A New Scintigraphic Method for Detecting the Esophageal Mucosal Lesions

—^{99m}Tc-Pertechnetate Coating and Wash-Out Esophageal Scintigraphy—

Masayuki Nakajo, Yuji Ito, Noboru Kuwahata,
Hiromichi Sakata and Shinji Shinohara
Department of Radiology, Kagoshima University School of Medicine
(Director: Prof. S. Shinohara)

Research Code No.: 705

Key Words: *Esophageal scintigraphy, ^{99m}Tc pertechnetate, Coating and wash-out, Esophagitis, Esophageal cancer*

食道粘膜病変検出を目的とした新しい核医学的検査法

—^{99m}Tc-pertechnetate 塗布・洗出し食道シンチグラフィー—

鹿児島大学医学部放射線医学教室（主任：篠原慎治教授）
中條　政敬　　伊東　祐治　　桑波田　昇
坂田　博道　　篠原　慎治

（昭和54年10月17日受付）
（昭和54年12月10日最終原稿受付）

食道粘膜病変の検出を目的とした簡便で新しい核医学的検査法（^{99m}Tc-CWES）を紹介した．原理は tracer で coating した食道粘膜面を水で wash-out し，正常と異常粘膜面の附着度の差を検出するものである．方法は被検者を立位にてガンマカメラの検出器に対向させ，coating の目的で ^{99m}Tc-pertechnetate 2～5mCi（容量 1～2ml）を経口投与し，その胃内流入までの通過時間の測定と共に，tracer の胃内流入を確認後，第1回目の撮像を，次に水30ccを3回に且ってえん下させ，食道粘膜面を wash-out して各回毎に撮像を行なう．食道正常9例では3回目の wash-out までに，頸部の軽度の activity を示した2例を除いて，食道全般の activity はほとんど消失した．逆流性ないし原因不明の食道炎7例と放射線食道炎15例では3回目（時に2回目でも）の wash-out で，すべて病変部に一致する residual activity が認められた．また放射線治療前に本法を実施していた症例では，照射前には認められなかった residual activity の出現により放射線食道炎の診断が可能であった．食道癌症例の高度狭窄2例では病変上部が，1例では病変上部と潰瘍病変部が，他の7例では潰瘍病変部のみが3回目 wash-out で，hot に描出された．食道炎と食道癌で治療後 follow up した症例では，その改善と共に residual activity の低下が認められた．食道粘膜面が intact と考えられた食道憩室，静脈瘤各2例と粘膜下腫瘍1例では，いずれも病変部に residual activity は認められず，X線学的に描出された病変が食道粘膜面のものか否かの鑑別にも本法は有

用と考えられた．更に coating の段階で，tracer の block があり，通過時間が60秒以上を示した5例のうち2例は機械的な，3例は機能的な閉塞であり，食道の dynamics を知る上でも有用であった．本法の最大の利点は，X線学的に描出困難な軽～中等度の食道炎の検出に鋭敏である点であると考えられた．

I. Introduction

While the radiographic and endoscopic examinations have routinely been employed in the study of the esophagus, the scintigraphic examinations to this organ have scarcely been reported. The articles so far reported include the detection of Barrett's esophagus with the intravenous use of ^{99m}Tc pertechnetate[1)2)3)], the dynamic study of the esophagus with the oral use of ^{99m}Tc pertecnetate[4)], and the tumor imaging with ^{67}Ga citrate[5)].

In this paper, a new scintigraphic method is proposed to detect the esophageal mucosal lesions with the use of a tracer radionuclide, 3 cups of water, and a gamma camera. This method is termed the "^{99m}Tc pertechnetate coating and wash-out esophageal scintigraphy (^{99m}Tc-CWES)".

II. Materials and Methods

The ^{99m}Tc-CWES is based on a theoretical concept that where the esophageal mucosa is pathologically deviated from the normal mucosal alignment, the radioactive tracer orally coated might be higher in this region than in the normal mucosa, and the lesion could be detected as the hot spots in the scintigraphic image after the whole esophageal tract is washed out by the water.

Nine adults with no evidence of the esophageal diseases were studied to learn the normal pattern of the scintigraphic image. Seven patients with esophagitis due to the reflux or the unknown causes, 15 patients with radiation esophagitis, 10 patients with esophageal cancer and 5 patients with other esophageal diseases were then studied. The conventional barium roentgenographies were performed in all patients. The endoscopic examinations were also performed in all patients except 9 normal subjects, 8 with radiation esophagitis and one with esophageal diverticulum. The radiographic and endoscopic examinations were performed at least within 7 days before or after the ^{99m}Tc-CWES.

Without any special preparation, the subject stands in front of the gamma camera RC-1C-1205 in upright position. The whole tract of the esophagus from the orfice to the esophagogastric junction is imaged with the use of a diverging collimator. A radioactive drink of 2 to 5 mCi ^{99m}Tc pertechnetate in a volume of 1 to 2 ml is prepared in a paper cup with a suitable lead shielding. The subject is instructed to hold the drink in his mouth and to swallow it with the sign. Its passage through the esophagus is observed on the monitor scope and the first imaging is performed immediately after the top of the drink come into the stomach. The transit time from the beginning of swallowing the tracer to the entrance of it into the stomach is also measured. The second imaging is taken after the oral administration of water in a volume of 30 ml. The third and the fourth images are obtained after the serial administration of the same volume of water. Fifty thousand counts were accumulated for each image. Hereafter, the first image is named the "coating image" and the second, the third and the fourth image is termed Ist, IInd and IIIrd "wash-out image" respectively.

III. Results

1. Normal esophagus

The tansit time was in the range of 3 to 7 seconds. The coating image showed 2 to 3 hot spots of radioactivity in the cervical and/or middle and/or lower esophagus with the constant hot spot in the recessus piriformis. These hot spots in the esophagus decreased with the repeated water administration (Fig. 1).

Almost all hot spots disappeared in the first wash-out image in one subject. They disappeared in the second wash-out images in 3 subjects, and in the third images in 3 subjects. The warm cervical

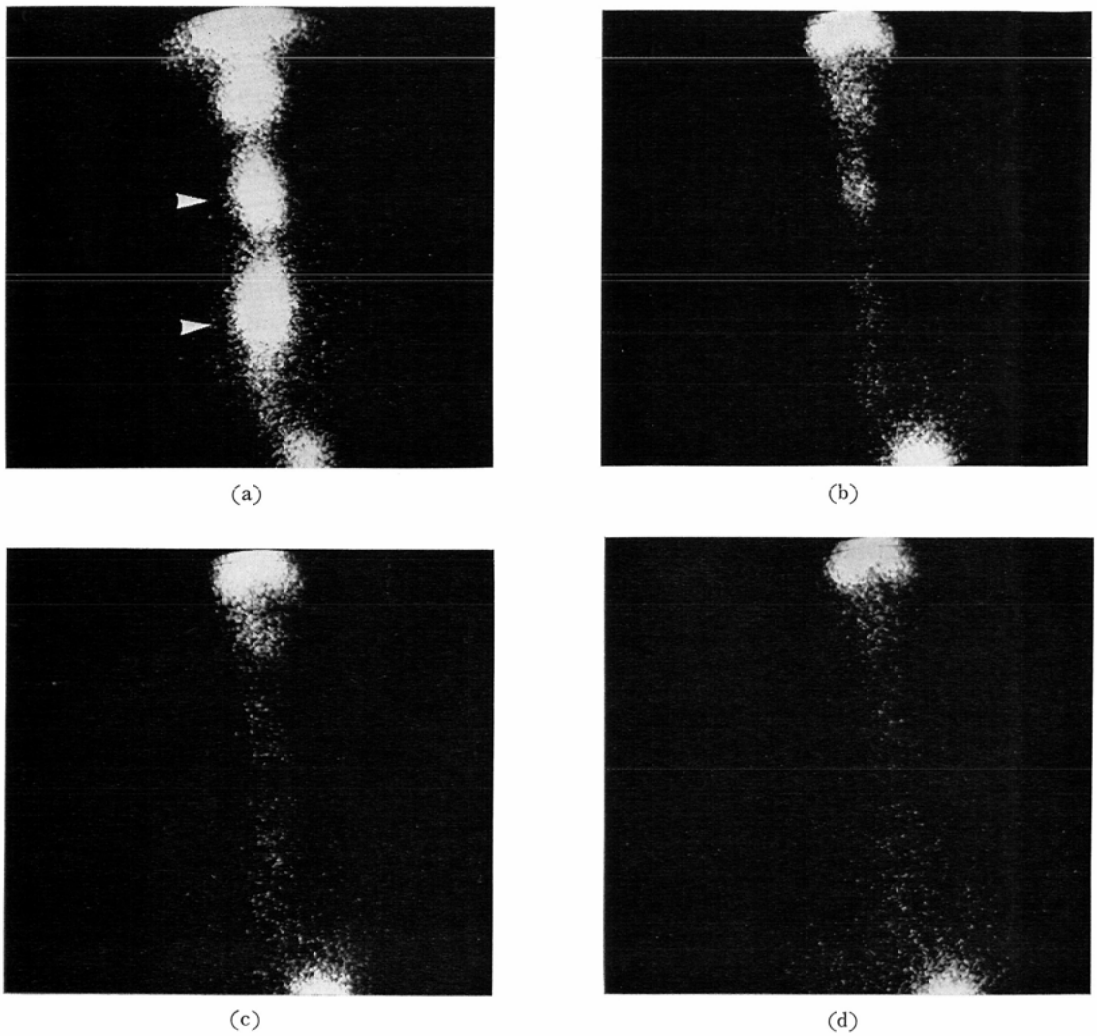


Fig. 1. Images of the normal esophagus.

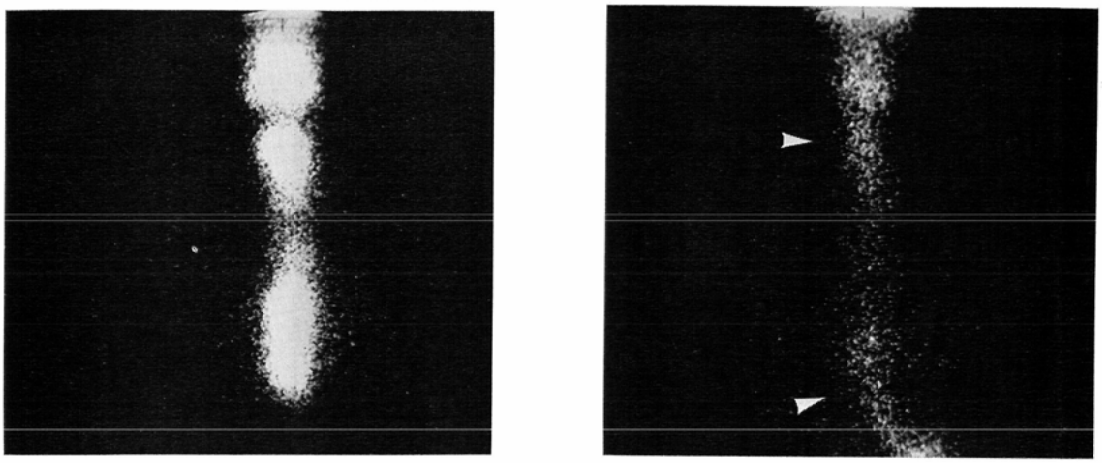
The coating image (a) shows 2 highly radioactive areas in the esophagus (arrowheads), and the first (b), the second (c), and the third (d) wash-out images show the gradual disappearance of the residual radioactive spots in the esophagus.

radioactive spots found in another 2 subjects in the third wash-out images might localize to the physiologically constricted portion of the cervical esophagus. In summary, the esophageal hot spots found in most of the normal subjects disappear or become faint in the third wash-out images.

2. Esophagitis

1) Esophagitis due to reflux or unknown causes

The transit time was in the range of 3 to 9 seconds in 5 patients, and more than 60 seconds in 2 patients whose coating images showed the blocked passage of the radioactive tracer at the lower end of the esophagus. In these 2 patients, the radiographic examination showed no mechanical obstruction due to the tumor or the extrinsic pressure. The area where the tracer remained was revealed the esophagogastric junction, and this blockade could be ascribed to esophageal aperistalsis (Fig. 2a).



(a) (b)

Fig. 2. Images of reflux esophagitis.

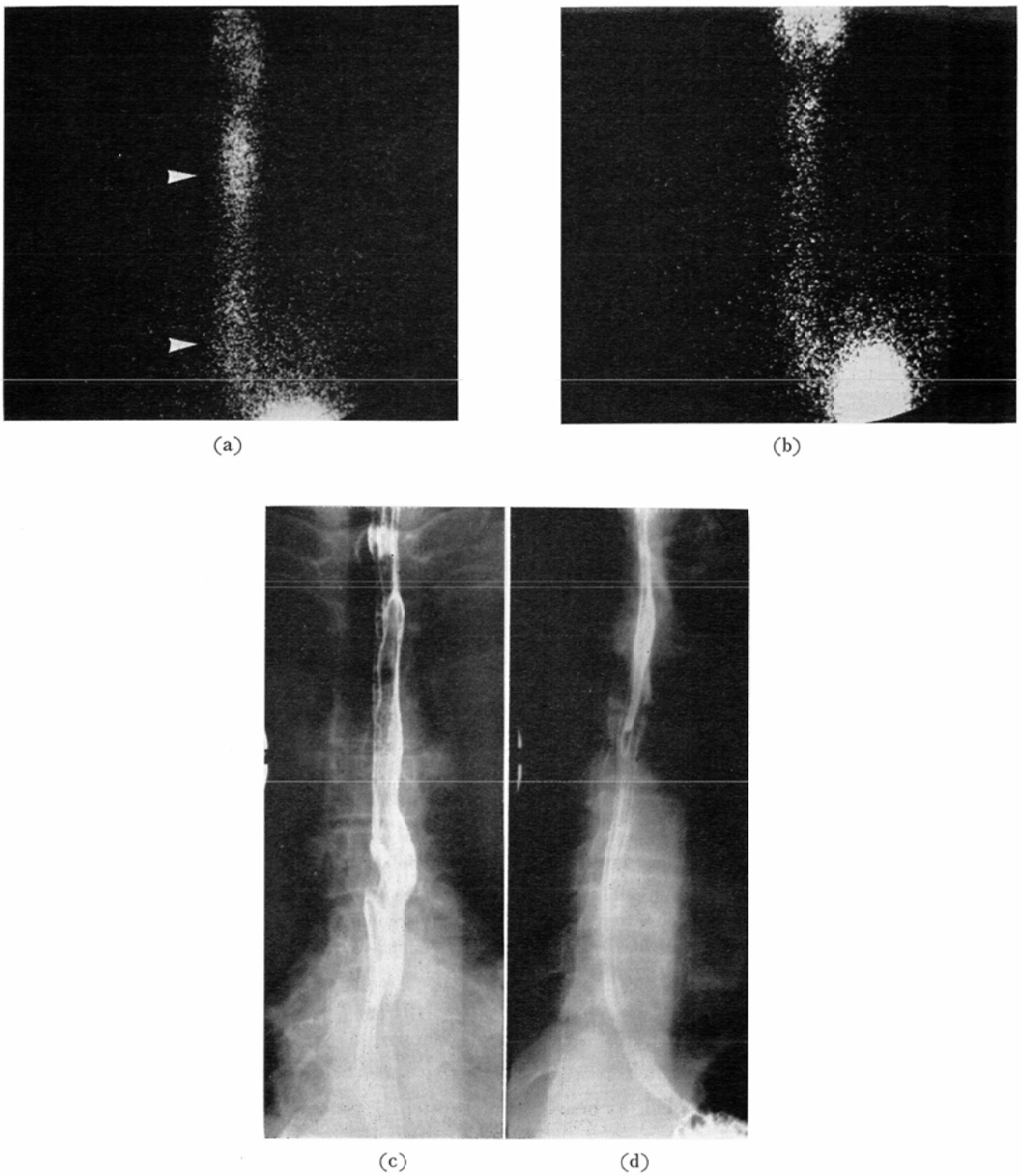
The coating image (a) shows the blockade of radioactivity at the lower region of the esophagus which is probably due to aperistalsis. The transit time is over 60 seconds. The third wash-out image (b) shows 2 residual radioactive spots, where the inflammatory lesions were found by the endoscopy (arrowheads).

The wash-out images (IIIrd or IInd) in this group showed the residual radioactive spots in the inflammatory lesions (Fig. 2b). Their residual radioactive spots became faint at the second studies performed when their symptoms such as heart burn, substernal pain and dysphagia were subsided and their radiographic and endoscopic findings were improved (Fig. 3).

The scintigraphic and endoscopic examinations revealed the presence of esophagitis in all 7 patients. But in 2 patients, the barium studies proved no abnormal findings such as the thickened folds, the serrated margins and the narrowed lumens (Table 1).

2) Radiation esophagitis

The patients in this group, 14 lung cancers and a malignant thymoma, were all received the radiation therapy to their mediastinum. The radiation dose given by a 10 MV X-ray linear accelerator ranged from 2,100 to 7,200 rad when a diagnosis of esophagitis was made. They usually complained of



(a)　(b)

(c)　(d)

Fig. 3. A 37-year-old man complaining of substernal pain which is aggravated by swallowing. Two residual radioactive spots (arrowheads) are demonstrated on the third wash-out image at the first examination (a). The endoscopy proved acute esophagitis at the upper region and chronic esophagitis at the lower part of the esophagus. At the second examination performed 2 months later, each residual radioactive spot is less intense than that of the first imaging (b). Thickened esophageal folds found in the first collapsed mucosal radiograph (c) disappeared in the second one (d).

Table 1. Results of 3 types of diagnostic methods in patients with esophagitis.

Cause	Number of patient	^{99m}Tc-CWES		Radiography		Endoscopy	
		POS*	NEG**	POS	NEG	POS	NEG
Reflux & unknown cause	7	7	0	5	2	7	0
Radiation							
confirmed°	7	7	0	3	4	7	0
not confirmed°°	8	8	0	7	1	–	–

*examination positive
**examination negative
°endoscopically confirmed
°°endoscopically not cofirmed

heart burn, substernal pain, burning pain on swallowing and dysphagia. Some patients received the ^{99m}Tc-CWES because of their high radiation dose.

The transit time was in the rage of 2 to 8 seconds and no significant difference was observed comparing to those of the normal subjects. Seven patients received the ^{99m}Tc-CWES before the mediastinal irradiation. The findings of their wash-out images (IIIrd or IInd) at that time were as follows: no hot area in the esophagus was observed in 4 patients, a small residual radioactivity at the cervical portion was observed in 2 patients and the radioactivity in the whole tract of the esophagus was proved in one patient. The latter patient had been already proved to have esophagitis in the entire tract before he received the mediastinal irradiation.

Abnormal residual radioactivities were demonstrated in the wash-out images (IIIrd or IInd) in 7 patients whose radiation esophagitis were endoscopically confirmed. The length of the residual hot areas matched to the longitudinal size of the irradiation fields in 4 patients, and it was longer than those of the irradiation fields in 3 patients. In another 8 patients with no endoscopic exminations, the residual radioactivities were also noticed. Their length matched to their irradiation fields in 4 patients, and was longer in 4 patients.

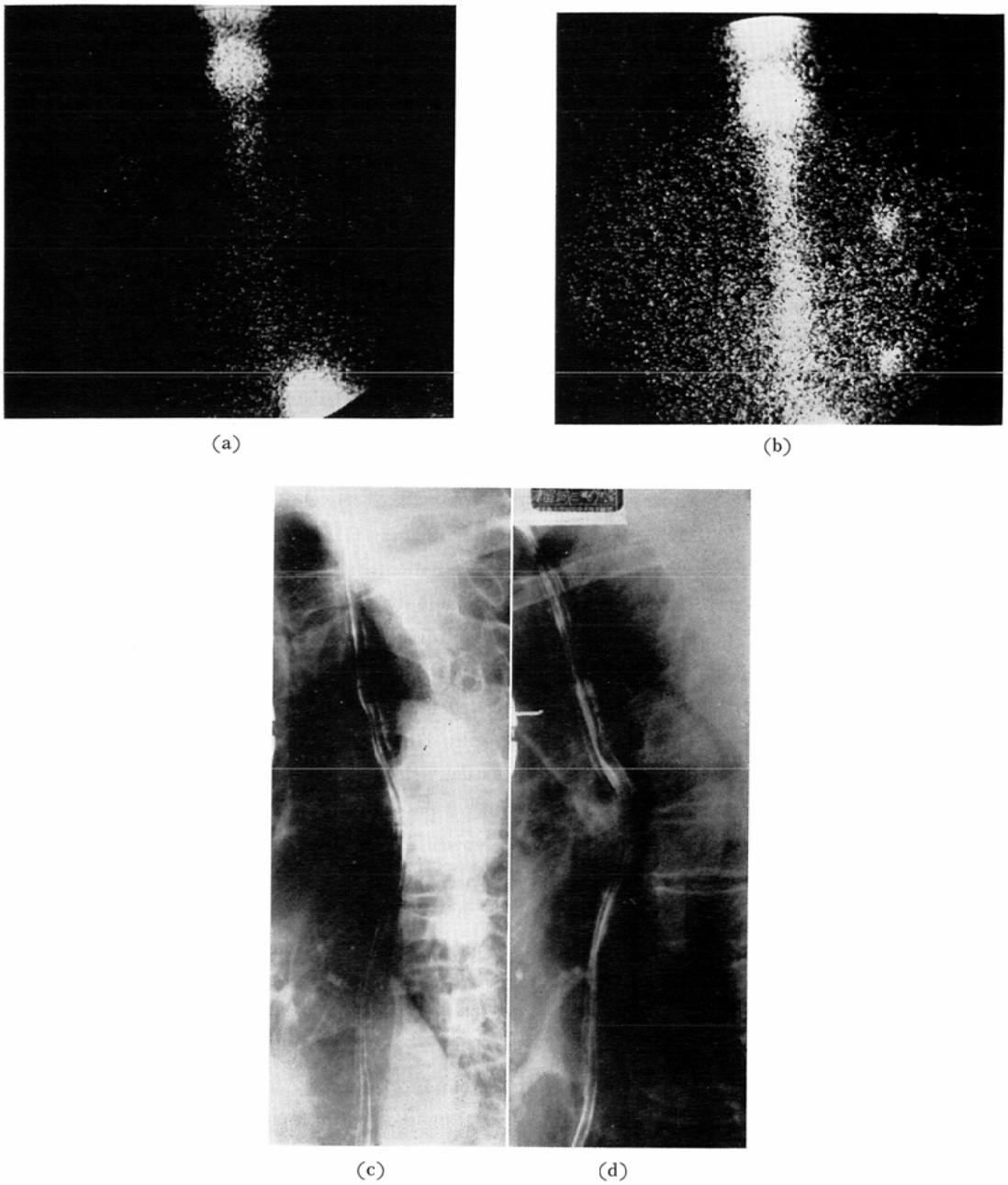
In 7 patients who had been performed the ^{99m}Tc-CWES before the mediastinal irradiation, both wash-out images before and after the irradiation enabled us to confirm the appearance of the new abnormal residual hot areas in the postirradiation images (Fig. 4). The barium studies did not prove the presence of esophagitis in 5 of 15 patients (Table 1).

3. Esophageal cancer

The length of the lesion in this group was ranged from 4 to 16 cm (6.7 cm mean) on the radiograph. The transit time did not show remarkable difference from those of normal subjects except 2 patients whose transit time were over 60 seconds because of the extremely narrowed esophageal lumen.

Table 2 shows the results of 3 types of examination methods performed before the radiation therapy. One patient (I.H.) whose examination was performed after 3,400 rad irradiation is included in this table. The high radioactive spots in the wash-out images (IIIrd) were found above the esophageal lesions in 2 patients (M.K. and Y.N.). The lesions themselves were low radioactive because of the strong esophageal constriction. The residual radioactivities in and above the lesion were presented in one patient (Fig. 5 H.U.).

In the wash-out images (IIIrd) of 7 patients, the lesions were delineated as hot areas and the other

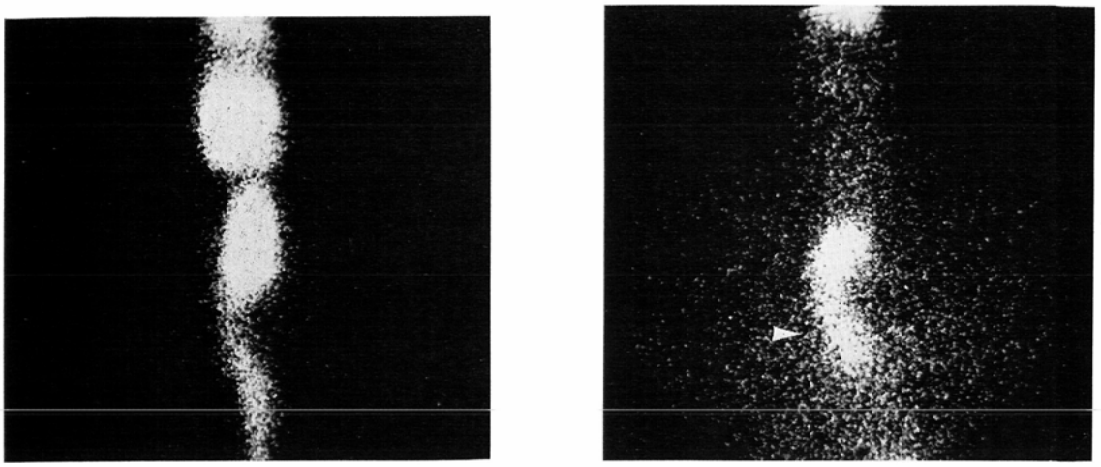


(a)　(b)

(c)　(d)

Fig. 4. A 69-year-old man with lung cancer whose primary lesion and mediastinum were irradiated.

The third wash-out image taken before the irradiation (a) shows no significant residual radioactivity. At the mediastinal dose of 5,800 rad, he complained of burning pain on swallowing and dysphagia. The wash-out image (IIIrd) at this time (b) showed considerable radioactivity in the whole esophagus. Two spots in the left pulmonary region indicate the longitudinal range of the irradiation field. The endoscopic examination proved the inflammatory process of the whole esophagus. But the apparent change in the radiographs of before (c) and after (d) the irradiation was not observed.



(a) (b)

(c)

Fig. 5. Images of esophageal cancer.

The coating image (a) shows the retention of the tracer in the recessus piriformis and in the area above the tumor. The cancer itself is revealed as the defect. The wash-out image (b) shows the slight retention of the tracer above the tumor and the residual radioactivity (arrowhead) in the area corresponds to the ulcer of the tumor. The radiograph (c) supports these findings.

Table 2. Results of 3 types of diagnostic methods in patients with esophageal cancer.

Patient	^{99m}Tc-CWES		Radiography	Endoscopy
	Area above lesion	Lesion		
M.K.	hot	cold	funnel type	not visible by stenosis
Y.N.	hot	cold	spiral type	not visible, ulcer formation
H.U.	hot	hot	spiral type	ulcer formation
S.H.	cold	hot	spiral type	ulcer formation
K.I.	cold	hot	serrated type	ulcer formation
I.H.	cold	hot	serrated type	ulcer formation
M.K.	cold	hot	serrated type	ulcer formation
T.S.	cold	hot	spiral type	ulcer formation
T.T.	cold	hot	spiral type	ulcer formation
H.T.	cold	hot	serrated type	ulcer formation

esophageal tracts as cold areas. The ulcer formations of the tumors were found in these patients by the radiographies and the endoscopies.

In the follow-up studies during or after the radiation therapies in 6 patients, the residual radioactivities were decreased in number and grade along with the improvement of diseases. In one patient, who complained of burning pain on swallowing during the radiation therapy, the residual radioactivity was found in the same extent as that of the irradiation field. It suggests the presence of radiation esophagitis which could not be detected by the radiographic examination (Fig. 6).

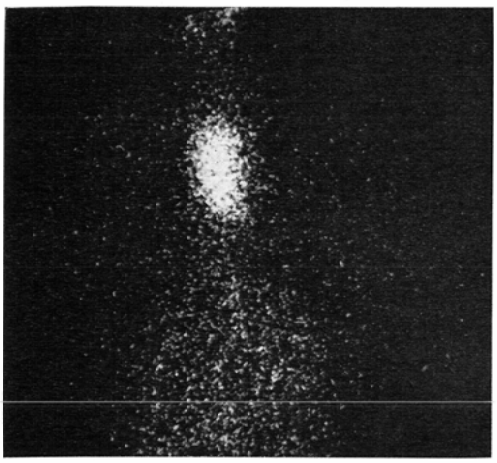
4. Other esophageal diseases

The residual radioactivities in the wash-out images (IIIrd) could not be detected in 2 patients with esophageal diverticula, in 2 patients with varices and in one patient with a submucosal tumor (Fig. 7). The transit time in one patient with a diverticulum was more than 60 seconds and his coating image showed a wedge-like blockade of the tracer at the lower end of the esophagus. The fact could suggest aperistalsis of the esophagus.

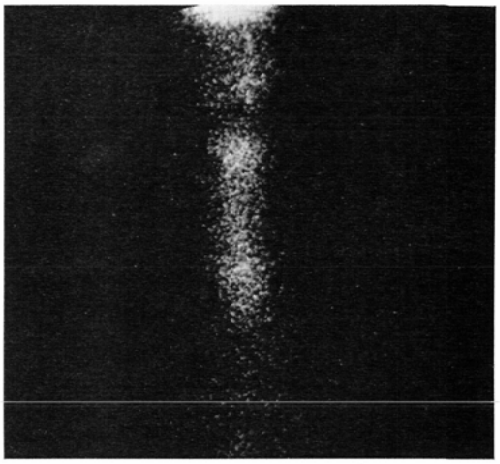
IV. Discussion

The ^{99m}Tc-CWES described in this paper is considered to be a simple, non-invasive and clinically valuable method in the study of the esophagus. Present studies of the normal subjects and of the patients with esophagitis or esophageal cancers showed that the third (second in some patients) wash-out images were quite useful in finding the esophageal mucosal lesions. In a few normal subjects, the slight residual radioactivities were found at the cervical region of the esophagus even in the third wash-out images. By comparing the scintigraphic images to the radiographic ones, these radioactivities were assumed to locate the physiologically constricted areas of the cervical esophagus. The endoscopic confirmation of this area has not been made.

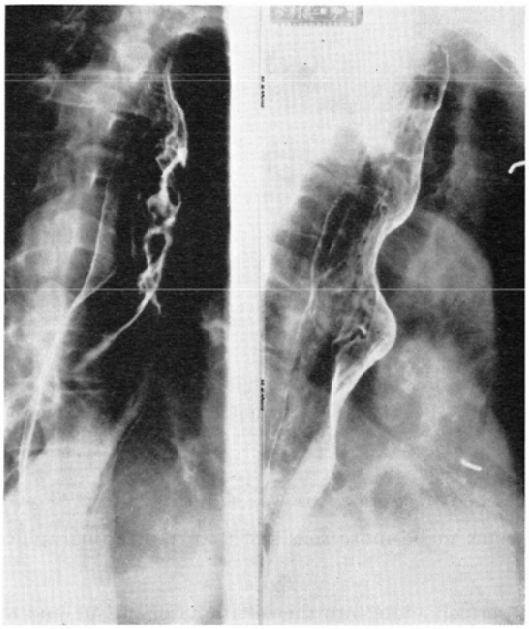
It is generally reported that superficial or mild esophagitis rarely causes the detectable morphological changes in the radiographs[6)7)8)]. In 6 of 14 patients in this series whose esophagitis were confirmed by the endoscopies, the presence of esophagitis could not be detected by the barium studies.



(a)



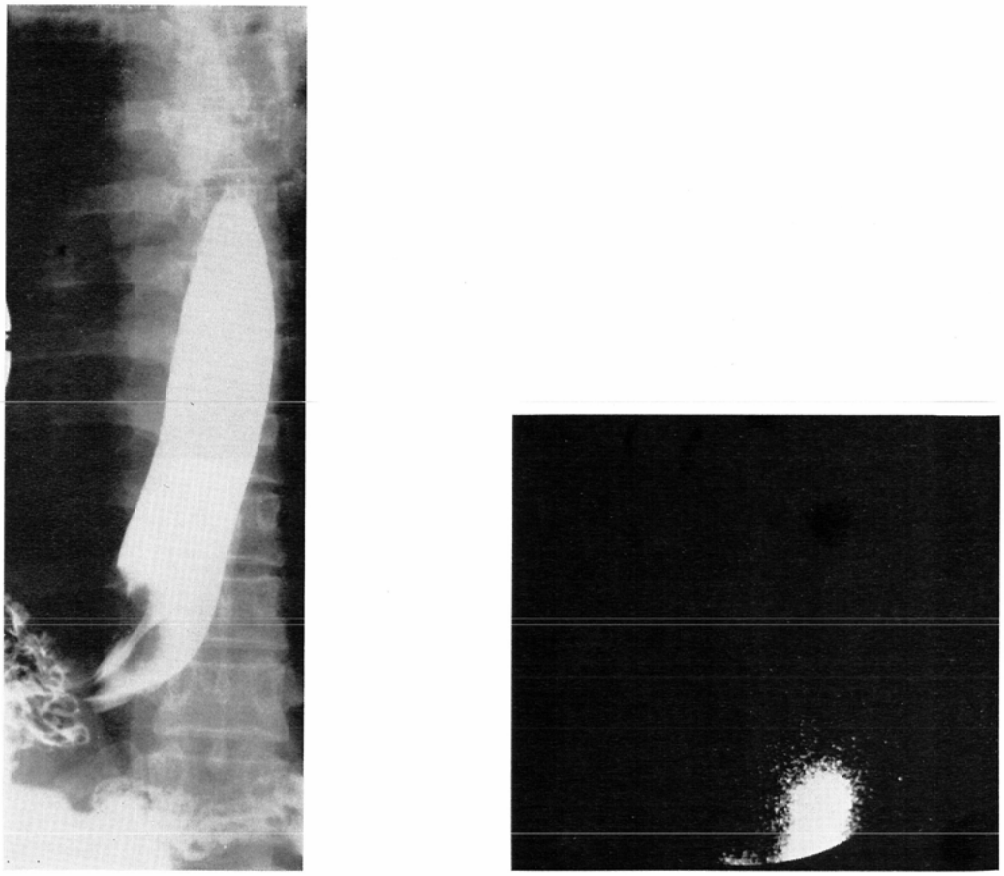
(b)



(c) (d)

Fig. 6. A 74-year-old man with the serrated type of esophageal cancer.

The wash-out image (IIIrd) taken before the radiation therapy (a) shows the localized residual radioactivity where the lesion is proved by the radiograph (c). He complained of burning pain on swallowing when his mediastinal dose came up to 4,000 rad. The wash-out image (IIIrd) at this time (b) revealed the localized residual radioactivity of which length corresponded to the irradiation field. It was less intense than the one obtained before the irradiation. Radiation esophagitis could not be detected in the radiograph at this time (d).



(a)　　(b)

Fig. 7. The image of submucosal tumor. Radiograph (a) demonstrates a smooth filling defect in the lower end of the esophagus which is caused by a submucosal tumor. No residual radioactivity is shown in the wash-out image (b).

On the other hand, the presence of esophagitis was shown by the ^{99m}Tc-CWES in all these patients. Therefore, this procedure seems to be more sensitive than the radiographic examination for detecting esophagitis.

The diffusion of ^{99m}Tc pertechnetate into the inflammatory tissue and the attachment of the tracer to the impaired mucosal texture are considered to be the principle of producing the residual hot spots. Both images obtained before and after the mediastinal irradiation enabled us to detect the presence of esophagitis. The new residual radioactive spots in the postirradiation wash-out images were the confirmative findings of irradiation esophagitis.

In esophageal cancers, the coating images showed the retention of the tracer above the lesions to the degree of the luminal narrowing. Their wash-out images (IIIrd) demonstrated the hot spots in the lesions except in 2 patients with almost complete obstruction of the lumen. The hot spots were considered to be the residual radioactivities in the ulcerative surface of the tumors. The method therefore is also useful for assessing the degree of the improvement of the obstruction and the

ulceration. The diagnostic value of this method for detecting early esophageal cancers is not yet certain because such a case is not included in this study. However, if most of early esophageal cancers appear in the plaque or the flat sessile polyps[9], and if they lack in the mucosal roughness or the ulcer formation, the diagnostic role of this method might not be so great.

In the other esophageal diseases such as diverticula, varices, and submucosal tumors, the wash-out images showed no significant residual radioactivities in the lesions. They must be ascribed to the intact mucosal surface in these diseases. Therefore, the ^{99m}Tc-CWES could be used in determining whether the radiographically proved lesions are mucosal or not.

Another application of this coating technique is the dynamic study of the esophagus. Especially the functional disorders such as achalasia or aperistalsis accompanied by esophagitis[10] could easily be detected. The use of a computer system along with this scintigraphic technique, as reported by Kazem[4], will offer the detailed functional data of the esophageal disorders.

V. Conclusion

A new scintigraphic method of detecting the esophageal mucosal lesions, named the ^{99m}Tc-CWES, was proposed. The method seems to be more sensitive than the radiographic examination in detecting esophagitis and the functional as well as the mechanical obstruction of the esophagus. Furthermore, the method may be valuable to determine whether the radiographically proved esophageal lesions are mucosal or not.

References

1) Berquist, T.H., Nolan, N.G., Carlson, H.C. and Stephens, D.H.: Diagnosis of Barrett's esophagus by pertechnetate scintigraphy. Mayo Clin. Staff Proc., 48: 276—279, 1973
2) Gordon, F., Ramirez-Degollado, J., Munoz, R., Cuaren, A. and Landa, L.: Diagnosis of Barrett's esophagus with radioisotopes. Am. J. Roentgenol., 121: 716—719, 1974
3) Berquist, T.H., Nolan, N.G., Stephens, D.H. and Carlson, H.C.: Radioisotope scintigraphy in diagnosis of Barrett's esophagus. Am. J. Roentgenol., 123: 401—411, 1975
4) Kazem, I. with technical assistance of Wagemakers, G. and Verbeeten, E.: A new scintigraphic technique for the study of the esophagus. Am. J. Roentgenol., 115: 681—688, 1972
5) Sonoda, K.: The clinical investigation of scintigraphy on esophageal cancer. Med. J. Kagoshima Univ., 28: 253—284, 1976
6) Goldstein, H.M., Rogers, L.F., Fletcher, G.H. and Dodd, G.D.: Radiological manifestations of radiation-induced injury to the normal upper gastrointestinal tract. Radiology, 117: 135—140, 1975
7) Dodds, W.J.: Current concepts of esophageal mortor function: Clinical implications for radiology. Am. J. Roentgenol., 128: 549—561, 1977
8) Ott, D.J., Gelfand, D.W. and Wu, W.C.: Reflux esophagitis: Radiographic and endoscopic correlation. Radiology, 130: 583—588, 1979
9) Koehler, R.E., Moss, A.A. and Margulis, A.R.: Early radiographic manifestations of carcinoma of the esophagus. Radiology, 119: 1—5, 1976
10) Simeone, J.F., Burrell, M., Toffler, T. and Smith, G.J.W.: Aperistalsis and esophagitis. Radiology, 123: 9—14, 1977