# Improved quantification of salivary gland scintigraphy by means of factor analysis

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Original Article

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## ABSTRACT

**Introduction:** In this study the automatic separation of oral and salivary gland activity and spontaneous secretion by means of factor analysis for quantitative salivary gland scintigraphy is introduced.

**Methods:** After intravenous administration of 99mTc sodium pertechnetate, dynamic scintigraphy was performed. 20 minutes after tracer application 2 ml of lemon juice was delivered to stimulate the glands. Applying elliptical regions of interest for oral cavity and four major salivary glands and using factor analysis of medical image sequences (FAMIS) results in factor images and curves, which are used for quantification of the oral, sublingual and glandular activity indexes.

**Results:** With FAMIS it is possible to automatically separate the three superimposed processes seen in salivary gland scintigraphy: glandular and oral activity and spontaneous secretion that results in significant different quantitative results.

**Conclusion:** The application of factor analysis improves the results of salivary gland scintigraphy by separation of superimposed dynamic processes of oral and glandular activity and spontaneous secretion.

**Key words:** Sjögren’s syndrome, Factor analysis, Salivary gland scintigraphy.

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## INTRODUCTION

Sjögren's syndrome is an autoimmune disease characterized by a chronic inflammatory process involving the salivary and lacrimal glands that leads to decreased water production for tears and eye and/or mouth dryness [1]. Cinically, it might be difficult to distinguish the early stage of Sjögren's syndrome from normal findings. It is important to make an accurate diagnosis because Sjögren's syndrome can be treated by various trial therapies including corticosteroids and other immunosupressants. Salivary gland scintigraphy with 99mTc sodium pertechnetate is an easy and non-invasive method to evaluate both parotid and submandibular glands for diagnosis and evaluation of Sjögren's syndrome [2-5]. Several studies for comparing the quantitative characteristics of salivary gland scintigraphy with the histopathologic grading of labial gland have been performed in patients with Sjögren's syndrome [6].

Recently, an interesting work quantified the behaviour of the oral radioactivity by region of interests (ROI) analysis [7]. This additional information is important since it has been shown that the coordinated analysis of oral activity and salivary gland activity is more helpful in improving diagnostic performance [8, 9]. Aung et al [7] correlated oral indices, histologic grades of labial gland biopsy specimens and the stage of Sjögren's syndrome for determination of the clinical stage of disease. However, conflicting views regarding the diagnostic merits of salivary gland scintigraphy in Sjögrens's syndrome persist. Uncertainty about which of several scintigraphic parameters are most useful for detection of mildly impaired parenchymatous function of salivary glands and determination of the clinical stage of Sjögren's syndrome have been problematic [7].

The critical step in quantitative evaluation of dynamic salivary gland scintigraphy is the drawing of ROIs, which is for this application particularly difficult and prone to errors. The variability in shape and location of manually selected ROIs reduces the reproducibility and both intra- and inter-observer comparison of results. Furthermore, several dynamic processes are superimposed, among them in the oral radioactivity, that may falsify the quantification.

One of the methods suggested for user independent definition of ROIs is factor analysis, which provides automatic separation of dynamic structures [10]. Factor analysis is a well known method in nuclear medicine useful for medical and physical applications [11-13].

Factor analysis assumes that any TAC is a weighted sum of a limited number of pure time activity evolutions, that corresponds to regions of similar temporal behaviour [14]. Factor analysis of medical image sequences (FAMIS) is based on a linear additive model and describes the information included in the whole series as the sum of several components that are physiologically or physically meaningful [15].

In this work we introduce the application of factor analysis for salivary gland scintigraphy that results in factor images and factor curves. After quantification following the schema by Aung et al [7] a comparison of the results was done by standard ROI analysis.

## METHODS

### Imaging Examinations

After intravenous administration of 180 MBq 99m Tc-sodium pertechnetate, dynamic salivary gland scintigraphy was performed with a dual head gamma camera (Infinia Hawkeye, General Electrics) using a low-energy high resolution collimator. As acquisition parameters a 128x128 matrix, zoom factor 1.3, 30 min, two frames/minute were used. Salivary gland secretion was stimulated using 2 ml oral lemon juice instilled with a syringe at 20 min after tracer injection.

### Image Processing

*Regions of Interest (ROIs) Analysis*

Oval shaped ROIs were drawn over the oral cavity and each of the four major salivary glands. Background regions were marked in the temporal and submental regions near the parotid and submandibular glands. With these ROIs time-activity curves were generated and used for quantification of oral activity and salivary glands.

To quantify oral activity, the pre-stimulatory oral activity index (PRI) and post-stimulatory oral activity index (POI) were calculated from numerical data obtained from the time activity curves (TACs) using a quantification schema presented by van den Akker et al [9]. Quantification of the salivary glands activity was done by calculation the maximum accumulation (MA), the maximum secretion (MS) and the secretion velocity (SV).

*Factor Analysis of Medical Image Sequences (FAMIS)*

Using the already drawn ROIs for the oral and salivary gland regions, we applied FAMIS using a three-factor model for the oral and two factors for the glandular activity. This process results in factor images and curves. The factor images were superimposed and to be distinguished coloured by the Pixies software package (red/blue/green). The curves were exported and analysed by the same quantification scheme as used for the ROI analysis.

## RESULTS

Applying FAMIS it is possible to fully automatic separate the different superimposed processes that exit for salivary gland scintigraphy: the oral cavity, the glandular activity and spontaneous secretion. Viewing the superimposed factor images (Fig. 1a, 2a, 3a) it is easy to distinguish the different structures. Although only the pixels inside the ROI are used for the FAMIS calculation, the software package colours the pixel of the whole image that belongs to the structure that shows a similar dynamic behaviour.

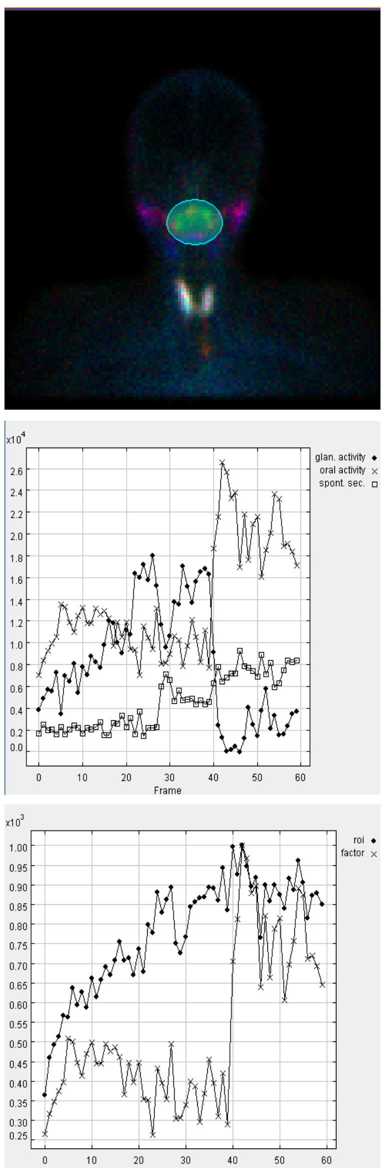


Fig 1. Oral cavity results: 1a) Superimposed factor images; 1b) Resulting factor curves using a three factor model show the fully automatic seperation of glandular and oral TAC, and the spontaneous secretion of the oral cavity; 1c) Comparing the oral activity curves obtained by ROI and FAMIS analysis.

In case of the oral activity clearly the separation of oral (green), glandular (blue) activity curves and spontaneous secretion (red) can been fully automatic visualized (Fig. 1a). Applying FAMIS factor curves are also obtained, representing the true oral TAC, the sublingual TAC and the spontaneous flow of the glands in the oral cavity (Fig. 1b). The TAC for the oral activity obtained by ROI analysis and FAMIS is shown in Fig. 1c. The sudden increase after salivary gland stimulation with lemon juice can be clearly observed. Table 1 shows the functional parameters that were found applying the quantification schema [7]. The visualisation of the spontaneous secretion of the glands in the oral cavity is only possible by FAMIS. Furthermore it is also possible to separate the oral from the sublingual activity curve. Quantitative results of the sublingual TAC are shown in Table 2. For the left parotid a two factor model was used and results in a separation of the parotid and oral activity curves (Fig. 2b). The increase of the oral curve is observed after the stimulation of the glands. The superimposed factor images are shown in Fig. 2a. The FAMIS results show lower count point after stimulation as found by ROI analysis that results in very different quantitative indices for the parotid gland. The functional parameters found by ROI analysis and FAMIS are indicated in Table 3. FAMIS results also in the case of the right submandibular gland in a separation of oral and glandular structures (Fig. 3a) and activity curves. In this patient a constant flow in the oral activity was found (Fig. 3b), whereas the submandibular gland curve shows the characteristic dynamic behaviour of the glands, that is also found for ROI analysis (Fig. 3c). The quantification of the ROI and the FAMIS curve are shown in Table 4.

**Table 1.** Indices for oral cavity.

| | ROI | FAMIS |
|---|---|---|
| PRI [%] | 36 | 20 |
| POI [%] | 50 | 60 |

**Table 2.** Measurement of the sublingual gland curve obtained by FAMIS.

| | |
|---|---|
| MA [%] | 67 |
| MS [%] | 88 |
| SV [%] | 75 |

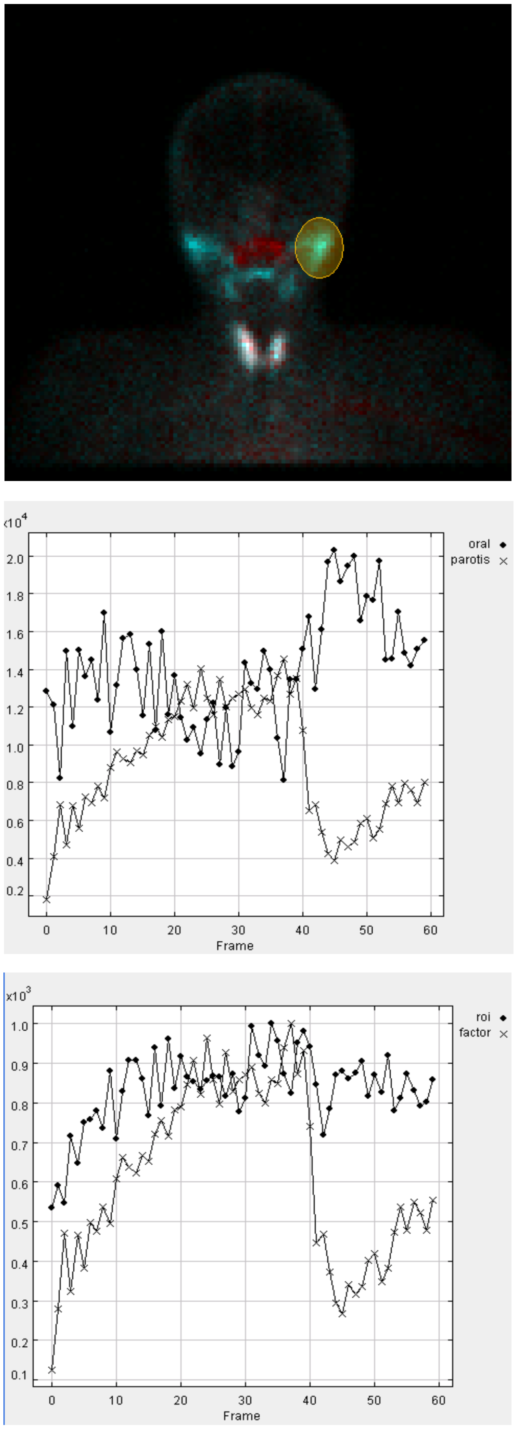


**Fig 2.** Parotid activity: 2a) superimposed factor images; 2b) factor curves of the parotid gland representing the separation of the parotid and oral activity; 2c) Comparison of the results obtained by ROI and FAMIS.

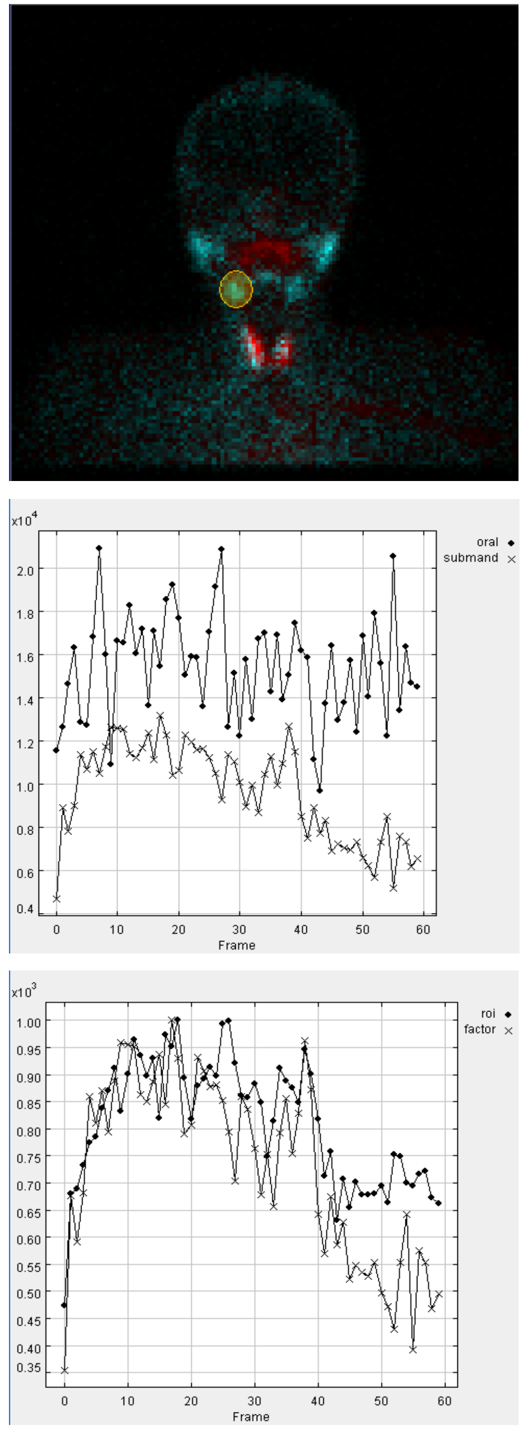


**Fig 3.** Submandibular gland activity: 3a) Superimposed factor images; 3b) Factor curves of the right submandibular gland representing the separation of the submandibular gland and oral activity; 3c) Comparison of the results obtained by ROI and FAMIS.

**Table 3.** Indices for parotid glands

| | ROI | FAMIS |
|---|---|---|
| MA [%] | 40 | 52 |
| MS [%] | 28 | 55 |
| SV [%] | 10 | 30 |

**Table 4.** Indices for submandibular glands

| | ROI | FAMIS |
|---|---|---|
| MA [%] | 32 | 32 |
| MS [%] | 35 | 42 |
| SV [%] | 13 | 26 |

## DISCUSSION

Salivary gland scintigraphy with 99m Tc-sodium pertechnetate has been proven as a helpful objective examination method, since patient complaints do not necessarily reflect the severity of salivary gland disease. Although this method appears to be objective and has been proven to be useful for diagnosis of Sjögren's syndrome, the quantitative parameters are difficult to obtain using ROIs analysis because the manual drawing of ROIs is critical for the quantitative evaluation. One major difficulty is the superimposed dynamic structures. Therefore, the separation of oral and glandular activity is necessary because the activity of both structures is superimposed and might falsify the quantitative factors. In this study FAMIS [14] was used to perform this separation fully automatic and user independent. Comparison of the FAMIS method was performed with our standard software package using ROI analysis. For the oral activity we applied a three factor model: true oral activity, sublingual activity and spontaneous secretion in the oral cavity. For the parotid a two factor model was used: glandular and spontaneous secretion in the oral cavity. The quantification of oral and glandular activity was done following a procedure described by Aung et al [7] for ROI and FAMIS analysis. This process allows the determination of functional parameters of oral (PRI and POI) and glandular (MA, MS, SV) activity**.** However, the amount of spontaneous salivary secretion (indicated by the value PRI) as measured by the ROI analysis is an assumption, since the dynamic behaviour is a summation of three processes: the first, the oral activity curve, the second, the flow into the salivary glands followed by secretion after stimulation and the third, the spontaneous secretion of the salivary glands in the oral cavity. The separation of these processes cannot be done by ROI analysis but is of clinical interest since this method may falsify the quantitative findings. FAMIS permits the separation of the TAC in an oral, a sublingual gland, and a spontaneous secretion curve by the separation of the three different dynamic behaviour that are visualized by the superimposed factor images (Fig. 1a, 2a, 3a). Applying a three factor model on the oral activity the three factor curves shows a pattern of the pre-stimulatory flow from the glands in the oral cavity (=the spontaneous secretion) and the amount of salivary secretion after stimulation (Fig. 1b). The value of PRI obtained by FAMIS (20%) is much lower than the value found by ROI analysis (36%) because only the pure (i.e. without superimposed spontaneous secretion) oral activity curve is taken for our quantification into account. The quantification of the sublingual glands was done by following the schema of the glands and results in functional parameters: MA, MS and SV. The spontaneous secretion of the glands in the oral cavity was visualised by superimposed factor images (red) and corresponding factor curves. The resulting factor curves of the parotid activity shows a glandular and oral pattern. The oral curve from the parotid clearly shows an increase of activity after stimulation (Fig. 2b). Applying FAMIS for the submandibular region results in the separation of the glandular curve, that is superimposed by the oral activity curve.

The separation of different dynamic processes by FAMIS allows to visualize the spontaneous secretion in the oral cavity and also allow the generation of user independent TAC which is especially important for small structures such as submandibular glands.

Future work need to be performed to compare the quantitative activity indices obtained by FAMIS for oral, parotid, submandibular and sublingual glands in healthy subjects and patients with early- and late-stage Sjögren syndrome.

## CONCLUSION

The application of FAMIS for salivary gland scintigraphy improves the scintigraphic information by separating the superimposed dynamic processes of oral and glandular activity. This results in a user-independent and fully automatic determination of the spontaneous salivary secretion.

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