Salivary gland imaging techniques for the diagnosis of Sjögren's syndrome

Extensive evaluation of the utility of newer imaging techniques in diagnosing Sjögren's syndrome has revealed that all of the techniques provide useful information that can help to differentiate between patients with Sjögren's syndrome and healthy individuals, with sensitivity and specificity ranging from 70–95%. However, there is a need for greater technique validation using disease-control patients with dry mouth and careful comparison with other diagnostic methods. Furthermore, a universally accepted grading of abnormal imaging findings observed in salivary glands is needed. Clarification of these matters will enable the clinician to choose the most reliable imaging technique to diagnose Sjögren's syndrome.

KEYWORDS: MRI ▪ salivary glands ▪ scintigraphy ▪ sialography ▪ Sjögren's syndrome ▪ ultrasonography ▪ xerostomia

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Sjögren's syndrome (SS) is a slowly progressing chronic autoimmune disease that primarily affects middle-aged women. It is fairly common, with an approximate 0.5% prevalence in the general population. The disease can manifest with various symptoms and is related to an autoimmune exocrinopathy involving mainly the salivary and lacrimal glands or systemic involvement affecting the joints, lungs, kidneys, blood vessels and muscles [1,2]. It can occur alone (primary SS) or in association with other autoimmune diseases (secondary SS). The diversity of the clinical presentation, particularly in the early stages of the disease, often delays the diagnosis of SS [3]. Many patients are therefore diagnosed many years after the onset of symptoms. As with most systemic autoimmune diseases, early diagnosis of SS is particularly important, as it allows clinicians to assess the extent of systemic involvement and optimize therapy. The diagnosis of SS is based on the classification criteria proposed by the American–European Study Group, introduced in 2002 and built on the 1992 European preliminary classification criteria [4]. In the era of high-resolution imaging technology, it is now possible to study the major salivary glands of patients with SS in depth, with the anticipation that the new information will provide the diagnostic armamentarium with noninvasive, sensitive and specific tools suitable for use in clinical trials, as well as everyday clinical practice.

Conventional imaging techniques

Over the past several years, various imaging techniques have been introduced to assess salivary gland involvement. In fact, sialography and scintigraphy have been validated and included in the classification criteria for disease diagnosis [4]. Sialography is a radiographic method that can detect anatomic changes in the salivary gland duct system [5], whereas scintigraphy provides useful information about salivary gland function by measuring the rate and density of technetium-99m (99mTc) pertechnetate uptake in the mouth after intravenous injection. However, these methods have drawbacks, primarily related to the need to cannulate the parotid ducts and inject the contrast medium through the narrow duct orifice [6,7]. Additional problems may arise in patients with allergies to the contrast medium or when severe obstruction of the duct diminishes diffusion of the radio-contrast material in the ductal system, thus limiting assessment of distal branches.

Ultrasonography

Ultrasonography is an inexpensive and noninvasive technique that is used to detect anatomic changes in the major salivary glands. With ultrasonography, the normal parotid gland is depicted as a homogeneous structure, with increased echogenicity relative to adjacent muscles. Increased echogenicity is due to fatty glandular tissue, which is abundant in the parotid and other major glands. Knowledge of the anatomy and evolution of pathological changes in SS is highly important for correctly interpreting ultrasonography images. However, a direct correlation between pathological changes and salivary gland images has not yet been established. Observational studies revealed that peripheral duct inflammation, with its associated intraglandular duct dilatation and increased

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parenchyma blood flow, produce multiple small, oval, hypoechoic or anechoic areas throughout the parenchyma that are usually well defined [8]. Hypoechoic or anechoic areas most probably represent lymphocytic infiltration, injury of salivary tissue or duct dilatation. In patients with long disease duration, appearance of cystic lesions may be related to progressive glandular destruction and prominent intraglandular sialectasis. Various ultrasonography studies in SS have shown that the sensitivity of these findings range from 70–95% [9]. A recent report by Wernicke *et al.* concluded that the submandibular glands of patients with SS, in addition to increased parenchymal heterogenicity, have lower glandular volume, compared with normal individuals [10]. Receiver operating characteristic (ROC) curve analyses showed that these findings could reliably discriminate between patients and healthy individuals (specificity >90%), but could detect only one-half to two-thirds of patients with SS (sensitivity 48–64%).

MRI

In recent years, MRI has been used to image the parotid glands of patients with SS. Areas of high signal intensity on time 1 (T1)-weighted magnetic resonance (MR) images, which indicate increased amounts of fatty tissue, are depicted in the glands of patients with SS [11]. Several MRI techniques are now available for identifying and staging the disease, including T1- and T2-weighted imaging [12], MR sialography [13] and diffusion-weighted MRI [14].

Conventional MRI, using a head/neck coil, is also useful for differentiation of other diseases (e.g., parotid tumors). High resolution MRI, using small surface coil, may provide additional information. Thus, T1- and T2-weighted imaging may disclose the architectural changes of the gland. MR sialography images the salivary ducts, whereas diffusion-weighted MRI provides information about salivary function [15].

In a study by El Miedany *et al.*, the MRI appearance of salivary glands was studied in 47 patients with SS, 20 patients with sicca manifestations without SS and 20 healthy individuals matched for sex and age [16]. Four patterns of salivary images have been identified; grade 0: normal homogeneous parenchyma was detected in 1/47 (2.1%) of patients and in 38/40 (95%) of the control group, grade 1: fine reticular or small nodular structure was identified in 7/47 (14.9%) of patients, grade 2: medium nodular pattern was detected in 12/47 (25.5%) of patient groups, grade 3: coarsely nodular. This was seen in 27/47 (57.4%) of patient groups.

Several studies aimed to define quantitative MRI criteria for the diagnosis of SS. In a study that included 83 patients with dry mouth (55 patients with SS, 28 without SS), MRI with a 47 mm microscopy coil, was performed [17]. MR images were obtained by T1-weighted and fat-suppressed T2-weighted imaging and by MR sialography of the parotid glands. Quantitative MRI of fat, intact gland lobule and number of sialoectatic foci were significantly found to be correlated with the severity of the disease. ROC analysis demonstrated that quantitative MRI of individual images yielded high diagnostic ability in differentiating between SS patients with xerostomia and those without SS. Thus, areas under the ROC curve (AUC-ROC) were 0.94 for fat area, 0.98 for intact lobule area and 0.91 for number of sialoectatic foci. The best cut off points by quantitative MRI were each associated with high sensitivity and specificity and, when used in combination, yielded 96% sensitivity and 100% specificity.

In a recent report, the appearance of labial salivary glands in patients with SS and healthy individuals was studied using MRI [18]. The upper and lower lip minor salivary glands consisted of one to three layers of gland clusters, each with high-signal intensity on T1-weighted and fat-suppressed T2-weighted images. The labial salivary gland imaging was readily enhanced after gadolinium injection. The labial gland areas were smaller in patients with SS than in patients without SS. However, no attempt was made to correlate these imaging data with findings from salivary gland biopsies. MRI of lacrimal glands was also evaluated. Diffusion-weighted MRI was performed in 31 healthy volunteers and 11 SS patients with impaired lacrimal function, revealing differences between normal and affected tissues, similar to those observed in major salivary glands [19].

Although these MRI techniques have certain advantages, their overall diagnostic utility remains to be clarified.

MR sialography

The earliest publications on MR sialography were those by Lomas *et al.* and Fischbach *et al.*, in which single-slice techniques were used [20,21]. Since then, MR sialography has been applied as an alternative to conventional sialography [13,22,23]. Compared with conventional sialography, MR sialography appears to be more sensitive in detecting salivary duct abnormalities. The initially reported MR sialography techniques were frequently associated with background noise from

neighboring structures, such as the neck vessels and muscles. More recently, dynamic MR sialography has been introduced. The technique is similar to dynamic MR cholangiopancreatography, in which images are acquired before and after administration of secretin [24,25]. Dynamic MR sialography visualizes the salivary ducts in a resting stage (baseline), following them up after filling with saliva in a time-dependent alternation and citric acid stimulation using dynamic MR sialographic images [26]. This method may overcome all or most of the above mentioned shortcomings, however, it requires long imaging time, since rapid exposure would result in poor sialographic images.

Quantitation of salivary gland involvement & functional evaluation

Current quantitative methods for the evaluation of glandular structure and function include classification of the glandular parenchyma according to the size of nodules, ducts and cavities [16,27], calculation of mean MR signal intensity in a portion of the gland [12], ultrasonography texture analysis [16,28] and, more recently, assessment of functional glandular change with diffusion-weighted MRI [29] and dynamic MR sialography [26]. Of note, none of these quantitative methods is widely approved and validated in consecutive SS patients.

The rich vasculature of the parotid gland allows studies to evaluate dynamic contrast material–enhanced MRI (i.e., dynamic MRI). Initially, dynamic MRI has been used in neoplastic disease [30], in which the tumor was described quantitatively in terms of the vascular plasma volume, transcapillary contrast agent transfer constant and extracellular extravascular volume, with the utilization of models of intravenously administered contrast agent kinetic parameters [31]. These parameters have been investigated as markers for the extension of the disease and outcome of treatment. This technique may yield significant information about tissue vascularization in non-malignant inflammatory diseases. The superficial location of the parotid gland facilitates an excellent signal:noise ratio with the use of the appropriate surface coil. A study of dynamic MRI of parotid glands in SS using tracer kinetic modeling found significant differences ($p < 0.001$) in summary statistics of model parameters between healthy volunteers and patients with SS. In brief, the volume of extracellular extravascular space was estimated to be larger in patients with SS than in healthy volunteers. In addition, a higher degree of microvascular heterogeneity was observed in the parotid glands of patients with SS compared with those of healthy volunteers [32].

Parotid scintigraphy

The main indication of salivary scintigraphy is the assessment of salivary gland function in patients with dry mouth. This is a functional method that allows for the simultaneous evaluation of major salivary gland parenchyma and function. After intravenous 99mTc-sodium pertechnectate administration, sequential head images, on anterior projection, are acquired in different time intervals, usually between 20–40 min. The images are stored and glandular regions of interest, as well as a background region, usually in the skull, are manually drawn, followed by a computerized generation of time–activity curves for each major salivary gland. Time–activity curves have two phases: the uptake phase, corresponding to tracer accumulation in the glandular parenchyma, and the excretion phase, initiated by the administration of a salivation stimulator agent, for example, citric acid. The excretion phase corresponds to tracer elimination through the oral cavity and provides information on the functional integrity of the ductal system [33]. In the early 1970s, Schall and colleagues proposed a classification scheme based on visual quality of glandular uptake and tracer excretion into the oral cavity [6,34]. Accordingly, salivary gland functional impairment is classified into four grades on the basis of intensity of uptake and presence of activity in the mouth after administration of the excretory stimulus; grade 1 is considered normal and grade 4 corresponds to the total absence of uptake and mouth excretion. This classification is considered the standard method for salivary scintigram interpretation.

The earliest and most common scintigraphic abnormality observed in SS is impairment of excretion, followed by a decrease in tracer accumulation, reflecting damage in the glandular parenchyma [35,36]. Submandibular glands are preferentially involved and their scintigraphic activity has been correlated to the degree of subjective xerostomia [33,37]. In a study comparing scintigraphic features of chronic sialadenitis and SS, Hermann *et al.* demonstrated that SS patients have more frequent multiglandular involvement, more biphasic kinetic defects and more severe dysfunction than chronic sialadenitis patients [35]. However, both conditions shared similar features, such as less frequent single-gland dysfunction, preferential submandibular

involvement and a tendency to slow isolated discharge failure over uptake failure. Salivary gland scintigraphy is sensitive enough to detect mild abnormalities, such as 25% destruction of glandular parenchyma, and its results correlate with clinicopathological features of SS, for example, the nonstimulated saliva production, sialography and focus scores in minor salivary gland biopsy.

Correlation of methods & diagnostic utility

Several studies have compared different imaging methods in an attempt to define the optimum sensitivity and specificity for disease diagnosis (TABLE 1). Parotid gland ultrasonography, contrast sialography and scintigraphy were compared in a study involving 77 patients with primary SS (male:female ratio: 3:74; mean age: 54 years) and in 79 patients with sicca symptoms but without SS [38]. Ultrasonography findings were graded using an ultrasonographic score ranging from 0–16, which was obtained by the sum of the scores for each parotid and submandibular gland. The sialographic and scintigraphic patterns were classified in four different stages. The AUC-ROC was employed to evaluate the performance of the screening methods. Of the 77 patients with primary SS, 66 had abnormal ultrasonography findings. Mean ultrasonography score in primary SS patients was 9.0, compared with 3.9 in healthy individuals ($p < 0.0001$). Sialography and scintigraphy showed abnormal findings in 59 and 58 SS patients, respectively. Among the three methods, ROC curves for ultrasonography gave the best performance, followed by sialography and salivary gland scintigraphy (AUC: 0.863, 0.804 and 0.783, respectively). In the study conducted by El Miedany *et al.*, which aimed to correlate ultrasonography and MRI findings with histopathology of minor salivary glands, parenchymal inhomogeneity by ultrasonography was seen in 93.6% of patients studied, while nodular pattern was seen in 97.8% of patients studied using MRI [16]. There was good agreement between ultrasonography and MRI findings ($r = 0.87$) in both SS cases and healthy individuals. The ultrasonography and MRI results correlated significantly with the histopathologic score of the minor salivary glands ($r = 0.82$, 0.84, respectively), as well as sialography score ($r = 0.69$, 0.60, respectively).

Niemelä *et al.* correlated MRI and MR sialography of both parotid glands in 26 SS patients and seven healthy controls [27]. MRI imaging revealed abnormalities in a total of 22 of the 26 patients. A total of 21 patients had a nodular or dendritic parenchymal pattern, five had cavities and six had duct dilatations. MR sialography revealed that 25 of the 26 patients had abnormalities of the ducts. One patient and all seven controls displayed normal images with both methods. The structural appearance of the parotid glands on MR images had a marginal linear association with the duct system changes, however, no correlation with the cavitary changes was seen using MR sialography. Both parenchymal and sialographic abnormalities were associated with the presence of antibodies to Ro/SSA intracellular autoantigen, however, there was no correlation with age of patients, disease duration and salivary flow rate, nor with the presence of hypergammaglobulinemia or extraglandular manifestations. In another study, ultrasonography examination of parotid, submandibular and sublingual glands was performed in 27 patients with primary SS, 27 healthy controls and 27 symptomatic controls without SS [39]. The results were compared

Table 1. Imaging techniques for the evaluation of salivary glands.

Technique	Information provided	Sensitivity (%)	Specificity (%)
Ultrasound	Structure of gland Volume of gland Areas of inflammation Areas of degenaration	50–70	>90
MRI	Structure of gland Architecture Areas of inflammation Differential diagnosis with other tumors	75–95	75–90
MR sialography	Ductal structure Sielectasias Dynamic evaluation of ducts	96	ND
Scintigraphy	Functional evaluation of salivary glands	72–98	ND

MR: Magnetic resonance; ND: Not defined.

with parotid MRI and MR sialography, as well as the clinical picture of the patients. Salivary gland abnormalities, parenchymal inhomogeneity or adipose degeneration were visualized in 21 (78%) SS patients, one healthy control and two symptomatic controls using ultrasonography. Two-thirds of patients showed changes in the parotid and submandibular glands, and one-third showed changes in the sublingual glands. By contrast, MR sialography was found to be the most sensitive method (96%) in detecting glandular changes, followed by MRI (81%) and ultrasonography (78%). The ultrasonography and MR results were related to anti-Ro/SSA positivity, however, not to saliva secretion. The salivary gland biopsy focus scores were related only to parotid MRI findings. In another study, 130 patients clinically suspected of having SS were examined by MR sialography and salivary gland scintigraphy [40]. Imaging findings of MR sialography and salivary gland scintigraphy were compared with the results of a labial gland biopsy. The diagnosis of SS was established in 80 patients. Abnormally high T2 signal intensity areas on MR sialography and decreased uptake and delayed excretion of (99mTc) pertechnetate on salivary gland scintigraphy were seen more frequently in patients with SS. For the diagnosis of SS, salivary gland scintigraphy showed higher sensitivity than MR sialography. On the other hand, MR sialography showed higher specificity and positive-predictive value than salivary gland scintigraphy. The overall diagnostic accuracy was 83% for MR sialography and 72% for salivary gland scintigraphy.

Despite the extensive work to elucidate the diagnostic utility of imaging techniques of major salivary glands in SS, several questions remain unanswered. First, how reliable is a given technique to discriminate between SS and other diseases mimicking it? In fact, differential diagnosis of SS includes other inflammatory diseases affecting the salivary glands, such as sarcoidosis, infection with hepatitis C virus or HIV. These diseases should be taken into consideration in cases in which multiple hypoechoic areas are shown to be scattered in salivary gland parenchyma using ultrasonography or in the case of pathologic changes visualized by MRI. So far, imaging studies in SS have not included disease control groups with these disorders. Second, concordance of imaging techniques with clinical or pathology data used for the diagnosis of the syndrome has not been clarified in large cohorts of unselected patients. The sensitivity of techniques, particularly those with a significant subjective component for the interpretation of the results, such as ultrasonography examination, should be carefully evaluated. Finally, a widely validated and accepted grading scale for all imaging techniques is needed. The clarification of these issues and the validation of the newer imaging techniques will enable their use as diagnostic criteria or even for the use of every day clinical practice, replacing older imaging techniques such as sialography.

Future perspective

The evolution and use of newer imaging techniques will most probably substitute older imaging techniques for the diagnosis of the disease. They might also be used as tools to evaluate the outcome of patients following targeted therapies. For the latter, quantification and clarication of the positive-predictive values of the methods are needed.

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Executive summary

- Sjögren's syndrome (SS) is a chronic systemic autoimmune disease affecting mainly the exocrine glands. The diagnosis is based on six criteria, including sialography and scintigraphy.
- Newer imaging techniques include ultrasonography, MRI, magnetic resonance sialography, dynamic MRI and quantitative scintigraphy. Their sensitivity and specificity range from 70–95%.
- There are advantages with each of these techniques. Ultrasonography and MRI disclose the structure, volume and pathology of the affected glands; magnetic resonance sialography visualizes the salivary ducts and dynamic MRI, along with scintigraphy, may provide useful information on the functional status of the salivary glands.
- Further studies are needed to evaluate the sensitivity and specificity in consecutive patients with SS and disease controls that mimic SS. Clarification of the diagnostic utility of these techniques would enable their use in everyday clinical practice.

Bibliography

Papers of special note have been highlighted as:
- ▪ of interest
- ▪▪ of considerable interest

1 Dafni UG, Tzioufas AG, Staikos P, Skopouli FN, Moutsopoulos HM: Prevalence of Sjögren's syndrome in a closed rural community. *Ann. Rheum. Dis.* 56, 521–525 (1997).

2 Skopouli FN, Dafni U, Ioannidis JP, Moutsopoulos HM: Clinical evolution, and morbidity and mortality of primary Sjögren's syndrome. *Semin. Arthritis Rheum.* 29, 296–304 (2000).

▪▪ **Describes the long term outcome of Sjögren's syndrome (SS) and factors of poor prognostic outcome.**

3 Kassan SS, Moutsopoulos HM: Clinical manifestations and early diagnosis of Sjögren syndrome. *Arch. Intern. Med.* 164, 1275–1284 (2004).

▪▪ **Describes the clinical presentation and pathogenetic characteristics of SS.**

4 Vitali C, Bombardieri S, Jonsson R *et al.*; European Study Group on Classification Criteria for Sjögren's Syndrome: Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American–European Consensus Group. *Ann. Rheum. Dis.* 61, 554–558 (2002).

▪ **Outlines classification criteria of the disease.**

5 Vitali C, Tavoni A, Simi U *et al.*: Parotid sialography and minor salivary gland biopsy in the diagnosis of Sjögren's syndrome. A comparative study of 84 patients. *J. Rheumatol.* 15, 262–267 (1988).

6 Schall GL, Anderson LG, Wolf RO *et al.*: Xerostomia in Sjögren's syndrome. Evaluation by sequential salivary scintigraphy. *JAMA* 216(13), 2109–2116 (1971).

7 Daniels TE, Benn DK: Is sialography effective in diagnosing the salivary component of Sjögren's syndrome? *Adv. Dent. Res.* 10, 25–28 (1996).

8 Madani G, Beale T: Inflammatory conditions of the salivary glands. *Semin. Ultrasound CT MR* 27, 440–451 (2006).

9 Tzioufas AG, Moutsopoulos HM: Ultrasonography of salivary glands: an evolving approach for the diagnosis of Sjögren's syndrome. *Nat. Clin. Pract. Rheumatol.* 4, 454–455 (2008).

▪ **Summarizes the major ultrasonographic findings in SS patients.**

10 Wernicke D, Hess H, Gromnica-Ihle E, Krause A, Schmidt WA: Ultrasonography of salivary glands – a highly specific imaging procedure for diagnosis of Sjögren's syndrome. *J. Rheumatol.* 35, 285–293 (2008).

11 Späth M, Krüger K, Dresel S, Grevers G, Vogl T, Schattenkirchner M: Magnetic resonance imaging of the parotid gland in patients with Sjögren's syndrome. *J. Rheumatol.* 18, 1372–1378 (1991).

12 Izumi M, Eguchi K, Ohki M *et al.*: MR imaging of the parotid gland in Sjögren's syndrome: a proposal for new diagnostic criteria. *AJR Am. J. Roentgenol.* 166, 1483–1487 (1996).

13 Tonami H, Ogawa Y, Matoba M *et al.*: MR sialography in patients with Sjögren syndrome. *AJNR Am. J. Neuroradiol.* 19, 1199–1203 (1998).

14 Sumi M, Takagi Y, Uetani M *et al.*: Diffusion-weighted echoplanar MR imaging of the salivary glands. *AJR Am. J. Roentgenol.* 178(4), 959–965 (2002).

15 Takagi Y, Sumi M, van Cauteren M, Nakamura T: Fast and high-resolution MR sialography using a small surface coil. *J. Magn. Reson. Imaging* 22, 29–37 (2005).

16 El Miedany YM, Ahmed I, Mourad HG *et al.*: Quantitative ultrasonography and magnetic resonance imaging of the parotid gland: can they replace the histopathologic studies in patients with Sjogren's syndrome? *Joint Bone Spine* 71, 29–38 (2004).

▪▪ **Compares ultrasonographic and MRI findings in the parotids of SS patients and correlates the findings with the histopathologic focus scores. A good agreement between MRI, ultrasonography and histopathology focus scores was observed.**

17 Takagi Y, Sumi M, Sumi T, Ichikawa Y, Nakamura T: MR microscopy of the parotid glands in patients with Sjögren's syndrome: quantitative MR diagnostic criteria. AJNR Am. J. Neuroradiol. 26, 1207–1214 (2005).

18 Sumi M, Yamada T, Takagi Y, Nakamura T: MR imaging of labial glands. *AJNR Am. J. Neuroradiol.* 28, 1552–1556 (2007).

19 Kawai Y, Sumi M, Kitamori H, Takagi Y, Nakamura T: Diffusion-weighted MR microimaging of the lacrimal glands in patients with Sjögren's syndrome. *AJR Am. J. Roentgenol.* 184, 1320–1325 (2005).

20 Lomas DJ, Carroll NR, Johnson G, Antoun NM, Freer CE: MR sialography. Work in progress. *Radiology* 200, 129–133 (1996).

21 Fischbach R, Kugel H, Ernst S *et al.*: MR sialography: initial experience using a T2-weighted fast SE sequence. *J. Comput. Assist. Tomogr.* 21, 826–830 (1997).

22 Murakami R, Baba Y, Nishimura R *et al.*: MR sialography using half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequences. *AJNR Am. J. Neuroradiol.* 19, 959–961 (1998).

23 Ohbayashi N, Yamada I, Yoshino N, Sasaki T: Sjögren syndrome: comparison of assessments with MR sialography and conventional sialography. *Radiology* 2093, 683–688 (1998).

24 Matos C, Metens T, Devière J *et al.*: Pancreatic duct: morphologic and functional evaluation with dynamic MR pancreatography after secretin stimulation. *Radiology* 203, 435–441 (1997).

25 Nicaise N, Pellet O, Metens T *et al.*: Magnetic resonance cholangiopancreatography: interest of IV secretin administration in the evaluation of pancreatic ducts. *Eur. Radiol.* 8, 16–22 (1998).

26 Morimoto Y, Habu M, Tomoyose T *et al.*: Dynamic magnetic resonance sialography as a new diagnostic technique for patients with Sjögren's syndrome. *Oral Dis.* 12, 408–414 (2006).

27 Niemelä RK, Pääkkö E, Suramo I, Takalo R, Hakala M: Magnetic resonance imaging and magnetic resonance sialography of parotid glands in primary Sjögren's syndrome. *Arthritis Rheum.* 45, 512–518 (2001).

28 Ariji Y, Ohki M, Eguchi K *et al.*: Texture analysis of sonographic features of the parotid gland in Sjögren's syndrome. *AJR Am. J. Roentgenol.* 166, 935–941 (1996).

29 Thoeny HC, De Keyzer F, Claus FG, Sunaert S, Hermans R: Gustatory stimulation changes the apparent diffusion coefficient of salivary glands: initial experience. *Radiology* 235, 629–634 (2005).

30 O'Connor JP, Jackson A, Parker GJ, Jayson GC: DCE-MRI biomarkers in the clinical evaluation of antiangiogenic and vascular disrupting agents. *Br. J. Cancer* 96, 189–195 (2007).

31 Evelhoch JL: Key factors in the acquisition of contrast kinetic data for oncology. *J. Magn. Reson. Imaging* 10, 254–259 (1999).

32 Roberts C, Parker GJ, Rose CJ *et al.*: Glandular function in Sjögren syndrome: assessment with dynamic contrast-enhanced MR imaging and tracer kinetic modeling – initial experience. *Radiology* 246, 845–853 (2008).

▪▪ **Evaluates the glandular function of patients with SS using dynamic MRI. Compared with normal individuals, patients with SS showed a significant difference in microvascular function of the parotid glands.**

33 Vinagre F, Santos MJ, Prata A, da Silva JC, Santos AI: Assessment of salivary gland function in Sjögren's syndrome: the role of salivary gland scintigraphy. *Autoimmun. Rev.* (2009) (Epub ahead of print).

▪ **Describes salivary gland scintigraphy and suggests methods for the development and standardization of quantitative indices that might prove useful for the assessment of glandular function in SS.**

34 Schall GL, Larson SM, Anderson LG, Griffith JM: Quantification of parotid gland uptake of pertechnectate using a γ scintilation camera and a 'region-of-interest' system. *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 115, 689–697 (1972).

35 Hermann GA, Vivino FB, Goin JE: Scintigraphic features of chronic sialadenitis and Sjögren's syndrome: a comparison. *Nucl. Med. Commun.* 20, 1123–1132 (1999).

36 Loutfi I, Nair MK, Ebrahim AK: Salivary gland scintigraphy: the use of semiquantitative analysis for uptake, and clearance. *J. Nucl. Med. Technol.* 31, 81–85 (2003).

37 Aung W, Murata Y, Ishida R, Takahashi Y, Okada N, Shibuya H: Study of quantitative oral radioactivity in salivary gland scintigraphy and determination of the clinical stage of Sjögren's syndrome. *J. Nucl. Med.* 42, 38–43 (2001).

38 Salaffi F, Carotti M, Iagnocco A *et al.*: Ultrasonography of salivary glands in primary Sjögren's syndrome: a comparison with contrast sialography and scintigraphy. *Rheumatology (Oxford)* 47, 1244–1249 (2008).

39 Niemelä RK, Takalo R, Pääkkö E *et al.*: Ultrasonography of salivary glands in primary Sjogren's syndrome. A comparison with magnetic resonance imaging and magnetic resonance sialography of parotid glands. *Rheumatology (Oxford)* 43, 875–879 (2004).

▪▪ **Evaluation of ultrasonography in patients with SS, patients with dry mouth without SS and in normal individuals, and comparison of findings with MRI and MR sialography. MR sialography was found to be the most sensitive method (96%) in detecting glandular changes, followed by MR imaging (81%) and ultrasonography (78%), with 94% specificity using ultrasonography. Focus scores in salivary gland biopsy were related only to parotid MR-imaging findings.**

40 Tonami H, Higashi K, Matoba M, Yokota H, Yamamoto I, Sugai S: A comparative study between MR sialography and salivary gland scintigraphy in the diagnosis of Sjögren syndrome. *J. Comput. Assist. Tomogr.* 25, 262–268 (2001).

▪ **Salivary gland scintigraphy showed higher sensitivity than MR sialography for SS diagnosis. On the other hand, MR sialography showed higher specificity and positive-predictive value than salivary gland scintigraphy. Overall diagnostic accuracy was 83% for MR sialography and 72% for salivary gland scintigraphy.**