# Scintigraphic Study of Duodenal-Gastric Reflux in Cases of Primary Gastropathy, Chronic Ulcer of the Duodenal Bulb, and Moynihan's Disease

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There are several methods for detection of bile in the stomach, but none has proven satisfactory. It appears that the scintigraphic study with quantitation of duodenal-gastric reflux after corrections for the overlap of the stomach by the liver and bowel is more reliable, noninvasive, and physiologic. Fifty-four patients were divided into groups according to their clinical presentation; seven asymptomatic volunteers, 20 patients with duodenal-gastric reflux gastropathy (DRG), 16 patients with recurrent ulcers of the duodenal bulb (RUD), and 11 patients with Moynihan's disease. Each of the 47 dyspeptic patients underwent an endoscopic examination and a scintigraphic study with [$^{99m}$Tc]disofenin for detection and quantitation of duodenal-gastric reflux. Endoscopy revealed the presence of bile in the stomach of 16 out of 20 DRG and four out of 16 RUD, while ten out of 11 patients with Moynihan's disease had clear gastric juice. Most of the DRG cases (15 out of 20) and half of the RUD (eight out of 16) presented reflux > 1.5%, while of the 11 Moynhihan, ten presented reflux < 1.5% and all the asymptomatic volunteer subjects < 1%. This quantitation method allowed us to perceive clearly the low % of reflux in the "normal asymptomatic" subjects compared with the DRG-type of dyspeptic patients. Among the dyspeptic, the distinction seems more evident between the DRG type and the Moynihan type. Occasionally, the scintigraphic method permits identification of patients with slower gallbladder evacuation (eight out of 47 dyspeptic in our study), adding valuable information for the diagnostic approach to dyspeptic patients.

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It has been demonstrated in animals as well as in man that reflux of duodenal content may injure the gastric mucosa, alter its function and cause such symptoms as pain, nausea, and bilious vomiting (*1–8*).

As there is no reliable technique for the quantitation of bile reflux, confusion persists as to whether the presence of bile in the stomach is a physiologic phenomenon, and what amount of duodenal-gastric reflux a stomach may tolerate without any pathologic modifications or clinical manifestations.

Since the advent of hepatobiliary tracers, several scintigraphic methods for measurement of reflux have been added to methods already in use, i.e., endoscopy and gastric intubation, but up to the present time none has proven satisfactory. The results of several quantification methods found in the literature (*9–14*) differ or are more or less satisfactory. Thomas (*9*) assessed reflux against liver and gallbladder activity using normalized time-activity curves. Dumont (*10*) measured the ratio of isotopic activity in the stomach to the injected dose. Fisher (*11*) expressed in percentages the ratio of $^{99m}$Tc activity in the stomach relative to the amount of $^{99m}$Tc activity which had emptied from the hepatobiliary tree. The two main problems encountered with quantification of duodenal-gastric reflux were the frequent overlap of one, the body of the stomach by the left hepatic lobe, and two, the antral region of the stomach by intestinal loops, which could result in a falsely increased

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percentage of reflux if no corrections were made. Sorgi (*15*) measured the percentage of reflux with and without corrections in 23 studies. The correction he used reduced the mean negative reflux from 1.9% to 1% ± 0.6, and the positive reflux from 5.8% to 1.7% ± 0.5. Therefore, Sorgi correlated the percentage of reflux after correction with the percentage of reflux assessed by nasogastric aspiration in 14 patients, obtaining satisfactory results of 3% versus 3.5%, respectively. However, this method for correction of bowel overlap consists in outlining an additional area of interest on a loop of bowel, equal in surface and adjacent to the overlap of the stomach by the bowel. Theoretically, this method is satisfactory. In practice, however, it is often impossible to discern the loops and to separate one from the other; furthermore, the loops of bowel move during the study and disappear from the area of interest, that is why we did not use this method.

The aim of our study was to develop a technique for the quantitation of bile reflux while allowing for corrections required by the background and by the overlap of the stomach by the liver and intestinal loops, and to ascertain whether this technique would enable us to distinguish categories among patients coming to their physicians with a clinical picture characteristic of dyspepsia.

## MATERIALS AND METHODS

### Patients

From September 1985 to May 1986, we studied 54 patients ranging in age from 22 to 72 yr (mean 46 yr). These patients were divided into groups according to their clinical presentation as follows:

1. *Seven volunteers.* (four female, three male, ranging in age from 22 to 53 yr) without any digestive symptoms or previous history of gastrointestinal disease.

2. *20 patients* (19 female, one male) with *duodenal-gastric reflux gastropathy* (DRG), a type of dyspepsia characterized by epigastric pain accentuated by food and accompanied by early satiety and abdominal bloating, frequently by nausea and occasionally, by vomiting of food or bile.

3. *16 patients* (10 male, six female) with *recurrent ulcers of the duodenal bulb* (RUD), evidenced by classic ulcer symptoms and presence of a lesion visualized at endoscopy and/or radiology.

4. *11 patients* (five male, six female) with Moynihan's disease (typical ulcer symptomatology although no lesion is visualized at endoscopy and/or radiology).

Of the 54 patients studied, seven had previously undergone a cholecystectomy, i.e., five DRG and two RUD.

## METHOD

Each of the 47 dyspeptic patients underwent both endoscopy and scintigraphy within 1 mo for detection and quantitation of duodenal-gastric reflux.

### Endoscopy

The gastroenterologist observed in particular the presence or absence of bile residue in the stomach and antral hyperemia, but chemical analysis of gastric contents was not performed. There is absolute correlation between the yellowish color of the gastric residue and the presence of bile salts and bile pigments (*7*).

### Scintigraphy

The patient in the fasting state (4–6 hr) was injected with 1.5 mCi (55 MBq) of technetium-99m ($^{99m}$Tc) disofenin intravenously. Twenty-five minutes after the injection he was placed in a semirecumbent position under a large field-of-view camera interfaced to a dedicated computer. Analogous images were obtained every 2 min for 40 min, i.e., from 25 to 65 min postinjection of the radiopharmaceutical. The data were collected simultaneously using a 64 × 64 × 8 matrix format, at the rate of 1 frame/10 sec. At 30 min after the injection, the patient drank a liquid meal rich in proteins and fatty acids, made up of one egg mixed with 250 ml of 2% milk and 5 ml of vanilla, to stimulate gallbladder evacuation.

At the end of the study, while remaining in the same position, the patient drank 100 ml of [$^{99m}$Tc]pertechnetate so as to locate the stomach precisely. The qualitative and quantitative analysis were then accomplished by two nuclear medicine physicians blinded to the clinical diagnosis. A study was deemed qualitatively positive when abnormal activity projected by the stomach was visualized on at least one scintiphoto.

### Quantitative Study of Reflux

Figure 1 shows the six regions of interest (ROIs) used for quantitation of reflux, i.e., the total stomach ($S_{tot}$), the proximal stomach ($S_{prox}$), the overlap of the stomach by the liver ($I_1$), a second ROI on the right lobe ($L_2$), the background (BKG), and the bowel ($B + S_{tot} - L_1$). $L_1$ is subtracted from $B + S_{tot}$ because activity in the left hepatic lobe is not yet in the gastrointestinal tract. After delineating the total stomach ($S_{tot}$) from the scintiphoto obtained after the ingestion of 100 ml of water labeled with [$^{99m}$Tc]pertechnetate, we visualized the 10-sec frames (240) in order to identify clearly the maximal overlap of the stomach by the bowel and liver. Another ROI was outlined on the proximal stomach so as to exclude any overlap by the intestinal loops, bile ducts, or gallbladder.

In order to remove the counts from the liver overlapping the stomach (Fig. 2A) without subtracting any underlying reflux, we outlined $L_1$ from the image made up of the first five frames of the study, and we used a second, identical ROI on the right lobe, excluding the main bile ducts and gallbladder. The ratio of the number of counts $L_1$ to $L_2$ gave us a factor x for the first five frames (first 50 sec) of the study, when there should not be any reflux. In the composite image of the first 50 sec, there were from 10,000 to 30,000 counts in $L_1$ or $L_2$. We assumed that excretion of the radiotracer by the liver was the same for the two liver ROIs because the slopes of the curves of $L_1$ and $L_2$ in control volunteers were similar for the two hepatic lobes. When $L_2$ was multiplied by this x factor the resulting curve $x \cdot L_2$ was paralleled to $I_2$ and represented liver activity overlapping the stomach. This $x \cdot L_2$ was subtracted from $S_{prox}$, giving us $S'_{prox}$ (Fig. 2B). The background region (BKG) was then outlined to the left of the stomach so that the cardiac pool and bowel activity were

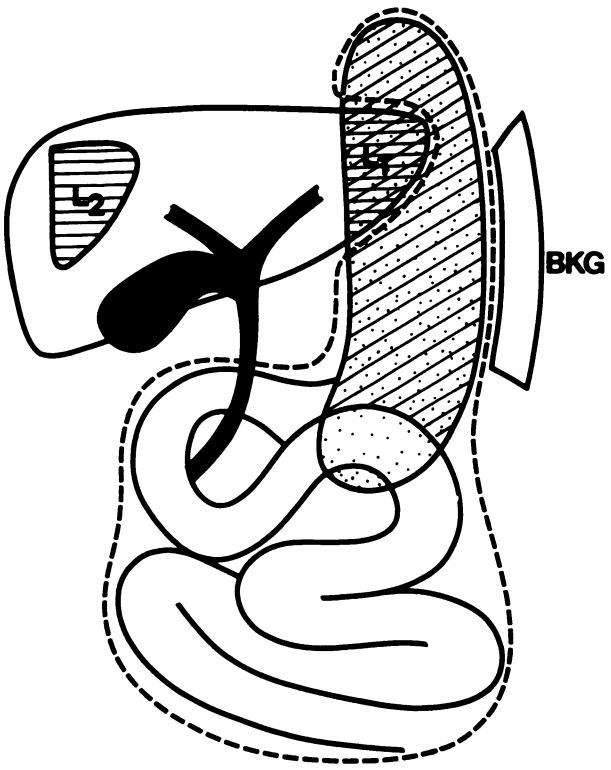


**FIGURE 1**
Diagram representing the six ROIs used for quantitation of duodenal-gastric reflux. (□) $S_{tot}$: Total stomach; (▨) $S_{prox}$: Proximal stomach; (■) $L_1$: Liver overlapping stomach; $L_2$: Duplicate of $L_1$ on right lobe; (----) $B + S_{tot} - L_1$: Bowel + total stomach − liver overlapping stomach; BKG: background.

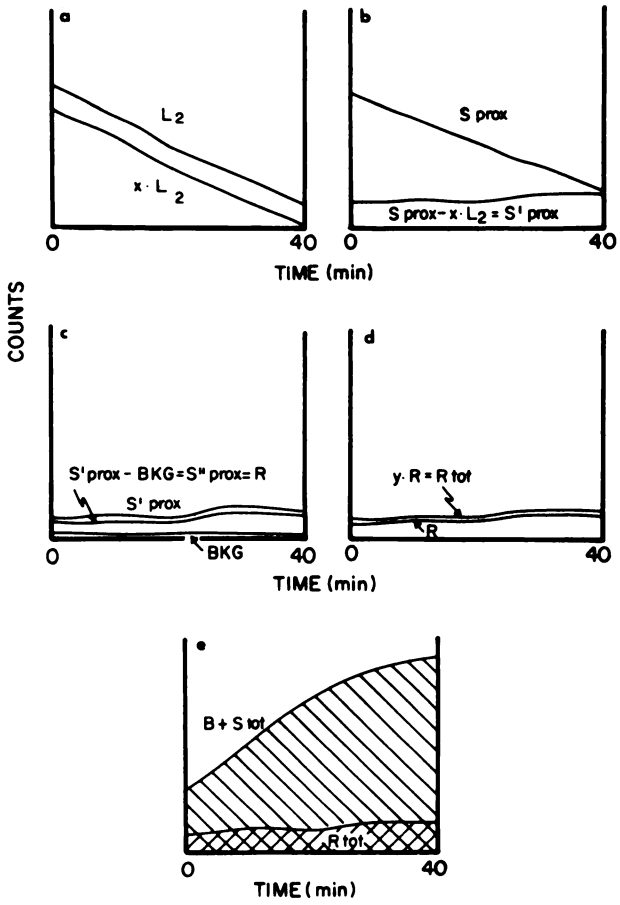


**FIGURE 2**
Schematic activity-time curves for each ROI, and of corrections made for the overlap of the stomach by the liver and bowel, and for the background. $S_{tot}$: Total stomach; $S_{prox}$: Proximal stomach; $L_1$: Liver overlapping stomach; $L_2$: ROI on right lobe; $X \cdot L_2$: Extrapolation of $L_1$ according to x; BKG: Background; R: Reflux in proximal stomach; $R_{tot}$: Reflux in total stomach; $B + S_{tot} - L_1$: Activity in bowel and stomach.

excluded. The BKG activity curve was corrected for the $S_{prox}$ surface and then subtracted from the $S'_{prox}$ curve (Fig. 2C). This $S''_{prox}$ curve ($S'_{prox}$ − BKG), that represented reflux (R) in this portion of the stomach, was finally corrected (Fig. 2D), (y factor = $S_{tot}$ surface divided by $S_{prox}$ surface) for the total stomach surface ($y.R = R_{tot}$). Background was not subtracted from ($B + S_{tot} - L_1$) because it was considered negligible compared with bowel activity.

The reflux index (Fig. 2E) equals the area under the activity curve of $R_{tot}$ divided by the area under the $B + S_{tot} - L_1$ curve.

## RESULTS

Forty-seven patients underwent upper endoscopy (Table 1). In most of the DRG patients there was bile present in the stomach (16 out of 20) and/or antral hyperemia (17 out of 20), while of the 16 RUD patients, 12 showed no trace of bile in the stomach although there was hyperemia of the antrum in eight. All but one of the cases of Moynihan's disease (ten out of 11) presented clear gastric juice.

The scintigraphic study of duodenal-gastric reflux was first interpreted qualitatively (Table 2) and reflux was visualized on at least one 2-min analog image in 13 of the 20 DRG patients, seven out of 16 RUD, and two out of 11 Moynihan. There was no evidence of reflux in the control subjects.

Results of the quantitative analysis appeared in Figure 3, i.e., the percentage of reflux for the different diseases studied. All volunteer asymptomatic subjects had < 1% reflux. Most cases (ten out of 11) of Moynihan's disease had a reflux < 1.5%. This is why we set 1.5% as a cutoff point for significant reflux. Most of the DRG cases (15 out of 20) and half (eight out of 16) of the RUD had a percentage of reflux > 1.5%. It is to be noted that subjects having undergone a cholecystec-

**TABLE 1**
Endoscopy

| | 20 DRG | 16 RUD | 11 Moynihan |
|---|---|---|---|
| Bile + | 16 | 4 | 1 |
| Bile − | 4 | 12 | 10 |
| Antral hyperemia | 17 | 8 | 3 |

TABLE 2
Scintigraphy: Qualitative Reflux

| | DRG | RUD | Moynihan | Controls |
|---|---|---|---|---|
| Reflux + | 13 | 7 | 2 | 0 |
| Reflux – | 7 | 9 | 9 | 7 |

tomy (five out of 20 DRG) are distributed in approximately the same proportion as the noncholecystectomized DRG subjects (four out of five and 11 out of 15, respectively having > 1.5% reflux).

## DISCUSSION

At present, there are several methods for detection of bile in the stomach, but none is perfect. Endoscopy (*16–17*) is probably the most commonly used. It often enables us to visualize bile residue, however, it is a nonphysiological method. Some authors (*18*) have demonstrated that the presence of an endoscope in the stomach may induce or increase bile reflux. Using scintigraphy, Wolverson (*14*) measured the percent of reflux before and after gastric intubation in 14 patients. He noted significantly increased reflux in three of them. Endoscopic quantitation of reflux remains subjective and limited in time to the short duration of the procedure.

Collection of gastric juice samples by means of gastric intubation may enable us to measure precisely the concentration of the various components of gastric juice (*19*), but as with endoscopy, this method is nonphysiological. It is also possible to aspirate from the stomach and measure artificial tracers such as BSP or indocyanine green (ICG) injected intravenously and excreted into the bile. But no extensive study using these tracers has yet been reported. As well, it is possible to aspirate in the gastric juice tracers instilled into the duodenum. According to the Mayo group (*20–21*), the small transpyloric tube used in this procedure would not have any effect on reflux.

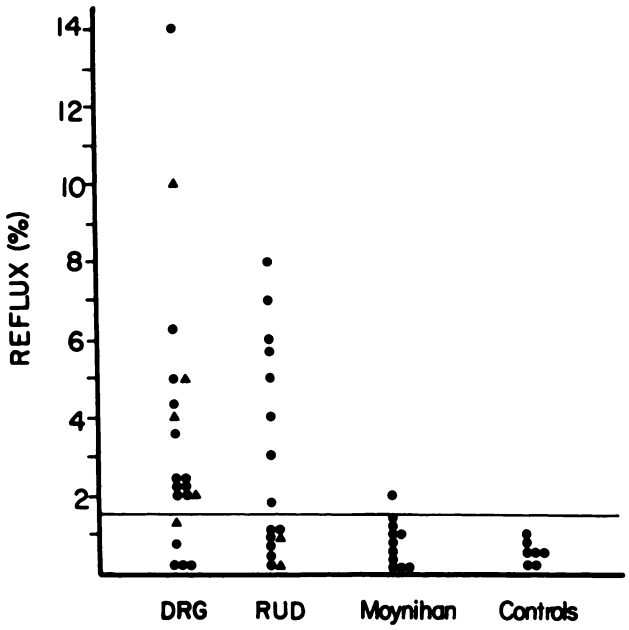


**FIGURE 3**
Quantitation of bile reflux. Distribution of the % of reflux (ordinate) for each group (abscissa). (·) Dyspeptic or normal; (▲) Dyspeptic with cholecystectomy.

A radiologic technique allows us to visualize reflux by introducing barium into the duodenum through a small tube (*22*). But there is a possibility that this tube may increase reflux. Moreover, this method is not quantitative. Recently, scintigraphic methods have allowed us to better visualize reflux and especially to quantify it. The scintigraphic study of duodenal-gastric reflux is probably the simplest method as well as being noninvasive and physiologic, and it enables us to assess reflux over a long period of time.

In our study we altered the methods already described in the literature so as to first exclude the region of the stomach which the loops of bowel overlapped, and then correcting for the total surface of the stomach. Quality and reproducibility of results depend upon a very strict methodology. We used a small dose of 1.5 mCi [$^{99m}$Tc] disofenin to avoid pixel overflow in digital acquisition. The patient was placed in a semirecumbent position (45°), sedentary for 40 min. This comfortable position decreases motion of the abdomen and bowel overlap on the stomach during the study. We did not try to separate the gastric antrum from the left lobe of the liver by left anterior oblique imaging. It would be more physiological to let the patient sit and walk between successive measurements of reflux, for instance in a study with 3 min scintiphotos every 15 min from 30 to 90 min, as reported (*23*). On the other hand, this method would increase manipulations during the computer analysis and would add to the inaccuracy of necessary corrections for organ overlap owing to repeated positioning of the subject. We could also miss intermittent or transient episodes of reflux. An egg-milk mixture was used to stimulate gallbladder evacuation because it contains significant amounts of fat which release considerable amounts of endogenous CCK. It also allows reflux, when present, to mix uniformly with radioactive gastric juice. In all cases of reflux on the qualitative study, reflux was seen not only at the level of the antrum, but at the level of the body and of the fundus as well. At the end of the study, [$^{99m}$Tc]pertechnetate was preferred to a nonabsorbable radiopharmaceutical such as DTPA or sulfur colloid, because it is more readily available, and it is considered a good anatomic marker of the stomach cavity in the minutes following its swallow.

Instead of quantitating in relation to the activity contained in the liver and gallbladder, we used a ROI

encompassing all the bowel and stomach, since the activity found in that region comes solely from the bile ducts and represents the activity (bile) which could potentially reflux in the stomach. Therefore, it is important to use a large field-of-view camera because the percentage of reflux could be incorrectly overassessed if part of the bowel activity was excluded. This is also true in such cases when biliary tract evacuation is very slow, for instance gallbladder dyskinesia (*24*). In our study of 47 dyspeptic patients, eight had a slower qualitative gallbladder evacuation and, consequently, little bowel activity during the study, which may occasionally explain false-positive results. In four of these patients, the scintigraphic study was repeated using CCK to have a quantitative and more reproducible evaluation of gallbladder function. All had a gallbladder ejection fraction < 20%. This technique enables us potentially to distinguish patients with reflux or dyskinesia when the clinical symptomatology is often similar.

We emphasize the importance of observing attentively the dynamic computer study before outlining the regions of interest, in order to identify precisely the organ overlap and the patient's breathing or shifting movements. In normal patients, the hepatic excretion of disofenin is uniform for each two ROIs outlined on the liver. However, our technique will not perform satisfactorily in cases of diseases affecting the segmental bile ducts, excretion from different portions of the liver may then vary.

We feel that the measurement of duodenal-gastric reflux in the manner described above is quite satisfactory, since it allowed us to note clearly the low percent of reflux in "normal asymptomatic" subjects compared to DRG-type dyspeptic patients. The percent of reflux as we measure it takes into account the extent of reflux and the length of time during which the gastric mucosa was exposed to bile. In our study, all volunteers had < 1% reflux and ten out of 11 Moynihan's disease had < 1.5% reflux. That value was then considered a cutoff point of reflux. A more elaborate study of reproducibility remains to be done to know if clinically asymptomatic subjects could have > 1.5% reflux by our method and if so what would be the significance.

In 13 subjects out of 54, we noted differing results between the qualitative and quantitative studies. Eight had a normal qualitative study although the percent of reflux was > 1.5%. Two of these cases can be explained by a large overlap of the stomach by the liver, and two others by lack of gallbladder contraction. The remaining four cases, whose percent of reflux varied between 1.5% and 2% are either false positive, or true positive who could not be identified visually because the percentage was too low. On the other hand, in five patients the qualitative study was positive, but the percentage of reflux was assessed from 0.9 to 1.5%, which we considered negative. Two of these patients were cholecystectomized; therefore, it is possible that absence of the gallbladder may account for a more rapid bile transit towards the bowel and an increase of the activity to be found there. This reduces falsely our measurement of the percentage of reflux. In fact, we think that reflux may be visualized when > 1%, depending on its extent and duration.

**TABLE 3**
Comparison Between Scintigraphic and Endoscopic Results

| | DRG | RUD | Moynihan |
|---|---|---|---|
| Bile + reflux > 1.5% | 13 | 3 | 0 |
| Bile − reflux < 1.5% | 2 | 6 | 9 |
| Bile − reflux > 1.5% | 2 | 5 | 1 |
| Bile + reflux < 1.5% | 3 | 2 | 1 |

There is no recognized gold standard for the measurement of reflux. A comparison of endoscopic and scintigraphic results (Table 3), i.e., the presence or absence of bile revealed by endoscopic examination compared with the percentage of reflux (< or > 1.5%), indicates that 33 results are in agreement and 14 are conflicting. In addition to the limits inherent to both techniques, the episodic character of duodenal-gastric reflux together with a relatively short assessment could account partly for these conflicting results. It should also be noted that slower gallbladder evacuation causes reduction of bowel activity during the whole study and overassessment of the percentage of reflux.

Moreover, Table 4 compares the percentage of reflux with the clinical diagnosis. Seventy-five percent (75%) of the DRG cases present reflux > 1.5% while 91% of subjects with Moynihan's disease had a percentage of reflux < 1.5%. It would seem that a scintigraphic study of duodenal-gastric reflux enables us to make a clear distinction between these two types of dyspeptic patients.

Concerning the four out of seven cholecystectomized patients presenting reflux > 1.5%, these results are in agreement with previous reports (*25–27*) which have already mentioned increased duodenal-gastric reflux in some cholecystectomized patients.

**TABLE 4**
Comparison Between Scintigraphic Results and Clinical Diagnosis

| | >1.5% | <1.5% |
|---|---|---|
| DRG | 15/20 (75%) | 5/20 (25%) |
| RUD | 8/16 (50%) | 8/16 (50%) |
| Moynihan | 1/11 (9%) | 10/11 (91%) |
| Controls | 0/7 (0%) | 7/7 (100%) |

## CONCLUSION

The physician is often faced with patients presenting a clinical picture of dyspepsia. Its etiology is not always easy to determine and the economic impact is considerable. The importance of duodenal-gastric reflux in several types of dyspepsia is not well known, since no study has documented it precisely.

It appears that our scintigraphic method allows reliable and reproducible quantitation of reflux, since our volunteer asymptomatic subjects did not present any significant reflux. As well it is possible to distinguish clearly at least two types of dyspeptic patients, i.e., those with Moynihan's disease and those with DRG. In addition, this technique has the advantage of being non-invasive, physiological, and acceptable to the patient. We could eventually include in this study a measurement of gastric emptying and move towards a more specific treatment of reflux when the patient is symptomatic.

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