Original article

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Validation of quantitative salivary gland scintigraphy in relation to the American–European concensus criteria for Sjögren's syndrome

Herman P. Kaldeway[a], Evert-Jan ter Borg[b], Ewoudt M.W. van de Garde[c], Jan B.A. Habraken[d] and Monique M.C. van Buul[a]

Purpose **The aim of this retrospective study was to evaluate the diagnostic value of semiquantitative parameters in salivary gland scintigraphy (SGS) in the diagnostic work-up of primary Sjögren's Syndrome (SS) using the American–European consensus criteria (AECC) as the gold standard.**

Patients and methods **99mTc-pertechnetate-SGS was performed in 110 patients with suspected primary SS. Uptake ratios (URs) and excretion fractions (EFs) for all parotid and submandibular salivary glands were calculated. Patients were divided into SS-positive, SS-negative, and SS-equivocal groups on the basis of the AECC criteria. SGS semiquantitative parameters were compared per group and cut-off values were defined.**

Results **Ninety-six (87%) women and 14 (13%) men with a mean age of 51 years (range: 18–77 years) were included. All patients underwent SGS, labial biopsy, Schirmer's test, and antibody tests (anti-SS-A and anti-SS-B). Twenty-four patients were SS positive, 56 patients were SS negative, and 30 patients were SS-equivocal. UR of the parotid glands did not differ between SS-positive and SS-negative groups [mean (range): 3.4 (1.4–6.9) and 3.9 (2.2–6.5), respectively], whereas UR of the submandibular glands were significantly lower in SS-positive patients [mean (range): 2.7 (1.1–5.6) and 3.5 (2.3–5.3), respectively]. EF in both parotid and submandibular glands was significantly lower in SS-positive patients compared with SS-negative patients: parotid 24% (range: −4 to 53%) and 36% (range: 15–58%), respectively; submandibular 16% (range: −5 to 46%) and 29% (range: 9–49%), respectively. On the basis of a cut-off value of 2.0 for UR and 20% for EF, the sensitivity, specificity, positive predictive value, and negative predictive value were 0.67, 0.86, 86, and 67%, respectively. Of 30 SS-equivocal patients, 15 had a positive SGS, whereas the other 15 were SGS negative. In both, there was no correlation with the AECC criteria IV (histopathology) and VI (antibodies). In these cases, the SGS result was decisive.**

Conclusion **Quantitative SGS is a valuable tool in the diagnostic management of patients with suspected primary SS, especially in those in whom the nonscintigraphic AECC criteria are not conclusive. The straightforward quantitative analysis of SGS used in this study can be implemented in any nuclear medicine department.** *Nucl Med Commun* **40:343–348**

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[a]Department of Nuclear Medicine, [b]Internal Medicine-Reumatology, [c]Clinical Pharmacology/Radiopharmacy and [d]Medical Physics and Instrumentation, St Antonius Hospital, Nieuwegein, The Netherlands

Correspondence to Herman P. Kaldeway, MD, St Antonius Hospital, Postbox 2500, 3435EM Nieuwegein, The Netherlands
Tel +31 883 207 512; fax +31 883 207 078;
e-mail: p.kaldeway@antoniusziekenhuis.nl

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Introduction

Primary Sjögren's Syndrome (SS) is an inflammatory autoimmune disease characterized by lymphocytic infiltration of the exocrine glands [1]. Predominantly, the lacrimal and salivary glands are affected, although SS can involve all other exocrine glands as well. The condition is relatively common, with a prevalence of 3%. SS occurs more frequently in women, with a female-to-male ratio of 9 : 1. For the diagnoses of SS, the American–European consensus criteria (AECC) are widely accepted (Table 1). These criteria include subjective ocular and oral symptoms, objective measurements of lacrimal and salivary flow rates, demonstration of lymphocyte infiltration in labial salivary gland biopsy, and the presence of antibodies anti-SS-A or anti-SS-B.

With respect to the criteria of salivary gland involvement, conventional salivary gland scintigraphy (SGS) is a safe and noninvasive method to evaluate the separate function of four salivary glands. Traditional SGS focus on the qualitative measurement of delayed uptake or reduced concentration or reduced excretion after provocation with a salivary stimulating agent. In the past decades, several studies have evaluated semiquantitative parameters using different methods [2–17]. Although there is no consensus on the amount of tracer activity, data acquisition, or calculation of parameters, a quantitative evaluation of data seems to be more diagnostic than a qualitative interpretation of the dynamic scan [18,19].

The aim of this study was to evaluate the diagnostic value of semiquantitative parameters in SGS in the

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diagnostic work-up in primary SS using the AECC as the gold standard.

Patients and methods

Data of all patients who underwent SGS in our department of nuclear medicine between February 2003 and March 2014 were reviewed. Patients who were referred with a suspicion of SS and who underwent a labial biopsy were included in the study. Symptom data, results of the Schirmer's test, and antibody test (anti-SS-A and anti-SS-B) were available for all the patients included. Informed consent was waived because of the retrospective nature of the study.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Salivary gland scintigraphy

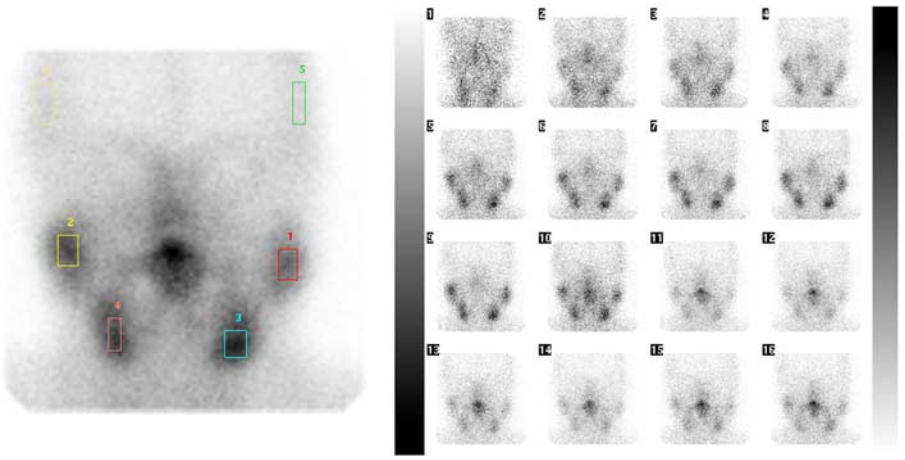
Anterior images were acquired in the supine position with the head placed on a fixing cushion directly after an intravenous administration of 100 MBq ^{99m}Tc-pertechnetate on a single-head gamma camera (Mediso Nucline TH; Mediso Medical Imaging Systems, Budapest, Hungary) with a low-energy high resolution collimator, dynamic scintigraphy, matrix 128 × 128, at 60 s/frame, acquired over 30 min. At the beginning of the tenth minute, 10 ml fresh lemon juice was administered in the mouth using a straw and immediately swallowed. Regions of interest were drawn manually on summed dynamic images: the left and right parotid, left and right submandibular glands, and the left and right parietotemporal bone as the background reference (Fig. 1).

Table 1 International classification criteria for Sjögren Syndrome (American–European Consensus Criteria) [1]

I	Ocular symptoms: a positive response to at least one of the following questions: Have you had daily, persistent, troublesome dry eyes for more than 3 months? Do you have a recurrent sensation of sand or gravel in the eyes? Do you use tear substitutes more than 3 times a day?
II	Oral symptoms: a positive response to at least one of the following questions: Have you had a daily feeling of dry mouth for more than 3 months? Have you had recurrently or persistently swollen salivary glands as an adult? Do you frequently drink liquids to aid in swallowing dry food?
III	Ocular signs, that is, objective evidence of ocular involvement defined as a positive result for at least one of the following two tests: Schirmer's test, performed without anesthesia (< 5 mm in 5 min) Rose Bengal score or other ocular dye score (>4 according to van Bijsterveld's scoring system)
IV	Histopathology: In minor salivary glands (obtained through normal-appearing mucosa) focal lymphocytic sialoadenitis, evaluated by an expert histopathologist, with a focus score > 1, defined as a number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes) per 4 mm^2 of glandular tissue
V	Salivary gland involvement: objective evidence of salivary gland involvement defined by a positive result for at least one of the following diagnostic tests: Unstimulated whole salivary flow (< 1.5 ml in 15 min) Parotid sialography showing the presence of diffuse sialectasias (punctate, cavitary, or destructive pattern), without evidence of obstruction in the major ducts Salivary scintigraphy showing delayed uptake, reduced concentration, and/or delayed excretion of tracer
VI	Antibodies to anti-SS-A or anti-SS-B, or both

In patients without any potentially associated disease, primary SS may be defined as follows:
The presence of any four of the six items is indicative of primary SS as long as either item IV (Histopathology) or VI (Serology) is positive. The presence of any three of the four objective criteria items (i.e. items III, IV, V, and VI).

Fig. 1



Region's of interest in the parotid, submandibular salivary glands, and background.

Table 2 Division of the three groups on the basis of criteria I, II, III, IV, and VI of the American–European consensus criteria

SS positive	SS negative	SS equivocal
III + IV + VI positive	IV + VI negative	All other cases
I + II + III + IV positive	Only IV or VI positive	I + II + IV positive
I + II + III + VI positive	Only IV + I positive	I + II + VI positive
I + II + IV + VI positive	Only IV + II positive	III + IV positive
	Only VI + I positive	III + V positive
	Only VI + II positive	

SS, Sjögren's Syndrome.

Uptake ratio (UR) and excretion fraction (EF) were calculated for each salivary gland. UR was defined as the highest count rate in the ninth or 10th minute divided by the average counts in the ipsilateral background reference between 10 and 20 min ($UR = maximum/BG^{average}$). EF was defined as 1 minus the lowest count rate 2–4 min after lemon juice stimulation divided by the highest count rate in the ninth or 10th minute [$EF = 1 - (minimum/maximum) \times 100\%$)] [3,14].

Gold standard

As there is no single test for the diagnoses of SS, the criteria of the AECC without the SGS results were used to divide the patients into three groups (Table 2):

(1) SS-positive (group 1): patients who fulfill the AECC irrespective of the result of the SGS;
(2) SS-negative (group 2): patients who did not fulfill the AECC irrespective of the result of SGS;
(3) SS-equivocal (group 3): if the result of the SGS would be necessary to determine whether the patient would fulfill the AECC or not.

For labial biopsy, a Chisholm score of 1 or higher was considered positive [1]. Schirmer's test was considered positive if less than or equal to 5 mm paper wetted after 5 min [1].

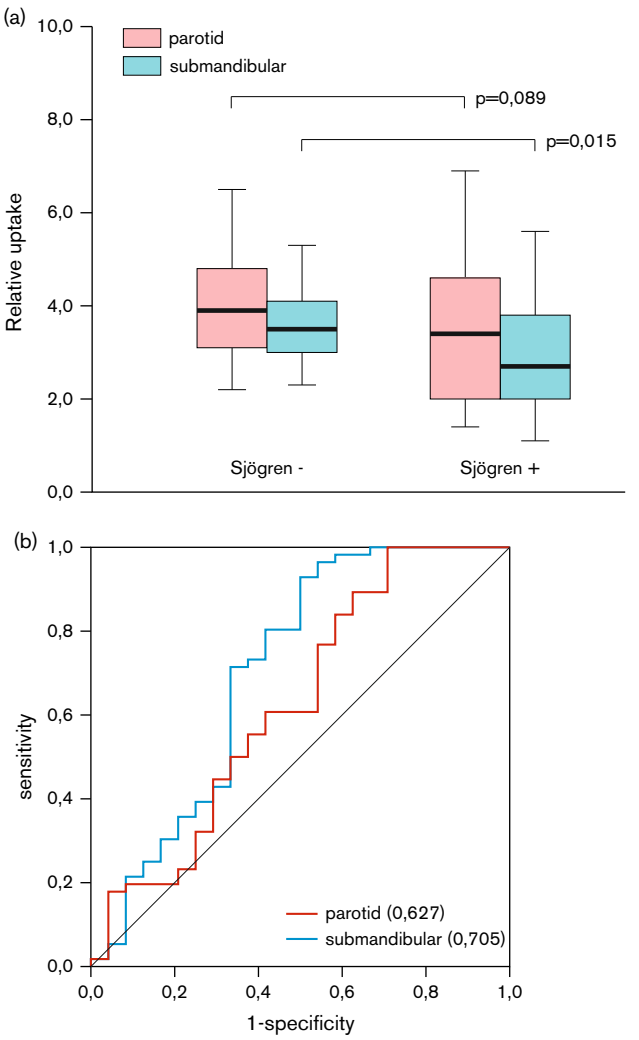
Statistical analysis

Differences between semiquantitative parameters were analyzed using the analysis of variance test. Receiver operating characteristics (ROC) were plotted for both the UR and EF to establish a cut-off value, which was used to determine the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of the SGS.

Results

Initially, 220 patients with suspected SS underwent SGS. In 124 patients, labial biopsy was performed. Fourteen patients were excluded because of incomplete data (in six patients, equivocal biopsy results or inadequate biopsy material were not available, and in eight patients, Schirmer's test was not available). Data of the remaining 110 patients were included for further analysis: 96 (87%) women and 14 (13%) men, with a mean age at the time of SGS of 52 years (range: 18–77 years). Ninety-seven patients reported mouth symptoms, in 77 patients, ocular symptoms were recorded, in 54 patients, Schirmer's test was positive, 40 patients had a biopsy

Fig. 2

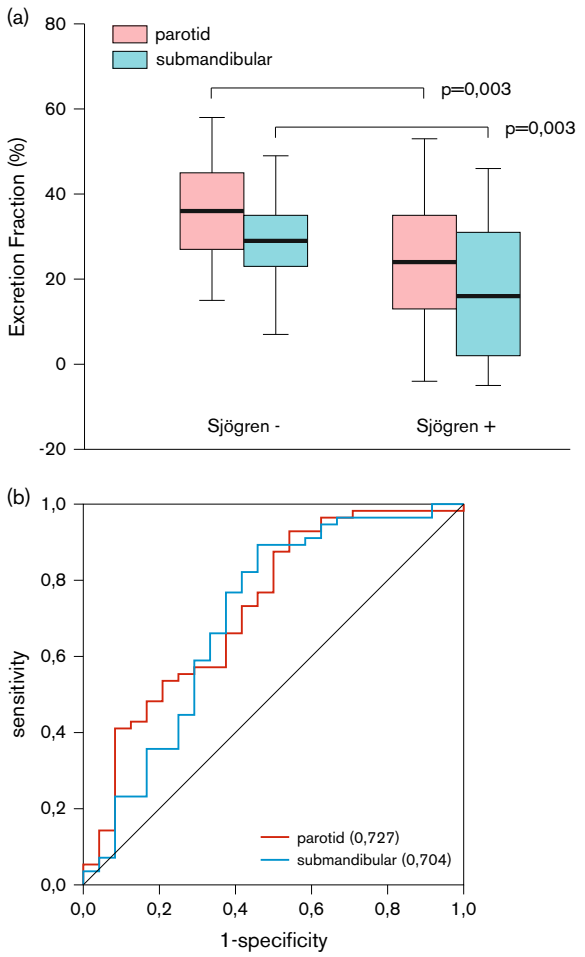


(a) Boxplot of the uptake ratio for both parotid and submandibular salivary glands in the SS-positive group ($N = 24$) and the SS-negative group ($N = 56$). (b) Receiver operating characteristic of uptake ratio in both parotid and submandibular salivary glands. SS, Sjögren's Syndrome.

with Chisholm score 1 or higher, and 40 patients had a positive test for anti-SS-A or anti-SS-B. On the basis of the algorithm described in Table 2, 24 patients could be classified as SS positive, 56 patients as SS negative, and 30 patients as SS-equivocal.

A significant difference in the relative tracer uptake in the parotid between de SS-positive and SS-negative patient groups could not be found [SS-positive 3.4 (range: 1.4–6.9), SS-negative 3.9 (range: 2.2–6.5), $P = 0.089$; Fig. 2a]. However, a significant difference in the relative tracer uptake in the submandibular salivary glands was found [SS positive 2.7 (range: 1.1–5.6), SS negative 3.5 (range: 2.3–5.3), $P = 0.015$; Fig. 2a]. The area under the curve for the relative tracer uptake in the ROC analysis was higher for the submandibular salivary glands than for the parotid glands (Fig. 2b).

Fig. 3



(a) Boxplot of excretion fraction for both parotid and submandibular salivary glands in the SS-positive group ($N = 24$) and the SS-negative group ($N = 56$). (b) Receiver operating characteristic of excretion fraction in both parotid and submandibular salivary glands. SS, Sjögren's Syndrome.

EF in both parotid and submandibular glands was significantly lower in SS-positive patients compared with SS-negative patients: parotid 24% (range: −4 to 53%) and 36% (range: 15–58%), respectively.

The same significant difference between SS-positive and SS-negative patients was observed in the submandibular glands, although the mean EF was slightly lower than that in the parotid glands: 16% (range: −5–46%) and 29% (range: 9–49%), respectively. The area under the curve of the EF in ROC was higher than that of the UR (Fig. 3b).

On the basis of the ROC of both the UR and the EF, a cut-off value of 2.0 was proposed for the UR and 20% for the EF. These values were used to evaluate the sensitivity and specificity of the salivary scintigraphy. If at least one out of four salivary glands had an UR below 2.0 or an EF below 20%, SGS was considered positive for SS; if all four glands had an UR of 2.0 or higher and an EF of 20% and higher, the test was considered negative.

Table 3 Results of salivary gland scintigraphy in Sjögren's Syndrome-positive and Sjögren's Syndrome-negative patients on the basis of cut-off values of a uptake ratio of 2.0 or an excretion fraction of 20%

	Clinical evaluation		
SGS	SS positive	SS negative	Total
Positive	16	8	56
Negative	8	48	24
Total	24	56	80

SGS, salivary gland scintigraphy; SS, Sjögren's Syndrome.

Table 4 No correlation between result of salivary gland scintigraphy, histopathology, and autoantibodies in the Sjögren's Syndrome-equivocal group

	Histopathology in SS-equivocal patients		Antibodies in SS-equivocal patients	
SGS	Positive	Negative	Positive	Negative
Positive ($n = 15$)	10	5	11	4
Negative ($n = 15$)	9	6	7	8
Total	19	11	18	12

SGS, salivary gland scintigraphy; SS, Sjögren's Syndrome.

Scintigraphic results

On the basis of this algorithm, 16 (67%) out of 24 SS-positive patients had a positive SGS, whereas 48 (86%) out of 56 SS-negative patients had a negative SGS, leading to a sensitivity, specificity, NPV, PPV, positive likelihood ratio, and negative likelihood ratio of the salivary scintigraphy of 0.67, 0.86, 86, 67, 4.8, and 0.38%, respectively (Table 3).

In 30 SS-equivocal patients, 15 had a positive SGS and the other 15 had a negative SGS. There was no correlation between the result of SGS and the AECC criteria IV (histopathology) and VI (antibodies) (Table 4). In these cases, SGS was decisive. In five patients, SS was confirmed, whereas labial biopsy was negative, in nine patients, SS was rejected, whereas labial biopsy was abnormal, in four patients, SS was confirmed with negative anti-SS-A or anti-SS-B antibodies, and in seven patients, SS was rejected in case of positive anti-SS-A or anti-SS-B antibodies.

Discussion

Planar SGS is a relatively easy and noninvasive method to explore salivary gland function for different indications such as developmental anomalies, obstructive disorders, autoimmune syndromes, or dysfunction after iodine-131 or radiotherapy [20,21]. One of the first methods used by Schall *et al.* [22] is based on tracer accumulation and unstimulated excretion. A grading system was introduced to determine the severity of salivary gland involvement in SS on the basis of the patterns of

Table 5 List of studies investigating salivary gland scintigraphy in correlation with Sjögren's Syndrome

References	Patients	Quantification method	Results
Bohuslavizki *et al.* [2]	13 SS patients 172 Controls	Uptake%, EF	Lower uptake and EF in SS compared with controls
Klutmann *et al.* [3]	312 Normal participants	Uptake%, EF	Lower limit of uptake and EF defined
Umehara *et al.* [4]	39 SS patients 12 Controls	UR, MA, MS, T_{max}, T_{min}	Lower UR, MA and MS in SS compared with controls
Aung *et al.* [5]	70 SS patients 21 Controls	UR, MA, MS, T_{max}, T_{min}, PRI, POI, SV	Decrease in POI, PRI, TI, MA, and UR with progression of disease
Adams *et al.* [6]	17 SS patients, 18 patients other autoimmune disease 15 Controls	UR, MA, MS, PRI, T_{max}	Lower UR in SS patients, large overlap in quantification parameters between groups
Loutfi *et al.* [7]	21 Controls	UR, EF	–
Shizukuiski *et al.* [8]	124 SS patients 11 Controls	EF, TSS	Inverse correlation with Saxon test
Booker *et al.* [9]	40 SS patients 43 patients with xerostomia 26 Controls	UR, MA, EF, PRI, POI, P : S ratio	Large overlap in parameters between groups
Nishiyama *et al.* [10]	45 SS patients 23 Controls	PC, US, ES, EF	Lower PC, US, and ES in SS patients compared with controls, no difference in EF
Hendriksen *et al.* [11]	Eight SS patients 16 Patients with isolated sicca	T_{max}, *C*%, *E*%	Decreased T_{max}, *C*% and *E*% in SS patients compared with patients with isolated sicca
Günel *et al.* [12]	27 SS patients 10 Controls	UR, MS	Decrease in UR and MS in advanced stage SS
Ramos-Casals *et al.* [13]	405 SS patients	Schall classification [20]	Higher classification showed a higher risk of developing systemic features and a lower survival rate
Aksoy *et al.* [14]	30 SS patients	EF	Correlation between EF and histopathologic grades
Zou *et al.* [15]	95 SS patients 36 Controls	UR, EF	UR and EF were signifantly lower in SS patients compared with the controls
Dugonjic *et al.* [16]	20 SS patients 10 Controls	T_{max}, T_{min}, MA, AV, MA, MS, SV, UR	Abnormal values of SGS parameters in SS patients compared with the controls
Kim *et al.* [17]	145 Patients clinically suspicious SS	Schall classification, UR, EF	UR and EF were lower in the SS group compared with the non-SS group

AV, accumulation velocity; *C*%, peak tracer distribution; *E*%, stimulated excretion; EF, excretion fraction; ES, excretion speed; MA, maximum accumulation; MS, maximum secretion; P : S ratio, ratio between parotid and submanibular salivary glands; pC, peak count; POI, poststimulatory oral index; PRI, prestimulatory oral index; SV, secretion velocity; T_{max}, time at maximum counts; T_{min}, time interval from stimulation to minimum counts; TSS, total scintigraphic scores; uptake%, percentage uptake of injected tracer; UR, uptake ratio; US, uptake speed.

pertechnetate accumulation in salivary glands. This method is still considered the standard method, despite the limitation that it is observer dependent and does not evaluate stimulated excretion.

In the past two decades, a wide variety of quantification methods used in SGS for the diagnosis of SS have been published in the literature (Table 5). The methods of SGS in these studies varied in ^{99m}Tc-pertechnetate dosage (85–555 MBq), acquisition duration (20–60 min), timing of salivary gland stimulation (10–40 min after injection), and method of salivary gland stimulation (lemon juice, vitamin C drops, carbachol injection, or hard lemon tablet). This variety in acquisition parameters does not allow a comparison between studies and trials [18,19,23].

The validation method in our study is unique as we compared SGS not only with histopathology but with all criteria of the AECC. We believe that by including oral and ocular symptoms, Schirmer's test, and anti-SS-A or anti-SS-B antibodies in the validation process, the final outcome is more precise and could potentially prevent false-positive or false-negative results.

In our study, the area under the curve in the ROC of the ejection fraction was higher than that of the UR, suggesting that EF is a more sensitive parameter in SGS than the UR. This has been confirmed by other studies [2,4,14–17]. However, one study by Nishiyama and colleagues could not confirm a difference in EF between SS patients and healthy controls [11]. A statistically significant difference in UR in the submandibular salivary glands between the SS-positive group and the SS-negative group could be established. Such a difference could not be confirmed for the parotids.

A considerable overlap in UR and to a lesser extent in EF was observed for both the parotid and submandibular glands between the SS-positive group and the SS-negative group. Such an overlap was also found in other studies [6,9].

Almost none of the studies that we found in the literature reported sensitivity, specificity, PPV, or NPV of SGS, except Kim *et al.* [17], who found a sensitivity, specificity, PPV, and NPV of 88.2, 48.6, 65.1, and 79.1%, respectively. In that study, visual analysis was found to have a greater diagnostic utility than a semiquantitative assessment. This might explain the higher sensitivity and much lower specificity compared with our study.

Study limitations

This was a retrospective study, which might have led to some bias in a sense that probably not all patients suspected for SS in our clinic were referred for SGS.

In addition, the use of concomitant medication at the time of salivary scintigraphy was not recorded methodically.

Anticholinergic drugs such as SSRIs or opioids could possibly influence the outcome of SGS, although, to our knowledge, no study has been carried out to determine the influence of concomitant medication on the outcome of SGS.

Conclusion

Quantitative SGS is a valuable tool in the diagnostic management of patients with suspected primary SS, especially in those in whom the nonscintigraphic AECC criteria are not conclusive. Therefore, it is worth keeping experience in this underused nuclear medicine investigation. The straightforward quantitative analysis of SGS carried out in this study can be implemented in any nuclear medicine department. Future review is necessary to harmonize the rules for preparation of the patient and acquisition protocols, and optimize quantification parameters and normal values.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, *et al*. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American–European Consensus Group. *Ann Rheum Dis* 2002; **61**:554–558.

2 Bohuslavizki KH, Brenner W, Wolf H, Sippel C, Tönshoff G, Tinnemeyer S, *et al*. Value of quantitative salivary gland scintigraphy in the early stage of Sjögren's syndrome. *Nucl Med Commun* 1995; **16**:917–922.

3 Klutmann S, Bohuslavizki KH, Kröger S, Bleckmann C, Brenner W, Mester J, *et al*. Quantitative salivary gland scintigraphy. *J Nucl Med Technol* 1999; **27**:20–26.

4 Umehara I, Yamada I, Murata Y, Takahashi Y, Okada N, Shibuya H. Quantitative evaluation of salivary gland scintigraphy in Sjörgen's syndrome. *J Nucl Med* 1999; **40**:64–69.

5 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* 2001; **42**:38–43.

6 Adams BK, Al Attia HM, Parkar S. Salivary gland scintigraphy in Sjögren's syndrome: are quantitative indices the answer? *Nucl Med Commun* 2003; **24**:1011–1016.

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

8 Shizukuishi K, Nagaoka S, Kinno Y, Saito M, Takahashi N, Kawamoto M, *et al*. Scoring analysis of salivary gland scintigraphy in patients with Sjögren's syndrome. *Ann Nucl Med* 2003; **17**:627–631.

9 Booker J, Howarth D, Taylor L, Voutnis D, Sutherland D. Appropriate utilization of semi-quantitative analysis in salivary scintigraphy. *Nucl Med Commun* 2004; **25**:1203–1210.

10 Nishiyama S, Miyawaki S, Yoshinaga Y. A study to standardize quantitative evaluation of parotid gland scintigraphy in patients with Sjögren's syndrome. *J Rheumatol* 2006; **33**:2470–2474.

11 Henriksen AM, Nossent HC. Quantitative salivary gland scintigraphy can distinguish patients with primary Sjøgren's syndrome during the evaluation of sicca symptoms. *Clin Rheumatol* 2007; **26**:1837–1841.

12 Günel S, Yilmaz S, Karalezli A, Aktaş A. Quantitative and visual evaluation of salivary and thyroid glands in patients with primary Sjögren's syndrome using salivary gland scintigraphy: relationship with clinicopathological features of salivary, lacrimal and thyroid glands. *Nucl Med Commun* 2010; **31**:666–672.

13 Ramos-Casals M, Brito-Zerón P, Perez-DE-Lis M, Diaz-Lagares C, Bove A, Soto MJ, *et al*. Clinical and prognostic significance of parotid scintigraphy in 405 patients with primary Sjogren's syndrome. *J Rheumatol* 2010; **37**:585–590.

14 Aksoy T, Kiratli PO, Erbas B. Correlations between histopathologic and scintigraphic parameters of salivary glands in patients with Sjögren's syndrome. *Clin Rheumatol* 2012; **31**:1365–1370.

15 Zou Q, Jiao J, Zou MH, Xu JH, Pan YF, Chen JN, *et al*. Semi-quantitative evaluation of salivary gland function in Sjögren's syndrome using salivary gland scintigraphy. *Clin Rheumatol* 2012; **31**:1699–1705.

16 Dugonjić S, Stefanović D, Ethurović B, Spasić-Jokić V, Ajdinović B. Evaluation of diagnostic parameters from parotid and submandibular dynamic salivary glands scintigraphy and unstimulated sialometry in Sjögren's syndrome. *Hell J Nucl Med* 2014; **17**:116–122.

17 Kim HA, Yoon SH, Yoon JK, Lee SJ, Jo KS, Lee DH, *et al*. Salivary gland scintigraphy in Sjögren's syndrome. Comparison of the diagnostic performance of visual and semiquantitative analysis. *Nuklearmedizin* 2014; **53**:139–145.

18 Vivino FB, Hermann GA. Role of nuclear scintigraphy in the characterization and management of the salivary component of Sjögren's syndrome. *Rheum Dis Clin North Am* 2008; **34**:973–986.

19 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; **8**:672–676.

20 van den Akker HP, Busemann-Sokole E. Absolute indications for salivary gland scintigraphy with ^{99m}Tc-pertechnetate. *Oral Surg Oral Med Oral Pathol* 1985; **60**:440–447.

21 Liem IH, Olmos RA, Balm AJ, Keus RB, van Tinteren H, Takes RP, *et al*. Evidence for early and persistent impairment of salivary gland excretion after irradiation of head and neck tumours. *Eur J Nucl Med* 1996; **23**:1485–1490.

22 Schall GL, Larson SM, Anderson LG, Griffith JM. Quantification of parotid gland uptake of pertechnetate using a gamma scintillation camera and a 'region-of-interest' system. *Am J Roentgenol Radium Ther Nucl Med* 1972; **115**:689–697.

23 Milic VD, Petrovic RR, Boricic IV, Marinkovic-Eric J, Radunovic GL, Jeremic PD, *et al*. Diagnostic value of salivary gland ultrasonographic scoring system in primary Sjogren's syndrome: a comparison with scintigraphy and biopsy. *J Rheumatol* 2009; **36**:1495–1500.