Application of diffusion-weighted magnetic resonance imaging in the diagnosis of salivary gland diseases: a systematic review

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Objectives. The aim of this systematic literature review was to focus on the use of diffusion-weighted magnetic resonance imaging (DWI) in the evaluation of salivary gland diseases.

Study Design. Databases were searched, and original research manuscripts up to 2018 were identified by using the keywords "diffusion" combined with "salivary gland," "salivary gland neoplasm," "sialadenitis," "parotid gland," "submandibular gland," "sublingual gland," "minor salivary gland," "salivary gland fistula," "salivary gland calculi," "salivary ducts," "xerostomia," and "sialorrhea." Only English language manuscripts and studies pertaining to DWI were selected.

Results. In all, 66 investigations regarding various salivary gland diseases, such as neoplasms, postirradiation changes, and inflammatory and autoimmune diseases, were included. Most study objectives involved the use of the apparent diffusion coefficient (ADC) in differentiating between benign lesions and malignant neoplasms. Histologic features of evaluated samples were heterogeneous.

Conclusions. DWI may improve the differential diagnosis of salivary gland diseases, particularly in distinguishing between benign and malignant neoplasms. A unique ADC cutoff value could not be established because of the heterogeneity of the methods applied for ADC assessment and the heterogeneity of the diseases. DWI and the ADC are valuable tools in the diagnosis of salivary gland disease. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;128:280−310)

Salivary gland disorders include inflammatory, bacterial, viral, neoplastic,[1] autoimmune,[2] and obstructive[3] diseases, as well as alterations caused by medical treatments, such as radiotherapy (RT) and chemotherapy. Imaging of major salivary glands is a diagnostic challenge because of the wide diversity of gland disorders with similar imaging findings.[3] Minor salivary glands are not often evaluated in imaging examinations unless they are associated with lesions or masses.[3]

Magnetic resonance imaging (MRI) is the preferred imaging modality for salivary gland assessment because of its ability to delineate lesions and their spread,[3] as well as salivary gland destruction or inflammation.[4] It is the complementary examination of choice for salivary gland assessment after ultrasonographic and clinical examinations.

Recently, diffusion-weighted MRI (DWI) has been mentioned in the literature as a complementary tool to traditional MRI that can allow characterization of tissue cellularity and physiologic processes.[5,6] DWI qualitatively describes the Brownian motion or random motion of water molecules when analyzing water diffusibility in an intercellular medium. Water molecule motion may vary qualitatively according to different tissues or intercellular conditions. DWI axial images generate apparent diffusion coefficient (ADC) maps,[7] which are applied to evaluate quantitative water molecule movement through ADC numerical values.

The ADC values from a determined region of interest (ROI) are calculated by assessing the difference in the signal intensity on DWI according to a monoexponential decay model, considering 2 or more b-values derived from DWI.[7] When the logarithm of relative signal intensity of the tissue is plotted (y-axis) against the b-values (x-axis), a linear behavior is observed, and the gradient of the observed line is the ADC.[6] The quantitative analysis provided by the ADC obtained from DWI findings can be accomplished only if at least 2 b-values are used for imaging. The optimal b-value depends on the tissue that is investigated.[6] Hence,

Statement of Clinical Relevance

Diffusion-weighted magnetic resonance imaging can provide information about tissue cellularity and depict physiologic processes. It can be used to study a wide range of salivary gland diseases; however, no systematic review regarding this is available in the literature.

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ADC values obtained from an ROI represent numerically the diffusibility of water molecules in the intercellular medium of a particular tissue. The higher the diffusibility, the higher are the ADC values.

In salivary gland imaging, DWI and ADC values have been studied in a wide range of disorders, mostly in the differentiation of neoplasms. The aim of the present study was to review the literature regarding the use of DWI and ADC in the evaluation of salivary gland diseases to offer an overview of the application of DWI and ADC. The following questions were addressed: (1) "What has been investigated regarding the application of DWI in salivary gland disorders, diseases, or lesions?" (2) "What were the results obtained by the researchers?" (3) "What is the application of DWI in salivary gland evaluation?"

MATERIALS AND METHODS

Protocol and registration

This review was registered at the National Institute for Health Research, International Prospective Register of Systematic Reviews (PROSPERO; No. CRD42018091554). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist was followed in this investigation.[8]

Data selection

The selection of studies potentially eligible for inclusion in this systematic review was performed by searching the PubMed, EMBASE (Excerpta Medica Database), Cochrane Central Register of Controlled Trials, Scopus, Web of Science, and Google Scholar databases. These databases were searched without language restrictions and 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 strategies: salivary gland AND diffusion, salivary gland neoplasm AND diffusion, sialadenitis AND diffusion, parotid gland AND diffusion, sublingual gland AND diffusion, submandibular gland AND diffusion, minor salivary gland AND diffusion, salivary gland fistula AND diffusion, salivary gland calculi AND diffusion, salivary ducts AND diffusion, xerostomia AND diffusion, sialorrhea AND diffusion. Three investigators participated in data selection, and an expert in DWI reviewed each study selected.

Eligibility criteria

Types of studies. Original studies (research articles) were considered appropriate for inclusion; however, case reports, abstracts, oral presentations, and literature reviews were considered ineligible. Original investigations that used MRI for the diagnosis of salivary gland disorders, lesions, or diseases and did not consider DWI and/or ADC were excluded. Investigations solely related to the technical evaluation of MRI protocols, software, and technical parameters were also excluded. Additionally, non−English language studies and non−human studies were excluded. The present review did not consider other imaging techniques, such as intravoxel incoherent motion, diffusional kurtosis imaging, diffusion tensor imaging, or split echo diffusion-weighted MRI.

Participant groups. Studies involving participant groups comprising patients with salivary gland disorders, lesions, or diseases (i.e., inflammation, infection, neoplasm, autoimmune, and RT- or chemotherapy-induced disorders) who underwent MRI complemented with DWI/ADC examinations were included in the data selection. However, participant groups comprising patients with mixed site lesions (i.e., head and neck lesions), including salivary gland abnormalities, were not included.

Data extraction

Data extraction was executed by 3 independent reviewers. Two reviewers initially screened the titles and abstracts and then evaluated the full text of each selected article to identify eligible studies. The third reviewer verified each study selected. Disagreements among the reviewers were resolved through discussion, and when an agreement could not be reached, a fourth coworker was consulted. The following data were extracted and documented: publication year; author information (e.g., investigator location); number of participants evaluated; nature of the salivary gland disorders, lesions, or diseases studied; investigation objective pertaining to DWI and ADC; how the salivary gland disorders, lesions, or diseases were grouped in the study; results (mainly ADC values); and conclusions. A single expert in DWI reviewed the reports selected to verify the MRI methodology. The investigators (authors or coauthors) of the selected reports were contacted when additional data were required.

Data analysis—risk of bias

The data search results are summarized in a flow chart (Figure 1) and in Tables I through VIII. Images from our own collection were added to illustrate the diseases discussed (Figures 2 and 3). The ADC values determined by the investigators are reported in a separate table, which includes the disorder, lesion, or disease studied.

As the ADC values may be subject to several sources of variability, direct comparisons between ADC values in the investigations were not performed.

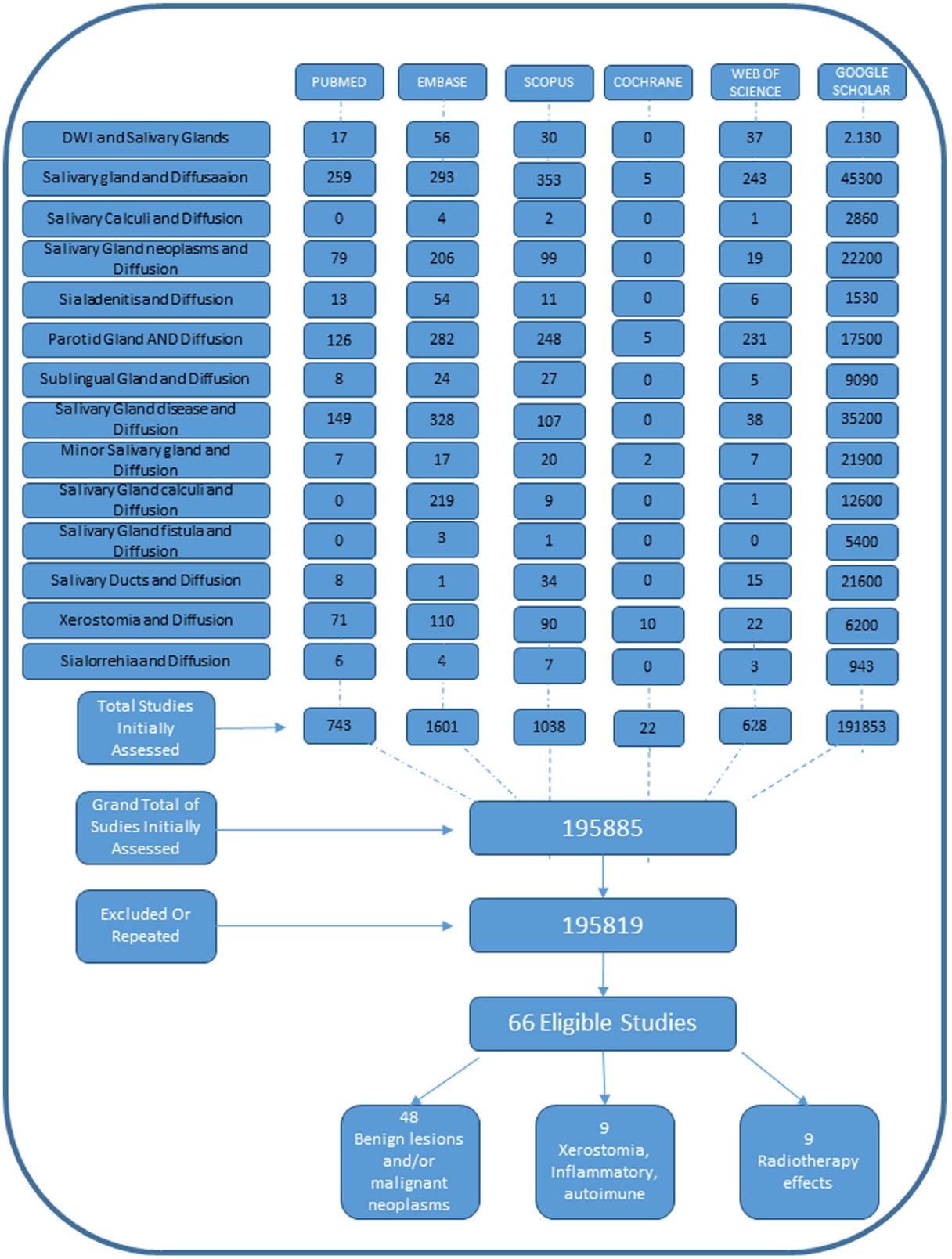

Fig. 1. Flow diagram of the literature search. Number of studies screened for each database and each keyword; number of studies excluded; number of eligible studies, and number of each study according to its main subject.

Table I. Year, authors, publication origin, main subject, Tesla value, and number of patients or lesions evaluated in the original articles selected in the review

Year	*Authors*	*Origin*	*Main subject*	*Tesla*	*Number*
2018	Domingo et al.[10]	Spain	Neoplasms	1.5	44
2018	Faheem et al. [11]	Egypt	Neoplasms	1.5	48
2018	Khamis et al.[12]	Egypt	Neoplasms	1.5	30
2018	Matsusue et al.[13]	Japan	Neoplasms	1.5	8
2018	Mikaszewski et al.[14]	Poland	Neoplasms	1.5	100
2018	Takahashi et al.[15]	Japan	Sjögren syndrome	3.0	9
2018	Wang et al.[16]	China	Neoplasms	1.5	78
2018	Zhang et al.[17]	China	Neoplasms	1.5	51
2018	Zhang et al.[18]	China	Neoplasms	1.5	36
2018	Zhang et al. [19]	China	Radiotherapy	3.0	26
2018	Zhang et al.[20]	China	Radiotherapy	3.0	28
2018	Zheng et al.[21]	China	Neoplasms	3.0	45
2018	Zheng et al.[22]	China	Neoplasms	3.0	112
2017	Kato et al.[23]	Japan	Neoplasms	1.5	45
2017	Loimu et al.[24]	Sweden	Radiotherapy	1.5	20
2017	Matsusue et al.[25]	Japan	Neoplasms	1.5	51
2017	Mikaswewki et al.[26]	Poland	Neoplasms	1.5	100
2017	Mikaszewski et al.[27]	Poland	Neoplasms	1.5	221
2017	Milad et al.[28]	Egypt	Neoplasms	1.5	46
2017	Nada et al.[29]	Egypt	Neoplasms and inflammatory lesions	1.5	73
2017	Razek et al.[30]	Egypt	Neoplasms	1.5	48
2017	Razek et al.[31]	Egypt	Neoplasms	1.5	31
2017	Tao et al.[32]	Japan	Neoplasms	1.5	148
2017	Terra et al.[33]	Brazil	Neoplasms and inflammatory lesions	1.5	22
2017	Xu et al.[34]	China	Sjögren syndrome	3.0	13
2017	Zhou et al.[35]	China	Radiotherapy	3.0	32
2016	Ding et al.[36]	China	Sjögren syndrome	1.5	39
2016	Eissa et al.[37]	Egypt	Neoplasms	1.5	53
2016	Karaman et al.[38]	Turkey	Neoplasms	1.5	36
2016	Kikuchi et al.[39]	Japan	Neoplasms	1.5	53
2016	Mukai et al.[40]	Japan	Neoplasms	1.5	193
2016	Yologlu et al.[41]	Turkey	Neoplasms	1.5	15
2016	Yuan et al.[42]	China	Neoplasms	1.5	207
2016	Zhu et al.[43]	China/United States	Neoplasms	1.5	43
2015	Doornaert et al.[44]	Netherlands	Radiotherapy and chemotherapy	1.5	15
2015	Juan et al.[45]	China	Radiotherapy	1.5	11
2015	Kato et al.[46]	Japan	Neoplasms	3.0	31
2015	Liu et al.[47]	China	Radiotherapy	1.5	13
2015	Salama et al.[48]	Egypt	Neoplasms	1.5	25
2014	Balçik et al.[49]	Turkey	Neoplasms	1.5	40
2013	Celebi et al.[50]	Turkey	Neoplasms	1.5	75
2013	Fruehwald-Pallamar et al.[51]	Austria	Neoplasms	3.0	38
2013	Zhang et al.[52]	China	Radiotherapy	3.0	28
2012	Kato et al.[53]	Japan	Neoplasms	1.5	10
2011	Lechner Goyault et al.[54]	France	Neoplasms	1.5	60
2011	Kato et al.[55]	Japan	Xerostomia	1.5	20
2010	Eida et al.[56]	Japan	Neoplasms	1.5	70
2010	Inci et al.[57]	Turkey	Neoplasms	1.5	32
2010	Li et al.[58]	China	Sjögren syndrome	1.5	42
2010	Yerli et al.[59]	Turkey	Neoplasms	1.5	25
2009	Habermann et al.[60]	Germany	Neoplasms	1.5	149
2009	Regier et al.[61]	Germany	Sjögren syndrome	1.5	65
2008	Abu et al.[62]	Japan	Neoplasms and inflammatory lesions	1.5	23
2008	Dirix et al.[63]	Belgium	Radiotherapy	1.5	8
2008	Ries et al.[64]	Germany	Inflammatory lesions	1.5	71
2008	Yabuuchi et al.[65]	Japan	Neoplasms	1.5	47
2007	Eida et al.[66]	Japan	Neoplasms	1.5	31
2007	Matsushima et al.[67]	Japan	Neoplasms	1.5	32
2007	Yerli et al.[68]	Turkey	Neoplasms	1.5	28

(*continued*)

Table I. Continued

Year	Authors	Origin	Main subject	Tesla	Number
2005	Habermann et al.[69]	Germany	Neoplasms	1.5	45
2005	Motoori et al.[70]	Japan	Neoplasms	1.5	9
2005	Motoori et al.[71]	Japan	Neoplasms	1.5	33
2004	Ikeda et al.[72]	Japan	Neoplasms	1.5	17
2004	Motoori et al.[73]	Japan	Neoplasms	1.5	46
2004	Patel et al.[74]	United States	Connective tissue disorders	1.5	97
2002	Sumi et al.[75]	Japan	Sjögren syndrome and inflammatory lesions	1.5	62

These sources of variability include patient-related differences, scanner stability, systematic reader errors (choice of ROI, intra-/interobserver repeatability),[9] lesion delineation in the DWI sequence,[5] and differences in MRI equipment, such as equipment potency (determined by Teslas) of each investigation (see Table I).

RESULTS

In total, 195,885 studies were initially identified in the databases with the use of all of the keywords. After applying the inclusion and exclusion criteria and removing duplicated studies, 195,815 studies were excluded. Four studies could not be fully evaluated and were excluded because of lack of accessibility (the Digital Object Identifier was incorrect; the paper was not available in our institution's library system; or the authors did not respond to our emails asking for a copy of the manuscript for evaluation in this review). In total, 66 investigations performed exclusively on salivary gland diseases were identified as appropriate for inclusion.[10-75] A flow diagram illustrating the literature search is presented in Figure 1. Studies selected according to the inclusion criteria are listed in Table I.

The oldest study identified was from 2002,[75] and 13 studies were found from the year in which the investigation was conducted (2018).[10-22] The number of patients or lesions analyzed ranged from 8[63] to 193.[40] Table I also includes the strength of the MRI equipment used in each investigation and the number of patients or lesions assessed.

With regard to the major salivary glands evaluated, most of the studies included the parotid gland, some of the studies included the submandibular gland,[19,20,30,33,37,44,56,62,63,70,73,75] and only one mentioned the minor salivary glands.[37]

Most studies focused on the use of the ADC in the assessment of salivary gland neoplasms,[10-13,16-18,21-23,25-28,30-32,37-43,46,48-51,53,54,56,57,59,60,65-73] although some of the studies included investigations of neoplasms with inflammatory disorders, such as sialadenitis,[29,33,62] or included inflammatory conditions and nonneoplastic lesions as well as benign neoplasms as a benign lesion group.[14,18,26,39,49,51,54,68] Salivary duct neoplasms were the main subject of 2 studies,[60,70] although other investigations included this type of neoplasm in their samples. Warthin tumors[10,12,13,16-18,23,25,30,38,41,46,48,49,51,54,56,57,59,60,65,67,69,71,72] and pleomorphic adenomas[10,12,16-18,21,25-28,33,38,40,41,46,48-51,54,57,59,60,62,65,68,69,73] were the neoplasms most frequently investigated. Comparisons between neoplasms and normal glandular tissue were also performed in some of the studies.[13,18,33,41,68,69] One study assessed malignant neoplasms exclusively.[53] Table II summarizes the data of the studies that investigated neoplasms, as well as their objectives, the sample features, and main conclusions. Table III presents the histologic types of lesions in each study.

Nine studies investigated the effects of RT on the salivary glands[19,20,24,35,44,45,47,52,63] and 1 of them compared patients experiencing the effects of RT with healthy volunteers.[47] Some studies performed imaging examinations with gustatory stimulation.[19,24,52,63] The main objectives, samples studied, and results pertaining to DWI and ADC of these studies are listed in Table IV.

Salivary gland inflammatory or immunologic diseases,[15,34,36,55,58,61,64,74,75] including Sjögren syndrome (SS),[15,34,36,58,61,75] acute or chronic parotitis,[61] and xerostomia without SS,[55] were also investigated. Among these studies, most compared patients with disease with healthy volunteers.[36,55,61,64,74,75] The main objectives, samples studied, and results pertaining to DWI and ADC of these studies are presented in Table V.

With regard to ADC, the data obtained by the investigators who studied mainly neoplasms, RT effects, and other diseases, as well as corresponding *P* values, are presented in Tables VI, VII, and VIII, respectively. With regard to neoplasms, pleomorphic adenomas frequently had the highest ADC values (Habermann et al.[60] reported the highest value, 2.09×10^{-3} mm/s^2), and Warthin tumors were reported as the benign neoplasm with the lowest ADC value.

Figure 2 demonstrates one of our cases to illustrate the review. The patient was a 37-year-old woman with pain in the salivary gland region for a duration of 4

Table II. Summarized data of the studies with neoplasms in their sample selected to the review*

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
Domingo et al., 2018[10]	Evaluation of dynamic contrast-enhanced and DWI	Patients with benign and malignant parotid neoplasms, with histopathologic confirmation, DWI, and DCE examinations.	• Warthin tumors presented lower ADC values compared with pleomorphic adenomas. • Malignant neoplasms and Warthin tumors presented lower ADC values, but malignant neoplasms in the sample were not frequent.
Faheem et al., 2018[11]	Determination of an ADC cutoff value for the differentiation of parotid gland benign and malignant neoplasms	Patients with benign and malignant parotid neoplasms, with histopathologic confirmation and DWI examinations.	• Benign neoplasms presented higher ADC values compared with malignant neoplasms. • Using 0.87×10^{-3} mm^2/s as a cut-off point to differ benign and malignant neoplasms, the sensitivity was 62.5%, and the specificity was 62.5%. • The ADC value is not conclusive enough to differentiate between benign and malignant neoplasms.
Khamis et al., 2018[12]	Evaluation of the diagnostic performance of ADC and Cho/Cr ratio in distinguishing subtypes of parotid gland neoplasms	Patients with parotid gland neoplasms (size greater than 1 cm), with histopathologic examination confirmation and DWI examinations.	• Benign neoplasms presented higher ADC values compared with malignant tumors. • PA presented higher ADC values compared with WT and malignant neoplasms. • The differentiation between benign versus malignant neoplasms, using a cutoff ADC value of 1.50×10^{-3} mm^2/s presented 100% sensitivity, 63.6% specificity, and 74.1% accuracy. • ADC values and Cho/Cr ratios are useful in the differentiation of parotid neoplasms subtypes.
Matsusue et al., 2018[13]	Evaluation of parotid vanishing neoplasms (with MRI homogeneity and isointensity to the normal parotid gland) using conventional MRI with and without postcontrast gadolinium-enhancement and on DWI	Patients with homogeneous enhanced neoplasms, with confirmed histopathologic diagnosis and DWI examinations.	• Neoplasms were classified as "low," "iso," and "high," according to its MRI features. No comparison between ADC values was performed. • All neoplasms evaluated demonstrated "low" T1-weighted signal and "high" DWI, except WT. • MRI evaluation of parotid neoplasms should be performed initially by T1-weighted and DWI.
Mikaszewski et al., 2018[14]	Creation of an algorithm for preoperative differential diagnosis of parotid gland neoplasms by using DWI.	Patients with parotid gland neoplasms, with histopathologic examination confirmation and DWI examinations.	• Using as a cutoff point an ADC value of $> 1.7 \times 10^{-3}$ mm^2/s for malignant neoplasms, investigators obtained 41.7% sensitivity and 98.5% specificity; • DWI provided similar accuracy of fine-needle biopsy in the differential diagnosis of parotid tumors.
Wang et al., 2018[16]	Creation of a scoring system to differentiate WT from carcinomas and PA	Patients with parotid gland neoplasms, with histopathologic diagnosis and DWI examinations.	• WT presented significantly lower ADC values compared with PA. • Carcinomas presented significantly higher ADC values compared with WT. • When using a cutoff ADC mean value of $\geq 1.01 \times 10^{-3}$ mm^2/s, combined with an SD ADC value of $> 0.11 \times 10^{-3}$ mm^2/s, patients age greater than 49 years and male gender, sensitivity was 87.5%, and specificity was 100%.
Zhang et al., 2018[17]	Evaluation of the use of CDFI and DWI in the differentiation of	Patients with parotid benign and malignant neoplasms, with histopathologic	• Benign and malignant lesions presented significantly differences in ADC values.

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Table II. Continued

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
	malignant parotid neoplasms from benign neoplasms	confirmation, CDFI, and DWI examinations.	• PA presented significantly higher ADC values compared with other neoplasms. • The mean ADC of WT was very close of carcinomas, possibly because Warthin tumors and carcinomas have rich cellularity.
Zhang et al., 2018[18]	Differentiation of benign and malignant parotid neoplasms by using DWI, SWI, and conventional MRI	Patients with parotid benign and malignant neoplasms, with histopathologic confirmation, MRI, SWI and DWI examinations.	• Mean ADC values from benign and malignant neoplasms did not present significant differences (PA and WT were included in the same group). • The differential diagnostic value of combined DWI and SWI is higher than that with these techniques used alone.
Zheng et al., 2018 (1)[21]	Differentiation of benign and malignant parotid gland neoplasms by using DWI, DCE, and conventional MRI	Patients with parotid benign and malignant neoplasms, with histopathologic confirmation, MRI, DCE, and DWI examinations.	• PA presented significantly higher ADC values compared with malignant neoplasms and adenolymphoma. • No significant differences between malignant and benign neoplasms ADC values were observed. • Combined techniques improved the accuracy in the differentiation of malignant and benign neoplasms.
Zheng et al., 2018 (2)[22]	Differentiation of benign and malignant parotid gland neoplasms by using semiquantitative and quantitative DCE and DWI	Patients with parotid benign and malignant neoplasms, with histopathologic confirmation, DCE, and DWI examinations.	• Using ADC threshold values 0.709×10^{-3} mm^2/s to 0.948×10^{-3} mm^2/s as malignant, sensitivity and specificity were 75% and 78%, respectively. • Combined techniques improved the accuracy in the differentiation of malignant and benign neoplasms.
Kato et al., 2017[23]	Differentiation between WT and oncocytoma of the parotid gland by using ADC values	Patients with WT (excluding purely cystic WT) and oncocytoma in parotid gland, who underwent DWI.	• WT presented lower ADC values compared with oncocytomas. • DWI images and ADC values may be useful in the differentiation of WT and oncocytoma in parotid glands.
Matsusue et al., 2017[25]	Differentiating pleomorphic adenomas, WT, and malignant tumors by using ADC and signal intensity of the enhancing neoplasms components	Patients diagnosed with parotid gland neoplasms, with histopathologic results, who also underwent DWI examinations.	• PA presented higher ADC values compared with WT or malignant neoplasms. • WT ADC values and malignant neoplasms presented no statistically significant difference. • Malignant lymphoma presented the lowest ADC values.
Mikaszewki et al., 2017[26]	To compare the accuracy of DWI and fine-needle biopsy in the differential diagnosis of malignant and benign parotid neoplasms in relation to the histopathologic examination	Patients diagnosed with parotid gland neoplasms, with histopathologic results, who also underwent DWI examination and fine-needle biopsy.	• DWI presented higher sensitivity and specificity in the differentiation of malignant and benignant neoplasms compared with fine-needle biopsy. • In the majority of the cases where fine-needle biopsy result was false-negative, the parotid malignancy was diagnosed as a PA with histopathologic examination. • DWI has a high cost and limited availability but should be performed in patients whose fine-needle biopsy examination results turn out to be nondiagnostic or show the presence of PA.
Mikaszewski et al., 2017[27]	The appropriate selection of ADC cutoff values to optimize sensitivity and specificity for PA and malignant neoplasms	Patients diagnosed with parotid gland neoplasms, with histopathologic results, who also underwent DWI examinations.	• Malignant neoplasms presented lower ADC values compared with PA. • The cutoff ADC value of 1.73×10^{-3} mm^2/s presented 100% sensitivity in the detection of malignant neoplasms.

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Table II. Continued

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
			• DWI is effective in the differential diagnosis of parotid malignancies and PAs.
Milad et al., 2017[28]	Evaluation of the added value of diffusion weighted magnetic resonance imaging (DW-MRI) in characterization of salivary gland lesions	Patients with salivary glands benign lesions (neoplasms, sialadenitis, cystic lesions) and malignant neoplasms, who underwent DWI and histopathologic examinations.	• ADC was 100% when the ADC value of 1.1×10^{-3} mm^2/s was set as a cutoff point in differentiating benign lesions from malignant neoplasms. • Malignant lesions' ADC values were lower than benign lesions' ADC values. • Parotid PAs presented the highest ADC values in the sample studied. • No significant difference was observed between carcinomas as lymphomas ADC values.
Nada et al., 2017[29]	Differentiation between inflammatory and neoplastic lesions and differentiation between parotid neoplasms	Patients with inflammatory, benign, and malignant neoplasms in parotid gland who underwent DWI and histopathologic examinations.	• Malignant neoplasms, benign neoplasms, and inflammatory lesions presented ADC values that were statistically significantly different. • When the ADC value 0.93×10^{-3} mm^2/s was set as a cutoff point to differentiate benign and malignant tumors, the sensitivity was 72%, and the specificity was 82%. • The use of DWI in the MRI protocol is recommended for the detection and discrimination of parotid neoplastic lesions.
Razek et al., 2017[30]	Characterization of parotid neoplasms with dynamic susceptibility contrast perfusion-weighted magnetic resonance MRI and DWI	Patients with parotid benign and malignant neoplasms, who had confirmed histopathologic diagnosis.	• ADC values of malignant neoplasms were lower than those of benign neoplasms. • ADC values of WT and malignant neoplasms presented no significant difference.
Razek et al.,2017[31]	Assessment of low versus high risk of salivary gland cancer and their diagnosis using ADC	Patients with submandibular benign and malignant neoplasms, who underwent histologic and DWI examinations.	• Malignant neoplasms presented lower ADC values compared with benign neoplasms. • Using an ADC value cutoff point of 1.26×10^{-3} mm^2/s, the differentiation between malignant and benign neoplasms presented sensitivity of 88% and specificity of 81%. • Lymphoepithelial carcinoma presented the lowest ADC value, and mucoepidermoid carcinoma exhibited the highest ADC value, with no statistically significant difference between neoplasms.
Tao et al., 2017[32]	Comparison between different methods (conventional MRI, DWI, and DCE-MRI) for the diagnosis of parotid gland tumors	Patients with benign and malignant neoplasms in parotid gland, who underwent MRI, DWI, DCE, and histologic examinations.	• Malignant neoplasms presented lower ADC values compared with benign neoplasms. • When stablished a cut-off point of 1.12×10^{-3} mm^2/s, it was obtained 91.5% sensitivity and 51.5% specificity. • Combined techniques have superior results in differentiating between benign and malignant neoplasms.
Terra et al., 2017[33]	Comparison between ADC values of normal salivary glands, sialadenitis, and PA of major salivary glands	Patients with sialadenitis (confirmed with histologic or cytologic analysis) and PA (confirmed with histologic analysis) in parotid or submandibular glands, who also underwent DWI.	• ADC values from nonaffected parotid glands were lower than sialadenitis or PA. • Sialadenitis parotid glands presented a lower ADC mean value compared with PA in parotid gland. • DWI allows for differentiating between reactive inflammatory and neoplastic lesions of the parotid glands.

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Table II. Continued

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
Eissa et al., 2016[37]	Evaluation of the DWI and DCE use in the preoperative characterization of salivary gland neoplasms	Patients with lesions suspected to be neoplasms in parotid, submandibular, and minor salivary glands. Final diagnosis was confirmed by surgery. Lesions were divided in groups, according to their ADC values.	• Low ADC values group included all parotid lymphoid lesions. • Intermediate ADC values group included mostly primary malignant neoplasms. • High ADC value groups included only benign neoplasms. • Combination of DWI and DCE is more helpful than the use of a single technique.
Karaman et al., 2016[38]	Differentiation of parotid gland neoplasms by using different b-values in DWI examination	Patients with parotid gland neoplasms, with histologic confirmation, who underwent DWI examinations, excluding patients with sialadenitis.	• PAs presented higher ADC values than WT or malignant neoplasms. • WT and malignant neoplasms presented no significant differences in ADC values. • Benign neoplasms presented higher ADC values than malignant neoplasms, for each b-value. • ADC values obtained from different b-values can add more information when differentiation of malignant and benign neoplasms is necessary; however, it is not useful to differentiate WT from malignant neoplasms.
Kikuchi et al., 2016[39]	Establishment of an algorithm by using DWI and technitium-99 m (Tc-99 m)pertechnetate scintigraphy for the diagnosis of parotid gland neoplasms, with the goal of reduction the number of patients who need core needle biopsy	Patients newly diagnosed with parotid gland neoplasms, with histopathologic results and DWI examinations.	• A preoperative algorithm using both techniques has an accuracy of 87%.
Mukai et al., 2016[40]	Parotid gland basal cell adenomas description of MRI features and comparison between basal cell adenomas with PA	Patients with basal cell adenomas and PA, who underwent DWI and histologic examinations.	• ADC values of basal cell adenomas was significantly lower than PA. • Using an ADC value cutoff point of 1.31×10^{-3} mm^2/s, the differentiation between PAs and basal cell carcinomas presented sensitivity of 92.7% and specificity of 91.7%.
Yologlu et al., 2016[41]	Parotid gland neoplasms ADC correlation with histopathologic results. Comparison between ADC values of neoplasms and contralateral normal gland	Patients with benign and malignant neoplasms in parotid gland, who underwent DWI and histologic examinations.	• PAs presented significantly higher ADC values compared with Warthin tumors or normal parotid parenchyma. • DWI and ADC maps are useful in the differentiation of parotid benign and malignant neoplasms.
Yuan et al., 2016[42]	Evaluation of the conventional MRI, DWI, and DCE in the differentiation of benign and malignant parotid neoplasms	Patients with benign and malignant primary neoplasms in parotid gland, who underwent DWI and histologic examinations.	• Benign lesions ADC values were higher than malignant neoplasms ADC values. • Using an ADC value of 1.01×10^{-3} mm^2/s as a cutoff point to differentiate between benign and malignant neoplasms, sensitivity was 86.4%, and specificity was 59.7%. • The combination of conventional MRI and DWI increases the diagnostic value of MRI in the differentiation of parotid benign and malignant neoplasms.
Zhu et al., 2016[43]	Differentiation and determination of mean parotid ADC values of	Patients with confirmed parotid benign lymphoepithelial lesion and mucosa-	• Using a b-value of b = 500 s/mm^2 statistically nonsignificant differences were observed between the two groups of lesions.

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Table II. Continued

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
	benign lymphoepithelial lesions and mucosa-associated lymphoid tissue lymphoma using different b-values	associated lymphoid tissue lymphoma, who underwent DWI examinations.	• Using a b-value of b = 1000 s/mm^2 benign lymphoepithelial lesion presented higher ADC values compared with mucosa-associated lymphoid tissue lymphomas. • When establishing an ADC value cutoff point of 0.669×10^{-3} mm^2/s to differ the lesions, sensitivity was 78.9% and specificity was 95.8%.
Kato et al., 2015[46]	Evaluation of DWI and ASL in the differentiation of parotid neoplasms	Patients with benign and malignant parotid neoplasms, who underwent DWI examinations.	PAs presented higher ADC values than WT and malignant neoplasms. No significant differences between ADC values when WT were compared with malignant neoplasms. • The combination of ASL and DWI are useful in the differentiation of PAs, WTs, and malignant neoplasms.
Salama et al., 2015[48]	Assessment of combined techniques ADC and metabolite spectrum acquired by magnetic resonance spectroscopy in the identification of various pathologic subtypes of parotid gland neoplasms	Patients with parotid gland neoplasms that underwent to fine-needle aspiration biopsy before DWI, with histologically confirmed diagnosis.	• PAs presented higher ADC values than WTs. • Carcinomas and WT ADC values presented no statistically significant differences. • PA presented higher ADC values than malignant neoplasms. • Combined techniques are useful modalities for identification of subtypes of parotid gland tumors.
Balçık et al., 2014[49]	Differentiation of benign lesions and malignant parotid neoplasms by using ADC values	Patients with parotid gland neoplasms, who underwent DWI examinations.	• The ADC values of PA were higher compared with WT and basal cell adenomas. • The ADC values of other malignant neoplasms were higher compared with WT. • The use of ADC values is helpful in the differential diagnosis of parotid gland neoplasms; DWI does not provide enough anatomic features of lesions and should be combined with MRI sequences.
Celebi et al., 2013[50]	Evaluation of the diagnostic usefulness of ADC values for differentiating between benign and malignant neoplasms	Patients with focal parotid lesions, who had undergone DWI examinations before biopsy or resection.	• ADC values of benign neoplasms were higher compared with malignant neoplasms. • PAs presented the highest ADC values among benign neoplasms with ADC values significantly higher than those of all the neoplasms studied. • Mucoepidermoid carcinomas presented higher ADC values among malignant neoplasms.
Fruehwald-Pallamar et al., 2013[51]	Evaluation of the combined use of MRI (using texture features) and DWI in the differentiation of parotid gland lesions	Patients with benign and malignant neoplasms, cysts, infections, and hemangioma, who underwent DWI examinations.	• WT presented lower ADC values compared with PA or other benign neoplasms. • All ADC values of benign lesions (when included in the same group of neoplasms and other lesions) presented higher ADC; values compared with malignant neoplasms. • WT presented lower ADC values compared with malignant neoplasms. • ADC values and MRI features (texture features) are useful in the characterization of parotid gland lesions.
Kato et al., 2012[53]	Description of MRI and DWI findings in patients with mucosa-associated lymphoid tissue lymphoma of the salivary glands	Patients with histologic proven mucosa-associated lymphoid tissue lymphoma, who underwent DWI examinations.	• DWI images demonstrated solid components areas of strong hyperintensity, and ADC values were low for all lesions examined.

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Table II. Continued

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
Lechner Goyault et al., 2011[54]	Evaluation of DWI and gadolinium-enhanced dynamic MRI for differentiating between benign and malignant parotid neoplasms	Patients with neoplasms or cystic lesions within the parotid gland with confirmed histopathologic diagnosis and DWI examinations.	• Malignant neoplasms ADC values were significantly lower compared with benign neoplasms. • PA ADC values were significantly higher compared with those of WT. • No significant differences were observed in PA ADC values and cystic lesions. • No significant difference was observed in the ADC values of malignant neoplasms compared with those of WT. • ADC can improve the performance of MRI in the characterization of distinct histologic types of neoplasms.
Eida et al., 2010[56]	Differentiation of benign and malignant neoplasms in salivary glands by using TICs and ADCs	Patients with benign and malignant neoplasms in parotid, submandibular, and sublingual glands, who underwent DWI examinations.	• ADC values of lymphomas were lower than those of WT. • Areas with low and extremely low ADC values in benign neoplasms were smaller than those in malignant neoplasms. • The combined use of DCE and DWI can be useful to differentiate between malignant and benign salivary gland neoplasms.
Inci et al., 2010[57]	Differentiation of benign and malignant parotid neoplasms by using ADC	Patients with benign and malignant parotid neoplasms and healthy patients as control patients, who underwent DWI examinations.	• Healthy parotid tissues presented lower ADC values compared with benign and malignant neoplasms. • Benign neoplasms presented higher ADC values compared with malignant neoplasms. • PA presented higher ADC values compared with WT and malignant neoplasms. • There was no difference in ADC values between WT and malignant neoplasms.
Yerli et al., 2010[59]	Evaluation of DWI diagnostic accuracy in comparison with fine-needle aspiration cytology in the differentiation of parotid gland neoplasms	Patients with parotid gland neoplasms, who underwent DWI, fine-needle aspiration cytology, and histologic examinations.	• Adenomas presented significantly higher ADC values compared with WT. • The ADC values of carcinomas overlapped the ADC values of benign neoplasms. • Compared with fine-needle aspiration cytology, the combination of MRI and ADC may have a similar diagnostic value for determining specific histologic types.
Habermann et al., 2009[60]	Comparison between ADC values of different salivary gland neoplasms by using echo-planar DWI examinations	Patients with benign and malignant neoplasms in parotid gland, who underwent DWI and histologic examinations.	• PA did not present differences in ADC values compared with myoepithelial adenomas. • ADC values of WT presented significantly difference from myoepithelial adenomas, lipomas, and salivary duct carcinomas. • Mucoepidermoid carcinomas, acinic cell carcinomas, and basal cell adenocarcinomas did not present significant differences from WT. • Malignant and benign neoplasms presented an overlap in ADC values. • The diagnosis of parotid salivary gland neoplasms should not be made using only ADC values.

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Table II. Continued

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
Abu et al., 2008[62]	Description of Kuttner tumors (a chronic sclerosing sialadenitis) and differentiation with other submandibular neoplasms	Patients with Kuttner tumors without evident sialoliths and patients with malignant and benign neoplasms, who underwent DWI examinations with confirmed histopathologic results.	• The ADC values of Kuttner tumors did not present significant differences compared with malignant neoplasms. • The ADC values of Kuttner tumors were lower than those of PAs. • PAs presented higher ADC values compared with malignant neoplasms. • Kuttner tumors and malignant neoplasms had some morphologic differences, although ADC values and enhanced patterns were similar.
Yabuuchi et al., 2008[65]	Determination of the usefulness of DWI and dynamic contrast material–enhanced MRI in the differentiation of benign and malignant neoplasms	Patients with benign and malignant neoplasms in parotid gland, who underwent DWI and histologic examinations.	• ADC threshold values were 1.4×10^{-3} mm^2/s between pleomorphic adenomas and carcinomas and 1.0×10^{-3} mm^2/s between WTs and carcinomas.
Eida et al., 2007[66]	Evaluation of preoperative ADC maps of benign and malignant in salivary gland neoplasms	Patients with benign and malignant neoplasms in major salivary glands, who underwent DWI and histologic examinations.	• WT presented heterogeneous ADC values: areas with extremely low ADC indicating lymphoid tissues, areas with intermediate ADC values corresponding to necrosis, and areas with low ADC values indicating cyst formation among lymphoid tissues. • Adenocarcinomas and adenoid cystic carcinomas presented heterogeneous ADC maps. • Malignant lymphomas presented extremely low ADC values. • Benign neoplasms presented higher ADC values compared with malignant neoplasms. • Using an ADC value cutoff point of $\geq 1.80 \times 10^{-3}$ mm^2/s, the differentiation between malignant and benign neoplasms presented sensitivity of 89% and specificity of 100% (when a malignant neoplasm had 5% of smaller areas with high ADC values).
Matsushima et al., 2007[67]	Differentiation between benign and malignant salivary gland neoplasms using ADC values	Patients with neoplasms in major salivary glands confirmed by biopsy or surgery who underwent DWI examinations.	• No significant differences were found between benign and malignant neoplasms, with considerable overlap in ADC values. • WT presented lower ADC values compared with PA or neurofibroma. • The ADC values of adenoid cystic carcinoma and myxoid lymphosarcoma were higher than those of the other malignant neoplasms studied. • No significant differences in ADC values were found between WT and malignant neoplasms. • ADC values may not contribute to a differential diagnosis between benign and malignant neoplasms.
Yerli et al., 2007[68]	Differentiation of malignant and benign neoplasms of parotid gland	Patients with benign and malignant neoplasms in parotid gland and healthy volunteers, who underwent DWI and histologic examinations.	• ADC values presented no significant differences when WT and malignant neoplasms were compared. • ADC values of parotid glands in healthy volunteers were significantly lower than the ADC values of WT, PAs, and malignant neoplasms. • ADC values are useful in differentiating PAs from other parotid gland neoplasms.

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Table II. Continued

Authors	*Objectives*	*Sample studied*	*Main results or conclusions*
Habermann et al., 2005[69]	Differentiation of primary parotid neoplasms using DWI EPI	Patients with suspect parotid tumors, who underwent sonography. Final diagnosis was confirmed with surgery. ADC values were obtained from both the affected side and he nonaffected parotid side.	• PAs presented higher ADC values than normal parotid tissue. • WT, lipomas, and mucoepidermoid carcinomas showed lower ADC values compared with normal parotid tissue. • WT and PA showed significant difference in ADC values in comparison with other neoplasms (lipoma, myoepithelial adenoma, salivary duct carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma).
Motoori et al., 2005[70]	Description of MRI features of salivary duct carcinoma	Patients with parotid and submandibular salivary duct carcinoma with DWI and histologic examinations.	• DWI showed irregularly high signal intensities; • The median ADC values was 1.16×10^{-3} mm^2/s.
Motoori et al., 2005[71]	To compare the accuracy of Tc-99 m pertechnetate scintigraphy and MRI in the diagnosis of WT	Patients with WT and malignant salivary gland neoplasms, who underwent MRI examinations and Tc-99 m pertechnetate imaging before surgery or fine-needle aspiration cytology.	• Traditional MRI, dynamic contrast-enhanced MRI, and DWI constitute a more useful method for evaluating Warthin tumor compared with Tc-99 m pertechnetate scintigraphy. • Traditional MRI, dynamic contrast-enhanced MRI, and DWI is a more useful method for differentiating WT from malignant neoplasms compared with Tc-99 m pertechnetate scintigraphy.
Ikeda et al., 2004[72]	Comparison of ADC values between WTs and other malignant neoplasms of the parotid gland	Patients with WT and other malignant neoplasms in parotid gland, who underwent DWI and histologic examinations.	• WT presented significantly lower ADC values compared with other malignant neoplasms. • DWI was useful to determine whether a salivary gland neoplasm was a WT.
Motoori et al., 2004[73]	Description of MRI features of pleomorphic adenomas	Patients with PA and malignant neoplasms in parotid and submandibular gland, with histopathologic results.	• PAs presented higher ADC values compared with malignant neoplasms. • The myxoid component of PAs presented high ADC values; • ADC values and other MRI parameters are valuable in differentiating PAs from other malignant neoplasms.

*Objectives, sample studied features, and main results or conclusions pertaining to diffusion-weighted magnetic resonance imaging and apparent diffusion coefficient.
ADC, apparent diffusion coefficient; *ASL,* $$ spin labelling; *CDFI,* color Doppler flow imaging; *Cho/Cr,* choline/creatinine; *DCE,* dynamic contrast-enhanced; *DTI,* diffusion tensor imaging; *DWI,* diffusion-weighted magnetic resonance imaging; *EPI,* echo-planar imaging; *FA,* fractional anisotropy; *MRI,* magnetic resonance imaging; *SS,* Sjogren syndrome; *SWI,* susceptibility-weighted imaging. *SWV,* shear-wave velocity; *TIC,* time−intensity curve.

Table III. Histologic types of lesions evaluated in each study selected: benign lesions (neoplasms or nonneoplastic lesions), and malignant neoplasms

Authors	*Benign lesions*	*Malignant neoplasms*
Domingos et al., 2018[10]	PA, WT, oncocytoma, basal cell adenoma, cystadenoma	Mucoepidermoid carcinoma, myoepithelial carcinoma, squamous cell carcinoma
Faheem et al., 2018[11]	PA, WT, basal cell adenoma, lymphoma, adenoid cystic carcinoma	Mucoepidermoid carcinoma, rhabdomyosarcoma
Khamis et al., 2018[12]	PA, WT	Mucoepidermoid carcinoma, adenoid cystic carcinoma, squamous cell carcinoma, acinic cell carcinoma
Matsusue et al., 2018[13]	PA, WT, oncocytoma	Small cell carcinoma, adenoid cystic carcinoma
Mikaszewski et al., 2018[14]	PA, WT, cysts, inflammatory disease	Adenocarcinomas, myoepithelial carcinomas, metastases, mucoepidermoid carcinomas, adenoid cystic carcinomas, acinic cell carcinomas, lymphomas, ductal carcinomas, planoephithelial carcinoma
Wang et al., 2018[16]	PA, WT	Adenoid cystic carcinoma, adenocarcinoma, squamous cell carcinomas, mucoepidermoid carcinoma, acinic cell carcinomas, carcinoma, salivary duct carcinoma
Zhang et al., 2018[17]	PA, WT, myoepithelial adenoma, hemangioma, schwannoma, granulomatous inflammation, branchial cleft cyst, Kimura disease	Acinic cell carcinoma, salivary duct carcinoma, carcinoma ex PA, lymphoma, metastasis
Zhang et al., 2018[18]	PA, WT, granulomatous inflammation	Acinic cell carcinoma, adenoid cystic carcinoma
Zheng et al., 2018[21]	PA, adenolymphoma, schwannoma, lymphangioma, basal cell adenoma	Acinar cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, carcinoma ex PA, carcinomas, branchial cleft cyst canceration
Zheng et al., 2018[22]	PA, WT, basal cell adenoma, oncocytic adenoma, monomorphic adenoma, schwannoma	Squamous cell carcinoma, acinic cell carcinoma, lymphoepithelial carcinoma, adenoid cystic carcinoma, lymphoma, mucoepidermoid carcinoma, duct carcinoma, basal cell adenocarcinoma, polymorphous low-grade adenocarcinoma
Kato et al., 2017[23]	WT, oncocytoma	
Matsusue et al., 2017[25]	PA, WT	Carcinoma ex PA, squamous cell carcinoma, adenoid cystic carcinoma, small cell carcinoma, malignant lymphoma
Mikaszewki et al., 2017[26]	PA, WT, myoepithelioma, cyst, oncocytic cystadenoma, basal cell adenoma, benign lymphoepithelial lesion, reactive lymph nodes, sialadenitis	Adenocarcinoma, acinic cell carcinoma, adenoid cystic carcinoma, myoepithelial carcinoma, metastasis, salivary duct carcinoma, mucoepidermoid carcinoma, carcinoma ex PA, adenoid cell carcinoma, metastatic clear cell carcinoma, carcinoma recidivans after RT, marginal zone B-cell lymphoma.
Mikaszewski et al., 2017[27]	PA	Adenocarcinomas, myoepithelial carcinomas, metastasis, mucoepidermoid carcinomas, adenoid cystic carcinomas, lymphomas, ductal carcinoma, planoepithelial carcinoma
Milad et al., 2017[28]	PA, WT, sialadenitis, hyperplasia, papillary cystadenoma, cystic lesion, calculous sialadenitis	Non-Hodgkin lymphoma, mucoepidermoid carcinoma, acinic cell tumor, carcinoma ex PA, adenoid cystic carcinoma, salivary duct carcinoma, Hodgkin lymphoma
Nada et al., 2017[29]	PA, WT, hemangioma, lymphangioma, basal cell adenoma and other inflammatory lesions*	Mucoepidermoid carcinoma, adenoid cystic carcinoma, basal cell carcinoma, mixed salivary gland tumor, rhabdomyosarcoma, lymphoma, leukemic infiltrates, metastatic intraparotid lesions, primitive neuroectodermal tumor.
Razek et al., 2017[30]	PA, WT, monomorphic adenoma, neurofibroma	Mucoepidermoid carcinoma, adenoid cystic carcinoma, carcinoma ex PA, lymphoma, metastasis
Razek et al., 2017[31]	PA, WT, papillary cystadenoma	Adenoid cystic carcinoma, mucoepidermoid carcinoma, salivary duct carcinoma, adenocarcinoma, carcinoma ex PA
Tao et al., 2017[32]	PA, WT, myoepithelioma, oncocytoma, basal cell adenoma	Adenoid cystic carcinoma, malignant PA, acinic cell carcinoma, mucoepidermoid carcinoma, metastatic carcinoma, papillary cystadenocarcinoma, tricholemmal carcinoma,

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Table III. Continued

Authors	*Benign lesions*	*Malignant neoplasms*
		adenocarcinoma, squamous cell carcinoma, lymphoepithelial carcinoma, malignant fibrous histiocytoma, leiomyosarcoma, malignant hemangiopericytoma, unclassified sarcoma, lymphoma
Terra et al., 2017[33]	PA, sialadenitis	
Eissa et al., 2016[37]	WT, schwannoma	Acinic cell carcinoma, squamous cell carcinoma, mucoepidermoid carcinoma, lymphoma, carcinoma ex PA, adenoid cystic carcinoma, metastasis
Karaman et al., 2016[38]	PA, WT, myoepithelioma, lipoma, hemangioma	Small cell lung metastasis, adenoid cystic cancer, squamous cell tumor, diffuse large B-cell lymphoma
Kikuchi et al., 2016[39]	PA, WT, oncocytoma, inflammatory granulation, neuroma, toxoplasma lymphadenitis	Diffuse large B-cell lymphoma, mucosa associated lymphoid tissue lymphoma, squamous cell carcinoma, basal cell carcinoma, acinic cell carcinoma, salivary duct carcinoma
Mukai et al., 2016[40]	PA, basal cell adenoma	
Yologlu et al., 2016[41]	PA, WT, reactive lymphoid hyperplasia, neurofibroma, lipoma	Mixed tumor, squamous cell carcinoma
Yuan et al., 2016[42]	PA, WT, basal cell adenomas, other benign parotid lesions	Lymphoepithelial carcinomas, malignant mixed tumor, mucoepidermoid carcinomas, other malignant lesions
Zhu et al., 2016[43]	Tumor-like benign lymphoepithelial lesion	Mucosa-associated lymphoid tissue lymphoma
Kato et al., 2015[46]	PA, WT	Mucosa-associated lymphoid tissue lymphoma, epithelial−myoepithelial carcinomas, follicular lymphoma, salivary duct carcinoma, carcinoma ex PA, small cell carcinoma
Salama et al., 2015[48]	PA, WT	Mucoepidermoid carcinoma, adenoid cystic carcinoma, acinic cell carcinoma
Balçık et al., 2014[49]	PA, WT, basal cell adenoma, dermoid cyst or high density cyst, lipoma	Mucoepidermoid carcinoma, adenoid cystic carcinoma, salivary duct carcinoma, adenocarcinoma, carcinoma ex PA, squamous cell carcinoma, metastasis
Celebi et al., 2013[50]	PA, WT, lymphadenopathy, cystic adenoma, infected cyst rupture	Lymphoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, metastasis, myoepithelial malignant tumor, salivary duct carcinoma, acinic cell carcinoma, basal cell carcinoma
Fruehwald-Pallamar et al., 2013[51]	PA, WT, cyst, lipoma, hemangioma, epidermoid cyst, infectious masses	Squamous cell carcinoma, acinic cell carcinomas, adenocarcinomas, sarcoma melanoma metastasis from previously unknown disease
Kato et al., 2012[53]	Mucosa-associated lymphoid tissue lymphoma	
Lechner Goyault et al., 2011[54]	PA, WT, cystic lesions	Malignant lymphoma, adenoid cystic carcinoma, high-grade mucoepidermoid carcinoma, epidermoid carcinoma, poorly differentiated high-grade carcinosarcoma, low-grade carcinosarcoma, salivary duct carcinoma, carcinoma, metastasis
Eida et al., 2010[56]	PA, WT, myoepithelioma, papillary cystadenoma, oncocytoma	Malignant lymphoma, adenocarcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, carcinoma ex PA, salivary duct carcinoma, epithelial−myoepithelial carcinoma, squamous cell carcinoma
Inci et al., 2010[57]	PA, WT, canalicular adenoma	Malignant lymphoma, carcinoma ex PA, adenoid cystic carcinoma, mucoepidermoid carcinoma
Yerli et al., 2010[59]	Adenoma, WT, lipoma, hemangioma, lymphadenopathy	Carcinoma
Habermann et al., 2009[60]	PA, WT, myoepithelial adenoma, lipoma, basal cell adenoma, cystadenoma, inverted ductal adenoma	Mucoepidermoid carcinoma, salivary duct carcinoma, acinic cell carcinoma, basal cell adenocarcinoma, adenoid cystic carcinoma, epithelial−myoepithelial carcinoma, carcinoma ex PA
Abu et al., 2008[62]	Kuttner disease (chronic sclerosing sialoadenitis, PA	Acinic cell adenocarcinoma, adenoid cystic carcinoma, adenocarcinoma, salivary duct carcinoma, epithelial−myoepithelial carcinoma
Yabuuchi et al., 2008[65]	PA, WT, branchial cleft cyst	Carcinoma ex PA, acinic cell carcinoma, non-Hodgkin lymphoma, adenoid cystic carcinoma, adenocarcinoma, mucoepidermoid carcinoma, salivary duct carcinoma, squamous cell carcinoma

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Table III. Continued

Authors	*Benign lesions*	*Malignant neoplasms*
Eida et al., 2007[66]	PA, WT, papillary cystadenoma	Adenoid cystic carcinoma, mucoepidermoid carcinomas, salivary duct carcinoma, adenocarcinoma, carcinoma ex PA
Matsushima et al., 2007[67]	PA, WT, neurofibroma	Adenoid cystic carcinoma, malignant lymphoma, carcinoma ex PA, lymphoepithelial carcinoma, squamous cell carcinoma, undifferentiated carcinoma, salivary duct carcinoma, malignant melanoma, myxoid liposarcoma
Yerli et al., 2007[68]	PA, WT, basal cell adenoma, cyst	Carcinoma, malignant lymphoma
Habermann et al., 2005[69]	PA, WT, lipoma, myoepithelial adenoma	Salivary duct carcinoma, adenoid cystic carcinoma
Motoori et al., 2005[70]		Salivary duct carcinoma
Motoori et al., 2005[71]	PA, WT, reactive lymphadenopathies	Acinic cell carcinoma, adenocarcinoma, squamous cell carcinoma and malignant lymphoma
Ikeda et al., 2004[72]	WT	Mucoepidermoid carcinoma, acinic cell adenocarcinoma, salivary duct carcinoma, squamous cell carcinoma, basal cell adenocarcinoma, carcinoma ex PA
Motoori et al., 2004[73]	PA	

*not specified.
PA, pleomorphic adenoma; *WT*, Warthin tumor.

months, but with no imaging alterations. T1-weighted and T2-weighted short tau inversion recovery (STIR) images are presented (see Figures 2A and 2B, respectively) with the ADC map (see Figure 2C). In the colored ADC maps, red areas indicate high facilitated diffusion; yellow areas indicate facilitated diffusion; green areas indicate restricted diffusion; and blue areas indicate high restricted diffusion.

Figure 3 illustrates the case of an 87-year-old female patient who had previously had surgical removal of a malignant neoplasm in the maxillary sinus and resection of a major neoplasm on the right side. This patient underwent DWI examinations because of suspicion of metastasis in the soft tissue on the left side, including the salivary gland. However, MRI showed no metastasis in the area investigated. T1-weighted and T2-weighted STIR images are presented (see Figures 3A and 3B, respectively) with the ADC map (see Figure 3C).

DISCUSSION

Major salivary glands are usually evaluated with conventional MRI because it is the imaging approach that offers superior soft tissue evaluation. The DWI technique can add more information for the elaboration of a diagnostic hypothesis because of its ability to detect tissue cellularity and the microstructural features of physiologic processes.[76] DWI qualitatively describes water molecule motion and can be translated to a numerical coefficient—the ADC. When the same parameters for data collection are used, comparisons between lesions or diseases of a distinct nature can be performed.[77] Furthermore, DWI is considered practical and simple to use and does not require additional time in the MRI examinations or the use of contrast agents.[78]

In this literature review, we observed that most of the investigators focused on the differentiation between benign and malignant neoplasms by using ADC values. Overall, the researchers succeeded in differentiating benign neoplasms from malignant neoplasms and found that the ADC values for benign lesions were higher than those for malignant neoplasms.[12,17,28,30-32,41,42,50,54,57,66] However, this is not in concordance with the findings of Faheem et al., who determined that ADC values are not conclusive in differentiating between benign and malignant tumors,[11] or those of Habermann et al.,[60] Yerli et al.,[59] and Matsushima et al.,[67] who observed an overlap in the ADC values of benign and malignant neoplasms. Other authors also discovered no differences between the ADC values of benign and malignant neoplasms.[18,60,67]

However, Warthin tumors, which are benign, had lower[16,23,51,72,49] or similar[17,25,30,38,46,48,54,57,67,68] ADC values compared with malignant neoplasms. The

Table IV. Studies regarding radiotherapy effects on salivary glands*

Authors	*Objective*	*Sample studied*	*Main results or conclusions*
Zhang et al., 2018[19]	Evaluation of early changes in ADC of the salivary glands and their association with xerostomia in patients under RT treatment	Patients with nasopharyngeal carcinoma under RT, within 1 week before RT and 2 weeks after the beginning of RT, at rest and with gustatory stimulation.	• At rest, ADC values were higher at 2 weeks after RT than before RT. • At gustatory stimulation, ADC values were lower at 2 weeks after RT than before RT. • For parotid glands, there was an inverse correlation with ADC and xerostomia at rest and at gustatory stimulation. • For submandibular glands, ADC and xerostomia didn't present correlation.
Zhang et al., 2018[20]	Evaluation of the use of DWI in patients with radiation-induced xerostomia	Patients with nasopharyngeal carcinoma, who received RT and CT treatment, 1 year after RT, with DWI examinations.	• Parotid and submandibular glands ADC values increased in all patients 1 week after RT. • ADC values decreased in parotid glands 1 year after RT, but not in submandibular glands. • ADC values are sensitive to salivary gland dysfunction.
Loimu et al., 2017[24]	Comparison between ADC values before and after CT (total treatment duration: 49 days) and RT	Patients without previous salivary gland disorders and head and neck cancer, who received CT and RT.	• Posttreatment ADC values were significantly higher than pretreatment values in unstimulated parotid and submandibular glands. • The maximum ADC value was significantly higher in posttreatment glands compared with pretreatment glands. • Posttreatment ADC values correlate with RT dose absorbed by salivary glands. • DWI could be a useful tool for detection of radiation-induced physiologic and functional changes in the major salivary glands in patients with head and neck cancer.
Zhou et al., 2017[35]	Parotid glands ADC histogram assessment before and after RT Correlation of ADC with xerostomia degrees	Patients with nasopharyngeal carcinoma, who received RT.	• ADC histogram parameters increased after RT. • Early mean changes rates of certain ADC histogram parameters increased after RT. • ADC histogram evaluation could be applied to assess RT-induced damage noninvasively and predict late xerostomia degrees in patients with nasopharyngeal carcinoma treated with RT.
Doornaert et al., 2015[44]	Evaluation of CT effect on salivary glands, before, after and during CT Assessment of the correlation of DWI changes in salivary glands	Patients with head and neck cancer, who under RT and CT	• Only simple descriptive statistics were applied. • Authors observed an increase in ADC values of submandibular and parotid glands after CT.
Juan et al., 2015[45]	Quantification of radiation-induced changes of parotic glands ADC in patients with nasopharyngeal carcinoma, treated with RT	Patients nearly diagnosed as nasopharyngeal carcinoma and treated with RT, who had DWI examinations before and after treatment.	• Post-RT parotid ADC values were significantly higher compared with pre-RT values. • The parotid ADC was negatively correlated with parotid volume. • The parotid ADC was positively associated with the radiation dose. • The increase of ADC was the result of the effect of acinar loss, rather than edema, at early to intermediate RT phases.
Liu et al., 2015[47]	Investigation of parotid gland DWI and ADC, by using EPDWI	Healthy volunteers and patients with head and neck cancer under RT.	• ADC values were higher in RT patients than in healthy volunteers.
Zhang et al., 2013[52]	Evaluation of the DWI in quantifying physiologic changes of the parotid gland during		• Before RT, the ADC values showed an initial increase and then fluctuated during stimulation.

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Table IV. Continued

Authors	Objective	Sample studied	Main results or conclusions
	gustatory stimulation before and after parotid-sparing RT	Patients with nasopharyngeal carcinoma, before and after RT, with DWI examinations.	• After RT, the mean ADC at rest increased, and the clinical xerostomia increased from grade 0 to grade 2. • When salivary gland function was decreased, which was measured by clinical xerostomia, ADC values increased. • Assessment of ADC may be useful in quantifying physiologic and pathologic changes in the parotid gland.
Dirix et al., 2008[63]	Evaluation salivary gland function before and after parotid-sparing RT, at rest, and after stimulation	Patients with squamous cell carcinoma of the oropharynx or oral cavity or lymph node metastases, who underwent RT and DWI examinations.	• At rest, before RT, ADC values of parotid were significantly lower than those of the submandibular gland. • During stimulation, before RT, ADC values increased, and ADC values peak was significantly higher compared with values at rest. • DWI allows for noninvasive evaluation of functional changes in the major salivary glands after RT.

*Authors, main objectives, sample studied features, and main results or conclusions pertaining to diffusion-weighted magnetic resonance imaging and apparent diffusion coefficient.
ADC, apparent diffusion coefficient; *CT*, chemotherapy; *DWI*, diffusion-weighted magnetic resonance imaging; *EPDWI*, echo-planar diffusion-weighted magnetic resonance imaging; *RT*, radiotherapy.

Warthin tumor is a common benign neoplasm in the parotid gland, with histologic features that can resemble malignant lesions, such as carcinomas, because of its high cellularity.[17] The histologic structure includes both an oncocytic epithelial component, forming cystic spaces with a papillary appearance, and lymphoid stroma.[79] Although there are cystic formations in the neoplasm, which was an exclusion criterion in a study by Kato et al. in their analysis of ADC values,[23] the heterogeneity of the tissue cellularity Warthin tumors was explored by Eida et al.,[66] who identified areas of extremely low ADC values corresponding to the lymphoid tissues and areas with low ADC values indicating cystic formation among lymphoid tissues.

Pleomorphic adenomas were reported as the benign tumors with the highest ADC values.[12,17,25,50,68] Pleomorphic adenomas exhibit a great variety of histopathologic characteristics, and the presence of both epithelial and mesenchymal-like tissues is the main diagnostic feature of these lesions.[80] Furthermore, pleomorphic adenomas typically have a rich stroma,[80] which leads to facilitated water diffusibility and, thus, the higher ADC values.

ADC comparisons were also performed in malignant neoplasms by the investigators, showing that lymphomas had lower ADC values compared with other malignant neoplasms.[25,66] Adenoid cystic carcinomas, myxoid lymphosarcomas,[67] and mucoepidermoid carcinomas[50] had higher ADC values compared with other malignant neoplasms. Heterogeneous ADC maps were seen in adenocarcinomas, adenoid cystic carcinomas,[66] and submandibular duct carcinomas,[70] which were associated with necrotic or cystic areas in neoplasm tissues.[66]

Normal salivary glands from healthy volunteers or the contralateral glands of patients were also compared with neoplasms on DWI examinations, and some investigators noted that normal glands had lower ADC values compared with those of benign and malignant neoplasms.[33,57,68,69]

In studies comparing neoplasms and inflammatory diseases, although significantly different ADC values were found between neoplasms and acute inflammatory diseases,[29,33] no differences were found between malignant tumors and chronic inflammatory sclerosing sialadenitis, such as Kuttner tumors.[62] The dissimilar results are related to the nature of the inflammatory diseases studied. Chronic inflammatory sclerosing sialadenitis is associated with focal squamous metaplasia with mild to moderate lymphoplasmacytic infiltrates in the prominent fibrotic specimens,[81] and this may restrict water molecule diffusibility.

In patients undergoing RT, some of the studies noted that ADC values increased after irradiation[19,20,24,35,45,52,63] and were higher in patients treated

Table V. Studies regarding inflammatory or autoimmune diseases and xerostomia*

Authors	*Objective*	*Sample studied*	*Main results or conclusions*
Takahashi et al., 2018[15]	Evaluation and prediction of response to abatacept therapy and detection of lymphocytic infiltration in patients with SS who had rheumatoid arthritis by using DWI	Patients with SS who had rheumatoid arthritis and underwent DWI examinations before and after abatacept therapy. Only the parotid glands were evaluated.	• The increase in salivary secretion tended to be higher in patients who showed decrease in signal intensity ratios in DWI. The increase in salivary secretion did not correlate with the rate of change in signal intensity ratios in DWI. • In patients who showed increased in salivary secretion, in response to the treatment, higher signal intensity was noticed before the treatment. This finding was not observed in patients who showed no response to the treatment. • Parotid DWI seems to be useful for evaluating and predicting the response in salivary secretion to abatacept in patients with SS and rheumatoid arthritis.
Xu et al., 2017[34]	Assessment of the influence of ROI methods on ADC measurement in patients with SS	Patients with confirmed SS, who underwent DWI examinations. Only the parotid gland was considered in this study.	• Authors suggested the use of the single-slice ROI in the clinical practice to ADC measurements. • The ROI methodology can influence the parotid gland ADC measurements and their diagnostic ability.
Ding et al., 2016[36]	Assessment of parotid gland DWI using different ROIs sizes in the diagnostic and evaluation of therapy in patients with SS.	Patients with SS, patients with dry mouth who did not meet diagnostic criteria for SS, and healthy volunteers, who underwent DWI examinations. Only the parotid gland was analyzed.	• The DWI signal intensity ratios were significantly higher in patients with SS compared with patients with dry mouth without SS or healthy volunteers, using a 5 mm^2 ROI. • No differences were observed when a larger ROI was used. • A small ROI DWI can provide morphologic and functional information on the parotid gland of patients with SS and can be useful in the diagnosis and evaluation of therapeutic efficacy.
Kato et al., 2011[55]	Evaluation of DWI applicability in patients with xerostomia by using a transient gustatory stimulation	Patients with complaints of xerostomia and healthy volunteers.	• No statistical difference in parotid gland ADC values was observed between prestimulated healthy volunteers and patients with xerostomia; • ADC increase rates showed a moderate positive correlation with washout rates by scintigraphy for parotid and submandibular glands.
Li et al., 2010[58]	Parotid gland ADC values comparison, before and after acid stimulation, between patients with CTD, primary SS, or secondary SS and healthy volunteers Also, comparison between the diagnostic values of ADC and PEF	Patients with primary and secondary SS or CTD and healthy volunteers.	• Without acid stimulation, ADC values in patients with primary SS were significantly lower than those in healthy volunteers and patients with CTD. • No significant differences in ADC values were found between patients with primary or secondary SS, without acid stimulation. • DWI and ADC values may help predict SS.
Regier et al., 2009[61]	Parotid gland ADC values comparison between patients with SS and healthy volunteers, before and after gustatory stimulation	Patients with SS and healthy volunteers, who underwent DWI examinations.	• In patients with early-stage SS, the parotid glands presented higher ADC values before and after stimulation compared with patients with advanced-state SS. • ADC values in healthy volunteers after gustatory stimulation were significantly higher compared with those in patients with early-stage SS, and significantly lower ADC values were observed at an advanced disease stage.

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Table V. Continued

Authors	*Objective*	*Sample studied*	*Main results or conclusions*
Ries et al., 2008[64]	Parotid gland ADC values comparison between healthy volunteers and patients with acute or chronic recurrent parotitis, before and after gustatory stimulation	Healthy volunteers and patients with acute or chronic recurrent parotitis, who underwent DWI examinations.	• In healthy controls, ADC values were significantly higher after gustatory stimulation. • Healthy controls presented significantly higher ADC values compared with patients with acute parotitis before and after oral stimulation. • ADC values in nonabscess edematous lesions were significantly higher compared with glands with abscess formations. • No significant differences were observed by measuring ADC values after oral stimulation when healthy volunteers were compared with patients with acute or chronic parotitis. • The results indicate the potential role of DWI in differentiating between acute and chronic inflammation.
Patel et al., 2004[74]	Comparison of parotid ADC values between patients with CTD and those without CTD.	Patients with CTD and those without CTD, who underwent DWI examinations.	• The ADC values of the parotid glands were higher in patients with CTD compared with those without CTD. • ADC may be useful in detecting parotid gland involvement in patients with CTD.
Sumi et al., 2002[75]	Determination of parotid and submandibular ADC values in patients with SS or sialadenitis and healthy controls.	Patients with SS or sialadenitis and healthy controls, who underwent DWI examinations.	• In healthy controls, the ADC values of the submandibular glands were significantly higher than those of the parotid glands. • Abscess formation in patients with sialadenitis was associated with decreased ADC values. • In patients with SS, ADC of the parotid gland was correlated with impairment of the salivary flow function. • A correlation was found between decreases in ADC values and severity of gland damage, as assessed on T1-weighted MRI.

*Authors, main objectives, sample studied features, and main results or conclusions pertaining to diffusion-weighted magnetic resonance imaging and apparent diffusion coefficient.
ADC, apparent diffusion coefficient; *CTD,* connective tissue disorders; *DWI,* diffusion-weighted imaging; *MRI,* magnetic resonance imaging; *PEF,* parotid gland excretion fraction; *RT,* radiotherapy; *ROI,* region of interest; *SS,* Sjogren syndrome.

Table VI. Investigations related to neoplasms included in the review, group of lesions studied, and mean/median ADC values found by the investigators, with respective *P* values (when comparison between ADC values were performed)—main results

Authors	*Group of lesions studied*	*ADC values found*	*P values*
Domingo et al., 2018[10]	Benign and malignant neoplasms	PA: 1.942×10^{-3} mm^2/s Warthin: 1.046×10^{-3} mm^2/s Malignant: 0.97×10^{-3} mm^2/s	Not specified
Faheem et al., 2018[11]	Benign and malignant neoplasms	Benign: 1.044×10^{-3} mm^2/s Malignant: 0.795×10^{-3} mm^2/s	Benign vs malignant: $P = .041$
Khamis et al., 2018[12]	Healthy parotid glands, benign and malignant neoplasms	Healthy glands: 0.53×10^{-3} mm^2/s Benign neoplasms: 1.61×10^{-3} mm^2/s Malignant: 1.53×10^{-3} mm^2/s PA: 1.99×10^{-3} mm^2/s Warthin: 0.93×10^{-3} mm^2/s	Benign vs malignant: $P = .002$ PA vs Warthin: $P < .001$ PA vs malignant: $P < .001$ Warthin vs malignant: $P = .008$
Matsusue et al., 2018[13]	Benign and malignant neoplasms	ADC values not specified	ADC values not specified
Mikaszewski et al., 2018[14]	Benign and malignant neoplasms	Mean/Median ADC values not specified	Mean/median ADC values not specified
Wang et al., 2018[16]	Warthin tumor, PA and malignant neoplasms	Cutoff ADC values for Warthin tumors ranged from: 1.016 to 0.117×10^{-3} mm^2/s ADC values not specified for the other neoplasms	PA vs Warthin: $P < .001$ Malignant vs Warthin: $P < .001$
Zhang et al., 2018[17]	Benign lesions (neoplasms and non-neoplastic lesions) and malignant neoplasms	PA: 1.57×10^{-3} mm^2/s Warthin: 0.83×10^{-3} mm^2/s Benign lesions: $0.79\,117 \times 10^{-3}$ mm^2/s Carcinomas: $1.16\,117 \times 10^{-3}$ mm^2/s Lymphomas: 0.57×10^{-3} mm^2/s	*P* values not specified for the different groups, although authors mentioned a statistical significantly difference between benign lesions and malignant neoplasms, except between Warthin tumors and benign lesions (apart from PA)
Zhang et al., 2018[18]	Benign and malignant neoplasms	Benign: 1.15×10^{-3} mm^2/s Malignant: 0.86×10^{-3} mm^2/s	Benign vs malignant: $P = .07$
Zheng et al., 2018[21]	Benign and malignant neoplasms	PA: 1.72×10^{-3} mm^2/s Malignant: 0.95×10^{-3} mm^2/s Adenolymphoma: 0.74×10^{-3} mm^2/s Benign: 1.33×10^{-3} mm^2/s	PA vs malignant: $P < .01$ Adenolymphoma vs malignant: $P < .01$ Benign vs malignant: $P < .05$
Zheng et al., 2018[22]	Benign and malignant neoplasms	PA: 1.367×10^{-3} mm^2/s Malignant: 0.859×10^{-3} mm^2/s Warthin: 0.700×10^{-3} mm^2/s	*P* values not specified for the different groups, although authors mentioned ADC values for PA were higher than malignant neoplasms and Warthin tumors presented lower ADC values than malignant neoplasms
Kato et al., 2017[23]	Warthin tumor and oncocytoma	Oncocytoma: 1.06×10^{-3} mm^2/s Warthin: 0.79×10^{-3} mm^2/s	Warthin vs oncocytoma: $P < .001$
Matsusue et al., 2017[25]	PA, Warthin tumors and malignant neoplasms	PA: 1.95×10^{-3} mm^2/s Warthin: 0.99×10^{-3} mm^2/s Malignant: 1.02×10^{-3} mm^2/s	PA vs Warthin: $P < .001$ PA vs malignant: $P < .001$ Warthin vs malignant: $P = .924$
Mikaszewki et al., 2017[26]	Benign and malignant neoplasms	Not reported	Not reported
	PA and malignant neoplasms		PA vs malignant: $P < .001$

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Table VI. Continued

Authors	*Group of lesions studied*	*ADC values found*	*P values*
Mikaszewski et al., 2017[27]		PA: 1.862×10^{-3} mm^2/s Malignant: 1.059×10^{-3} mm^2/s	
Milad et al., 2017[28]	Benign lesions (neoplasms and non-neoplastic lesions) and malignant neoplasms	Benign lesions: 1.67×10^{-3} mm^2/s Malignant: 0.8×10^{-3} mm^2/s	Benign vs malignant: $P < .0001$
Nada et al., 2017[29]	Benign and malignant neoplasms, inflammatory diseases and healthy parotid glands	Healthy: 1.12×10^{-3} mm^2/s Benign: 1.16×10^{-3} mm^2/s Malignant: 0.82×10^{-3} mm^2/s Inflammatory: 0.86×10^{-3} mm^2/s	Inflammatory vs neoplasms: $P < .001$ Benign vs malignant: $P < .001$
Razek et al., 2017[30]	Benign and malignant neoplasms	PA: 1.22×10^{-3} mm^2/s Malignant: 0.94×10^{-3} mm^2/s	Benign vs malignant: $P < .001$
Razek et al., 2017[31]	Benign and malignant neoplasms	Benign: 1.55×10^{-3} mm^2/s Malignant: 1.15×10^{-3} mm^2/s	Benign vs malignant: $P < .001$
Tao et al., 2017[32]	Benign and malignant neoplasms	Benign: 1.16×10^{-3} mm^2/s Malignant: 0.91×10^{-3} mm^2/s	Benign vs malignant: $P < .001$
Terra et al., 2017[33]	PA, sialadenitis and healthy parotid glands	Parotid gland: Healthy: 0.53×10^{-3} mm^2/s Sialadenitis: 1.39×10^{-3} mm^2/s PA: 1.91×10^{-3} mm^2/s Submandibular gland: Healthy: 0.84×10^{-3} mm^2/s Sialadenitis: 0.97×10^{-3} mm^2/s	Parotid gland: Healthy vs sialadenitis: $P = .001$ Sialadenitis vs PA: $P = .020$ Submandibular gland: Sialadenitis vs healthy: $P = .466$
Eissa et al., 2016[37]	Benign and malignant neoplasms	Warthin: 0.69×10^{-3} mm^2/s Lymphoma: 0.58×10^{-3} mm^2/s Malignant: 0.97×10^{-3} mm^2/s PA: $> 1.4 \times 10^{-3}$ mm^2/s	Not specified, although authors mentioned that PA presented significantly higher ADC values than Warthin, lymphomas and malignant neoplasms. Additionally, Warthin tumors presented lower ADC values than malignant neoplasms; and Warthin presented higher values than lymphomas
Karaman et al., 2016[38]	Benign and malignant neoplasms	b-value = 100: Benign: 1.85×10^{-3} mm^2/s Malignant: 2.23×10^{-3} mm^2/s b-value = 500: Benign: 1.59×10^{-3} mm^2/s Malignant: 0.98×10^{-3} mm^2/s b-value = 1000: Benign: 1.38×10^{-3} mm^2/s Malignant: 0.90×10^{-3} mm^2/s	b-value = 100: Benign vs malignant: $P = .31$ b-value = 500: Benign vs malignant: $P = .004$ b-value = 1000: Benign vs malignant: $P = .026$
Kikuchi et al., 2016[39]	Benign lesions (neoplasms and non-neoplastic) and malignant neoplasms	PA: 1.60×10^{-3} mm^2/s Warthin: 0.87×10^{-3} mm^2/s Other benign lesion: 0.93×10^{-3} mm^2/s Carcinoma: 1.13×10^{-3} mm^2/s Malignant Lymphoma: 0.69×10^{-3} mm^2/s	Not specified

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Table VI. Continued

Authors	*Group of lesions studied*	*ADC values found*	*P values*
Mukai et al., 2016[40]	Basal cell adenomas and PA	Basal cell adenomas: 1.24×10^{-3} mm^2/s PA: 1.86×10^{-3} mm^2/s	PA vs basal cell adenomas: $P < .001$
Yologlu et al., 2016[41]	Benign lesions (neoplasms and non-neoplastic), malignant neoplasms and healthy parotid gland	Healthy: 863−761 for b-values: 750-1000 seconds/mm^2 Benign: 1016−931 for b-values 750−1000 1000 seconds/mm^2 Malignant: 999−894 for b-values 750−1000 1000 seconds/mm^2	PA vs Warthin tumors: $P = .021$ Healthy vs benign lesions and malignant neoplasms = P = .016
Yuan et al., 2016[42]	Benign and malignant neoplasms	Benign: 0.89×10^{-3} mm^2/s Malignant: 1.19×10^{-3} mm^2/s	Benign vs malignant: $P < .0001$
Zhu et al., 2016[43]	Benign lymphoepithelial lesions and mucosa-associated lymphoid tissue lymphoma	b-value = 500 Benign lymphoepithelial lesions: 1.16×10^{-3} mm^2/s Lymphoma: 1.06×10^{-3} mm^2/s b-value = 1000 Benign lymphoepithelial lesions: 0.992×10^{-3} mm^2/s Lymphoma: 0.634×10^{-3} mm^2/s	b-value = 500 Benign lymphoepithelial lesions vs lymphoma: $P = .359$ b-value = 1000 Benign lymphoepithelial lesions vs lymphoma: $P < .001$
Kato et al., 2015[46]	Benign and malignant neoplasms	PA: 1.70×10^{-3} mm^2/s Warthin: 0.78×10^{-3} mm^2/s Malignant: 0.88×10^{-3} mm^2/s	PA vs Warthin: $P < .01$ PA vs malignant: $P < .01$ Warthin vs malignant: $P = .701$
Salama et al., 2015[48]	Benign and malignant neoplasms	PA: 1.89×10^{-3} mm^2/s Warthin: 0.92×10^{-3} mm^2/s Malignant: 1.03×10^{-3} mm^2/s	Benign vs malignant: $P = .037$
Balçık et al., 2014[49]	Benign lesions (neoplasms or non-neoplastic) and malignant neoplasms	Benign lesions: 1.74×10^{-3} mm^2/s Malignant: 1.13×10^{-3} mm^2/s	Benign vs malignant: $P = .006$
Celebi et al., 2013[50]	Benign and malignant neoplasms	Benign: 1.72×10^{-3} mm^2/s Malignant: 1.05×10^{-3} mm^2/s	Benign vs malignant: $P < .001$
Fruehwald-Pallamar et al., 2013[51]	Benign lesions (neoplasms or non-neoplastic) and malignant neoplasms	Large ROI: Benign: 1.86×10^{-3} mm^2/s Malignant: 1.51×10^{-3} mm^2/s PA: 1.76×10^{-3} mm^2/s Warthin: 1.58×10^{-3} mm^2/s Small ROI: Benign: 1.70×10^{-3} mm^2/s Malignant: 1.18×10^{-3} mm^2/s PA: 1.54×10^{-3} mm^2/s Warthin: 1.05×10^{-3} mm^2/s	Large ROI: Warthin vs PA: $P = .03$ Warthin vs benign: $P = .042$ Small ROI: Malignant vs benign: $P = .025$ PA vs Warthin: $P = .001$
Kato et al., 2012[53]	Mucosa-associated lymphoid tissue lymphoma	Mucosa-associated lymphoid tissue lymphoma: 0.64×10^{-3} mm^2/s	Statistical tests not performed for numerical comparison of ADC values

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Table VI. Continued

Authors	*Group of lesions studied*	*ADC values found*	*P values*
Lechner Goyault et al., 2011[54]	Benign lesions (neoplasms and non-neoplastic lesions) and malignant neoplasms	PA: 1.87×10^{-3} mm^2/s Warthin: 0.84×10^{-3} mm^2/s Cystic lesions: 1.90×10^{-3} mm^2/s Malignant: 0.83×10^{-3} mm^2/s	Benign vs malignant: $P < .001$ PA vs Warthin: $P < .001$
Eida et al., 2010[56]	Benign and malignant neoplasms	Lymphomas:0.43×10^{-3} mm^2/s Warthin: 0.78×10^{-3} mm^2/s	Lymphomas vs Warthin: $P = .039$
Inci et al., 2010[57]	Healthy parotid gland, benign and malignant neoplasms	Benign: 1.51×10^{-3} mm^2/s Malignant: 1.05×10^{-3} mm^2/s Healthy: 0.27×10^{-3} mm^2/s	Malignant vs control: $P = .001$ Malignant vs benign: $P = .03$ Healthy vs malignant: $P = .001$ Healthy vs benign: $P = .001$
Yerli et al., 2010[59]	Benign lesions (neoplasms and nonneoplastic) and malignant neoplasms	Warthin: 1.02×10^{-3} mm^2/s Adenomas: 1.75×10^{-3} mm^2/s Carcinomas: 1.31×10^{-3} mm^2/s	Not reported, although authors mentioned statically significant differences between Warthin tumors and adenomas
Habermann et al., 2009[60]	Benign and malignant neoplasms	PA: 2.09×10^{-3} mm^2/s Warthin: 0.89×10^{-3} mm^2/s Myoepithelial adenomas: 1.86×10^{-3} mm^2/s Lipomas: 0.62×10^{-3} mm^2/s Salivary duct carcinomas: 1.10×10^{-3} mm^2/s Mucoepidermoid carcinoma:1.05×10^{-3} mm^2/s Basal cell adenocarcinoma: 0.96×10^{-3} mm^2/s Acinic cell carcinoma: 0.79	PA vs other lesions (except myoepithelial adenomas): $P = .054$ Warthin vs myoepithelial adenomas: $P < .001$ Warthin vs lipomas: P = .013 Warthin vs salivary duct carcinomas: $P = .37$ Warthin vs mucoepidermoid carcinoma: $P = .094$ Warthin vs basal cell adenocarcinoma: $P = .604$ Warthin vs acinic cell carcinomas: $P = .396$
Abu et al., 2008[62]	Kuttner tumors, benign and malignant neoplasms	Kuttner tumor: 1.19×10^{-3} mm^2/s Malignant: 1.20×10^{-3} mm^2/s PA: 1.83×10^{-3} mm^2/s	Kuttner vs PA: $P = .000$ PA vs malignant: $P = .001$ Kuttner vs malignant: $P = 1.0$
Yabuuchi et al., 2008[65]	Benign and malignant neoplasms	PA: 1.92×10^{-3} mm^2/s Warthin: 0.86×10^{-3} mm^2/s Carcinomas: 1.12×10^{-3} mm^2/s Malignant lymphomas: 0.88×10^{-3} mm^2/s	Not specified
Eida et al., 2007[66]	Healthy salivary glands, benign and malignant neoplasms	Healthy Parotid: 0.63×10^{-3} mm^2/s Healthy Sublingual:0.87×10^{-3} mm^2/s Healthy Submandibular: 0.97×10^{-3} mm^2/s Mean or median ADC values for neoplasms were specified as "extremely low"; "low", "intermediate" and "high".	Parotid vs submandibular: $P < .001$ Submandibular vs sublingual: $P = .012$ Parotid vs sublingual: $P < .001$
Matsushima et al., 2007[67]	Benign and malignant neoplasms	Benign: 1.40×10^{-3} mm^2/s Malignant: 1.09×10^{-3} mm^2/s	Benign vs malignant: $P > .05$
Yerli et al., 2007[68]	Healthy parotid gland, benign and malignant neoplasms	PA: 1.74×10^{-3} mm^2/s Warthin: 0.97×10^{-3} mm^2/s Malignant:1.04×10^{-3} mm^2/s Healthy: 0.34×10^{-3} mm^2/s	Warthin vs PA: $P < .05$ PA vs Warthin: $P < .05$ Warthin vs malignant: $P > .05$ Healthy vs Warthin: $P < .05$

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Table VI. Continued

Authors	Group of lesions studied	ADC values found	P values
			Healthy vs PA: $P < .05$
			Healthy vs malignant: $P < .05$
Habermann et al., 2005[69]	Healthy parotid gland, benign and malignant neoplasms	Healthy: 1.14×10^{-3} mm^2/s	PA vs other neoplasms: $P = .001$
		Warthin: 0.85×10^{-3} mm^2/s	Warthin vs other neoplasms: $P = .001$
		PA: 2.14×10^{-3} mm^2/s	Mucoepidermoid carcinoma vs other neoplasms: $P = .001$
		Mucoepidermoid carcinoma: 1.04×10^{-3} mm^2/s	PA vs Warthin: $P < .001$
			Warthin vs mucoepidermoid carcinoma: $P < .001$
			PA vs mucoepidermoid carcinoma: $P < .001$
Motoori et al., 2005[70]	Salivary duct carcinoma	Salivary duct carcinoma: 1.16×10^{-3} mm^2/s	Statistical test not performed for numerical comparison of ADC values
Motoori et al., 2005[71]	Benign lesions (neoplasms and non-neoplastic) and malignant neoplasms	Not specified	Statistical test not performed for numerical comparison of ADC values
Ikeda et al., 2004[72]	Warthin tumor and malignant neoplasms	Warthin: 0.96×10^{-3} mm^2/s	Warthin vs malignant: $P < .01$
		Malignant: 1.19×10^{-3} mm^2/s	
Motoori et al., 2004[73]	PA and malignant neoplasms	Mean or median values not specified.	Statistical test not performed to median or mean values

ADC: Apparent diffusion coefficient; PA: Pleomorphic adenoma; SS: Sjogren syndrome.

with RT than in healthy volunteers.[47] This shows that ADC values are sensitive to salivary gland dysfunction[20,52] and may be correlated with the RT dose absorbed by the salivary glands during treatment.[24] RT is described as a tissue-nonspecific treatment modality for patients with head and neck cancers. RT is associated with inadvertent, but considerable, damage to the surrounding normal tissues, including the salivary glands, which may exhibit chronic and acute responses to radiation damage at a tissue level. [82]

Other investigators focused on autoimmune disorders, such as SS and other connective tissue disorders (CTDs),[15,34,36,58,61,74,75] other inflammatory diseases (e.g., sialadenitis, acute and chronic parotitis),[33,64,75] and xerostomia.[55] Studies confirmed that patients with CTDs show higher DWI signal intensity or ADC values compared with healthy volunteers[36,64,74] and noted a correlation between the severity of gland damage and ADC values.[75] Some authors compared patients with healthy volunteers[36,55,61,64,74,75] and showed that the DWI signal ratio was higher in patients with SS[36] and that ADC values can differ according to the stage of SS.[58,64] ADC values were similar between healthy volunteers and patients with xerostomia.[55]

Parotitis was the single research subject of 1 study by Ries et al.,[64] who noted that patients with acute parotitis had higher ADC values compared with healthy volunteers and that patients with chronic parotitis had higher ADC values compared with patients with acute parotitis. Nevertheless, abscesses in the glands had lower ADC values compared with parotitis with edema and no abcess.[64] The biologic mechanism associated with water molecule diffusibility in abscesses is not fully understood, but it probably relates to the contents of these areas, which consists of a collection of highly concentrated proteins, inflammatory cells, and necrotic tissues.[83]

Although the main objective of this systematic review was the collection and discussion of data pertaining to DWI, it was observed that some researchers also compared different techniques with DWI, mostly for the diagnosis of neoplasms,[12,17,22,26,30,32,37,39,42,46,51,54,56,59,65,69,71] such as scintigraphy,[39,71] color Doppler flow imaging,[17] dynamic contrast-enhanced MRI,[10,21,22,30,42,54,65] time intensity curves,[56] fine-needle aspiration cytology,[26,59] arterial spin labeling,[46] conventional MRI,[32,51] and echo-planar imaging.[32,37,69] Overall, a number of authors reported that combined techniques could improve diagnostic capabilities.

Another observation was that investigators aimed to set certain limits for ADC values or determine cutoff numerical ADC values to verify the accuracy of the ADC in the differentiation of distinct neoplasms.[11,12,16,25,27-29,31,32,40,42,43,65,66,70] As

Table VII. Investigations related to effects of radiotherapy on salivary glands included in the review, group of lesions studied, and mean/median ADC values found by the investigators, with respective *P*-values (when comparison between ADC values were performed)—main results

Authors	*Group of lesions studied*	*ADC values found*	*P values*
Zhang et al., 2018[19]	Effects of RT, at rest and gustatory stimulation, before and two weeks after RT.	Parotid gland: At rest, before RT: 1.35×10^{-3} mm^2/s At rest, 2 weeks after RT: 0.94×10^{-3} mm^2/s After stimulation, before RT: 0.27×10^{-3} mm^2/s After stimulation, 2 weeks after RT: 0.36×10^{-3} mm^2/s Submandibular gland: At rest, before RT: 1.24×10^{-3} mm^2/s At rest, 2 weeks after RT: 1.57×10^{-3} mm^2/s After stimulation, before RT: 0.13×10^{-3} mm^2/s After stimulation, 2 weeks after RT: 0.15×10^{-3} mm^2/s	Parotid gland: At rest, before RT vs after RT: $P < 0.01$ After stimulation, before vs after RT: $P < 0.01$ Submandibular gland: At rest, before RT vs after RT: P < 0.01 After stimulation, before vs after RT: $P = 0.19$
Zhang et al., 2018[20]	Effects of RT and CT, one year after RT.	Parotid gland: Pre-RT: 1.26×10^{-3} mm^2/s One-week post-RT: 1.75×10^{-3} mm^2/s One year post-RT: 1.57×10^{-3} mm^2/s Submandibular gland: Pre-RT: 1.32×10^{-3} mm^2/s One-week post-RT: 1.70×10^{-3} mm^2/s One year post-RT: 1.69×10^{-3} mm^2/s	Parotid gland: Before vs one week after RT: $P < 0.001$ Before vs one year after RT: $P < 0.001$ Submandibular gland: Before vs one week after RT: $P < 0.001$ Before vs one year after RT: $P = 0.581$
Loimu et al., 2017[24]	Effects of CT and RT.	Parotid gland: Baseline at rest: 1.15×10^{-3} mm^2/s Post-RT: 1.48×10^{-3} mm^2/s Submandibular gland: Baseline at rest: 1.35×10^{-3} mm^2/s x 10^{-3} mm^2/s Post-RT: 1.73×10^{-3} mm^2/s	Baseline at rest, parotid vs submandibular: $P < 0.001$ Post-RT vs baseline: $P < 0.001$ (parotid and submandibular)
Zhou et al., 2017[35]	Effects of RT before RT, one month after and two months after RT.	Before RT: 0.726×10^{-3} mm^2/s One month after: 1.084×10^{-3} mm^2/s Two months after: 1.136×10^{-3} mm^2/s	Before RT vs one month after: $P < 0.001$ Before RT vs two months after: $P < 0.001$
Doornaert et al., 2015[44]	Effects of RT and CT.	Not reported.	Statistical test not performed for numerical comparison of ADC values.
Juan et al., 2015[45]	Effects of RT, before and after 100 days of RT, and considering grades of xerostomia.	Before RT: 0.8×10^{-3} mm^2/s ADC values for xerostomia grades were not reported.	Pre-RT vs stage 1 and 2: $P < 0.05$ (higher ADC values at pre-RT) Pre-RT vs stage 3: $P = 0.153$ (higher ADC values at pre-RT)
Liu et al., 2015[47]	Effects of RT and healthy parotid glands.	Not reported.	Statistical test not performed for numerical comparison of ADC values.
Zhang et al., 2013[52]	Effects of RT, at rest and with stimulation.	At rest, before RT: 1.24×10^{-3} mm^2/s After stimulation, before RT: 1.40×10^{-3} mm^2/s At rest, after RT: 1.75×10^{-3} mm^2/s After stimulation, after RT: 1.90×10^{-3} mm^2/s	At rest, before RT vs stimulation before RT: $P = 0.001$ Before RT and after RT: $P = 0.001$
Dirix et al., 2008[63]	Effects of RT, at rest and with stimulation.	Parotid gland: At rest, before RT: 0.85×10^{-3} mm^2/s Submandibular gland: rest, before RT: 1.14×10^{-3} mm^2/s	At rest, parotid vs submandibular: $P < 0.0001$

ADC: Apparent diffusion coefficient; CT: Chemotherapy; RT: Radiotherapy.

Table VIII. Investigations related to other diseases affecting salivary glands included in the review, group of lesions studied, and mean/median ADC values found by the investigators, with respective *P*-values (when comparison between ADC values were performed)—main results

Authors	*Group of lesions studied*	*ADC values found*	*P values*
Takahashi et al., 2018[15]	SS before and after abatacept therapy.	Not reported.	Statistical test not performed for numerical comparison between ADC values.
Xu et al., 2017[34]	SS and healthy glands.	SS gland: ROI based on a reader based-circular: 1.124×10^{-3} mm^2/s ROI based on a single slice: 1.145×10^{-3} mm^2/s ROI based on a whole gland: 1.163×10^{-3} mm^2/s Healthy gland: ROI based on a reader based-circular: 1.038×10^{-3} mm^2/s ROI based on a single slice: 1.036×10^{-3} mm^2/s ROI based on a whole gland: 1.037×10^{-3} mm^2/s	Healthy vs SS (ROI based on a whole gland): P <0.001 Healthy vs SS (ROI based on a single slice): P < 0.001 Healthy vs SS (ROI based on a reader based-circular): P = 0.001
Ding et al., 2016[36]	SS, dry mouth without SS and healthy volunteers.	SS: 1.16×10^{-3} mm^2/s Dry mouth: 1.29×10^{-3} mm^2/s Healthy: 1.31×10^{-3} mm^2/s (ADC ratios were reported)	SS vs dry mouth: P = 0.001 SS vs healthy: P = 0.001 Healthy vs dry mouth: P = 0.887
Kato et al., 2011[55]	Xerostomia and Healthy volunteers, at rest.	Xerostomia: Parotid, at rest: 0.94×10^{-3} mm^2/s Submandibular, at rest: Healthy: 1.27×10^{-3} mm^2/s Parotid, at rest: 0.91×10^{-3} mm^2/s Submandibular, at rest: 1.17×10^{-3} mm^2/s	Parotid, at rest, xerostomia vs healthy: P < 0.01 Submandibular, at rest, xerostomia vs healthy: Not specified, although authors mentioned it wasn't significant.
Li et al., 2010[58]	Primary and secondary SS, CTD and healthy volunteers.	Bilaterally Parotid glands: Primary SS: 0.88×10^{-3} mm^2/s Secondary SS: 0.98×10^{-3} mm^2/s CTD: 0.99×10^{-3} mm^2/s Healthy:1.01×10^{-3} mm^2/s	Primary SS vs CTD: P < 0.05 Primary SS vs Healthy: P < 0.05
Regier et al., 2009[61]	SS (early and advanced stage) and healthy volunteers, at rest and after stimulation.	Healthy: At rest: 1.14×10^{-3} mm^2/s After stimulation: 1.2×10^{-3} mm^2/s Early stage SS: At rest: 1.22×10^{-3} mm^2/s After stimulation: 1.29×10^{-3} mm^2/s Advanced stage: At rest:0.97×10^{-3} mm^2/s After stimulation: 1.01×10^{-3} mm^2/s	Healthy, at rest and after stimulation: P = 0.009 Early SS vs advanced SS (at rest and after stimulation): P < 0.001 Early SS vs healthy after stimulation): P = 0.04 Advanced SS vs healthy after stimulation): P = 0.001
Ries et al., 2008[64]	Healthy volunteers and patients with acute or chronic recurrent parotitis, at rest and after stimulation.	Healthy: At rest: 1.14×10^{-3} mm^2/s After stimulation: 1.2×10^{-3} mm^2/s Acute inflammation: At rest: 1.22×10^{-3} mm^2/s After stimulation: 1.32×10^{-3} mm^2/s Chronic inflammation: At rest: 1.05×10^{-3} mm^2/s After stimulation: 1.20×10^{-3} mm^2/s	Healthy vs acute inflammation at rest: P = 0006 Healthy vs acute inflammation after stimulation: P < 0001 Healthy vs chronic at rest: P = 0.04 Acute vs chronic at rest: P = 0.005 Healthy vs chronic after stimulation: P = 0.94 Acute vs chronic after stimulation: P = 0.15
Patel et al., 2004[74]	CTD and healthy patients.	Healthy: 0.50×10^{-3} mm^2/s CTD: 0.96×10^{-3} mm^2/s	Healthy vs CTD: P = 0.001
Sumi et al., 2002[75]	Patients with SS, sialadenitis and healthy patients.	Healthy; Parotid:0.28×10^{-3} mm^2/s Submandibular: 0.37×10^{-3} mm^2/s Sialadenitis: Mean/median ADC for the entire sample not informed SS: Mean/median ADC for the entire sample not informed	Healthy, parotid vs submandibular P < 0.0001

ADC: Apparent diffusion coefficient; CTD: Connective tissue disorders; ROI: Region of interest; RT: Radiotherapy; SS: Sjogren syndrome.

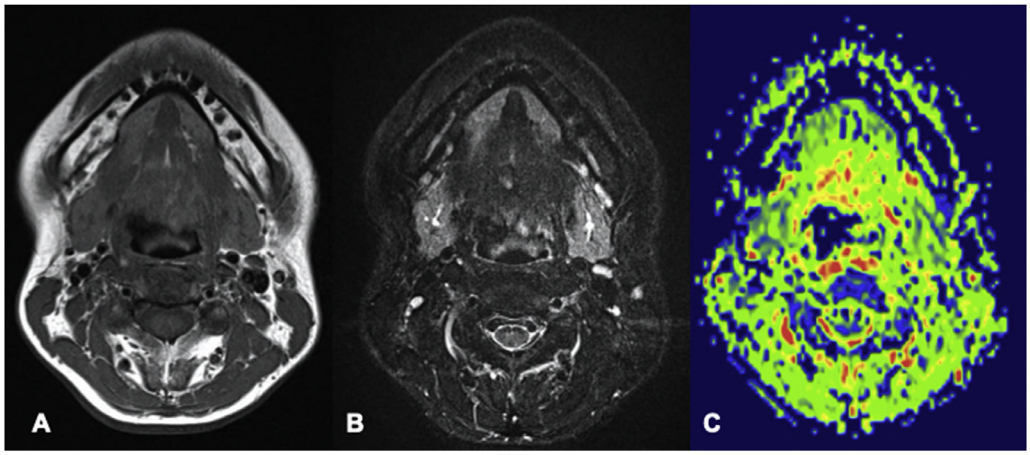

Fig. 2. A 37-year-old woman complaining of pain in the salivary gland region with a duration of 4 months, but no imaging alteration. **(A)** T1-weighted axial slices. **(B)** T2-weighted short tau inversion recovery (STIR) axial slices. **(C)** Its correspondent apparent diffusion coefficient (ADC) map.

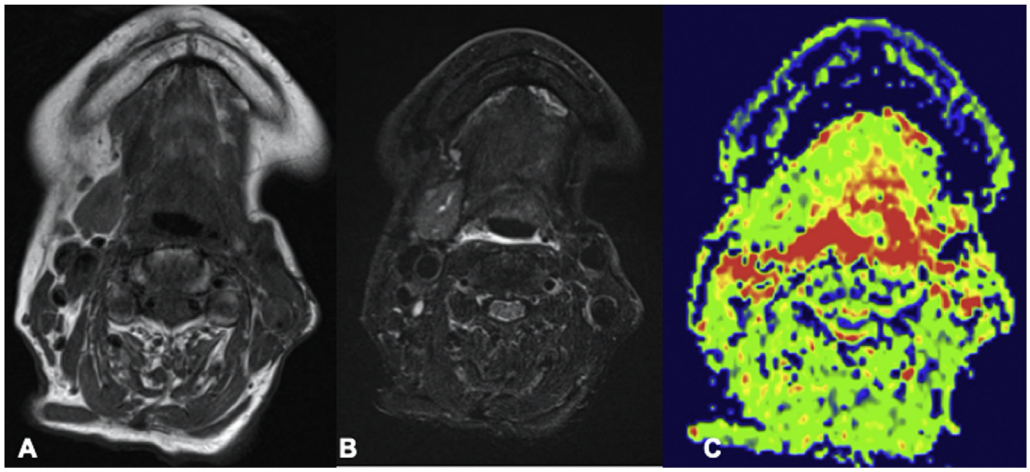

Fig. 3. A 87-year-old female patient who had undergone resection of a malignant neoplasm in the maxillary sinus on the right side. **(A)** T1-weighted axial slices. **(B)** T2-weighted short tau inversion recovery (STIR) axial slices. **(C)** Its correspondent apparent diffusion coefficient (ADC) map.

mentioned, ADC values may be subject to several sources of variability,[5,9,84] which can affect the wide applicability of these cutoff points. Additionally, direct comparison between ADC values from the studies in this review is not appropriate because of the differences in DWI acquisition parameters (shown in Table I; MRI strength varied from 1.5 T to 3.0 T), differences in equipment used, and ROI positioning strategies. Ideally, direct comparisons should be performed only when the equipment, parameters, ROI strategies, and diseases (i.e., same inflammatory condition, same histologic type neoplasm) are equal.

Limitations

The limitations of the present review include the small number of available studies investigating the effects of RT and other inflammatory or autoimmune diseases in the salivary glands, as well as the impossibility of comparing the ADC values collected.

CONCLUSIONS

DWI and ADC may improve the quality of imaging in the diagnosis of salivary gland disorders, mainly by differentiating between benign and malignant neoplasms. A unique cutoff value for the ADC could not be established because of the heterogeneity of methods used for ADC assessment and the heterogeneity of the diseases evaluated in each study. Overall, DWI and ADC are valuable methods in the diagnosis of salivary gland diseases, adding information to the diagnostic hypothesis and improving the differentiation of salivary gland diseases by assessment of ADC values.

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