Quantitative Texture Analysis of Parotid Gland Ultrasound Images Yield Higher Correlation with Scintigraphy than Semiquantitative Scoring in Primary Sjögren's Syndrome Patients

CME Credits

Cheng-Hsun Lu[1,2], Yi-Min Huang[3], Song-Chou Hsieh[1], Ko-Jen Li[1]*

[1]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [2]Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan, [3]Department of Internal Medicine, National Taiwan University Hospital, Yunlin, Taiwan

Abstract

Background: Ultrasound (US) can detect salivary gland abnormalities in primary Sjögren's syndrome (SS). This study aimed to compare the correlation among the semiquantitative US scores, texture features, and the quantitative salivary gland scintigraphy (SGS) results. **Methods:** This retrospective study included 11 patients who were diagnosed with primary SS and underwent US examinations of the parotid glands and SGS simultaneously. We evaluated SGS quantitatively based on the calculation of maximum accumulation ratio (MAR) and stimulated excretion fraction (EF). The US findings were accessed through the semiquantitative Outcome Measures in Rheumatology scoring system and by gray-level co-occurrence matrix (GLCM) texture analysis. Spearman's rank correlation tests were performed. **Results:** A significant moderate negative correlation was noted between the semiquantitative US score and MAR (rho = −0.57, $P = 0.006$), but not with EF (rho = −0.11, $P = 0.613$). The GLCM texture metrics, including contrast, dissimilarity, and homogeneity, were all determined to be significantly associated with both MAR and EF. The GLCM contrast correlated moderately to MAR (rho = −0.66, $P = 0.001$). The GLCM homogeneity highly correlated to EF (rho = 0.74, $P < 0.001$). The contrast and homogeneity can still discriminate the changes in MAR and EF in the subgroups with the same semiquantitative US scores. **Conclusion:** US findings on parotid gland can correlate with SGS results when analyzed based on GLCM texture features. With the GLCM texture metrics, US appears to be an excellent imaging tool for the assessment of the parotid glands in primary SS patients.

Keywords: Gray-level co-occurrence matrix texture analysis, parotid gland, scintigraphy, Sjögren's syndrome, ultrasound

Introduction

Primary Sjögren's syndrome (SS) is a common systemic autoimmune disease.[1] This disease is often characterized by exocrinopathy, and especially affects the salivary and lacrimal glands. Biopsy of minor salivary glands is invasive, but may help to establish the diagnosis of primary SS. The typical histopathological SS features are included in the revised classification criteria proposed by the American–European Consensus Group (AECG) and the 2016 American College of Rheumatology (ACR)–European League Against Rheumatism (EULAR) classification criteria.[2,3] Xerostomia associated with salivary gland dysfunction has been identified as the hallmark symptom of primary SS. Salivary gland scintigraphy (SGS) has been used for a long time in the evaluation of primary SS.[4] SGS correlates with histopathological findings within salivary glands of primary SS patients, and is a validated imaging technique that provides an objective means to detect dysfunction of each major salivary gland.[5-7] Quantitative SGS has been proved to be a sensitive and reliable method. The

Received: 25-08-2021 **Revised:** 28-11-2021 **Accepted:** 01-05-2022 **Available Online:** 05-07-2022

Supplementary material available online

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jmut

DOI: 10.4103/jmu.jmu_173_21

Address for correspondence: Dr. Ko-Jen Li, Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, National Taiwan University Hospital, No. 7, Chung Shan S. Road, Taipei 10002, Taiwan. E-mail: dtmed170@gmail.com

How to cite this article: Lu CH, Huang YM, Hsieh SC, Li KJ. Quantitative texture analysis of parotid gland ultrasound images yield higher correlation with scintigraphy than semiquantitative scoring in primary sjögren's syndrome patients. J Med Ultrasound 2023;31:112-8.

maximum accumulation ratio (MAR) and stimulated excretion fraction (EF) can be calculated to quantify glandular activity, and these parameters derived from SGS can contribute to the detection of salivary gland dysfunction in SS patients.[5,7-10] Even though SGS was omitted from the 2016 ACR–EULAR classification criteria, it is still often used as a reference benchmark for the investigation of other imaging techniques.[11-13]

The 2016 ACR–EULAR classification criteria for primary SS also provide an opportunity for the use of new diagnostic tests, such as parotid ultrasonography.[3,13] Ultrasound (US) is a valuable noninvasive tool used for the detection of salivary gland abnormalities, and it also has the advantage of accessibility, repeatability, and low cost. Nevertheless, its diagnostic reliability has not been investigated extensively.[14] Thus, a validated and standardized US definition of salivary gland in primary SS is required. One early study showed significant differences between salivary gland US and SGS examinations.[11] Another research reported a good intermodality agreement between the parotid US and sialography, despite the fact that the ability of the parotid US to diagnose SS was significantly lower.[15] To facilitate the use of US for diagnosing and monitoring of changes in the glands, the emerging Outcome Measures in Rheumatology clinical trials (OMERACT) consensus-based semiquantitative grayscale scoring system for major salivary gland lesions was developed. Substantial inter-reader and intra-reader reliabilities have been demonstrated.[16,17]

In addition, the gray-level co-occurrence matrix (GLCM) is a common method used for texture feature extraction that has been applied for the quantitative analysis of US image data of various lesions.[18-20] The GLCM contains objective and quantitative information on image texture characteristics, such as homogeneity. Inhomogeneity is exactly one of the characteristic US features in SS.[16] However, only a few studies have applied the GLCM technique on the ultrasonic texture evaluations of salivary glands. The sonographic parotid gland features may serve as imaging signatures to assess radiation-induced injury and to predict xerostomia.[21,22] To this date, no other research study has validated the features of GLCM with SGS in patients with primary SS. More evidence for the application of US GLCM texture analysis is thus required.

As such, we conducted this retrospective study involving patients classified with primary SS who underwent simultaneous US examination and SGS of parotid glands. Our aim was to explore the correlation among the US texture features, semiquantitative scores, and the quantitative evaluation of SGS.

Patients and Methods

Study design

This retrospective study was conducted at the National Taiwan University Hospital, Taipei, Taiwan. All the datasets from the 70 patients with xerostomia who underwent US examinations of the parotid glands in the department of rheumatology from July 2011 to June 2019 were reviewed. The patients who were diagnosed of primary SS were then screened for eligibility. The classifications of primary SS were based on the 2002 AECG classification criteria and the 2016 ACR–EULAR classification criteria.[2,3] Those who simultaneously underwent SGS with ^{99m}Tc sodium pertechnetate were included in this study. We excluded patients with ages <20 years, parotid gland infection, parotid tumors, and a history of parotidectomy. Eleven patients met the eligibility criteria for this study. Their clinical features are summarized in Table 1. Their median age was 46.1 years, and 10 (90.9%) of them were female.

Quantitative evaluation of salivary gland scintigraphy

After intravenous injection of 8 mCi ^{99m}Tc sodium pertechnetate, serial images were acquired every 60 s for 30 min. At the 15th min after the injection, an ascorbic acid tablet (500 mg) was administered intraorally as a stimulus. To quantify the glandular activity, three values were obtained for each parotid gland: (A) the ratio of the uptake to the background activity during the 1st min represents the baseline perfusion, (B) the ratio of the uptake to the background activity at the 15th min represents the maximum activity point before stimulation, and (C) the ratio of the uptake to the background activity at the 30th min represents the minimum activity point after stimulation. The MAR and EF can be calculated as described previously.[7-9] MAR is expressed in the form of $\left(\frac{B-A}{B}\right)\times 100\%$, and EF is $\left(\frac{B-C}{B}\right)\times 100\%$. No patient received pilocarpine or cevimeline within 1 day before scintigraphy.

Table 1: Demographics and clinical biomarkers of the patients with Sjögren's syndrome included in this study (n=11)

Variable	*N* (%) (or median [IQR])
Age (years), median (IQR)	46.1 (40.0-53.0)
Gender (female)	10 (90.9)
Antinuclear antibody (positive)	7 (63.6)
Anti-SSA antibodies (positive)	7 (63.6)
Anti-SSB antibodies (positive)	5 (45.5)
RF (positive)	3 (27.3)
IgG (mg/dl), median (IQR)	1680 (1300-2300)
Abnormal histopathology (positive)‡	4 (36.4)
ESSDAI, median (IQR)	2 (2-3)
SGS of parotid glands (n=22)§	
Maximum accumulation ratio, median (IQR)	66.7 (57.2-71.4)
Excretion fraction, median (IQR)	6.0 (−21.4-36.4)
Semiquantitative OMERACT US score (n=22)§	
OMERACT Grade 0	1 (4.5)
OMERACT Grade 1	10 (45.5)
OMERACT Grade 2	9 (40.9)
OMERACT Grade 3	2 (9.1)

‡Histopathology reports were available only in four patients, §Bilateral parotid glands of each patient were analyzed separately. IQR: Interquartile range, RF: Rheumatoid factor, IgG: Immunoglobulin G, SGS: Salivary gland scintigraphy, US: Ultrasound, OMERACT: Outcome measures in rheumatoid arthritis clinical trials, ESSDAI: European Eague Gainst Heumatism Sjögren's Syndrome Disease Activity Index, SS: Sjögren's syndrome

Ultrasound assessment and semiquantitative scoring

US examinations were conducted with a Toshiba Xario XG US system (Toshiba Medical Systems Corporation, Tochigi, Japan), with the use of a broadband 7.2–14 MHz linear array transducer. The US examinations were conducted by rheumatologists who had been certified by the Chinese Taipei Society of US in Medicine and had >2 years of experience in scanning salivary glands. Ultrasonographies of the parotid glands were performed with the standard imaging technique, as reported previously.[23] The emerging OMERACT semiquantitative grayscale scoring system for SS was then applied, and the grading was conducted by an experienced assessor blinded to the clinical information. The validated scoring system graded the ultrasonographic changes of major salivary glands: Grade 0, normal; Grade 1, minimal inhomogeneity without anechoic or hypoechoic areas; Grade 2, moderate inhomogeneity with focal anechoic or hypoechoic areas; and Grade 3, severe inhomogeneity with diffuse anechoic or hypoechoic areas occupying the entire gland or fibrous gland.[16,17]

Ultrasound gray-level co-occurrence matrix texture analysis

The GLCM texture metrics in the study were calculated through the use of software R (version 4.0.5, R Foundation for Statistical Computing, Vienna, Austria) with the package GLCM Textures (Ilich, Alexander R. 2020.http://doi.org/10.5281/zenodo. 4310187). The GLCM feature extraction method consisted of several steps [Figure 1]. At the beginning, the longitudinal US image that contained maximum parenchymal area was selected for each parotid gland. The image was then cropped to a rectangular shape. After the intensities were normalized and after all the values of the raster graphics were converted to a numeric mode, GLCMs were then created. There were eight exploratory metrics of GLCM adopted in this study: contrast, dissimilarity, homogeneity, angular second moment, entropy, mean, variance, and correlation. The definitions of these textural features have been described in detail in the literature.[21,24] These metrics can be divided into three groups: the contrast group (contrast, dissimilarity, and homogeneity), the orderliness group (angular second moment and entropy), and the descriptive statistics group (mean, variance, and correlation). These measures were calculated by setting the inter-pixel distance of one in four directions (shifts of 0°, 45°, 90°, and 135°), and were then combined to one rotation-invariant texture [Figure 1c]. The metrics from the rotation-invariant texture were used for statistical analyses.

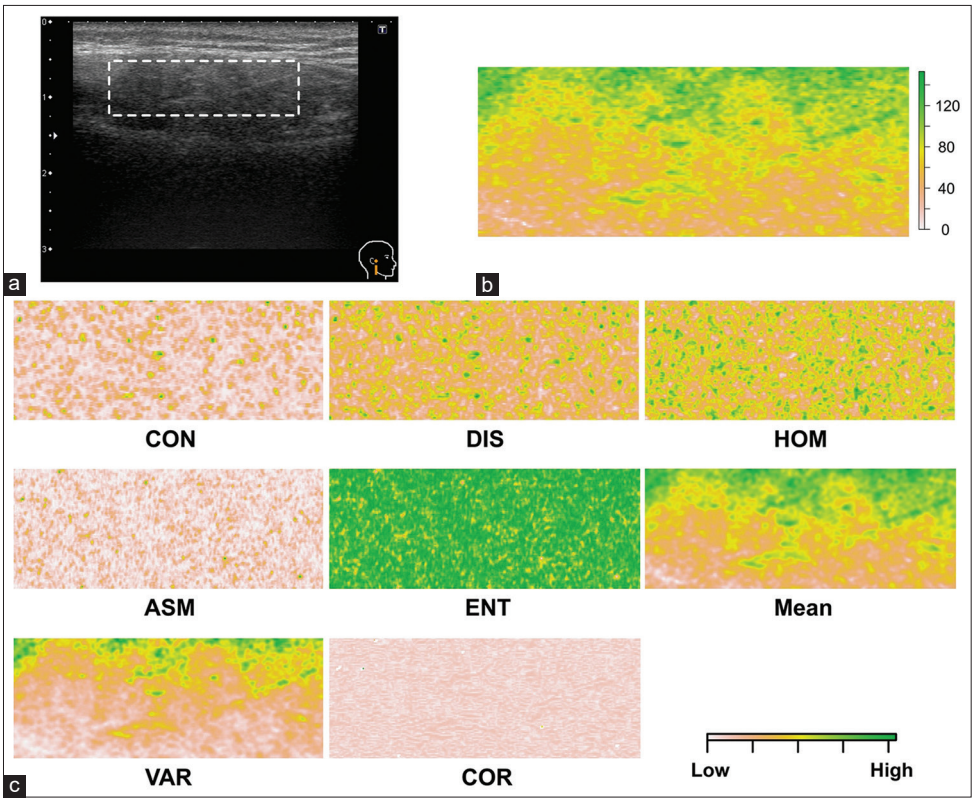

Figure 1: Example demonstrating texture analysis using the GLCM. A left parotid gland with Grade 1 findings was examined with US, wherein mild inhomogeneity without anechoic area was found (a). The images containing maximized parenchymal area would then be selected for analysis (a, dotted-line rectangle). After cropping the image into a rectangular shape, the raster graphics were converted to a matrix (b). Subsequently, GLCMs could be created with the R package GLCMTextures. Eight GLCM metrics were then explored and adopted in this study: CON, DIS, HOM, ASM, ENT, mean, VAR, and COR. The textural features were calculated in all four directions (0°, 45°, 90°, and 135°), and were then combined to one rotation-invariant texture (c). GLCM: Gray-level co-occurrence matrix, US: Ultrasound, CON: Contrast, DIS: Dissimilarity, HOM: Homogeneity, ASM: Angular second moment, ENT: Entropy, VAR: Variance, COR: Correlation

Statistical analyses

All statistical analyses were conducted with the use of software R. Spearman's rank correlation analysis was used to evaluate the correlation among the parotid glandular activity of SGS, OMERACT scores, and the metrics of GLCM. A Spearman's correlation coefficient (rho) ≥0.5 or ≤−0.5 indicated a moderate to high correlation.[25] Associations with $P < 0.05$ were considered a statistically significant.

Ethics statement

The study protocol was approved by the Institutional Review Board and Ethical Committee of National Taiwan University Hospital, Taipei, Taiwan (202001077RINC). The patient consent was waived by the IRB.

Results

Clinical features of patients

Table 1 lists a summary of the demographics and clinical biomarkers of the participants. The diagnosis of primary SS was mainly based on the clinical evaluation and the presence of specific autoantibodies. Four cases received salivary gland biopsies for diagnosis, and the histopathological findings were both indicative of primary SS. In the clinical interpretation of US findings, the median number (interquartile range) of the OMERACT semiquantitative score was 1.5 (interquartile range = 1–2).

Correlation between US findings and quantitative salivary gland scintigraphy

The associations among the semiquantitative scores, the US texture features, and the quantitative glandular activity of SGS are summarized in Table 2. With the OMERACT scoring system, the semiquantitative score exhibited a significant negative correlation to MAR (rho = −0.57, $P = 0.006$), but not to EF (rho = −0.11, $P < 0.613$). Among the contrast group of GLCM texture metrics, the contrast was significantly negatively and moderately correlated to MAR (rho = −0.66, $P = 0.001$), and yielded a low correlation to EF (rho = −0.46, $P = 0.032$). The dissimilarity was significantly negatively and moderately correlated to both MAR (rho = −0.62, $P = 0.003$) and EF (rho = −0.52, $P = 0.014$). The homogeneity was significantly positively and moderately correlated to MAR (rho = 0.53, $P = 0.012$), and was highly correlated to EF (rho = 0.74, $P < 0.001$). Among the orderliness and descriptive statistics groups of GLCM texture metrics, only a low negative correlation was determined between the variance and MAR.

Table 2: Correlation between the parotid glandular activity of salivary gland scintigraphy and the indices of outcome measures in rheumatoid rthritis clinical trials scores and gray-level co-occurrence matrix texture features ($n = 22$)

Variables	Spearman's rho (P)	
	MAR	EF
Age at ultrasound assessment	0.03 (0.889)	<0.01 (0.984)
ESSDAI	−0.20 (0.362)	−0.22 (0.321)
OMERACT score	−0.57 (0.006)**	−0.11 (0.613)
GLCM texture features		
Contrast	−0.66 (0.001)**	−0.46 (0.032)*
Dissimilarity	−0.62 (0.003)**	−0.52 (0.014)*
Homogeneity	0.53 (0.012)*	0.74 (<0.001)**
Angular second moment	0.09 (0.705)	−0.05 (0.813)
Entropy	−0.16 (0.479)	0.14 (0.544)
Mean	−0.30 (0.175)	0.06 (0.797)
Variance	−0.44 (0.042)*	−0.33 (0.133)
Correlation	−0.13 (0.561)	−0.13 (0.551)

*$P<0.05$, **$P<0.01$. ESSDAI: European league against rheumatism Sjögren's syndrome disease activity index, GLCM: Gray-level co-occurrence matrix, MAR: Maximum accumulation ratio, EF: Excretion fraction, OMERACT: Outcome measures in rheumatoid arthritis clinical trials

Subgroup analysis of gray-level co-occurrence matrix texture metrics defined by Outcome measures in rheumatoid arthritis clinical trials score

For all the parotid glands, the GLCM contrast demonstrated the best significant correlation to MAR, while the GLCM homogeneity yielded the best and a significant correlation to EF. The scatter plots are displayed in Figure 2. For the subgroup of parotid glands with the semiquantitative score of 1 ($n = 10$), the GLCM contrast tended to be associated negatively with MAR (rho = −0.64, $P = 0.054$), and the GLCM homogeneity still showed significant and high positive correlation to EF (rho = 0.85, $P = 0.004$). For the subgroup of the parotid glands with the semiquantitative score of 2 ($n = 9$), the GLCM contrast exhibited significant and high negative correlation to MAR (rho = −0.87, $P = 0.005$), and the GLCM homogeneity tended to be positively associated with EF (rho = 0.62, $P = 0.086$). In the parotid glands with the same semiquantitative score, GLCM texture features were still able to discriminate different SGS activities.

Discussion

Various imaging techniques are currently applied for the diagnosis and follow-up of patients with primary SS.[26] The identification of the best imaging tool for primary SS remains a challenge in clinical practice. SGS and sialography have been frequently used for the diagnosis of SS and have been included in the 2002 AECG classification criteria.[2] However, no imaging modality was included in the 2016 ACR–EULAR classification criteria.[3] This provides an opportunity for the use of novel imaging diagnostic techniques, such as US.[3,16,27,28] The OMERACT task force group has developed US definitions and a semiquantitative scoring system with good interobserver and intraobserver reliabilities.[16] One recent study found that adding the semiquantitative score to the 2016 ACR–EULAR criteria can improve the diagnostic utility of primary SS.[13] Salivary gland US may be a prospective tool in the diagnosis and follow-up of primary SS.

The parotid gland is the largest of the salivary glands and is easy for US evaluations.[23] In this study, we retrospectively included

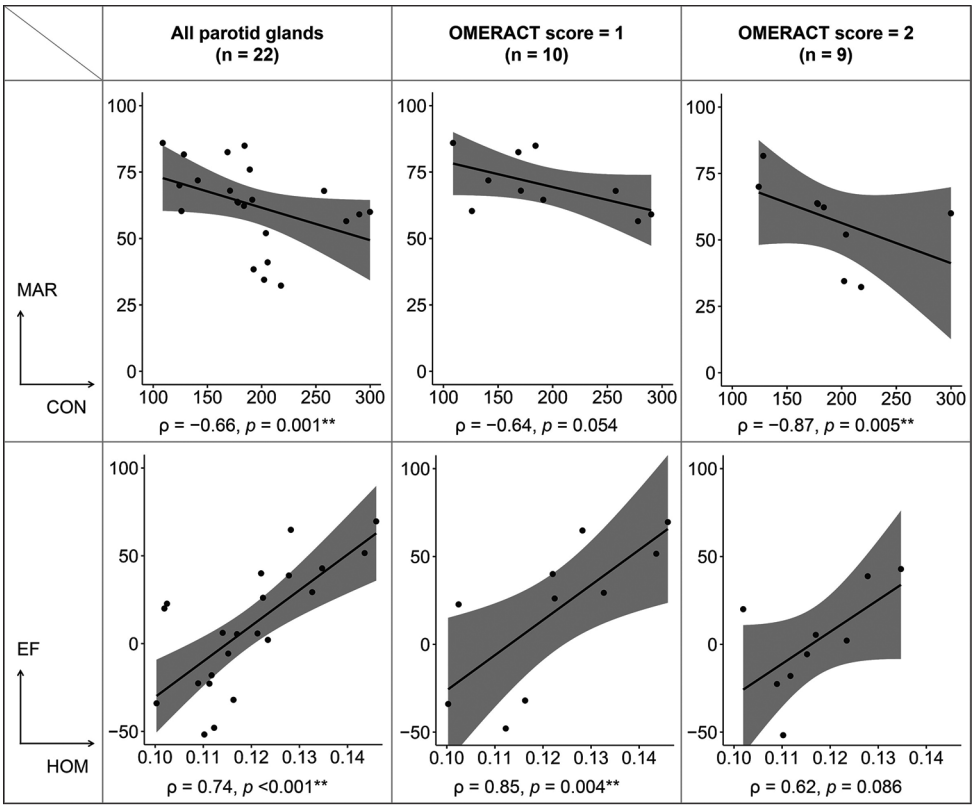

Figure 2: The scatter plots display the strongest correlation between the GLCM texture features and the activity of scintigraphy, with linear regression fit (solid lines) and 95% confidence intervals (gray bands). Spearman's rho was calculated to test the association. For all parotid glands ($n = 22$), the CON shows significantly moderate negative correlation to the MAR, and the HOM shows significantly high positive correlation to EF. For the subgroup of parotid glands with the semiquantitative OMERACT US score of one ($n = 10$), the CON tended to be negatively associated with MAR, whereas the HOM still yielded significantly high positive correlation to EF. For the subgroup of parotid glands with the semiquantitative OMERACT US score of two ($n = 9$), the CON yielded significantly high negative correlation to the MAR, while the HOM tended to be positively associated with EF. These findings suggest that GLCM CON and HOM were better markers for discriminating the activity of scintigraphy compared with the semiquantitative scoring system (*$P < 0.05$; **$P < 0.01$). GLCM: Gray-level co-occurrence matrix, CON: Contrast, MAR: Maximum accumulation ratio, HOM: Homogeneity, EF: Excretion fraction, OMERACT: Outcome measures in rheumatoid arthritis clinical trials, US: Ultrasound

11 patients with primary SS who received simultaneous US examinations of parotid glands and SGS. With the use of quantitative SGS evaluation as a reference benchmark, we assessed the association between the parotid gland function and US assessments. This study evaluated the US findings of 22 parotid glands in two ways: (1) with the use of the semiquantitative OMERACT scoring system and (2) with the use of GLCM texture analysis. The semiquantitative OMERACT scoring system classified US findings on salivary glands into four grades (from Grade 0 to 3); nevertheless, quantitative continuous parameters can be obtained with the use of GLCM texture analysis of the US findings. The GLCM method is a popular approach for texture feature extraction. Based on closed-form formulas, GLCM texture metrics can provide objective and unbiased information on US findings.[21,22,24]

Among the 22 parotid glands, the semiquantitative scores were mainly 1 and 2, thus indicating minimal to moderate inhomogeneity. Although a significant and moderate negative correlation between semiquantitative score and MAR could be found [Table 2], there was no significant correlation between the semiquantitative score and EF. The semiquantitative scores yielded poor correlation outcomes with EF in our study. Given that EF has been reported to be a sensitive indicator of salivary gland dysfunction, the semiquantitative scoring system alone may not be sensitive enough to predict salivary gland dysfunction.[5,8-10] A recent study supported the incorporation of US in the diagnosis of primary SS using the OMERACT US scoring system with a cut-off score ≥2 in at least one gland; however, 47% of the primary SS patients had parotid glands that were scored with Grade 0 bilaterally.[29] Parotid gland changes usually develop gradually overtime. The discrimination ability of the semiquantitative scoring system that only divided US findings into four grades may not be adequate for the slowly progressive nature of SS.[1,30] Conversely, using the GLCM texture analysis, quantitative continuous parameters can be obtained from the US images of parotid glands.[21,22] The texture metrics in the orderliness group (angular second moment and entropy) and descriptive statistics group (mean, variance, and correlation) yielded only low to negligible correlations to MAR or EF. As expected, the texture metrics in the contrast group including contrast,

dissimilarity, and homogeneity, were all significantly associated with either MAR or EF. Furthermore, the highest correlation was found in the relation between the GLCM contrast and MAR (rho = −0.66, P = 0.001) and between the GLCM homogeneity and EF (rho = 0.74, P < 0.001). SS will result in heterogeneous changes in the echotexture of the salivary glands. The OMERACT scoring system evaluates the parenchymal inhomogeneity and focal anechoic or hypoechoic areas. Based on the statistical properties, the texture metrics in the contrast group measure the intensity contrast between a pixel and its neighbor over the whole image. Therefore, the analysis of contrast, dissimilarity, and homogeneity are based on the same concept of the OMERACT scoring system. These quantitative continuous parameters may be more sensitive to changes.

For further investigation of the discrimination ability of GLCM texture analysis, subgroup analysis was performed for the parotid glands with the same semiquantitative score. The moderate to high correlations were deemed persistent among the subgroups [Figure 2]. Based on the above findings, we may conclude again that GLCM texture analysis appears to be more sensitive than the semiquantitative OMERACT US scoring system in determining the function of individual parotid glands in primary SS patients.

We also analyzed the differences in the results of semiquantitative US scores and GLCM texture analysis between anti-SSA/SSB-positive and anti-SSA/SSB-negative patients. However, no significant differences were found. In addition, the semiquantitative US scores did not correlate with European Eague Gainst Heumatism Sjögren's Syndrome Disease Activity Index (ESSDAI) (rho = 0.16, P = 0.475). Among the eight GLCM texture features, only homogeneity poorly correlated to ESSDAI scores (rho = 0.46, P = 0.030). The ESSDAI scores can be influenced by prominent extraglandular involvement, and thus poorly correlate to the changes in the echotexture of the salivary glands.

GLCM texture analysis is a well-developed method.[18-20] The texture metrics can be computed automatically and rapidly using free and ready-to-use software packages. It is possible for US machines to be equipped with a feature extraction function based on the use of GLCM. Future studies are warranted to determine the normal range and the cut-off value of each GLCM texture metric. A prospective observational study that integrates grayscale US, elastography, SGS, and novel biomarkers has been approved by the National Taiwan University Hospital Research Ethics Committee (202006082RINC), and is now in progress.

The present study was limited owing to its retrospective nature and the small sample size of participants. Only 11 primary SS patients received simultaneous US and SGS for the evaluations for the assessments of xerostomia [Table S1]. No analysis based on the underlying histopathological features could be performed. However, the adoption of the emerging OMERACT grading system and the application of GLCM texture analysis can still allow us to demonstrate how routine US examinations of parotid glands can discriminate the parotid gland function in clinical practice. GLCM is a well-established texture analysis method, which possesses the capacity to automatically assess a vast number of images in a quicker and more error-free manner. These facts would contribute to reliable quantitative texture analysis by even less-expert sonographers. Thus, we may expect that future US machines will be equipped with GLCM functions.

Conclusion

We provided real-world data such that the US outcomes of parotid glands can correlate to quantitative SGS outcomes using GLCM texture analysis. US is accessible, repeatable, and low cost. It is envisaged that in conjunction with the ready-to-use, objective, and unbiased GLCM texture metrics, US may become an essential clinical imaging tool for the evaluation of salivary glands in patients with primary SS.

Financial support and sponsorship

This work was supported by the National Taiwan University Hospital (Grant No. NTUH.110-M4880).

Conflicts of interest

There are no conflicts of interest.

References

1. Mariette X, Criswell LA. Primary Sjögren's Syndrome. N Engl J Med 2018;378:931-9.
2. 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;61:554-8.
3. Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, *et al.* 2016 American college of rheumatology/European league against rheumatism classification criteria for primary Sjögren's syndrome: A consensus and data-driven methodology involving three international patient cohorts. Arthritis Rheumatol 2017;69:35-45.
4. Schall GL, Di Chiro G. Clinical usefulness of salivary gland scanning. Semin Nucl Med 1972;2:270-7.
5. Kang JY, Jang SJ, Lee WW, Jang SJ, Lee YJ, Kim SE. Evaluation of salivary gland dysfunction using salivary gland scintigraphy in Sjögren's syndrome patients and in thyroid cancer patients after radioactive iodine therapy. Nucl Med Mol Imaging 2011;45:161-8.
6. Aksoy T, Kiratli PO, Erbas B. Correlations between histopathologic and scintigraphic parameters of salivary glands in patients with Sjögren's syndrome. Clin Rheumatol 2012;31:1365-70.
7. García-GonzálezM,González-SotoMJ,GómezRodríguez-BethencourtMÁ, Ferraz-Amaro I. The validity of salivary gland scintigraphy in Sjögren's syndrome diagnosis: Comparison of visual and excretion fraction analyses. Clin Rheumatol 2021;40:1923-31.
8. 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;40:64-9.
9. 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.
10. Kaldeway HP, Ter Borg EJ, van de Garde EM, Habraken JB, van Buul MM. Validation of quantitative salivary gland scintigraphy in relation to the American-European concensus criteria for Sjögren's syndrome. Nucl Med Commun 2019;40:343-8.
11. Salaffi F, Carotti M, Iagnocco A, Luccioli F, Ramonda R, Sabatini E, *et al.* Ultrasonography of salivary glands in primary Sjögren's

syndrome: A comparison with contrast sialography and scintigraphy. Rheumatology (Oxford) 2008;47:1244-9.
12. Milic V, Petrovic R, Boricic I, Radunovic G, Marinkovic-Eric J, Jeremic P, *et al.* Ultrasonography of major salivary glands could be an alternative tool to sialoscintigraphy in the American-European classification criteria for primary Sjogren's syndrome. Rheumatology (Oxford) 2012;51:1081-5.
13. Geng Y, Li B, Deng X, Ji L, Zhang X, Zhang Z. Salivary gland ultrasound integrated with 2016 ACR/EULAR classification criteria improves the diagnosis of primary Sjögren's syndrome. Clin Exp Rheumatol 2020;38:322-8.
14. Jousse-Joulin S, Milic V, Jonsson MV, Plagou A, Theander E, Luciano N, *et al.* Is salivary gland ultrasonography a useful tool in Sjögren's syndrome? A systematic review. Rheumatology (Oxford) 2016;55:789-800.
15. Takagi Y, Kimura Y, Nakamura H, Sasaki M, Eguchi K, Nakamura T. Salivary gland ultrasonography: Can it be an alternative to sialography as an imaging modality for Sjogren's syndrome? Ann Rheum Dis 2010;69:1321-4.
16. Jousse-Joulin S, D'Agostino MA, Nicolas C, Naredo E, Ohrndorf S, Backhaus M*, et al.* Video clip assessment of a salivary gland ultrasound scoring system in Sjögren's syndrome using consensual definitions: An OMERACT ultrasound working group reliability exercise. Ann Rheum Dis 2019;78:967-73.
17. Finzel S, Jousse-Joulin S, Costantino F, Hánová P, Hocevar A, Iagnocco A, *et al.* Patient-based reliability of the outcome measures in rheumatology (OMERACT) ultrasound scoring system for salivary gland assessment in patients with Sjögren's syndrome. Rheumatology (Oxford) 2021;60:2169-76.
18. Kim N, Amin V, Wilson D, Rouse G, Udpa S. Ultrasound image texture analysis for characterizing intramuscular fat content of live beef cattle. Ultrason Imaging 1998;20:191-205.
19. Alvarenga AV, Pereira WC, Infantosi AF, Azevedo CM. Complexity curve and grey level co-occurrence matrix in the texture evaluation of breast tumor on ultrasound images. Med Phys 2007;34:379-87.
20. Alvarenga AV, Teixeira CA, Ruano MG, Pereira WC. Influence of temperature variations on the entropy and correlation of the Grey-Level Co-occurrence Matrix from B-Mode images. Ultrasonics 2010;50:290-3.
21. Yang X, Tridandapani S, Beitler JJ, Yu DS, Yoshida EJ, Curran WJ, *et al.* Ultrasound GLCM texture analysis of radiation-induced parotid-gland injury in head-and-neck cancer radiotherapy: An *in vivo* study of late toxicity. Med Phys 2012;39:5732-9.
22. Nardone V, Tini P, Nioche C, Mazzei MA, Carfagno T, Battaglia G, *et al.* Texture analysis as a predictor of radiation-induced xerostomia in head and neck patients undergoing IMRT. Radiol Med 2018;123:415-23.
23. Gritzmann N, Rettenbacher T, Hollerweger A, Macheiner P, Hübner E. Sonography of the salivary glands. Eur Radiol 2003;13:964-75.
24. Hall-Beyer M. Practical guidelines for choosing GLCM textures to use in landscape classification tasks over a range of moderate spatial scales. Int J Remote Sens 2017;38:1312-38.
25. Akoglu H. User's guide to correlation coefficients. Turk J Emerg Med 2018;18:91-3.
26. Jousse-Joulin S, Coiffier G. Current status of imaging of Sjogren's syndrome. Best Pract Res Clin Rheumatol 2020;34:101592.
27. Ramos-Casals M, Brito-Zerón P, Bombardieri S, Bootsma H, De Vita S, Dörner T, *et al.* EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. Ann Rheum Dis 2020;79:3-18.
28. Price E, Allen A, Rauz S, Tappuni A, Sutcliffe N, Bombardieri M, *et al.* The management of Sjögren's syndrome: British society for rheumatology guideline scope. Rheumatology (Oxford) 2021;60:2122-7.
29. Fana V, Dohn UM, Krabbe S, Terslev L. Application of the OMERACT Grey-scale Ultrasound Scoring System for salivary glands in a single-centre cohort of patients with suspected Sjögren's syndrome. RMD Open 2021;7:e001516.
30. Brito-Zerón P, Baldini C, Bootsma H, Bowman SJ, Jonsson R, Mariette X, *et al.* Sjögren syndrome. Nature reviews Disease primers 2016;2:16047.

Supplementary Material

Table S1: Participating patient clinical profiles and the classification of primary Sjögren's syndrome according to both the American-European consensus group criteria and the 2016 American College of Rheumatology-European league against rheumatism criteria

Number	Age	Gender	Ocular dryness‡	Oral dryness‡	Schirmer's test¶	Salivary scintigraphy	Autoantibodies			Salivary gland histopathology§	AECG criteria	2016 ACR/EULAR criteria
							ANA	SSA	SSB			
1	62	Female	Yes	Yes	+	Abnormal	+	+	+	N/A	Yes	Yes
2	39	Male	Yes	Yes	+	Abnormal	−	−	−	+	Yes	Yes
3	65	Female	Yes	Yes	+	Abnormal	+	−	−	+	Yes	Yes
4	41	Female	Yes	Yes	N/A	Abnormal	+	+	−	N/A	Yes	N/A
5	50	Female	Yes	Yes	N/A	Abnormal	+	+	+	N/A	Yes	N/A
6	41	Female	Yes	Yes	+	Abnormal	−	−	−	+	Yes	Yes
7	36	Female	Yes	Yes	N/A	Abnormal	+	+	+	N/A	Yes	N/A
8	46	Female	Yes	Yes	+	Abnormal	+	+	+	N/A	Yes	Yes
9	53	Female	Yes	Yes	+	Abnormal	−	−	−	+	Yes	Yes
10	53	Female	Yes	Yes	+	Abnormal	+	+	+	N/A	Yes	Yes
11	25	Female	Yes	Yes	N/A	Abnormal	−	+	−	N/A	Yes	N/A

‡Symptoms for at least 3 months, ¶A Schirmer's test ≤5 mm/5 min in at least one eye was considered positive, §The presence of focal lymphocytic sialadenitis was considered positive. Patients 2 and 9 received labial salivary gland biopsy in another hospital. ANA: Antinuclear antibodies, SS: Sjögren's syndrome, AECG: American-European consensus group, 2016 ACR-EULAR: 2016 American College of Rheumatology-European League Against Rheumatism, N/A: Not available, +: Positive, -: Negative