Origin and Location of the Oral Activity in Sequential Salivary Gland Scintigraphy with ^{99m}Tc-Pertechnetate

H. P. van den Akker, E. Busemann Sokole, and J. B. van der Schoot

University of Amsterdam, Amsterdam, The Netherlands

Conflicting views exist regarding the origin and location of the oral radioactivity seen in salivary gland scintigraphy with ^{99m}Tc-pertechnetate. The normal accumulation of oral activity was studied in a series of healthy subjects by sequential scintigraphy (anterior and lateral views) after intravenous injection of 2 mCi of ^{99m}Tc-pertechnetate. Ligation of the parotid ducts and/or cannulation of the submandibular ducts, which prevented their secretions from reaching the oral cavity, established that the oral activity was due entirely to radioactive saliva secreted by the parotid and submandibular glands. Pertechnetate mouthwash studies confirmed that radioactive saliva is adsorbed to oral mucosa and that adsorption to the lingual mucosa is the major contributor to the oral activity. Pertechnetate uptake in sublingual and minor salivary glands of the oral cavity was not visualized, thereby invalidating scintigraphy in the study of these glands. In the diagnosis of salivary gland disorders, oral activity is a useful indicator of major salivary gland function.

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Scintigraphy of the salivary glands using ^{99m}Tc-pertechnetate was introduced into clinical practice by Börner et al. in 1965 (*1*). During the ensuing 10 years both static and dynamic scintigraphy have become increasingly popular as noninvasive means of investigating salivary gland disorders, even though the diagnostic limitations have not yet been fully established. The major difficulty with these scintigraphic studies is the disagreement regarding the origin of the "oral activity," the radioactivity seen to accumulate in the oral region. This activity has been attributed by some to pertechnetate uptake in the sublingual and minor salivary glands (*1–5*) and by others to radioactive saliva secreted by the parotid and submandibular glands (*6,7*). To further complicate the matter, many investigators have accepted both sources, but without reference to their relative contributions (*8–16*).

In the present study, the exact origin and location of the oral activity were investigated in a series of volunteers in order to establish the significance of this activity in salivary gland scintigraphy.

MATERIALS AND METHODS

Sequential scintigraphy was performed in 18 healthy volunteers, none having a history of salivary gland disorder, to study the accumulation of ^{99m}Tc-pertechnetate in the region of the oral cavity. Informed consent was obtained from each subject before his participation. A Searle Radiographics Pho/Gamma III HP scintillation camera and a low-energy high-resolution parallel-hole collimator were used, together with a 4,096-channel analyzer and magnetic tape data-processing system. In all subjects sequential studies were carried out in the frontal view, with the subject in the supine position and with the head slightly extended. Immediately after intravenous injection of 2 mCi of ^{99m}Tc-pertechnetate, consecutive 2-min scintiscans were made up to 10 min, followed by 5-min scintiscans every 10 min up

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For reprints contact: E. Busemann Sokole, Dept. of Nuclear Medicine, University Hospital "Wilhelmina Gasthuis," le Helmersstraat 104, Amsterdam, The Netherlands.

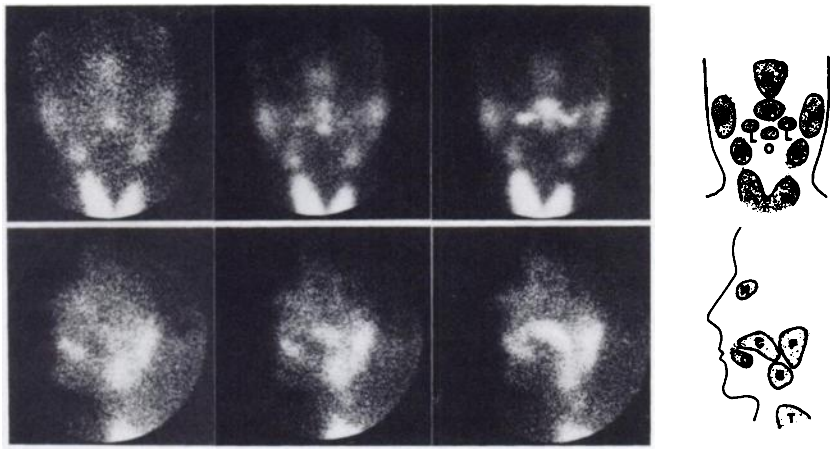

FIG. 1. Normal sequential images in frontal (top) and left lateral (bottom) views after intravenous injection of ^{99m}Tc-pertechnetate. Diagrams show locations of parotid gland (P), submandibular gland (S), central activity (C), lower activity (O), lateral activity (L), nasal activity (N), and thyroid gland (T).

to 65 min after injection. The digitized data were stored on magnetic tape at 2-min intervals and later replayed to obtain time–activity curves for selected regions over the right and left parotid and submandibular glands (4 cm^2) and different parts of the oral activity (2.5 cm^2). Positional changes resulting from opening the mouth were investigated after completion of the sequential series: scintiscans in frontal and lateral views were obtained with the mouth closed and with the mouth held maximally open with a bite block. In four subjects the position of the palate was established in frontal and lateral views by an acrylic palatal plate containing a small ^{99m}Tc marker in the midline. In two subjects, lateral sequential studies up to 65 min after injection were carried out to follow the accumulation of oral activity in this projection.

The effects of radioactive saliva secreted by the major salivary glands were studied in eight subjects. In five subjects saliva from these glands was prevented from reaching the mouth by ligation of both parotid ducts and cannulation of both submandibular ducts, after which the sequential study was started. The individual contributions of these glands were studied in three subjects in whom, respectively, one parotid duct was ligated, both parotid ducts were ligated, and both submandibular ducts were cannulated. In each subject, the sequential study was continued up to 55 min after injection of ^{99m}Tc-pertechnetate and compared with a normal study performed 1 week previously. Ligation merely involved tying a suture around the parotid duct under local anesthesia. The temporary obstruction caused no adverse effects throughout a 1-year followup.

In two subjects, a submandibular duct was located by inserting a polyethylene catheter cut to the length of the duct and containing a small ^{99m}Tc source at each end. Before introducing the catheter into the submandibular duct, the lingual nerve was anesthetized with a 2% lidocaine solution. This also blocked the secretory–motor fibers to the submandibular gland, thereby preventing obstructive symptoms from developing. In two other subjects the orifice of the parotid duct was located on the scintiscans using only the tip of a catheter containing a small ^{99m}Tc marker.

Frontal and lateral scintiscans were obtained in three subjects after a saline mouthwash containing 0.5 mCi of ^{99m}Tc-pertechnetate had been held in the mouth for 10 min. Scintiscans were then repeated twice, each time after thoroughly rinsing the mouth with saline solution for 10 min. The data were stored on magnetic tape and replayed to calculate the percentage of activity retained in the oral cavity after each rinse.

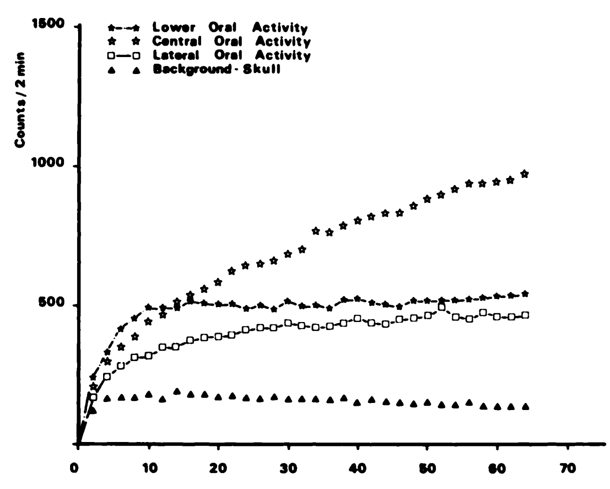

FIG. 2. Relative shapes and magnitudes of time–activity curves from 2.5-cm^2 regions in oral activity after intravenous injection of 2 mCi of ^{99m}Tc-pertechnetate. Curves are averaged from ten normal subjects and are uncorrected for background activity because of its variable magnitude in different oral regions.

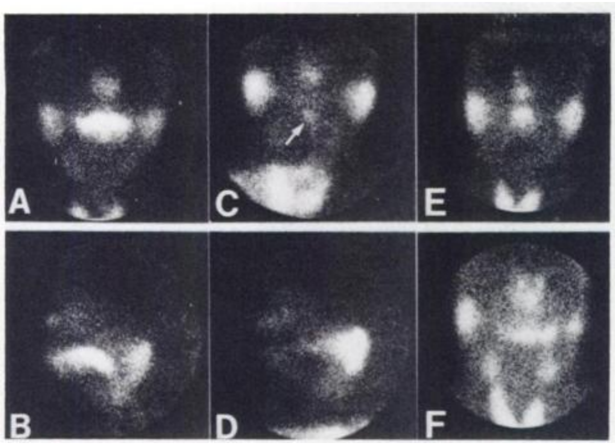

FIG. 3. Oral activity seen frontally (A) and laterally (B) in normal study is absent after ligation of both parotid ducts and cannulation of both submandibular ducts (C,D). Radioactive saliva in submandibular duct catheters is visible on frontal image in midline, particularly where catheters run briefly toward detector after emerging from mouth (C arrow). Haze over thyroid region (C,D) is due to leakage from catheters onto absorbent paper. Ligation of parotid ducts (without submandibular cannulation) suppresses lateral oral activity, both for bilateral ligation (E) and for right ligation only (F). Note retention of activity in obstructed glands (C,F). Images obtained 50–65 min after injection.

RESULTS

In all normal frontal and lateral sequential studies, radioactivity became visible in the oral region during the first 10 min after the intravenous injection of ^{99m}Tc-pertechnetate. As early as 4 min after injection, the frontal images showed weak diffuse bands of activity extending cranially from the submandibular glands to the midline. These bands were followed by distinct activity in the midline ("lower activity"), which in lateral studies corresponded to activity ventrally in the oral region (Fig. 1). Activity in the upper part of the mouth ("central activity") became discernible by 10 min and increased until it became the predominant feature, surpassing submandibular gland activity within 20 min and parotid gland activity within 40 min after injection. In the lateral projection the central activity was seen to be crescent-shaped and nonuniform (Fig. 1), with its most intense part situated posteriorly. The lower activity gradually seemed to merge with the increasing central activity, subsequently becoming less distinct. Activity laterally in the oral cavity ("lateral activity") appeared at the same time as, or slightly later than the central activity and accumulated to form either separate collections of activity or lateral extensions of the central activity (Fig. 1). As with the lower activity, the central and lateral activities were preceded by the appearance of weak diffuse bands extending from the parotid glands to the oral region.

Time–activity curves of the central, lower, and lateral activities generally showed consistent shapes (Fig. 2). The central activity continuously increased, whereas the lower activity either increased gradually to a plateau or decreased after reaching a maximum at 10–20 min. The two lateral activities were usually equal and tended to increase gradually. In 8 of the 18 subjects, sudden decreases were observed in glandular curves. Such a decrease in submandibular gland activity always correlated with a concurrent peak or increase in lower activity; similarly, a sudden decrease in parotid gland activity always correlated with a concurrent sharp increase in lateral activity.

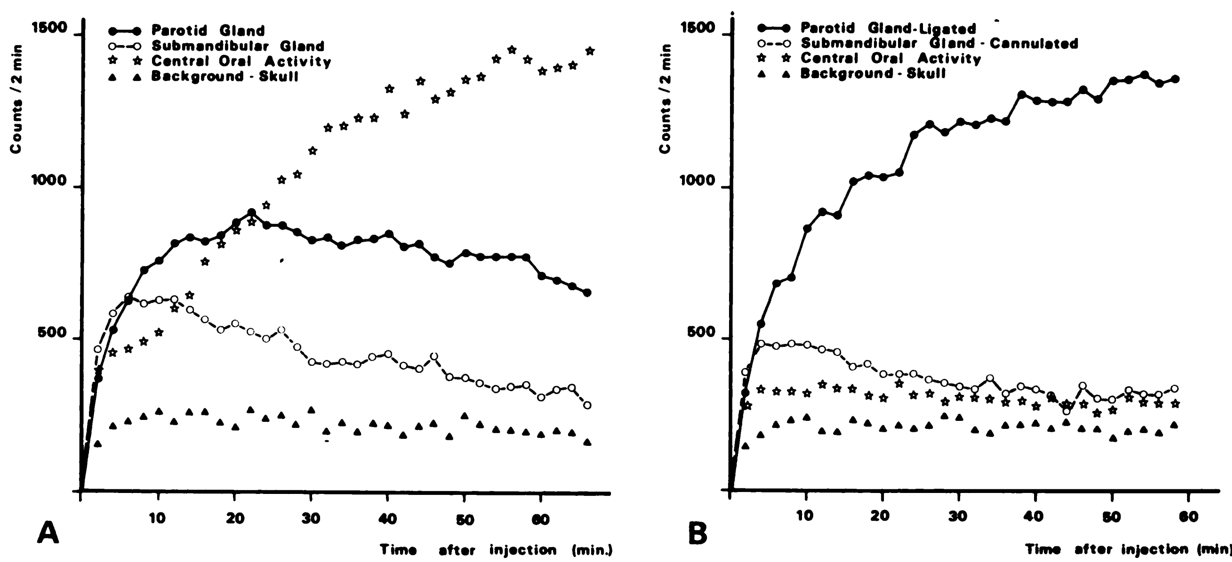

FIG. 4. Time–activity curves from subject shown in Figs. 3A–D. (A) Normal study and (B) after ligation of both parotid ducts and cannulation of both submandibular ducts. All regions of interest are 4 cm^2.

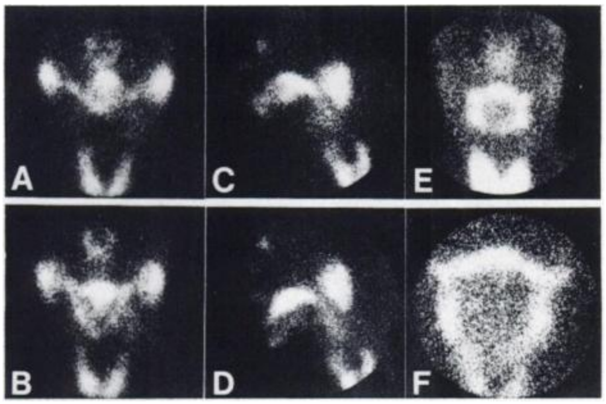

FIG. 5. Frontal images with mouth closed (A) and open (B) show downward displacement of oral activity and separation of nasal and central oral activity when mouth is opened. Note triangular configuration of oral activity when mouth is open. Lateral images with mouth closed (C) and open (D) further elucidate changes (see text). (E) Frontal mouth-open image; (F) repeat with pinhole collimator. Note almost circular configuration of oral activity and central area of diminished radioactivity.

In sequential studies after ligation of both parotid ducts and cannulation of both submandibular ducts, no accumulation of oral activity was observed (Figs. 3 and 4). Only ligation of parotid duct(s) resulted in absence or slight accumulation of lateral activity (Figs. 3E and 3F). As seen in lateral views, only cannulation of submandibular ducts resulted in absence of lower activity. This effect was obscured in frontal views by radioactive saliva in the cannulas (see cannula artifact in Fig. 3C).

The scintiscans obtained with the mouth closed and open showed a striking difference both in the configuration and in the position of the oral activity (Fig. 5). In frontal views with the mouth open, the oral activity as a whole was displaced downwards; in addition, the central and lower activities were separated, leaving an area of diminished activity between them, and the lateral activities lengthened in a downward and medial direction. On lateral images, the oral activity shifted in a ventrocaudal direction when the mouth was opened with the most intense posterior part changing from a dorsocaudal to a horizontal or even a ventrocaudal direction. Radioactive markers established the location of the palate, the submandibular duct, and the parotid duct orifice and related these structures to the oral activity (Fig. 6).

Radioactivity was retained in the mouth after a ^{99m}Tc-pertechnetate mouthwash. Figure 7 shows that this retained oral activity closely resembles the oral activity seen after intravenous injection not only in configuration, but also in displacement when the mouth is opened. After the mouth was thoroughly rinsed with saline solution, the distribution of the oral radioactivity remained the same, although the total activity decreased on the average by 25% after the first rinse (range, 10–37%) and a further 7% after the second rinse (range, 4–10%).

DISCUSSION

Within 2–4 min after intravenous injection of ^{99m}Tc-pertechnetate in normal subjects, areas of increased activity in the salivary gland region were recognized and could be identified with the parotid and submandibular glands. Increased activity in the region of the oral cavity appeared during the initial 10 min after injection, but its correspondence with anatomic structures could not be so readily ascertained. Moreover, this oral activity became greater than either parotid or submandibular gland uptake and usually was still increasing at 1 hr after injection, whereas the parotid and submandibular glands reached their maximum uptake considerably earlier (*17*). In the literature, two unrelated explanations for the oral activity are presented. Several authors (*1–5*) attribute the oral activity solely to uptake in the sublingual and the minor salivary glands, particularly the palatine glands. They suggest that scintigraphy provides the only method of investigating minor salivary gland function, and therefore diminished or absent oral activity is interpreted as con-

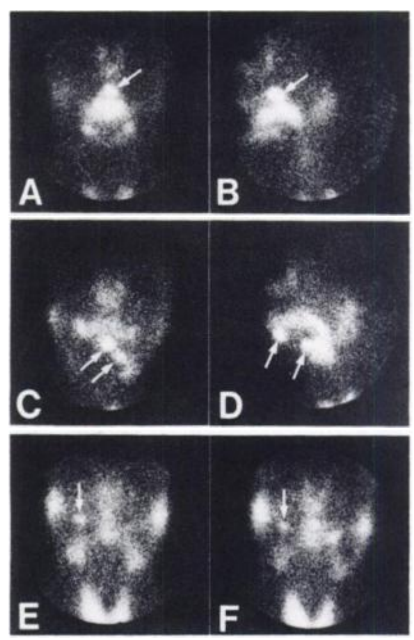

FIG. 6. Radioactive markers on palate (arrows) appear as small areas of activity separate from and above oral activity when mouth is open: (A) frontal; (B) lateral. Compare with mouthwash images (Figs. 7B and 7D). On frontal (C) and lateral (D) images, markers in catheter show course and length of left submandibular duct (arrows). Early (10–15 min) frontal image (E) shows marker blocking right parotid duct orifice (arrow). Later (40–45 min) lateral oral activity is seen on left side, opposite to marker (F). Note obstructive retention in right parotid gland.

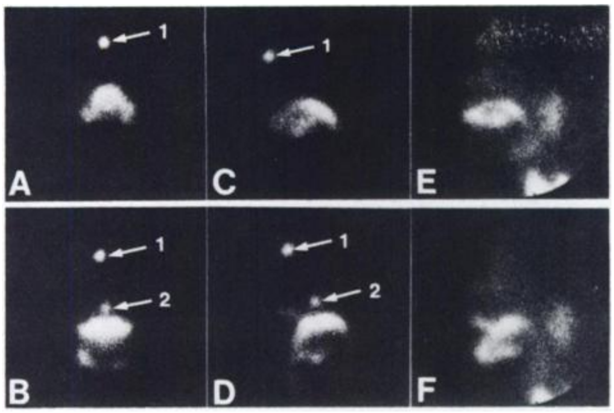

FIG. 7. Retained pertechnetate mouthwash activity viewed frontally (A,B) and laterally (C,D) with mouth closed (A,C) and open (B,D). Markers are on bridge of nose (Arrow 1) and on palate (Arrow 2). Note configuration and displacement of retained activity on opening mouth and separate location of palatal marker. Mouthwash activity (C,D) closely resembles oral activity after intravenous injection of pertechnetate, viewed laterally with mouth closed (E) and open (F).

clusive evidence of minor salivary gland involvement in systemic glandular disorders, such as Sjögren's disease. On the other hand, Harden et al. (*6*) suggest that the oral activity is mainly due to saliva from the major salivary glands; they conclude that adsorption of pertechnetate to the oral mucosa takes place, since the small volume of radioactive saliva in the mouth would not account for the oral activity seen. While they do not rule out the minor salivary glands altogether, they consider adsorption to be the more important factor. Most authors accept both these explanations for the oral activity (*8–16*). However, without a clear indication as to the relative contributions of radioactive saliva and minor gland uptake, the oral activity cannot be properly interpreted.

Our ligation and cannulation studies clearly show that the oral activity visualized during the normal sequential studies was entirely dependent on radioactive saliva secreted by the parotid and submandibular glands. It follows that scintigraphy cannot be used to investigate the function of minor salivary glands. However, since pertechnetate concentration in minor salivary gland tissue does occur (*18*), our observations show that uptake in these glands does not become visible above background.

Although we have shown that oral activity is due to radioactive saliva, the continuous increase and considerable magnitude of this oral activity cannot be accounted for solely by saliva circulating in the oral cavity. Adsorption of pertechnetate to the oral mucosa, as suggested by Harden et al. (*6*), must therefore be considered. Our pertechnetate mouthwash studies support Harden's thesis, since the radioactivity was not only partially retained in the oral cavity after the mouthwash, but it maintained the same activity distribution. The similarity in activity distributions from mouthwash and intravenous pertechnetate further indicates mucosal adsorption of pertechnetate from radioactive saliva. We are currently exploring this further with autoradiographic studies.

Valuable insight into the location of the oral activity was gained from the views obtained when the mouth was open. The downward displacement of the central activity, resulting in distinct separation from the palatal marker, ruled out the palate as the location of this activity. Particularly in the lateral view, the configuration and displacement of central activity suggests its location on the tongue. This might be explained by the numerous lingual papillae which provide a large surface area for mucosal adsorption of pertechnetate.

The lateral activity originated mainly from parotid secretions, since this activity did not accumulate when salivary flow from the parotid gland was obstructed. The diffuse bands of activity often seen between the parotid glands and the mouth represented radioactive saliva in the parotid ducts. Lateral activity appeared to be situated in the region of the buccal mucosa near the parotid duct orifice, as suggested by Grove and Di Chiro (*8*) and Sorsdahl et al. (*9*). When seen in frontal images, the lengthening of the lateral activity in a downward direction corresponds to the stretching of the buccal mucosa that occurs when the mouth is opened. Activity in the horseshoe-shaped mandibular sulcus now also became discernible due to the change in the angle between the mandible and the detector.

Markers placed at each end of a submandibular duct not only located the length and course of the duct on the scintiscans, but also defined the position of the sublingual gland, whose medial surface is in close contact with the duct. In our series, no accumulation of pertechnetate was observed in the sublingual glands. Furthermore, in a patient, we were able to measure the concentration of pertechnetate in a histologically normal sublingual gland, removed during surgery, in the floor of the mouth at 1 hr after intravenous injection of 2 mCi of ^{99m}Tc-pertechnetate. Plasma samples obtained at the time of excision were also measured, and a gland-to-plasma (G/P) concentration ratio of 0.69 was found [G/P = (percent dose/gm gland)/(percent dose/ml plasma)]. By comparison, also at 1 hr after injection of pertechnetate, Lazarus et al. (*19*) found a mean G/P ratio of 2.50 ($n = 6$) for excised parotid tissue. For rat muscle, Papadopoulos et al. (*20*) found a tissue-to-plasma ratio of 0.21 ± 0.010 (mean $\pm$ s.e.m., $n = 6$). Assuming typical weights of 30 gm for the parotid gland and 5 gm for the sublingual gland, we calculated that total pertechnetate uptake of the parotid should be about 20 times that of the sublingual gland. From these data it is understandable that sublingual gland uptake is not visualized on scintiscans. The submandibular duct markers showed definitely that the lower activity could not be attributed to uptake in the sublingual glands, as suggested by zum Winkel et al. (*15*). In agreement with Sorsdahl et al. (*9*), we consider the lower activity to represent radioactive saliva in the floor of the mouth near the orifices of the submandibular ducts. Radioactive saliva in the duct itself is usually seen early during the study as a weak diffuse band of activity. The relation between submandibular gland saliva and the lower activity was also supported by the time-activity curves that showed peaks or sharp increases in the lower activity concurrent with sudden decreases in submandibular gland activity.

In clinical practice, oral activity is not due to pertechnetate uptake in sublingual and minor salivary glands and should only be regarded as a useful indicator of major salivary gland function.

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