

# Can ulceration in carcinoma of the oesophagus be detected by $^{99m}\text{Tc}$ -sucralfate scan?

**V Sharma**

MD, PhD

Johannesburg Hospital and  
Tata-Memorial Hospital and Radiation Medicine Centre  
Mumbai, India

**S Awasare**

MSc

**V Rangrajan**

DRM, DNB

**H H Shimpi**

MSc

**U Mahantshetty**

MD, DNB

Tata Memorial Hospital and Radiation Medicine Centre  
Mumbai, India

**P S Choudhary**

DRM, DNB

Rajeev Gandhi Hospital and Research Institute  
New Delhi, India

oesophagus were acquired at 2 minutes, 2 hours, 4 hours and 6 hours following ingestion. In some patients images were also

acquired at 24 hours and at follow-up. The comparison was done with endoscopy as the gold standard.

**Results and observations.** The overall positivity of the test was 83% at 4 hours (24 of 29 patients), 34% at 6 hours (10 of 29 patients) and 24% at 24 hours (7 of 29 patients). The sensitivity of the test was 85%, and the positive predictive value 50%.

**Conclusion.** Due to low positive predictive value, this investigation cannot

## Abstract

**Objective.** To test: (i) the sensitivity and positive predictive value of tagged material in delineating ulcerations of the oesophagus in the pre- and post-treatment periods and at follow-up; and (ii) whether tagging could reduce the need for invasive endoscopic procedures in patients with carcinoma of the oesophagus.

**Materials and methods.** Twenty-nine patients with carcinoma of the oesophagus selected for radiation therapy underwent the  $^{99m}\text{Tc}$  sucralfate scintimaging prior to radiation therapy. Patients were asked to drink 10 ml suspension of 10 mCi  $^{99m}\text{Tc}$  sucralfate. The sequential images of the

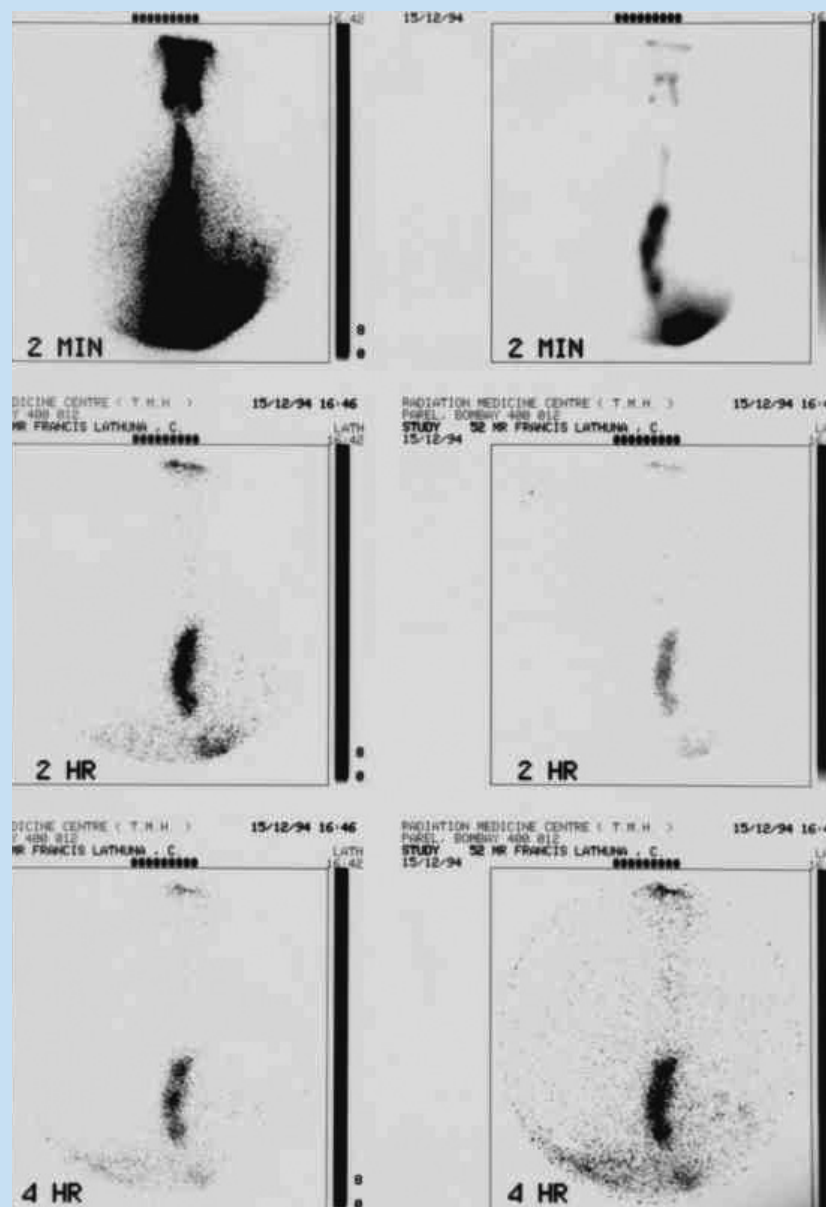


Fig. 1a. Pre-radiation scan. Static sucralfate study scans at varying intensities at 2 minutes, 2 hours and 4 hours post ingestion.

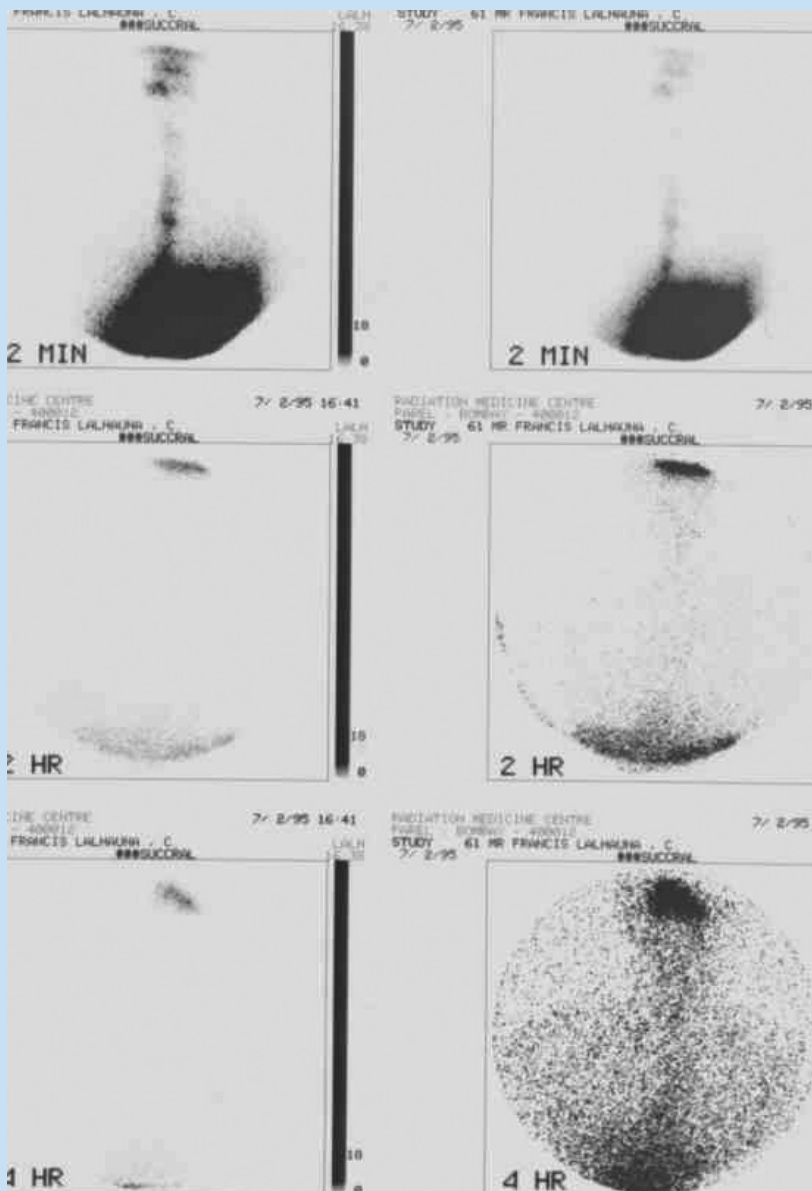


Fig. 1b. Post radiation scan. Static sucralfate study scans at varying intensities at 2 minutes, 2 hours and 4 hours post ingestion.

replace endoscopy to diagnose ulcerative disease in patients with carcinoma of the oesophagus.

## Introduction

The diagnosis of presence of deep ulceration in the oesophagus due to disease has value for both diagnosis and management. Patients with ulcerative tumours are treated with surgery as the first choice unless found inoperable because of advanced disease at presentation or poor

general condition. Radiation therapy can aggravate the condition of the patient as ulceration may become worse with higher doses of radiation leading to severe pain and sometimes fistula formation. Sucralfate (the aluminium salt of sulphated sucrose) labelled with selenium<sup>75</sup> and <sup>99m</sup> technetium (<sup>99m</sup> Tc) has been shown to give variable results for detection of ulceration throughout the gastrointestinal tract (GIT).<sup>1-5</sup> The results have, however, been mainly negative for oesophageal ulceration

from static imaging scans. A non-invasive scan would be much better tolerated by patients than oesophagoscopy and might be more accurate than a barium swallow which is frequently non-diagnostic in patients with oesophagitis.<sup>6</sup>

## Objectives

The purpose of the study was to test: (i) the sensitivity and positive predictive value of tagged material in delineating ulcerations in the oesophagus pre-treatment, post-treatment and at follow-up; and (ii) whether it could reduce the need for invasive endoscopic procedures in patients with carcinoma of the oesophagus.

We evaluated the use of <sup>99m</sup>Tc labelled sucralfate in the investigation of oesophageal mucosal ulcerations in the pre- and post-radiotherapy periods in patients with carcinoma of the oesophagus with endoscopy as the gold standard. The results form the basis of this report.

## Material and methods

Twenty-nine patients with carcinoma of the oesophagus selected for radiation therapy underwent the <sup>99m</sup>Tc sucralfate scintigraphy prior to starting radiation therapy. The lesions involved the upper-third in 2 patients, mid-third in 20 patients and lower-third in 7 patients. All patients had endoscopy to confirm the diagnosis of malignancy. The morphological appearances of the lesions were grouped into ulcerative in 14 patients (ulcerative 6, ulceroproliferative in 8) and non-ulcerative in 15 patients (infiltrative in 8, polypoidal in 7).

## Labelling and sucralfate tagging with <sup>99m</sup>Tc

Sucralfate and other chemicals were obtained from commercial sources. <sup>99m</sup>TcO<sub>4</sub> was obtained from alkaline 99M004 using 2 butanole by the solvent extraction process and further processed into an injectable form.<sup>7</sup> Instant labelling kits of sucralfate prepared at the Radiation Medicine Centre in Mumbai, India were used.<sup>8</sup> The lyophilised sucralfate was suspended in 2.0 - 3.0 ml of distilled water. A desired amount

**Table I. Correlation between sucralfate tagging and endoscopy pre-radiotherapy**

	Sucralfate technetium-99m scan	Endoscopy	
		Positive	Negative
Positive (N)	24	12	12
Negative (N)	5	2	3
Total (N)	29	14	15
Sensitivity		12/14 = 85%	
Specificity		03/15 = 20%	
Positive predictive value		12/24 = 50%	
Negative predictive value		03/05 = 60%	

**Table II. Correlation between sucralfate tagging and endoscopy at follow-up**

	Sucralfate technetium-99m scan	Endoscopy	
		Positive	Negative
Positive (N)	5	2	3
Negative (N)	1	0	1
Total (N)	6	2	4
Sensitivity		2/2 = 100%	
Specificity		1/4 = 25%	
Positive predictive value		2/5 = 40%	

of  $^{99m}\text{Tc}$  04- in 0.5 - 1.5 ml was added to it and incubated for 10 minutes at room temperature. Unlabelled  $^{99m}\text{Tc}$ 04 was removed following centrifugation for 1 - 2 minutes at 3 000 revolutions per minute (rpm). Distilled water was used for additional rinses. The percentage of labelling was calculated from the observed radioactivity in the final suspension and that present in the combined supernatant layer.<sup>9</sup>

### Imaging protocol

Patients were asked to drink a 10 ml suspension of 10 mCi  $^{99m}\text{Tc}$  sucralfate. An initial dynamic acquisition was carried out for 30 seconds with a frame rate of 0.5 seconds/frame. One minute post ingestion an oesophageal view was acquired and the patient was then asked to drink 20 ml water to wash out the labelled sucralfate that had not adhered to the affected mucosa. Following this sequential images of the

oesophagus were acquired for 2 minutes, 2 hours, 4 hours and 6 hours (Fig 1a and b). In some patients images were also acquired at 24 hours and at follow-up. Pre-radiotherapy scans were performed on 29 patients, pre-radiotherapy scans as well as post-radiotherapy scans on 13 patients, and post-radiotherapy scans on 18 patients. All patients underwent endoscopy at follow-up evaluation to confirm whether ulceration was present.

### Results and observations

The criteria used for positivity of the scans were an increased concentration of the tagged material, for at least 4 hours. The criteria used for positivity were taken from the report by Bailer *et al.*<sup>10</sup>

True-positive was defined as ulceration on endoscopy and increased concentration

on scan. True-negative was defined as no ulceration on endoscopy and no uptake on scan. False-positive was defined as no ulceration on endoscopy but increased uptake on scan. False-negative was defined as ulceration on endoscopy but no uptake on scan.

The overall positivity of the test was 83% at 4 hours (24 of 29 patients), 34% at 6 hours (10 of 29 patients), and 24% at 24 hours (7 of 29 patients). The sensitivity of the test was 85% at 4 hours but the positive predictive value was 50%. The specificity of the test was 20% and negative predictive value was 60%. The false-positive rate was 50% and it was due to stasis of the radioisotope in the cases with no evidence of ulceration on endoscopy (Table I).

In 18 patients, for whom only post-radiotherapy scans were done, an increased uptake was noted in 9 patients (50%) at 4 hours, 4 patients (22%) at 6 hours and 3 patients (17%) at 24 hours.

In the 13 patients who had pre- and post-radiation scans, 6/13 patients (46%) at 4 hours, 3/13 patients (23%) at 6 hours and 2/13 patients (15%) at 24 hours had positive scans.

Six patients were followed up between 3 months and 6 months post-radiation; 5/6 patients (83%) showed positivity at 4 hours, with evidence of ulceration in 2 patients on endoscopy and a positive predictive value of 40% (Table II).

### Discussion

Dynamic radionuclide scintigraphy is becoming an established test in the assessment of functional abnormalities of the oesophagus such as strictures, spasm and achalasia.<sup>11</sup> It is non-invasive, simple to perform, is well tolerated by patients, and can produce quantitative indices of function. However, this technique will only identify sites of mucosal damage in the oesophagus if they are gross enough to precipitate transit abnormalities, and as such it is of no value in the early detection and follow-up of oesophageal ulceration. Reports have described the labelling of sucralfate with selenium-75 and technetium-99m with variable results for the detection of ulceration throughout the GIT.<sup>1-5</sup>

The results in our study showed almost similar uptake in 13 patients who had scans both before and on completion of radiation at 4 hours, 6 hours and 24 hours when compared with 18 patients who had scans only on completion of radiation at the same intervals. Mearns *et al*<sup>11</sup> have shown a 92% positive predictive value for dynamic sucralfate imaging of oesophageal ulceration. The present study, however, showed the sensitivity of the test to be 85%, but the positive predictive value was only 50%. The most probable explanation for the low positive predictive value is the stasis of the radioisotope in cases with non-ulcerative disease at endoscopy.

Previous work has focused on the applications of labelled sucralfate in the imaging of the stomach and small and large bowel, but its use has been documented in the oesophagus<sup>11</sup> with mainly negative results from static imaging techniques.

Due to positive results from their study, Mearns *et al*<sup>11</sup> suggest limiting endoscopy to initial evaluation using histological examination to exclude the possibility of a malignant process. This is not supported by the present study due to the low positive

predictive value. Although Mearns *et al.* suggested that the <sup>99m</sup>Tc sucralfate dynamic study has a real value, firstly as a screening test in deciding who should be endoscoped, and secondly as a test suitable for following the progress of patients undergoing therapy for oesophageal ulceration, we are unable to recommend the use of sucralfate tagging in the follow-up period.

In conclusion, this study does not support the use of sucralfate tagging to replace endoscopy in cancer of the oesophagus due to a low positive predictive value.

We would like to sincerely acknowledge Professor Bernard Donde, Head of Department of Radiation Oncology, Johannesburg Hospital, for corrections to the manuscript.

## References

1. Vasquez TE, Bridges RL, Braunstein P, Jansholt AL, Meshkinpour H. Gastrointestinal ulceration: detection using a technetium-99m. Labelled ulcer avid agent. *Radiology* 1983; **148**: 227-231.
2. Dawson DJ, Khan AN, Nuttall P, Shreeve DR. Technetium-99m labelled sucralfate isotope scanning in the detection of peptic ulceration. *Nucl Med Commun* 1985; **6**: 319-325.
3. Dawson DJ, Khan AN, Miller V, Ratcliffe JF, Shreeve DR. Detection of inflammatory bowel disease in adults and children: evaluation of a new isotope technique. *BMJ* 1985; **291**: 1227-1230.
4. Maurer AH, Knight IC, Kollman M *et al.* Validation of binding of <sup>75</sup>Se-labelled scralfate to sites of gastrointestinal ulceration (abstract). European Nuclear Medicine Society Congress, London, 1985.
5. Crump BJ, Field S, Rake MO, Kettle AG, Buxton Thomas MS, Coakley AJ. <sup>99m</sup>Tc sucralfate imaging in inflammatory bowel disease – Poor correlation with radiology (abstract). London: British Nuclear Medicine Society Annual Meeting, 1987.
6. Goff JS, Adcock KA, Schmelter R. Detection of esophageal ulcerations with Technetium-99m albumin sucralfate. *J Nucl Med* 1986; **27**: 1143-1146.
7. Naronha OPD. Solvent extraction technology of <sup>99</sup>Mo-<sup>99m</sup>Tc-generator system performance, characteristics. Proceedings of the 1984 Radiopharmaceuticals and Labelled Compound Conference, Tokyo: 223-232.
8. Shimpi HH, Naronha OPD, Samuel AM. Development of <sup>99m</sup>Tc. Sucralfate as a diagnostic agent for ulcers of gastrointestinal (GI) tract: Physicochemical factors affecting the oral dosage form. *Indian Journal of Nuclear Medicine* 1996; **11**: 42 - 46.
9. Shimpi HH, Naronha OPD, Samuel AM. Transport patterns and orally fed <sup>99m</sup>Tc sucralfate in ulcer induced animal model. *Indian Journal of Nuclear Medicine* 1996; **11**: 93 - 97.
10. Bailer JC, Mosteller F. Medical technology assessment. In: Bailer JC III, Mosteller F, eds. *Medical Uses of Statistics*. 2nd ed Boston: N Engl J Med Books, **1992**: 393 - 411.
11. Mearns AJ, Hart GC, Cox JA. Dynamic radionuclide imaging with <sup>99m</sup>Tc-sucralfate in the detection of oesophageal ulceration. *Gut* 1989; **30**:1256-1259.