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Original Research Article

Functional assessment of major salivary glands using scintigraphy

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Abstract

Objective: To demonstrate a methodology of scintigraphy imaging interpretation considering pixel intensity values in groups of patients presenting lupus erythematosus, Sjögren's Syndrome (SS), SS associated to systemic lupus erythematosus, parotiditis, drug-induced sialorrhea and salivary glands disease-free. **Material and methods:** A total of 36 salivary gland scintigraphy images that were from patients with lupus erythematosus, SS, SS combined lupus, parotiditis, and drug-induced sialorrhea were assessed. The pixel intensity of the scintigrams was also evaluated using the standardized grayscale at 8 bits, Images were analyzed under a region of interest (ROI) of 2 cm2 at maximum uptake using ImageJ. **Results:** Significant differences between the groups were obtained both for parotid (p=0.026) and submandibular glands (p=0.0952). Statistical significant differences were observed in post-hoc tests between Lupus combined with SS patients, for parotid and submandibular glands, when compared to normal group (p=0.04 and p=0.03 respectively). Pixel values were higher for Lupus combined with SS patients, representing a lower uptake. **Conclusion:** The pixel intensity assessment was able to differentiate and point to lower salivary flow rates for the systemic lupus erythematosus combined with SS patients when compared to other disorders affecting the salivary gland function.

Introduction

Salivary glands are responsible for the oral cavity lubrification, food digestion and teeth integrity preservation. Salivary glands dysfunction may manifest as painful swelling, thick or purulent discharge, or dry mouth, named as "xerostomia" [4]. The degree of xerostomia varies from subtle to severe, resulting in oral dysfunction and leading to psychosocial morbidities [7].

Salivary glands evaluation is performed by several techniques such as sialometry, scintigraphy, magnetic resonance, computed tomography and contrast sialography [15]. Although sialography is considered the gold standard technique, it is invasive and presents limited information about glandular function and may induce to complications, such as pain, ductal perforation, fistula formation and glandular infection [18].

Salivary gland scintigraphy (SGS) is useful to analyze functional activity of salivary glands [9]. This non-invasive imaging technique, in which a radiotracer can be administered intravenously, orally, inhaled or subcutaneously, which is well-tolerated by patients [15]; also, it provides data on the glandular parenchymal involvement and excretion from all major salivary glands in a single examination [15].

SGS is widely used to assess patients in diverse functional salivary pathologies, such as Sjögren's Syndrome (SS) [2], obstructive sialadenitis with or without parenchymal destruction [19], and iatrogenic irradiation-related sialadenitis [17]. Diverse categorical classifications for SGS imaging interpretation were already proposed in literature, such as the degree of glandular uptake and isotope secretion in oral cavity [12] and visual assessment [16]. However, the measurement of isotope excretion is oral cavity depends on the saliva swallowing during the examination, which may interfere in results [20], and visual assessment is highly observer-dependent, which is its main advantage [5].

Thus, the objective of the present investigation was to demonstrate a methodology of scintigraphy imaging interpretation considering pixel intensity values in groups of patients presenting lupus erythematosus, SS, SS associated to systemic lupus erythematosus, parotiditis, drug-induced sialorrhea and salivary glands disease-free.

Material and methods

Ethnics Committee approval was obtained at the university (approval number 3.565.450) and the guidelines of Helsinki were followed in this investigation. All the patients signed a consent form.

A total of 36 salivary gland scintigraphy images that were performed for diagnostic purposes, were obtained from patients with lupus erythematosus, SS, SS combined lupus, parotiditis, and drug-induced sialorrhea. Patients that performed the SGS due to the complaints of xerostomia but did not present any salivary gland alteration were classified as "normal". In figure 1, cases from the sample studied is exhibited. Examinations with technical problems or patients with inconclusive diagnosis were excluded.

All images were obtained from the same equipment, a computerized scintillation camera with a low-energy, high-sensitivity collimator was employed: Millennium MG® gamma camera (GE Medical Systems). Patients were positioned in a supine position under the camera. After intravenous administration of technetium sodium pertechnetate 99mTc at 185MBq, static images in the anterior projection were obtained in 41 min, using a 128x128 matrix and a zoom factor of 1.41. After 30 min, salivary secretion was stimulated by a sialagogue – 5 ml citric acid/lemon juice. To capture the images, a gamma camera was placed in front of the head and neck region, ensuring that the four main salivary glands and the thyroid were included in the image area. The static approach was chosen because the dynamic SGS is susceptible to artifacts caused by patient movement during lemon juice stimulation.

A medical radiologist and three dental radiologists with experience in SGS evaluated the images. The dynamics of glandular functions were observed following the uptake and subsequent elimination of the radiopharmaceutical after the stimulation of salivation through the consumption of lemon.

The pixel intensity of the scintigrams was also evaluated using the standardized grayscale at 8 bits, ranging from 0 (black) to 255 (white) for comparison with the visual analysis. Images were analyzed under a region of interest (ROI) of 2 cm2 at maximum uptake using ImageJ (National Institute of Health public domain software, Bethesda, MD, USA) (figure 1). The ROIs were positioned in the center of each image.

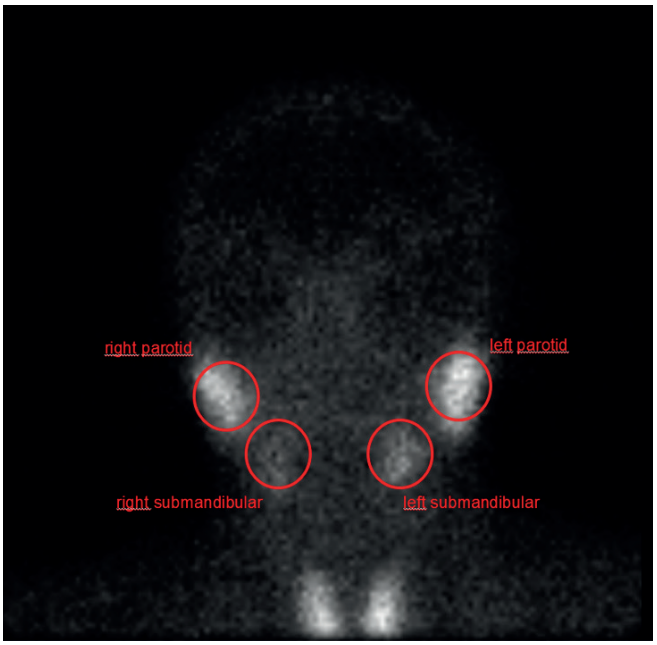

Figure 1 – Regions of interest selected in the scintigraphy imaging for the pixel-intensity assessment

Statistical assessment

Interobserver agreement was performed using the Kappa test. Kappa values characterize different ranges according to the degree of agreement. Thus, values greater than 0.75 represent excellent agreement, values below 0.40 represent low agreement and values between 0.40 and 0.75 represent median agreement.

For quantitative data, adherence to the normality curve was verified using the Shapiro-Wilk test. Due to the absence of data normality, comparisons were made between groups using the nonparametric Kruskal-Wallis test, complemented with post-hoc tests. Values of pixel intensity comparisons were tested for each salivary gland pair (parotid and submandibular), according to the disease presented by the patient.

All statistical analyzes were performed at a significance level of 5%, using IBM SPSS Statistics 17 software, SPSS®, Inc, Chicago, IL.

Results

From the 36 images initially included in the sample, 6 were excluded due to lack of conclusive diagnosis. Thirty examinations were included (28 females and 2 males; age range 35 to 80 years old) A total of 120 salivary glands (right and left parotid and right and left submandibular glands) were evaluated. The final sample description, according to the disease presented is available on table I.

Table I – Descriptive statistics. Sample size according to the diseases reported, considering females and males

	Sample	**Normal**	**SS**	**SS associated with SLE**	**SLE**	**Parotitis**	**Drug-induced syalorreia**
Total of patients	30	6	13	3	5	2	1
Female	26	3	13	3	4	2	1
Male	4	3	0	0	1	0	0
Mean age	43.17 (±18.12)	35.33 (±20.69)	46.75 (±18.03)	41.33 (±24.90)	42.80 (±7.32)	32.50 (±0.70)	78.00

Abbreviations: SS: Sjögren's syndrome; SLE: systemic lupus erythematosus

Descriptive data on the pixel values obtained for parotid and submandibular gland are available on table II. Significant differences between the groups were obtained both for parotid (p=0.026) and submandibular glands (p=0.0952). Statistical significant differences were observed in post-hoc tests between Lupus combined with SS patients, for parotid and submandibular glands, when compared to normal group (p=0.04 and p=0.03 respectively). Pixel values were higher for Lupus combined with SS patients, representing a lower uptake.

Moreover, interobserver agreement, according to Kappa test was 0.83 (p=0.002).

Table II – Pixel intensity values in maximum uptake for parotid and submandibular according the disease

	Right parotid	Left parotid	Right submandibular	Left Submandibular
Normal	81.00 (+60.50)	82.66 (+58.28)	64.83 (+45.67)	63.66 (+36.09)
SS	86.58 (+52.12)	89.83 (+53.82)	88.33 (+47.56)	93.08 (+55.43)
SS and SLE	156.66 (+68.63)	142.00 (+62.00)	109.66 (+24.94)	105.66 (+29.53)
SLE	128.66 (+37.07)	92.00 (+28.00)	119.00 (+46.29)	106.33 (+60.54)
Parotiditis	93.50 (+109.60)	104.00 (+121.62)	61.50 (+71.41)	72.50 (+81.31)
Sialorrhea	57.00	77.00	45.00	65.00

Abbreviations: SS: Sjögren's syndrome; SLE: systemic lupus erythematosus

Discussion

In the present investigation, higher pixel intensities values in maximum uptake, representing lower radioisotope uptake, was observed in patients with SS combined with systemic erythematosus lupus when compared to patients without any salivary gland disease. SS is a complex autoimmune disorder, that affects salivary gland functional activity [11] that is classified as primary, when the SS is not associated to other autoimmune disease, and secondary SS, when SS is associated to other autoimmune disease as systemic lupus erythematosus; however, the terms "overlapping" or "associated" SS can also be employed [14]. Both disorders are connective tissue disorders [13], sharing genetic backgrounds and the influence of additional immunogenetic, environmental, or hormonal factors [14].

Although the sample size was small, and statistically significant results were not detected, it was verified that systemic lupus erythematosus patients also presented higher pixel values, even when compared to SS patients. These results could be influenced by the clinical status of the patient, which it wasn't available [3]. Salivary gland decreased flow in systemic lupus erythematosus patients is not new and might express the multisystemic presentation of the disease [3]. Histological findings point to enhanced lymphocyte proliferation in the salivary glands [3], similar to those seen in SS.

SGS stands alone in evaluating the functional status of the salivary glands, with limited recent research on its application published [4]. A normal SGS shows symmetrical and normal glandular shape, with clear contrast [4]. Moreover, fast and spontaneous excretion is seen, with a gradual radioisotope concentration increase succeeded by a sudden drop, with a good response to acidic stimulation [4]. In contrast, abnormal SGS presents less contrast uptake with a slight variation in contrast concentration and emptying [1].

Additionally, submandibular glands, showed greater involvement than the parotid glands, despite no significantly differences in pixels values were detected, which is in agreement with what has been reported in the literature [8]. Håkansson *et al.* [10], when comparing patients with and without symptoms of dry mouth and/or dry eyes, observed that the submandibular glands had a lower response to stimulated secretion when compared to the parotid glands, with no differences between the left and right side submandibular glands.

The aforementioned differences between submandibular and parotid glands could be explained by the size and composition of them, which is markedly distinct: while the parotid gland consists of serous acini, producing watery and serous saliva, the submandibular gland contain both mucous and serous acini [6]. These diverse glandular constitution results in distinct saliva type production, probably affecting the radioisotope excretion and changing the SGS results, as it is very susceptible to salivary flows variations.

The limitation of the present study is the small sample size, particularly for the sialorrhea investigation.

Conclusion

The pixel intensity assessment was able to differentiate and point to lower salivary flow rates for the systemic lupus erythematosus combined with SS patients when compared to other disorders affecting the salivary gland function.

Conflict of interest statement

Luciana Munhoz, Emiko Saito Arita, Christyan Hiroshi Iida and Plauto Watanabe declare they have no conflicts of interest.

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