

# SIALOSCINTIGRAPHY with $^{99m}\text{Tc}$ PERTECHNETATE

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## ABSTRACT

In recent year, the technique of nuclear medicine with  $^{99m}\text{Tc}$  pertechnetate is widely accepted for the evaluation of salivary gland function because of its less invasion. This technique has two types of examinations; 1) static sialoscintigraphy and 2) sequential sialoscintigraphy. The static sialoscintigraphy shows the morphology of the glandular parenchym, and furthermore the sequential sialoscintigraphy, from which we obtain informations as the time activity curve, provides the salivary gland informations of uptake, accumulation and excretion of  $^{99m}\text{Tc}$  pertechnetate for us. These functional informations are necessary and useful to determine exact diagnosis of salivary diseases.

## INTRODUCTION

The investigation of the functional condition of the salivary gland is of great importance to determine the exact diagnosis because most of salivary gland diseases are usually associated with a functional disturbance. Clinical evaluation of the patients with salivary gland diseases are usually performed by the radiographic examination with or without the use of contrast materials and other clinical examinatiois. This radiographic examination offers some informations but is limited to the morphological informations, for example, salivary calculus and certain forms of inflammatory and tumorous disease. Therefore this method does not fill the need of the functional informations.

In 1962 Harper first reported the accumulation of  $^{99m}\text{Tc}$  pertechnetate in the salivary gland.<sup>1)</sup> Since then this technique of nuclear medi-

cine with  $^{99m}\text{Tc}$  pertechnetate is widely employed for the evaluation of salivary gland function because of its less invasion.<sup>2-10)</sup> This imaging technique with  $^{99m}\text{Tc}$  pertechnetate provides a lot of informations about uptake, accumulation and excretion of  $^{99m}\text{Tc}$  pertechnetate in the salivary gland. These informations are useful in detecting salivary gland diseases and in determining the appropriate therapeutic management of patients. In this article sialoscintigraphy, especially sequential sialoscintigraphy, with  $^{99m}\text{Tc}$  pertechnetate was performed in some kinds of salivary gland diseases. The author attempted to describe the normal pattern of sialoscintigraphic findings and the characteristic view of functional disturbance in comparison with the normal manifestation.

1) THE PROCEDURE OF SIALOSCINTIGRA-  
PHY WITH  $^{99m}\text{Tc}$  PERTECHNETATE

$^{99m}\text{Tc}$  pertechnetate was administered in-

travenously in a dose of  $3.7 \times 10^8$  Bq (10 mCi)  
The sialoscintigraphy was carried out using the  
Gamma View scintillation camera (HITACHI Co.)

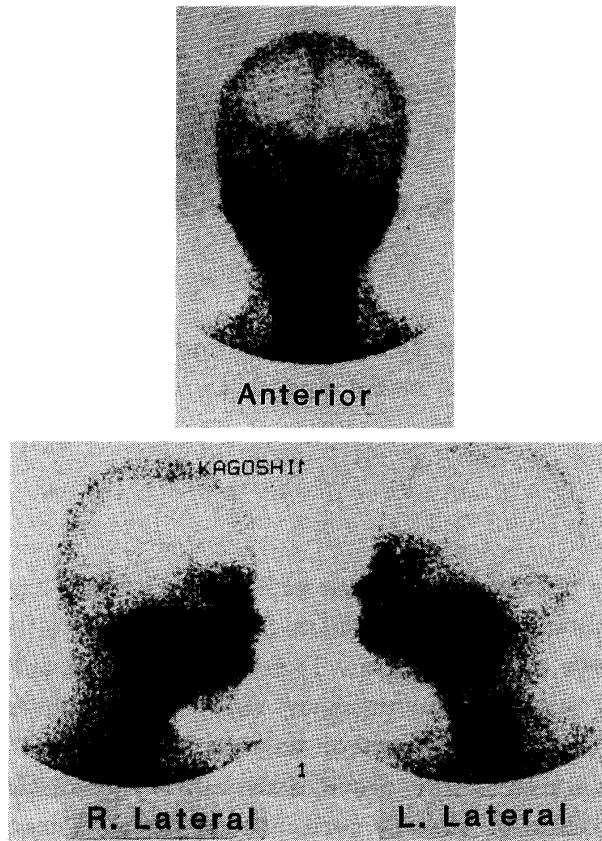


Fig. 1 Static Images of Sialoscintigraphy

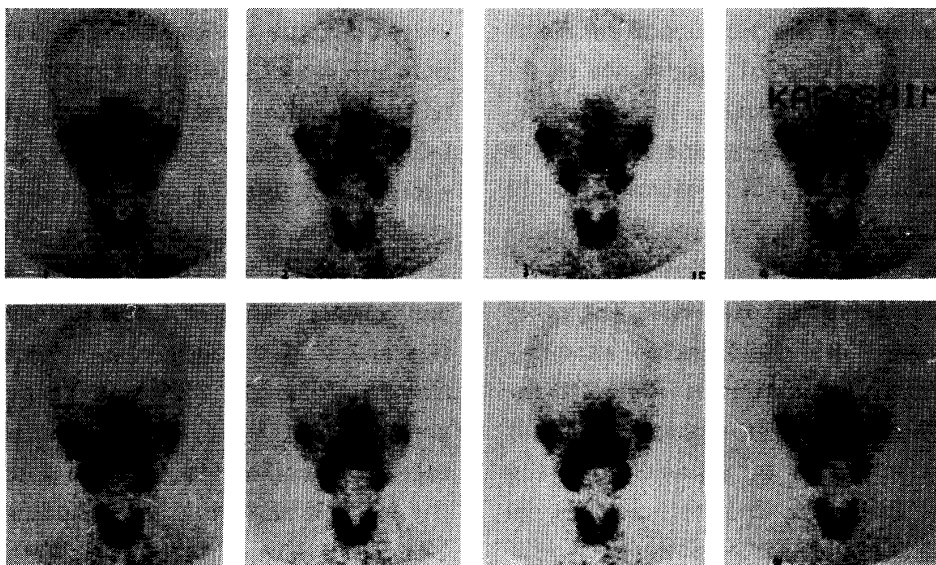


Fig. 2 Sequential Sialoscintigraphy

Each frame data was obtained by consecutive twenty-second scintiscan.

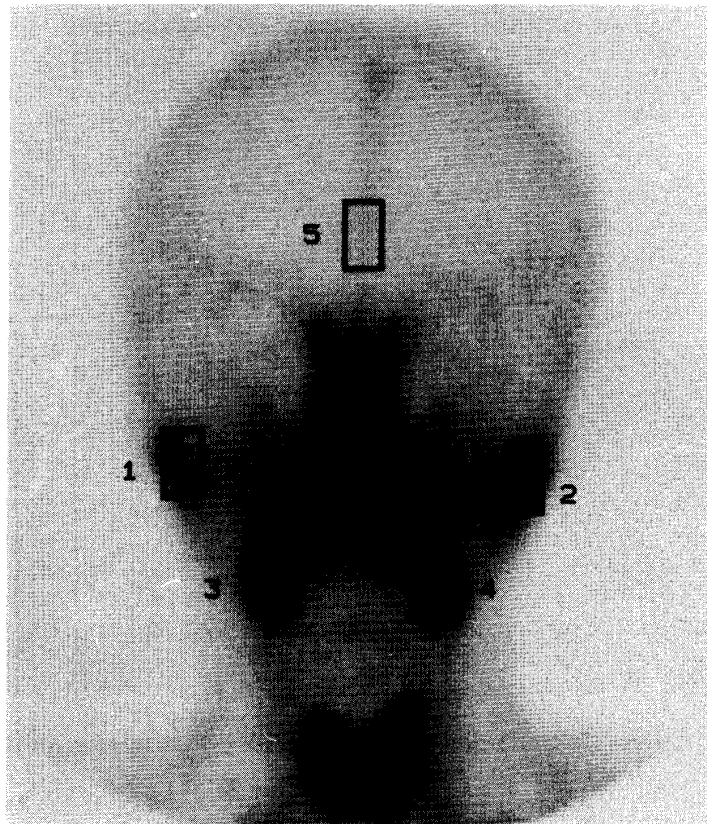


Fig. 3 ROIs of Salivary Glands of Sequential Sialoscintigraphy

- (1): Right Parotid Gland
- (2): Left Parotid Gland
- (3): Right Submandibular Gland
- (4): Left Submandibular Gland
- (5): Background as control

with a low-energy high-resolution parallel-hole collimator. Two types of sialoscintigraphies were performed. One was a static sialoscintigraphy and the other was a sequential sialoscintigraphy (dynamic sialoscintigraphy). The static sialoscintigraphy of salivary glands, which showed the uniform distribution of radioactivity in normal salivary glands, described the decrease and the lack of radioactivity, and the mottled distribution of radioactivity (space-occupying lesion) in diseases (figure 1). The sequential sialoscintigraphy was performed in the

anterior view. The patient was placed on a bed in a supine position under the scintillation camera, with the head slightly extended. Immediately after injection of  $^{99m}\text{Tc}$  pertechnetate, consecutive twenty-second scintiscans were made up to fifty minutes. A twenty-second scintiscan was recorded as one frame data, and one hundred and fifty frames were obtained (figure 2). On each frame, four regions of interest (ROI) covered bilateral parotid glands and submandibular glands were employed to recognize visually the patterns of the

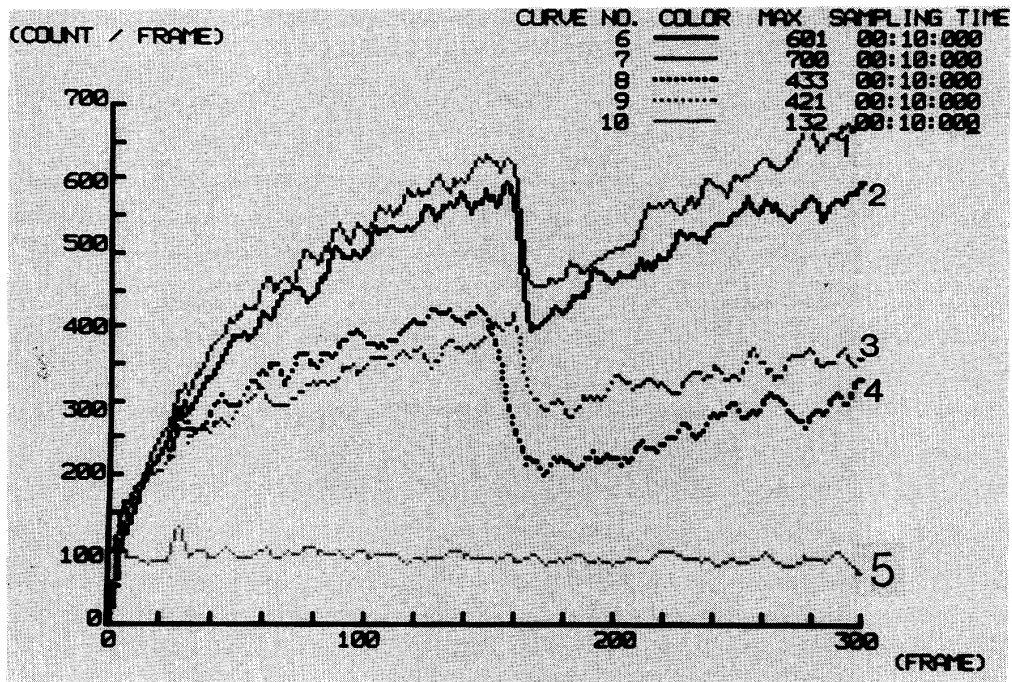


Fig. 4 Time Activity Curves of Sequential Sialoscintigraphy  
 (1),(2): Parotid Glands  
 (3),(4): Submandibular Glands  
 (5) : Background

uptake, accumulation and excretion of  $^{99m}\text{Tc}$  pertechnetate by the salivary glands. Another one ROI in the frontal area was added as a control of background count of radioactivity (figure 3). ROI numbers of 1 and 2 covered the bilateral parotid glands and numbers of 3 and 4 covered submandibular glands. Number of 5 covered the area of control. The stimulation agent (ascorbic acid) was regularly used to accelerate the functions of secretion and excretion. A stimulation provided a rapid way of investigating the secretory function of glandular parenchym and the patency of the major excretory duct without forfeiting any information. When a stimulation was used, a small amount of solution of ascorbic acid was dropped on the surface of the tongue at thirty minutes after intravenously injection of  $^{99m}\text{Tc}$  pertechnetate. The data of radioactive accumulation in the area of each ROI was collected as digital data by the

image analyzer and these digital data were used to obtain "Time Activity Curves" of sequential sialoscintigraphy (dynamic sialoscintigraphy) for selected five interested regions over the major salivary glands and the area of control (figure 4). The ordinate is the radioactive count per frame and the abscissa is the frame number that is time. These curves indicate the uptake, accumulation and excretion of  $^{99m}\text{Tc}$  pertechnetate by salivary glands as a function of time elapsed.

## 2) ANALYSIS OF SIALOSCINTIGRAPHY OF NORMAL PATTERN

Thirty-five patients with inflammation, Sjögren's syndrome, tumor and others underwent this sialoscintigraphic examination with  $^{99m}\text{Tc}$  pertechnetate. They were referred to Kagoshima University Dental Hospital from 1985 to 1989. From them salivary glands of intact were selected and

Tab. 1 Subjects for Analysis of Sialoscintigraphy

	Parotid Gland		Submandibular Gland	
	Right	Left	Right	Left
Disorder	3	5	15	16
Intact	32	30	20	19

(number of glands)

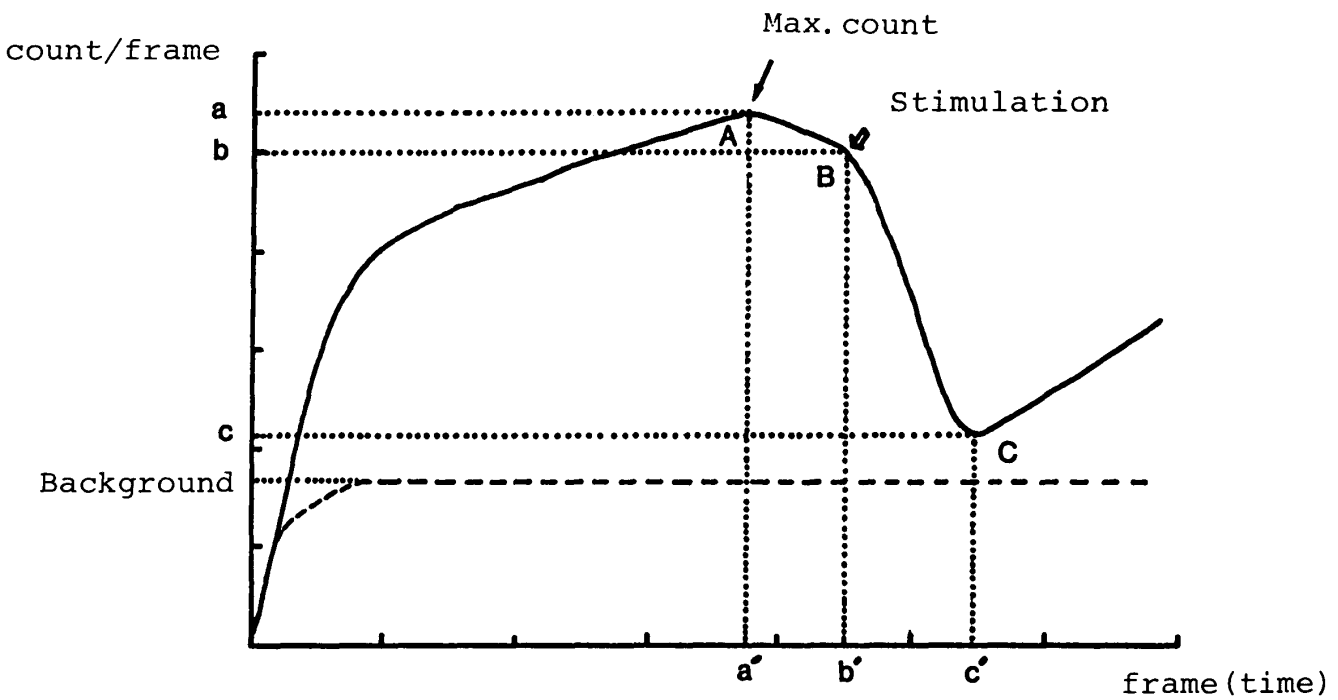


Fig. 5 Analysis of Time Activity Curve

1. Maximum uptake time --- (a')
2. Excretion rate after stimulation  
---  $(1-c/b)$
3. Reaction time ---  $(c' - b')$
4. Ratio of salivary radioactive count to background radioactive count  
---  $(a/\text{background})$

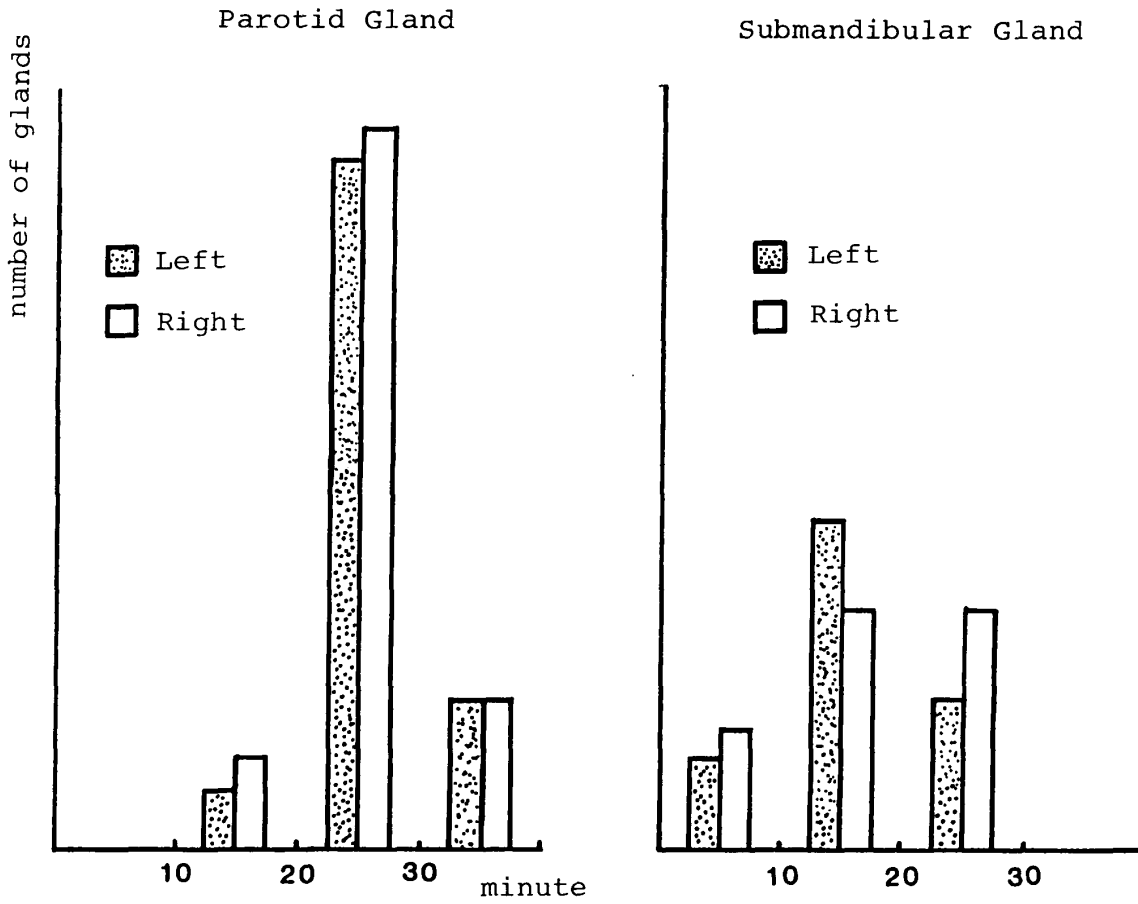


Fig. 6 Maximum Uptake Time

Tab. 2 Maximum Uptake Time

	Parotid Gland		Submandibular Gland	
	Right	Left	Right	Left
Average	25.5	25.9	22.7	20.8
	25.7		21.7	

(minute)

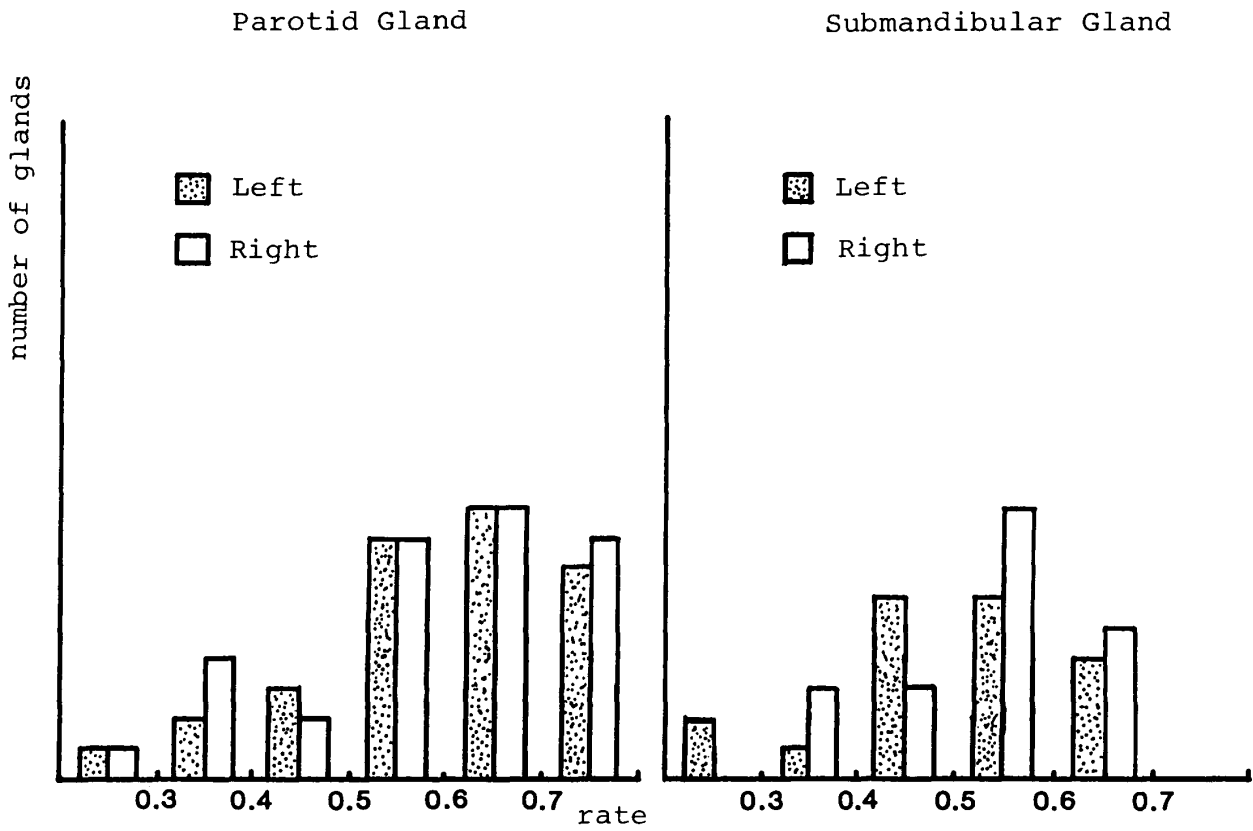


Fig. 7 Excretion Rate after Stimulation

Tab. 3 Excretion Rate after Stimulation

	Parotid Gland		Submandibular Gland	
	Right	Left	Right	Left
Average	0.58	0.60	0.53	0.52
	0.59		0.53	

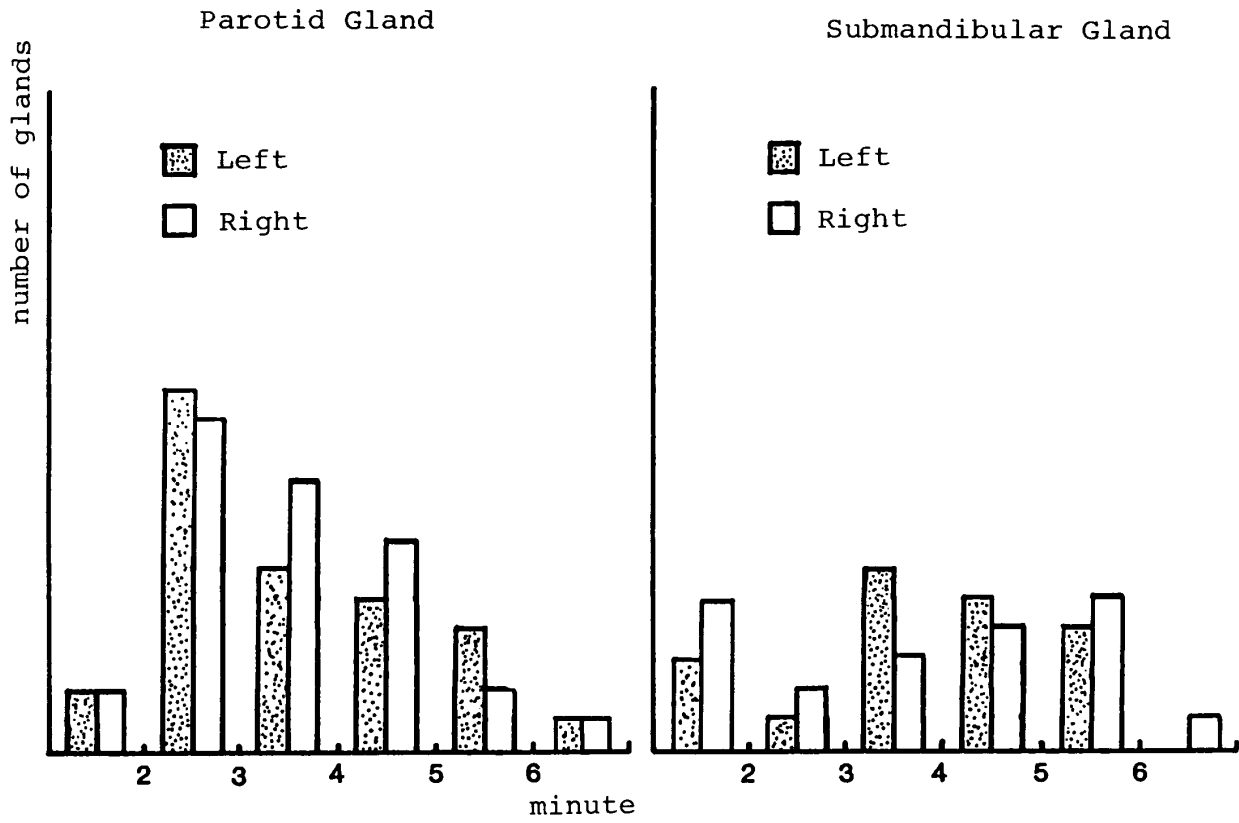


Fig. 8 Reaction time

Tab. 4 Reaction time

	Parotid Gland		Submandibular Gland	
	Right	Left	Right	Left
Average	3.53	3.54	3.70	3.64
	3.53		3.67	

(minute)



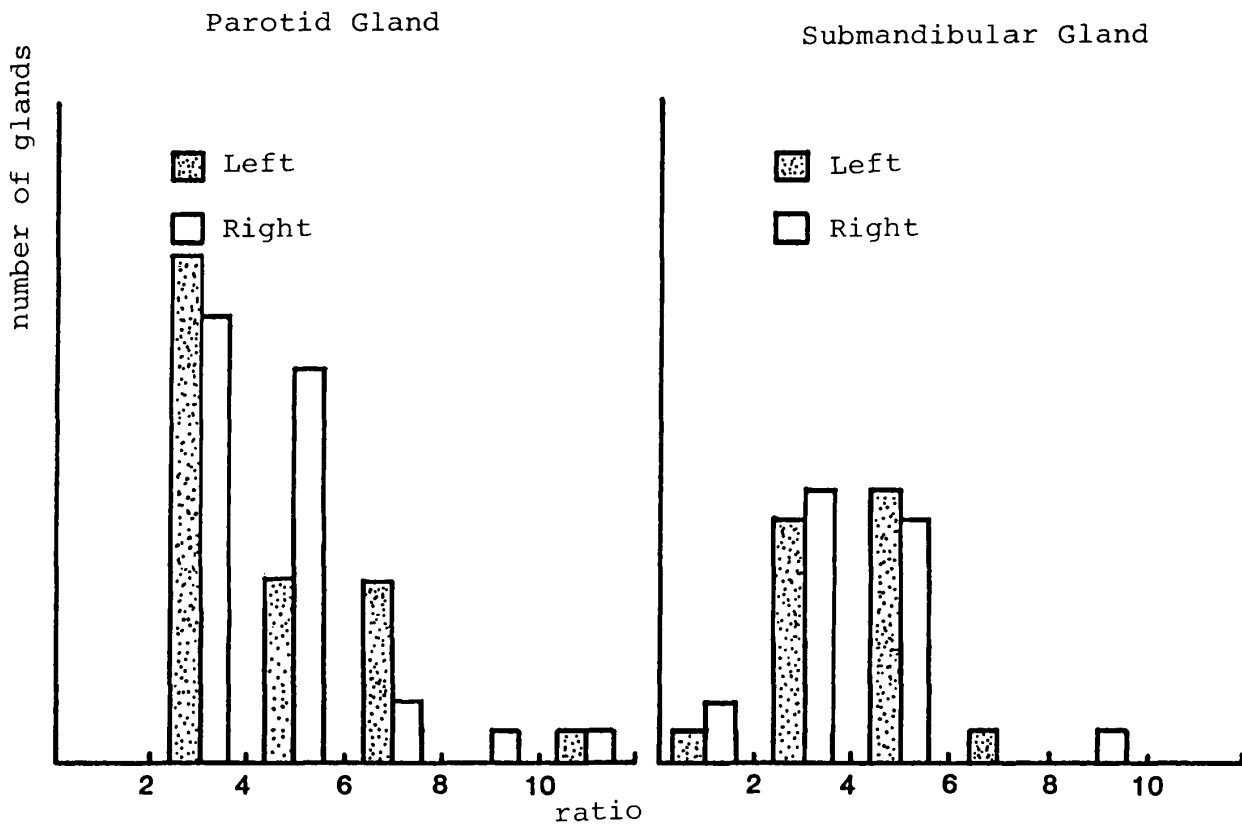


Fig. 9 Ratio of Salivary Radioactive Count to Background Radioactive Count

Tab. 5 Ratio of Salivary Radioactive Count to Background Radioactive Count

	Parotid Gland		Submandibular Gland	
	Right	Left	Right	Left
Average	4.37	4.60	3.88	3.92
	4.48		3.90	

examined to obtain normal pattern of time activity curve and normal static images (table 1). These subjects consisted of thirty-two right, thirty left parotid glands, and twenty right, nineteen left submandibular glands.

The analysis of time activity curves was made by determining parameters as follows; 1) maximum uptake time, 2) excretion rate after stimulation with ascorbic acid, 3) reaction time to stimulation and 4) ratio of salivary radioactive count to background radioactive count (figure 5). The normal pattern of time activity curves of parotid glands and submandibular glands were made by use of the data of intact salivary glands from patients in this investigation.

The results of investigation were as follows. Incidence for maximum uptake time of intact parotid glands and submandibular glands were shown in figure 6. Most of parotid glands reached max-

imum count within twenty or thirty minutes. On the other hand, the maximum uptake time of submandibular glands varied and distributed widely from ten to thirty minutes. There was a slight difference between parotid glands and submandibular glands. Table 2 showed the average of maximum uptake time of parotid glands and submandibular glands respectively. The average of maximum uptake time was about 25.7 minutes in parotid glands and 21.7 minutes in submandibular glands. The submandibular glands reached the maximum radioactive count faster than the parotid glands. The incidence for excretion rate after stimulation, reaction time to stimulation and ratio of salivary radioactive count to background radioactive count were shown in figures 7, 8 and 9 respectively. The average of them were shown in tables 3, 4 and 5. The average of excretion rate were 0.59 in parotid glands and 0.53 in submandibular glands,

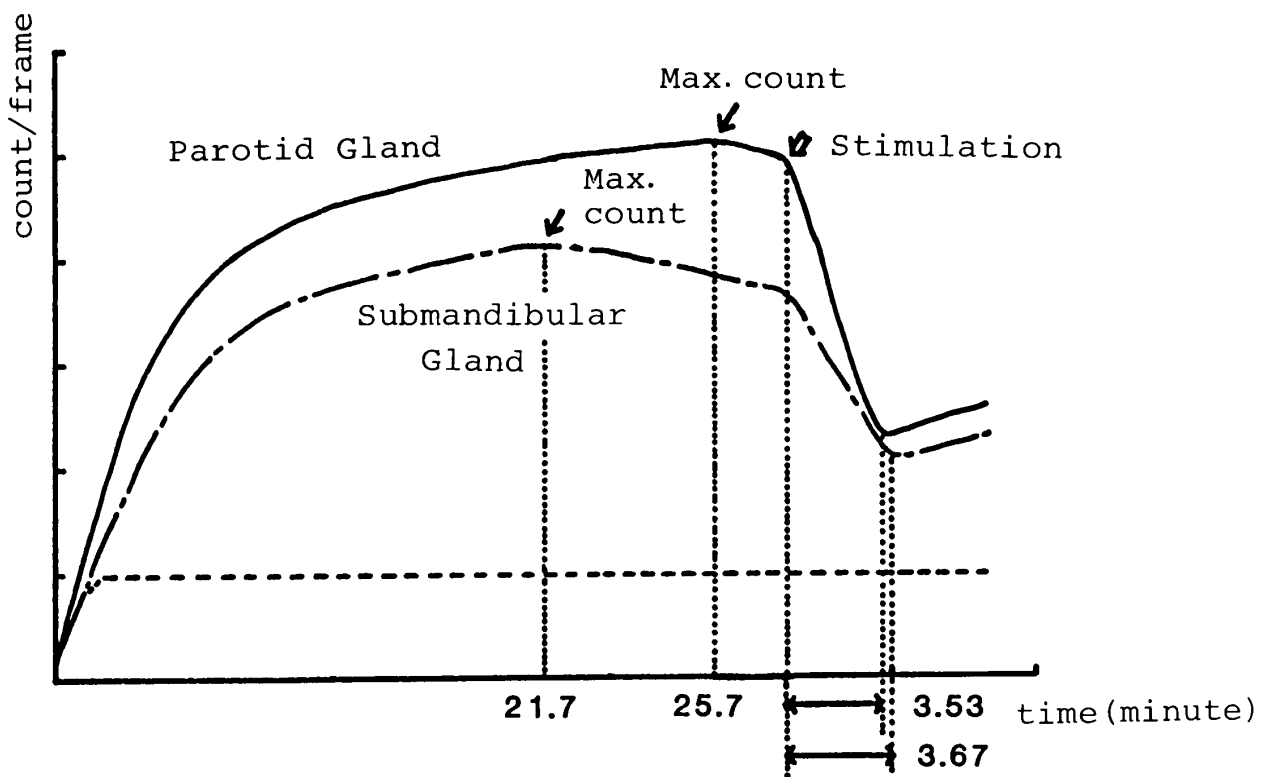


Fig. 10 Time Activity Curve of Normal Pattern

of reaction time were 3.53 minutes in parotid glands and 3.67 minutes in submandibular glands, and of the ratio of salivary radioactive count to background radioactive count were 4.48 in parotid glands and 3.90 in submandibular glands. Both of parotid glands and submandibular glands showed mostly a similar tendency, but the parotid glands were slightly dominant concerning these parameters except for maximum uptake time in comparison with the submandibular glands. On the basis of these results, normal pattern of time activity curves of parotid glands and submandibular glands shown in figure 10 were obtained. The parotid glands and submandibular glands showed a similar pattern of time activity curve essentially. Time activity curves showed a rapid ascent immediately after intravenously injection of  $^{99m}\text{Tc}$  pertechnetate and subsequently showed a gentle rising slope. This phase of rapid ascent showed that the active uptake of  $^{99m}\text{Tc}$  pertechnetate in salivary glands was more predominant than the excretion. The curves continuing to rise gradually

reached the maximum count within 20 or 30 minutes and subsequently described descent. When the stimulation with ascorbic acid was done, the curves fall down head over heels promptly and subsequently reached near the background level within a few minutes, and then showed reuptake. There was no obvious difference between parotid glands and submandibular glands except for maximum uptake time and ratio of salivary radioactive count to background radioactive count. The author determined this pattern of time activity curves shown in figure 10 as normal.

### 3) CASES

Figures 11 and 12 showed a 57 year-old male with inflammation of the right submandibular salivary gland (case 1). This patient was referred to our hospital with a chief complaint of swelling and spontaneous pain in that region and diagnosed as sialolithiasis by radiographic examination. He had an operation for removal of calculus and did not present any symptom after that. But three

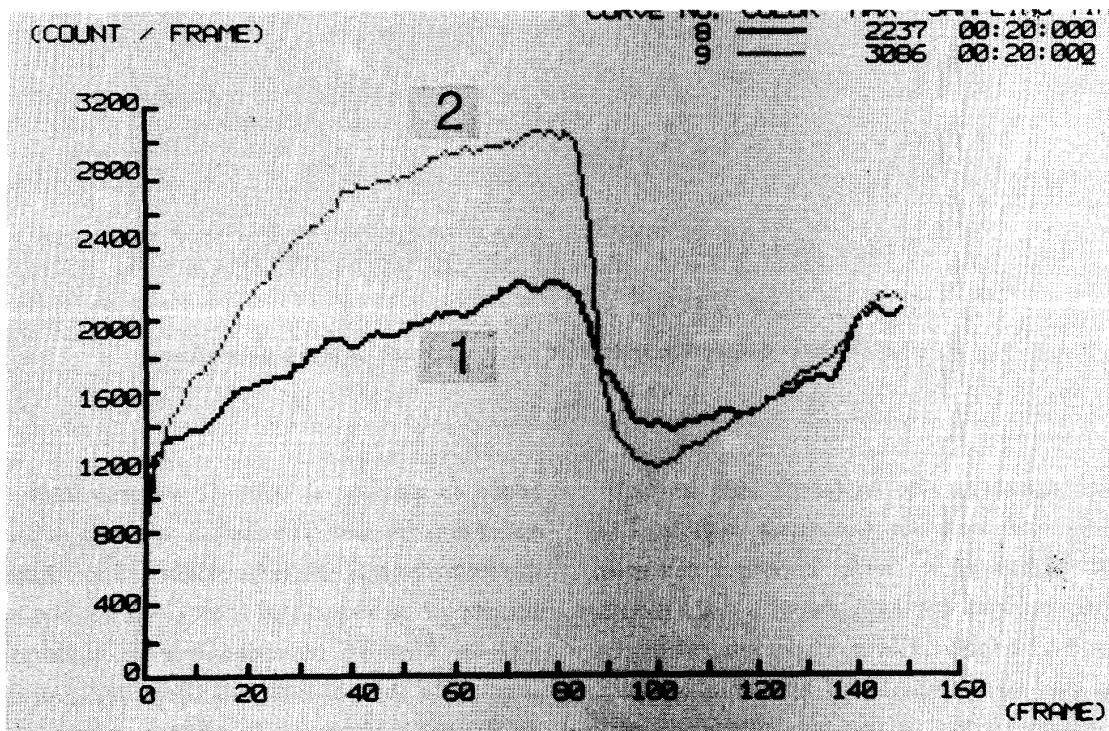


Fig. 11 Time Activity Curve of Submandibular Glands of Case 1. (1): Right, (2): Left  
A remarkable decrease in uptake of  $^{99m}\text{Tc}$  pertechnetate of right gland was shown.

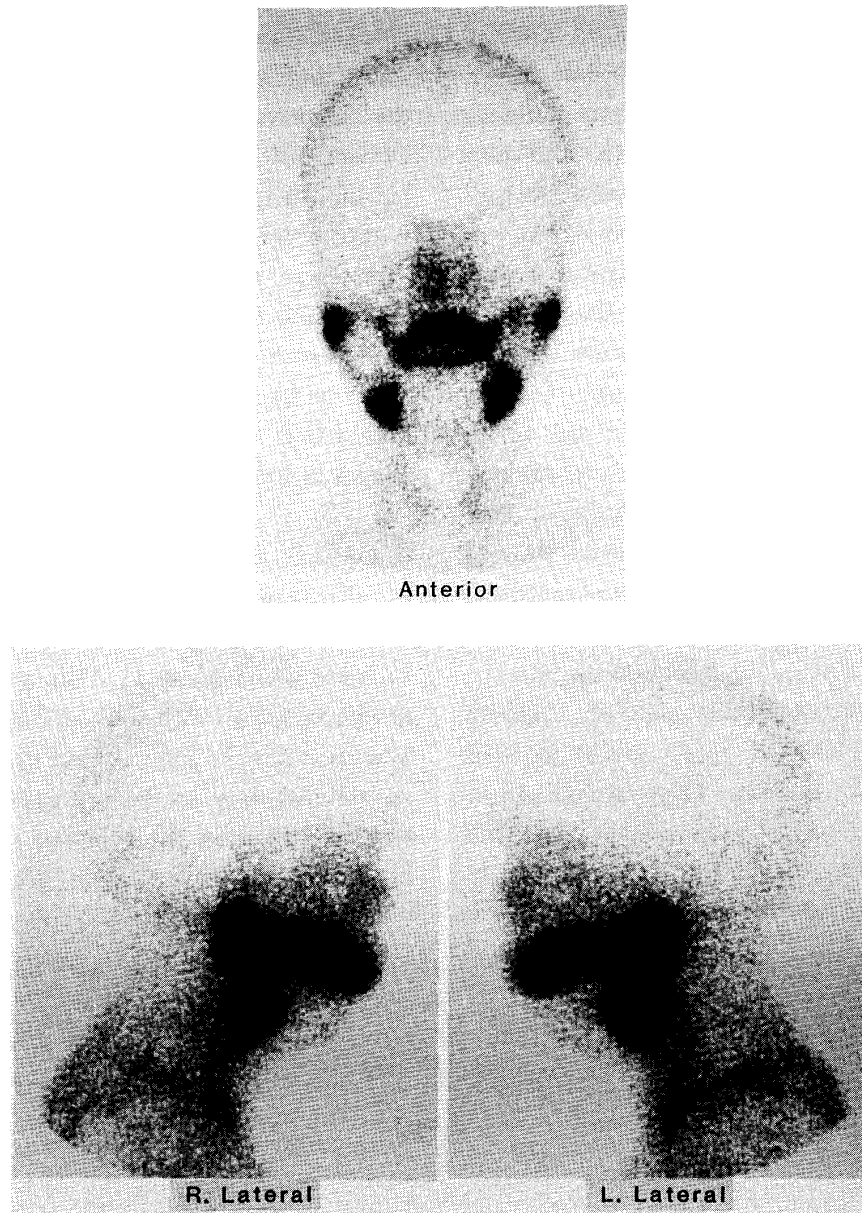


Fig. 12 Static Images of Case 1

No significant difference between right and left glands was shown.

months after operation he suffered from a recurrent swelling and pain in the same region. The findings of sialography with contrast material showed a pronounced enlargement of a main excretory duct and a disappearance of peripheral ducts. Concerning the manifestation of sialoscintigraphy, the time activity curve in the left submandibular gland showed normal pattern which was stated previously. On the other hand, the pattern of right submandibular gland showed a remarkable dec-

rease in uptake of  $^{99m}\text{Tc}$  pertechnetate. But the excretion by the stimulation with ascorbic acid indicated normal pattern (figure 11). About static images of anterior and lateral views, the accumulation of  $^{99m}\text{Tc}$  pertechnetate of right gland was similar to that of left and there was no significant difference (figure 12). These sialoscintigraphic findings indicated the slightly decreased function of uptake and accumulation of right submandibular salivary gland.

Figures 13 and 14 showed a 73 year-old female with a chief complaint of xerostomia (case 2). This patient did not have swelling and pain. She did not undergo sialographic examination but she was suspected as Sjögren's syndrome by other clinical findings. Time activity curves showed abnormal patterns except for that of right parotid gland (figure 13, curve No.1). The left parotid gland (curve No.2) demonstrated the marked decrease in accumulation of 99m-Tc pertechnetate which was fallen down about half in count of right normal parotid gland. Besides the function of excretion was severely disturbed. Both of submandibular glands (curve No. 3 and 4) revealed a decrease in uptake, and showed remarkable lower in func-

tion of excretion. About static images there was no significant change (figure 14). These time activity curves of sialoscintigraphy well explained the clinical feature of xerostomia. The author determined this case 2 as Sjögren's syndrome of stage 2 of Alarcón-Segovia according to sialoscintigraphic manifestations.

Figures 15, 16 and 17 showed a 57 year-old male with a chief complaint of tumor formation in the left parotid gland which was as large as hen's egg and elastic hard (case 3). The sialograph with contrast material showed an enlargement of main excretory duct and a displacement of peripheral ducts. This was a typical finding so-called as "ball in hand" (figure 15). The static images of sialos-

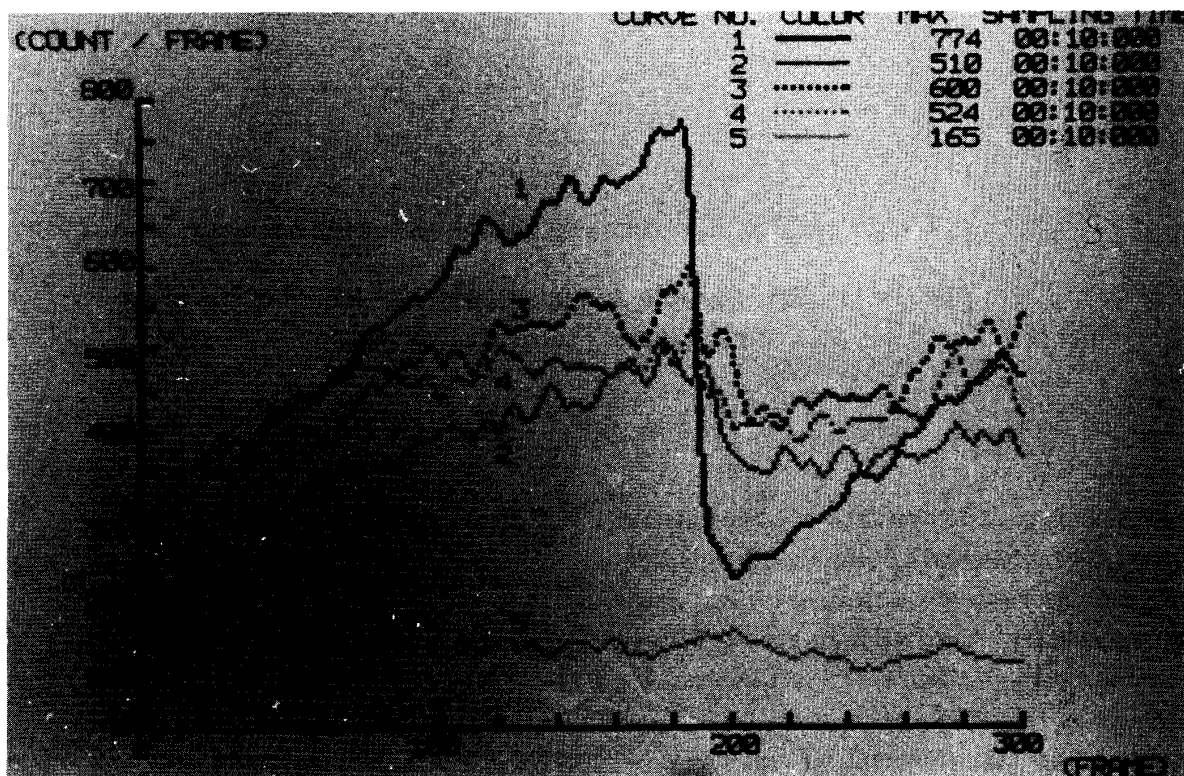


Fig. 13 Time Activity Curves of Case 2

- (1): Right Parotid Gland
- (2): Left Parotid Gland
- (3): Right Submandibular Gland
- (4): Left Submandibular Gland
- (5): Background as control

The curves showed abnormal patterns except for right parotid gland and a typical lower in function of excretion.

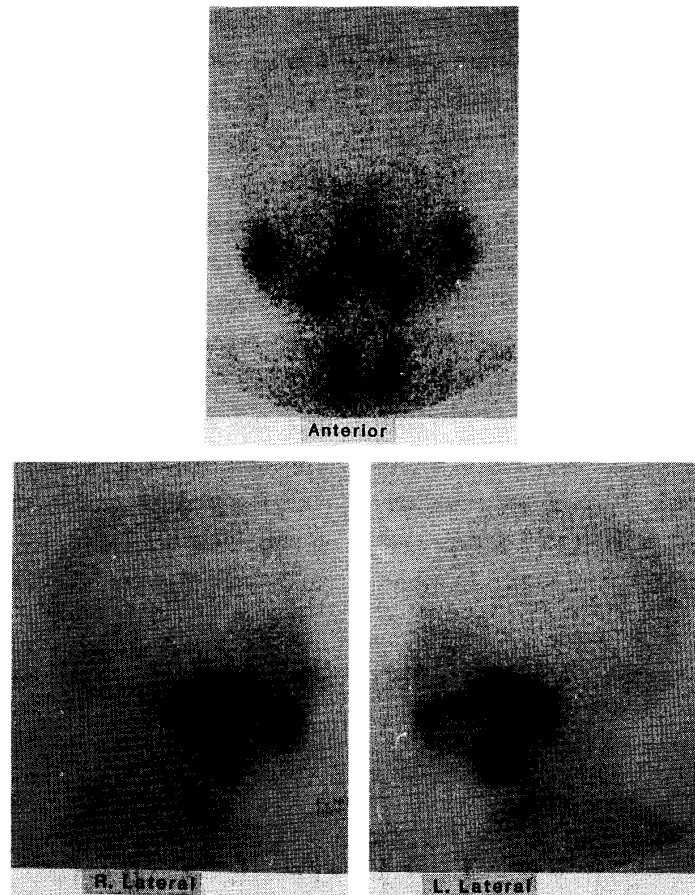


Fig. 14 Static Images of Case 2  
No significant change was shown.

cintigraphy showed the decrease in accumulation (left lateral view, figure 16) and typical displacement of glandular parenchyma (anterior view, figure 16). On the contrary, time activity curves showed mostly normal pattern (figure 17). In this case, the displacement of salivary gland was the typical manifestation, but the function of uptake, accumulation and excretion of  $^{99m}\text{Tc}$  pertechnetate were not severely disturbed. The histopathological diagnosis of this case 3 was adenoid cystic carcinoma in pleomorphic adenoma.

Figures 18 and 19 showed a 67 year-old female with a chief complaint of tumor formation in the inferior part of the left parotid gland which was elastic hard and a size of baby's fist (case 4). Figure 18 taken immediately before and after a

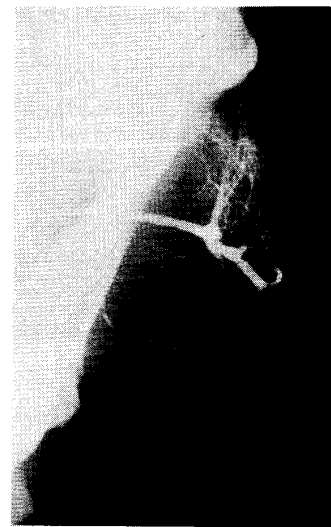


Fig. 15 Sialography of Left Parotid Gland of Case 3  
An enlargement of main excretory duct and a displacement of peripheral duct were shown (so-called as "ball in hand").

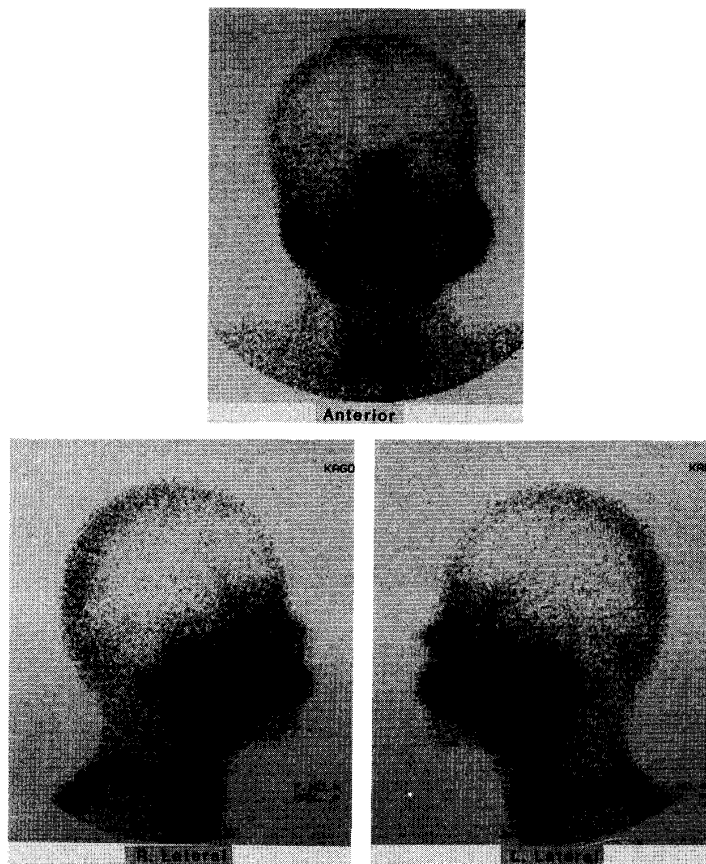


Fig. 16 Static Images of Case 3

A decrease in accumulation and a displacement of left parotid glandular parenchym were shown.

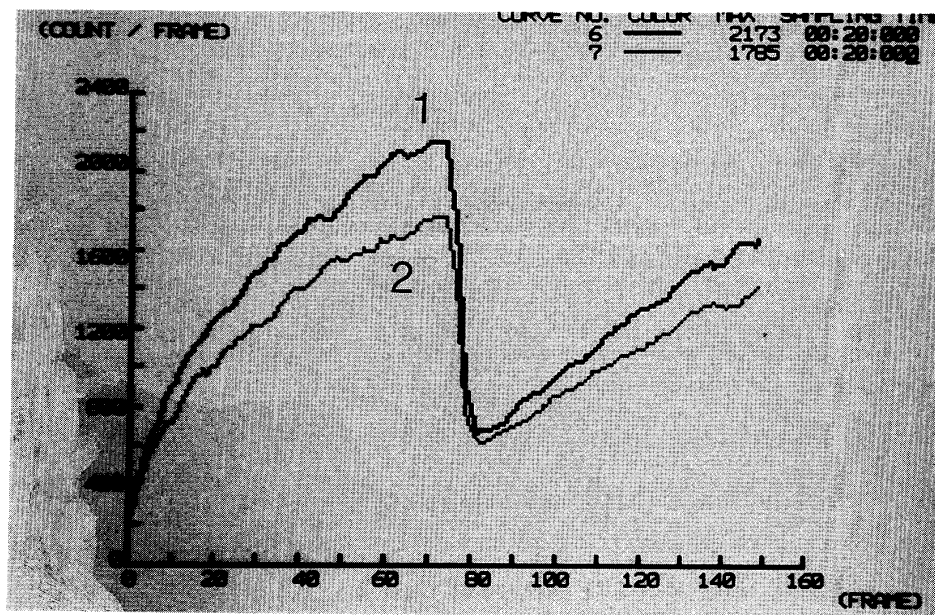


Fig. 17 Time Activity Curves of Case 3

(1): Right Parotid Gland

(2): Left Parotid Gland

No significant difference between right and left parotid glands was shown.

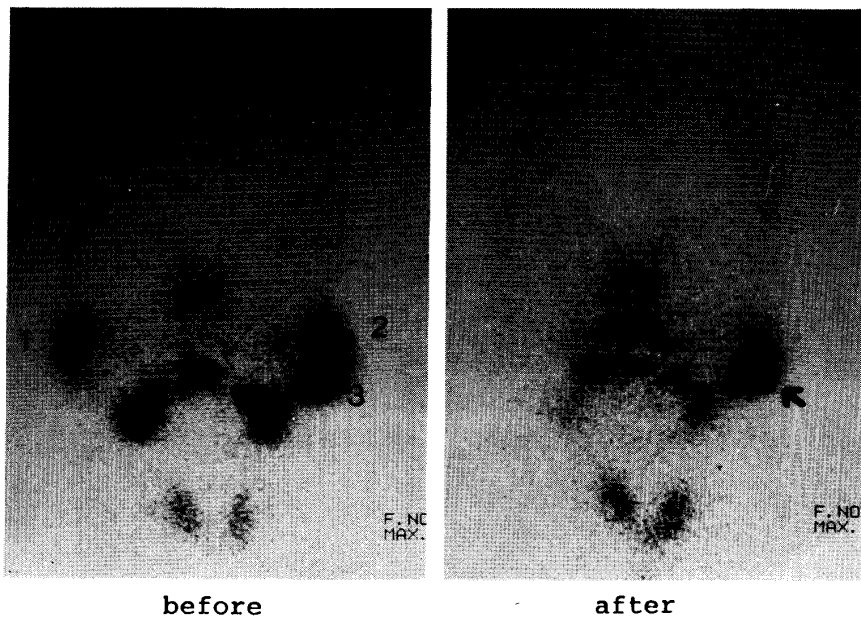


Fig. 18 Static Images of Case 4

- (1): Right Parotid Gland
- (2): Left Parotid Gland
- (3): Region of Tumor

These scintigraphs taken immediately before and after a stimulation with ascorbic acid showed a prompt excretion from all salivary glands. On the contrary, a significant retention in the region of tumor was shown (↑).

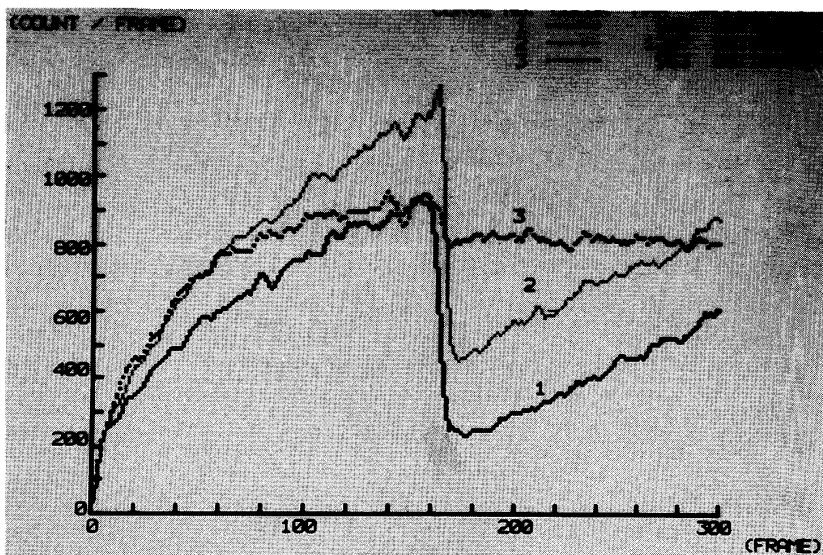


Fig.19 Time Activity Curves of Case 4

- (1): Right Parotid Gland
- (2): Left Parotid Gland
- (3): Region of Tumor

The curve of tumor showed no reaction to stimulation (No.3)



stimulation with ascorbic acid revealed that there was a remarkable increase in accumulation of 99m-Tc pertechnetate in the tumor lesion (before) and a prompt excretion of 99m-Tc pertechnetate from all salivary glands by stimulation (after). However on the contrary, there was a significant retention of 99m-Tc pertechnetate in the region of tumor (after, figure 18). Figure 19 showed time activity curves and the curve of tumor region (curve No.3) revealed no reaction to stimulation. This sialoscintigraphic manifestations suggested the identification of Warthin's tumor.

## DISCUSSION

Radiological examination of salivary glands may be desirable for two reasons; 1) to study the morphology of the gland and any space-occupying lesions, and 2) to evaluate the salivary function of the glands. Sialography with contrast material is useful primarily for the study of morphology of a main excretory duct and peripheral ducts. While the technique of nuclear medicine is utilized for evaluation of the morphology of the glandular parenchyma and the salivary function of glands. Especially concerning the salivary function, the sialoscintigraphy of nuclear technique is more predominant than the sialography.<sup>11-15)</sup> As an agent of nuclear scanning for the salivary glands, iodine was used in 1950's<sup>16)</sup> but in recent years 99m-Tc pertechnetate has displaced iodine.<sup>2)</sup> The distribution of iodine and 99m-Tc pertechnetate in salivary glands were qualitatively similar.<sup>5)</sup> 99m-Tc pertechnetate is well suitable for human scanning because it has a gamma radiation (140 keV, 87.9%), short physical half-life of six hours and lack of beta radiation.<sup>17)</sup> These excellent properties permit the introduction of large amounts of radioactivity to improve scintigraphic reliability while minimizing radiation exposure of the patient. About the sialoscintigraphy, we selected four parameters from the time activity curve with reference to previous report.<sup>18)</sup> The parameters of maximum uptake time and ratio of salivary radioactive count to background radioactive count exhibit the func-

tion of active uptake and accumulation, and excretion rate and reaction time showed the function of secretion and excretion. The initial sharp ascent of time activity curve was the phase of active uptake of 99m-Tc pertechnetate by glandular parenchyma and this phase mostly depends on arterial blood supply.<sup>9)</sup> Subsequently the curve gradually rises to the maximum count and this phase indicates that the uptake rate was generally similar to the secretion rate of saliva. The difference of curve pattern between parotid glands and submandibular glands resulted from the fact that the flow rate of submandibular glands is two to three times greater than that of parotid glands,<sup>9)</sup> and partly depends on the glandular volume. The reaction time and excretion rate reflect the function of glandular secretion and ductal excretion. In our normal series, there was an interindividual variability of time activity curve and a broad normal extent.<sup>13)</sup> But the time activity curves of both parotid glands and submandibular glands are generally similar to each other. Besides the symmetry between right and left glands generally observed. So it is possible to make an interindividual comparison between right and left glandular function in unilateral disease.<sup>9)</sup> Kessler and others concluded that serous glands accumulate 99m-Tc pertechnetate faster than either mixed glands or mucous glands.<sup>19)</sup> However in our normal series, the submandibular gland reached the maximum count earlier than the parotid gland. So our investigation suggests that the time activity curve are reflected not by the histological type of glands but by the flow rate. The static images, which reflect the function of accumulation of 99m-Tc pertechnetate in glandular parenchyma, provided a visual information and were useful for unilateral diseases (shown in case 1 and case 3), but mostly powerless in slight and bilateral diseases (shown in case 2). The accumulation in time activity curve were interpreted as a data of proportion to background radioactive count, so this data had an objectivity. In our clinical series, the decrease in accumulation of 99m-Tc pertechnetate was shown in most of salivary diseases except for Warthin's tumor and the decrease in excretion

was shown in Sjögren's syndrome.<sup>20-24)</sup> These manifestations were characteristic in the functional disturbance. However it was not able to differentiate accurately the diseases by sialoscintigraphy only except for Warthin's tumor.<sup>25,26)</sup>

In conclusion, sialoscintigraphy with 99m-Tc pertechnetate provided to us the informations of the glandular function, the ductal function and morphology of glandular parenchym without any invasion.<sup>27)</sup> These informations permitted us to dermine the salivry gland diseases under considering the functions as well as clinical features.

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