblastomas	2.30×10^{-3} mm^2/second	
	Odontogenic keratocysts	0.92×10^{-3} mm^2/second	< .001
	Dentigerous cysts	1.25×10^{-3} mm^2/second	
	Odontogenic keratocysts		Not significant
	Multicystic ameloblastomas (cystic areas)	1.93×10^{-3} mm^2/second	Other comparisons were
	Multicystic ameloblastomas (solid areas)	1.36×10^{-3} mm^2/second	not performed
Peters et al.[23]	Myxoma	2.07×10^{-3} mm^2/second	Single neoplasm in the benign lesion group
Salodiya et al.[24]	Odontogenic myxoma	Not reported	Not applicable (case report)
Panyarak et al.[25]	Ameloblastic carcinoma	1.13×10^{-3} mm^2/second	Comparisons between odontogenic lesions were
	Myxofibroma	1.76×10^{-3} mm^2/second	not performed
	Ameloblastoma	1.56×10^{-3} mm^2/second	
	Odontogenic keratocyst	0.94×10^{-3} mm^2/second	
Ogura et al.[26]	Odontogenic keratocysts	1.03×10^{-3} mm^2/second	
	Other cysts	1.98×10^{-3} mm^2/second	.038
	Simple bone cyst	2.79×10^{-3} mm^2/second	Other comparisons were not performed
	Nasopalatine duct cyst	2.28×10^{-3} mm^2/second	
	Radicular cyst	1.82×10^{-3} mm^2/second	
	Dentigerous cyst	1.67×10^{-3} mm^2/second	

ADC, apparent diffusion coefficient.

Table V. Histologic features of the samples assessed in the articles included in the review, and the number (n) of the cases in each investigation

Authors	Benign neoplasms or tumor-like lesions	n	Malignant neoplasms	n	Inflammatory lesions	n
Sumi et al.[13]	Ameloblastoma	9				
	Odontogenic keratocyst	7				
Wang et al.[14]	Schwannoma	4	Squamous cell carcinoma	8	Inflammatory diseases	14
	Neurofibroma	5	Adenoid cystic carcinoma	5		
	Ameloblastoma	2	Mucoepidermoid carcinoma	3		
	Fibrous dysplasia	2	Adenocarcinoma	3		
	Pleomorphic adenoma	2	Lymphoepithelial carcinoma	1		
	Leiomyoma	2	Malignant ameloblastoma	1		
	Eosinophilic lymphogranuloma	2	Rhabdomyosarcoma	5		
	Synovial chondromatosis	1	Osteosarcoma	4		
	Giant cell granuloma	1	Malignant fibrous histiocytoma	2		
	Desmoplastic fibroma	1	Synovial sarcoma	2		
	Nodular fasciitis	1	Ewing sarcoma	1		
			Plasmacytoma	1		
			Leiomyosarcoma	1		
			Angiosarcoma	1		
			Myxofibrosarcoma	2		
			Undifferentiated sarcoma	1		
Casseta et al.[15]	Dentigerous cyst	8				
	Unicystic ameloblastoma	1				
	Solid/multicystic ameloblastoma	1				
Eida et al.[16]	Ameloblastoma	5				
	Simple bone cyst	4				
	Dentigerous cyst	9				
	Radicular cyst	4				
	Odontogenic keratocyst	5				
Neubauer et al.[17]	Hemangioma	6	Ewing sarcoma	3		
	Nonossifying fibroma	5	Osteosarcoma	1		
	Lymphangioma	4	Desmoplastic small round cell tumor	1		
	Arteriovenous malformation	3	Primitive myxoid sarcoma	1		
	Osteochondroma	2	Local recurrence of alveolar rhabdomyosarcoma	1		
	Synovial epidermoid sarcoma	2				
	Langerhans cell histiocytosis	2	Local recurrence of synovial sarcoma	1		
	Benign desmoid tumor	1				
	Desmoid fibromatosis	1	Osseous metastasis of neuroblastoma	1		
	Inflammatory soft tissue tumor	1	Metastasis of adrenocortical carcinoma	1		
	Osteoid osteoma	1				
	Aneurysmal bone cyst	1				
	Fibrous dysplasia	1				
	Neurofibroma	1				
	Schwannoma	1				
	Ameloblastic fibro-odontoma	1				
	Benign myofibroblastic soft tissue tumor	1				
Srinivasan et al.[18]	Ameloblastoma	10				
	Odontogenic keratocyst	5				
	Odontogenic myxoma	3				
	Dentigerous cyst	2				
Cassetta et al.[19]	Solid/multicystic ameloblastoma	1				
Zhu et al.[20]	Odontogenic keratocyst	2				
Seno et al. [21]	Ameloblastoma	1				
Oda et al.[5]	Ranula	4	Malignant melanoma	1	Odontogenic abscess	6
	Nasopalatine duct cyst	2				
	Hemangioma	4				
	Squamous cell carcinoma	19				
	Pleomorphic adenoma	3				
	Basal cell carcinoma	1				

(*continued*)

Table V. Continued

Authors	Benign neoplasms or tumor-like lesions	n	Malignant neoplasms	n	Inflammatory lesions	n
	Medication-related osteonecrosis	10				
	Osteoradionecrosis of the jaw	4				
	Odontogenic keratocyst	3				
Han et al. [22]	Unicystic ameloblastoma	11				
	Odontogenic keratocyst	15				
	Multicystic ameloblastoma	11				
	Dentigerous cyst	3				
Peters et al.[23]	Adenoma	11	Carcinoma	17	Myositis	1
	Hemangioma	3	Metastasis	12	Inflammatory	1
	Warthin tumor	2	Lymphoma	12	Pseudotumor	1
	(Fibro)lipoma	2			Focal parotitis	1
	Schwannoma	1			Post-therapeutic inflammation	1
	Meningioma	1				
	Glomus tumor	1				
	Myxoma	1				
	Lymphangioma	1				
	Lymphoepithelial cyst	1				
Salodiya et al.[24]	Odontogenic myxoma	1				
Panyarak et al.[25]	Pleomorphic adenoma	8	Adenoid cystic carcinoma	4		
	Hemangioma	6	Ameloblastic carcinoma	1		
	Lipoma	3	Mucoepidermoid carcinoma	2		
	Central ossifying fibroma	1	Osteosarcoma	1		
	Fibroma	2	Pleomorphous carcinoma	1		
	Myxofibroma	1	Spindle cell carcinoma	1		
	Neurofibroma	1				
	Ameloblastoma	2				
	Basal cell adenoma	1				
	Odontogenic keratocyst	1				
	Lymphoplasmacytic lesion	1				
	Spindle cell or pleomorphic lipoma	1				
	Spindle cell tumor	1				
	Warthin tumor	1				
Ogura et al.[26]	Odontogenic keratocyst	5				
	Other cysts	11				
	Simple bone cyst	1				
	Nasopalatine duct cyst	3				
	Radicular cyst	3				
	Dentigerous cyst	4				

N, No. of cases in the sample provided by the investigators.

using ADC values. It was possible to distinguish ameloblastomas from odontogenic keratocysts,[13,16,18] ameloblastomas from dentigerous cysts,[16] and nasopalatine duct cysts from odontogenic keratocysts.[5] Some investigators also detailed the morphology of ameloblastomas and split the lesions into solid and cystic areas[13,16,18] or classified these lesions as unicystic and multicystic to perform comparisons between groups.[22] The greater diffusibility in ameloblastomas, shown by higher ADC values, compared with keratocysts, is inherent to the histologic features of these tumors.

The authors agreed that ameloblastomas have higher ADC values than keratocysts,[13,16,22] even when comparisons between distinct regions of ameloblastomas were performed, such as solid[13] versus fluid/cystic areas.[16,18,22] Ameloblastomas show variable morphology in distinct areas[30] on the basis of liquid and solid components, which can be fully evaluated by MRI.[31] Hence, it was expected that these different areas would be evaluated according to fluid or solid contents when comparisons were performed, although not all researchers considered this.[14] Furthermore, compared with dentigerous cysts, fluid areas of ameloblastomas also demonstrated higher ADC values.[16,22] In contrast, when dentigerous cysts were compared with keratocysts, no significant differences in ADC values were found.[22]

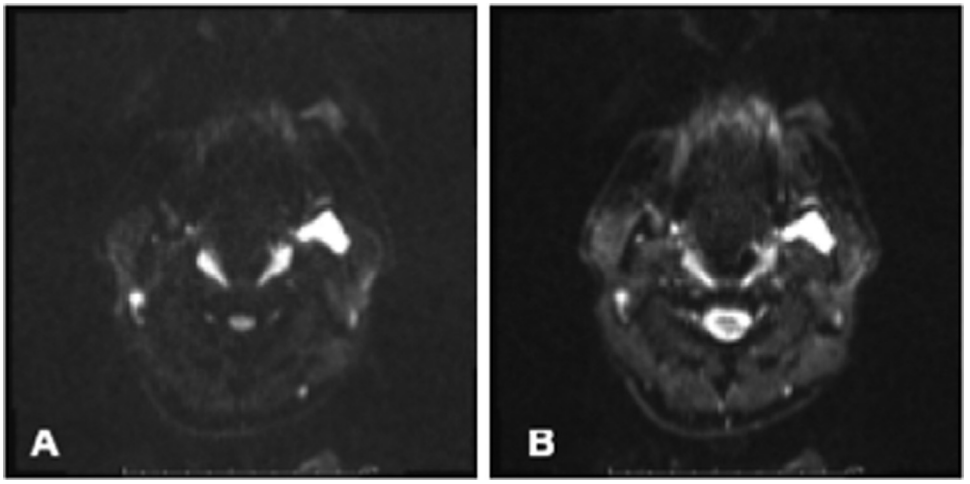

Fig. 3. Diffusion-weighted imaging (DWI) using 2 distinct b values **(A)** b = 0; **(B)** b = 800. The lesion was an odontogenic keratocyst in the left posterior mandibular region of a 22-year-old male. The lesion exhibits a hyperintense pattern (axial slices).

Odontogenic keratocysts were accepted for a time by the WHO as neoplasms, with the designation "keratocystic odontogenic tumor." The 2017 WHO restored the name *odontogenic keratocyst* and moved the lesion back into the cyst classification.[32] Exclusively solid variants of odontogenic keratocysts are rarely described in the literature.[33] Considering the morphologic features of ameloblastomas, Sumi et al.[13] attempted to compare the solid areas of odontogenic keratocysts with the solid areas of ameloblastomas, but failed because investigators could not measure ADC values in their cases; the solid areas of the keratocysts were too small. Other researchers did not consider the presence of solid areas in the keratocyst when ADC values were obtained.[5,18,22,26]

Odontogenic lesions were also compared with nonodontogenic lesions,[16] such as other cysts in the jaw,[26] salivary gland neoplasms,[5] ranulas,[5] inflammatory diseases,[14] and malignant neoplasms.[14] Ogura et al.[26] observed that odontogenic keratocysts have lower water diffusibility compared with other cysts in the jaw. Oda et al.[5] confirmed that keratocysts have lower ADC values compared with ranulas and nasopalatine duct cysts and that nasopalatine duct cysts, which present high signal intensity in T1-weighted images because of the presence of keratin and viscous fluid,[34]

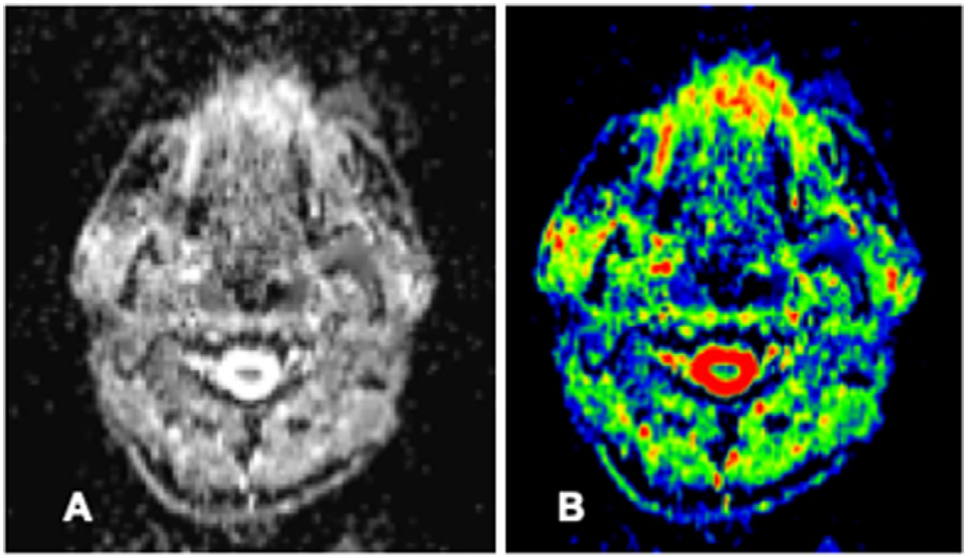

Fig. 4. Apparent diffusion coefficient (ADC) maps, **(A)** black and white, **(B)** colored, of the same case using the same slices. In the ADC map colored image, the blue areas show highly restricted water molecule diffusion, the green areas illustrate restricted diffusion, the yellow areas represent facilitated diffusion, and the red areas show highly facilitated diffusion.

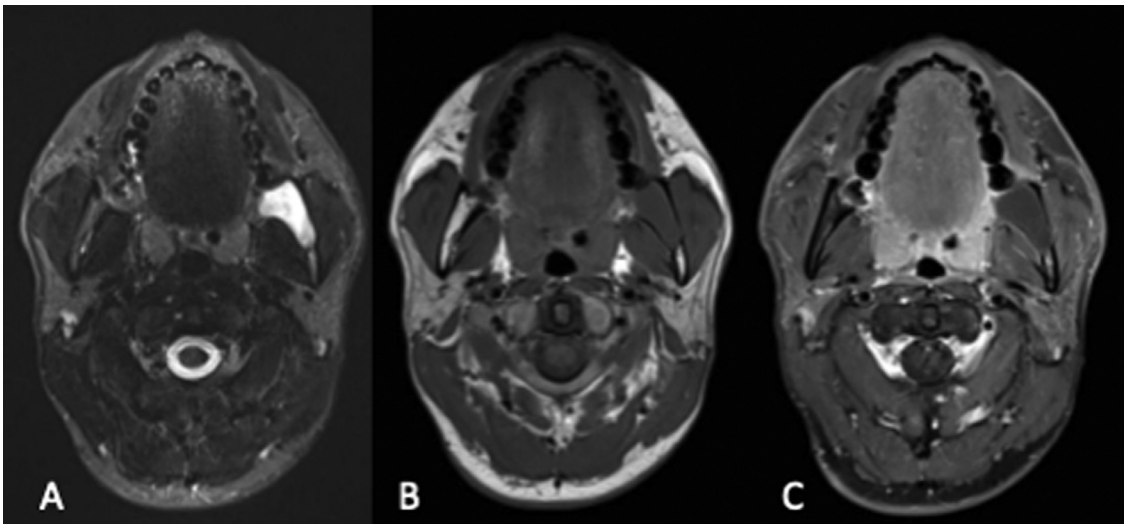

Fig. 5. **(A)** Short tau inversion recovery (STIR) image. **(B)** T1-weighted image. **(C)** Contrast-enhanced T1-weighted image of the same case (odontogenic keratocyst) in axial slices.

show lower water diffusibility compared with odontogenic abscesses and hemangiomas.[5] These findings were expected because of the cytomorphologic nature of abscesses and hemangiomas; however, surprisingly, researchers found that nasopalatine duct cysts have lower water diffusibility than squamous cell carcinomas.[5] These findings could have been affected by the limited number of nasopalatine duct cysts included in the researchers' samples (2 cases).

Although the aim of this systematic review was to collect and discuss data regarding the application of DWI in the assessment of benign odontogenic lesions, we ultimately selected studies that included nonodontogenic lesions[17,23] and case reports[19,20,21,24] due to the fact that only a few research articles were available because of the novel subject matter. The case reports included 1 case of odontogenic myxoma,[24] 1 of ameloblastoma,[19,21] and 2 of peripheral odontogenic keratocysts.[20]

In one of the case reports, DWI was used to differentiate inflammatory from neoplastic lymph nodes near a primary odontogenic lesion,[19] and the same methodology was applied in a study with a larger number of cases.[35] The investigators' basic assumptions were that neoplastic lymph nodes have restricted water diffusibility and that the absence of neoplastic lymph nodes could indicate that the lesion is benign, which may contribute to the differential diagnosis in early lesion imaging evaluations.[19]

The investigations in which limited numbers of benign odontogenic lesions were compared concluded that ADC could be useful in the differentiation of some types of lesions.[13,14,16,18,22,26] However, the results

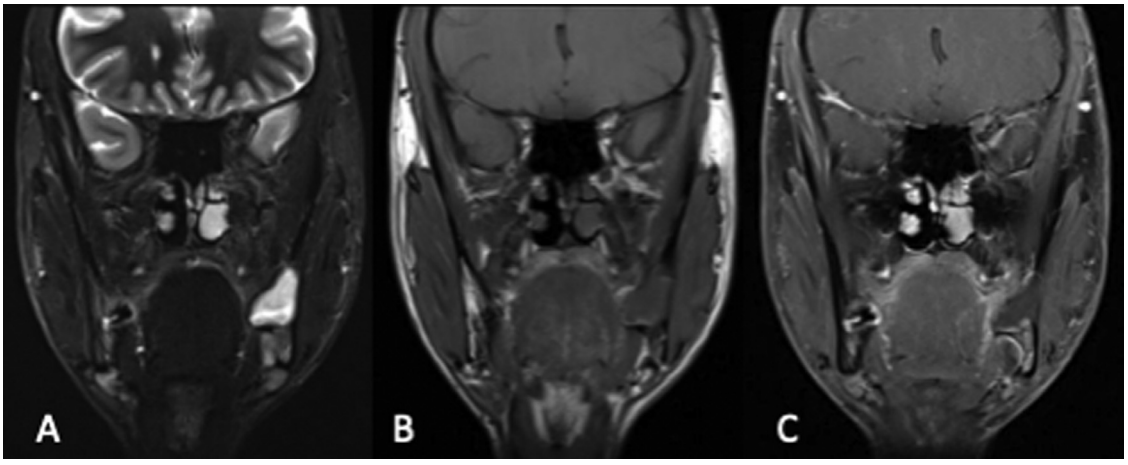

Fig. 6. **(A)** Short tau inversion recovery (STIR). **(B)** T1-weighted image. **(C)** Contrast-enhanced T1-weighted image of the same case (odontogenic keratocyst) in coronal slices.

obtained by these investigators could not be compared directly because DWI and ADC values can be influenced by a number of factors, such as the type and the strength of the equipment, acquisition parameters, scanner stability,[10] lesion delineation in the DWI sequence,[11] and ROI positioning strategies. The ROI positioning strategy is crucial in heterogeneous lesions, mainly ameloblastomas and odontogenic keratocysts that have fluid and solid contents.

The limitations of the present review include the small number of available studies on only benign odontogenic lesions, which could have facilitated comparison between these abnormalities, and the small number of cases of each lesion included in the research.

CONCLUSIONS

The application of DWI in the diagnosis of benign odontogenic lesions has been studied by few researchers. These investigations focused mainly on the differentiation of ameloblastomas and odontogenic keratocysts from other odontogenic and/or nonodontogenic lesions. The samples in the investigations on histologic types of lesions were highly heterogeneous. Overall, it is too early to reach a conclusion based on the available data in the literature that DWI and ADC can provide useful information in the differentiation of the histologic types of some benign odontogenic lesions.

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APPENDIX

Big flow chart