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

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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 $^{99m}$Tc-sucralfate scintimaging prior to radiation therapy. Patients were asked to drink 10 ml suspension of 10 mci $^{99m}$Tc sucralfate. The sequential images of the 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
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 and technetium has been shown to give variable results for detection of ulceration throughout the gastrointestinal tract (GIT). 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.

**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 $^{99m}$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 $^{99m}$Tc labelled sucralfate scintimagining 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 $^{99m}$Tc**

Sucralfate and other chemicals were obtained from commercial sources. $^{99m}$Tc04 was obtained from alkaline 99M004 using 2 butanole by the solvent extraction process and further processed into an injectable form. Instant labelling kits of sucralfate prepared at the Radiation Medicine Centre in Mumbai, India were used.

The lyophilised sucralfate was suspended in 2.0 - 3.0 ml of distilled water. A desired amount...
of 99mTc 04- in 0.5 - 1.5 ml was added to it and incubated for 10 minutes at room temperature. Unlabelled 99mTc04 was removed following centrifugation for 1 - 2 minutes at 3000 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.

### Imaging protocol

Patients were asked to drink a 10 ml suspension of 10 mCi 99mTc sucrafate. 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 sucrafate 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. 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 85% 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. 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 sucrafate with selenium-75 and technetium-99m with variable results for the detection of ulceration throughout the GIT.

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

<table>
<thead>
<tr>
<th>Sucrafate</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>99mTc04m</td>
<td>24</td>
<td>12</td>
</tr>
<tr>
<td>Negative (N)</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Total (N)</td>
<td>29</td>
<td>14</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>12/14 = 85%</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>03/15 = 20%</td>
<td></td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>12/24 = 50%</td>
<td></td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>03/05 = 60%</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Sucrafate</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>99mTc04m</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Negative (N)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total (N)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>2/2 = 100%</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>1/4 = 25%</td>
<td></td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>2/5 = 40%</td>
<td></td>
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</tbody>
</table>
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\(^1\) have shown a 92% positive predictive value for dynamic sucralafate 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 sucralafate in the imaging of the stomach and small and large bowel, but its use has been documented in the oesophagus\(^1\) with mainly negative results from static imaging techniques. Due to positive results from their study, Mearns et al.\(^1\) 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 \(^{99m}\text{Tc}\) sucralafate 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 sucralafate tagging in the follow-up period.

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

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References


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