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Comparison of three with six regions of interest analyses in patients with idiopathic constipation undertaking colon transit scintigraphy using ^{67}Ga-citrate

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Abstract. – OBJECTIVE AND INTRODUCTION: Preparation of data from 6 geometric regions of interest in the colon is time consuming, and can become impractical in the environment of busy Nuclear Medicine Departments. Therefore, we have investigated and demonstrated an alternative method for obtaining the same diagnostic information from an analysis of patients with idiopathic constipation who underwent colon transit scintigraphy using ^{67}Ga-citrate. Data analysis methods using three regions of interest are compared to the results obtained using the more time consuming 6 regions of interest method to analyze the data.

MATERIALS AND METHODS: In this study, we report our results of the comparative reanalysis of data obtained by more traditional methods. We compare 3 regions of interest (ROI) which were taken from areas including the right colon, left colon and the rectosigmoid colon, with original work using our alternative 6 (ROI) diagnostic methodology. In addition, the proximal colonic emptying (PCE) was determined at 24 hr post ingestion among members of 3 identified subject groups.

RESULTS: The distribution of activity as the ingested 67Ga-citrate passes through the colon constitutes an activity profile. The mean activity position in the colon can be determined from subsequent radiographic images and from this the mean clearance time can be calculated. In quantitative assessment, this represents the time at which half of activity was eliminated from colon (mean half clearance time – MCT) which did not appear different in the reanalysis. There is no significant difference in the current study in GMC 24h, GMC 48h and GMC 72h between two groups using the Man Whitney u test (p > 0.05), while in the previous work the results were statistically significant for the two later time periods GMC (GMC 48h and GMC 72h) (p = 0.016 and p = 0.027 respectively). The PCE in the group 1 was = 2.50 (0.37); group 2, 1.57 (0.47) and group 3, 2.97. The PCE was not different between the two groups (p = 0.21).

CONCLUSIONS: This investigation demonstrated that the radionuclide colon transit study using 67Ga-citrate is a safe, physiologic, and quantitative method for evaluating the transit of fecal material from cecum to rectum. Although, the visual assessment of diagnosis of the subjects in the two analyses is the same, it was not completely supported by quantitative measurements. Therefore, further studies need to be done.

Key Words:
Idiopathic constipation, Colon transit scintigraphy, ^{67}Ga-citrate, Colonic inertia pattern, Functional rectosigmoid obstruction (FRSO).

Introduction

This study compares the analysis of data from patients with idiopathic constipation who underwent colon transit scintigraphy using ^{67}Ga-citrate. A comparison is made between the diagnosis of activity (normal pattern, colonic inertia, and functional rectosigmoid obstruction) using three regions of interest to determine: direct observation, mean half-clearance time (MCT), activity profile, and geometric center

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analysis (GMT) as well as subsequent retention times for various regions of the colon. These results were compared to those obtained previously using the same data sets but analyzing the data using activity profiles based on six regions of interest[1].

In this study of 13 patients with idiopathic constipation demonstrated clear delineation between normal and abnormal groups on the basis of total and segmental percent colonic retention over 3 days using 6-7 MBq ^{67}Ga-citrate. The acquired data were produced from geometric mean center (GMC) of segmental retention of tracer, colonic tracer half-clearance time and mean activity profiles. Three patterns of colonic transit scintigraphy were observed: nine patients with normal pattern, for whom propagation of activity was acceptable during the study (group 1); three patients with colonic inertia pattern with mark retention of activity in the transverse colon, splenic flexure and rectosigmoid regions in 48h and 72h (group 2); one patient with significant retention of activity in the rectosigmoid in 72h defined as functional rectosigmoid obstruction (FRSO) (group 3). However, preparation of these data from 6 geometric regions of interest (ROI) including ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon and rectosigmoid colon, is time consuming, particularly in the busy environment of Nuclear Medicine Departments and, therefore, we have investigated an alternative method for analysis. In this study, we report the results of reanalyzing the data according to a method which involves using just three ROIs including right colon, left colon and the rectosigmoid colon. The results of this work are compared to those obtained from our original work involving analysis using all six ROI. In addition, we have developed new comparison formula for analysis of data between the three groups defined in the earlier study. This paper investigates the feasibility of using ^{67}Ga chelates as radioactive tracers for colonic transit in conjunction with simpler image analysis procedures.

Materials and Methods

Three regions were defined: right colon (cecum to mid-transverse colon); left colon (mid-transverse colon to descending colon sigmoid colon junction); and rectum and sigmoid colon (see Figure 1). The amount of activity in the abdomen at 6 hr was taken as 100%. The geometric means of the count rates in corresponding regions in each pair of anterior and posterior views were corrected for background counts and for radioactive decay and were calculated at 24, 48 and 72 hr for the three subject groups.

To calculate the geometric center, the number of counts in a given region was divided by the corrected number of total counts from the start of the study and multiplied by the region number. This calculation represents the geometric center for a given time. The formula used to calculate the geometric center is:

$$\text{Geometric center} = \frac{\sum^{3}_{1} \text{ROIi}}{\text{Instilled counts}} \times i \qquad (1)$$

where i and ROIi represent the ROI number and the counts in ROI number i, respectively.

The proximal colonic emptying (PCE) was determined at 24 hr according to the formula:

$$\text{PCE [\%/hr]} = \frac{(\text{LT} + \text{RS} + \text{STO})^{*}\ 100}{(\text{RT} + \text{LT} + \text{RS} + \text{STO})^{*}\ 24\text{hrs}} \qquad (2)$$

where LT = left colon; RT = right colon; RS = rectosigmoid colon; STO = stool.

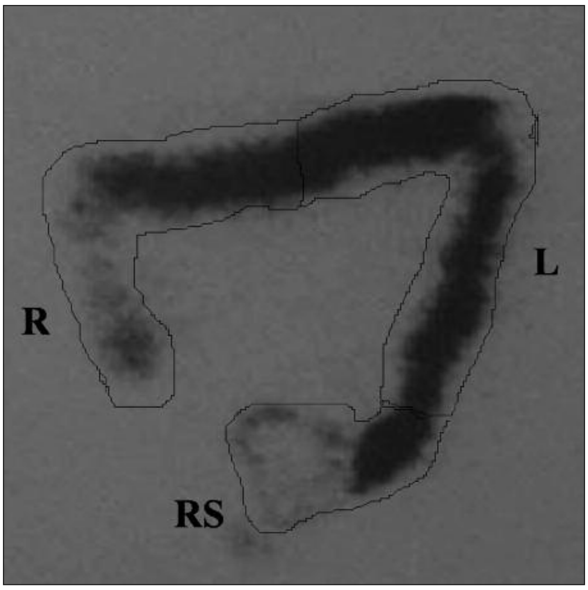

Figure 1. Three ROIs for different colonic segments. (LT = left colon; RT = right colon; RS = rectosigmoid colon).

Results

Thirteen patients, age; 35±13 years, 9 men and 4 women were studied[1]. In current and prior qualitative evaluations, the same results were acquired for these three groups. In quantitative assessment, the time for which half of the activity was eliminated from colon (mean half clearance time (MCT)) was not affected by reanalysis (Table I). There was no significant difference in GMC_{24h}, GMC_{48h} and GMC_{72h} between the two groups using Man Whitney test ($p > 0.05$) in the current study while in the previous work there was statistically significant differences in the two later geometric mean center analysis(GMC_{48h} and GMC_{72h}) ($p = 0.016$ and $p = 0.027$ respectively) (Table I).

The PCE in the group 1 was = 2.50 (0.37); group 2, 1.57 (0.47) and group 3, 2.97. The PCE was not different in two groups ($p = 0.21$).

The time activity profile of the percent retention in the different patterns of colonic transit was shown in Figures 2-4. Retention profiles of activity for the different groups are shown in Figure 5. The mean count activity for the three groups over the three different time periods are shown (Table II).

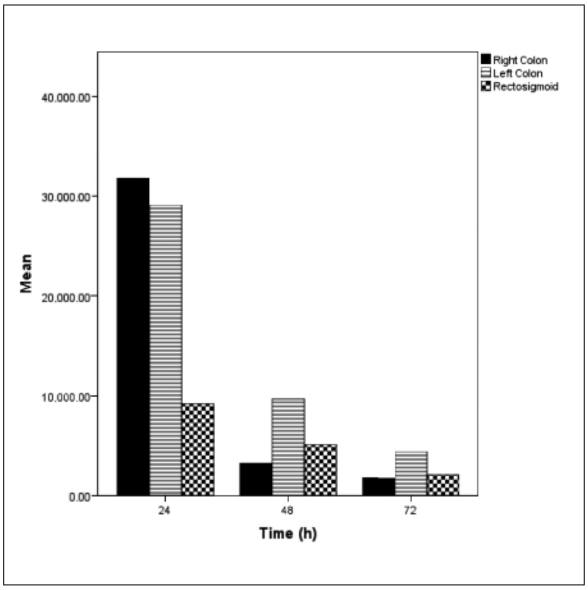

Figure 2. Activity retention profiles for three different patterns of colonic transit scintigraphy. Group 1 with normal pattern colonic transit. (ROI = right colon, ROI = left colon, ROI = rectosigmoid).

Table I. The geometric mean center (GMC) and mean half clearance time (MCT) in three groups of subjects.

Diagnosis	N (f/m)	Age	Time of scintigraphy 24 H GMC	24 H *p* value	48 H GMC	48 H *p* value	72 H GMC	72 H *p* value	MCT Hours	MCT *p* value
Normal (Group 1)	9 (6/3)	38 ± 0.67	2.47 ± 0.67		3.07 ± 0.22		3.17 ± 0.44		31 ± 11	
Inertia (Group 2)	3 (2/1)	43 ± 9	1.52 ± 0.19	0.21	3.63 ± 0.84	0.73	3.85 ± 1.01	0.65	95 ± 16	0.017
FRSO	1 (m)	21	3.81		4.75		5.68		120	

FRSO = functional rectosigmoid obstruction.

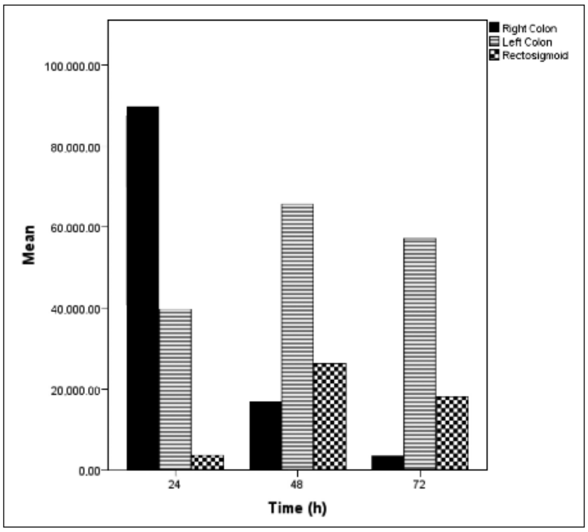

Figure 3. Activity retention profiles for three different patterns of colonic transit scintigraphy. Group 2 with slow propagation of activity throughout the colon. (ROI = right colon, ROI = left colon, ROI = rectosigmoid).

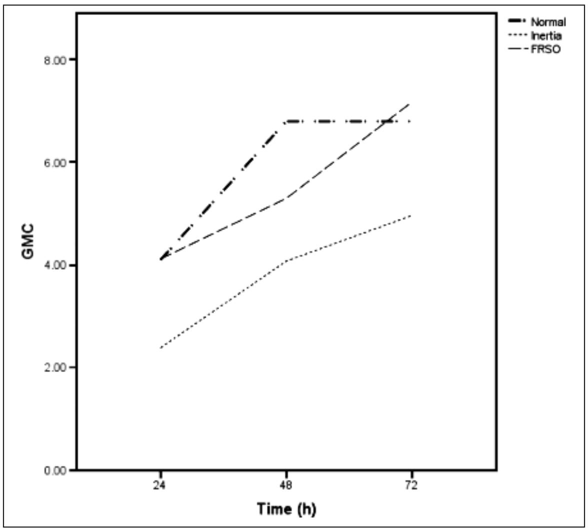

Figure 5. Curve of GMCi in the three patterns defined by colonic transit scintigraphy. The greatest amount of GMC24h and sharpness of initial slope are seen in patients with normal pattern, but in patients with colonic inertia, there is minimum of GMC_{24h}, but greater sharpness of the second slope. In patients with FRSO, there is acceptable GMC_{24h}.

Discussion

Assessment of colonic motility is especially important in patients with refractory constipation who may be referred for surgery based on this symptom. However, objective confirmation of disturbed colonic transit is necessary before proceeding with such invasive measures.

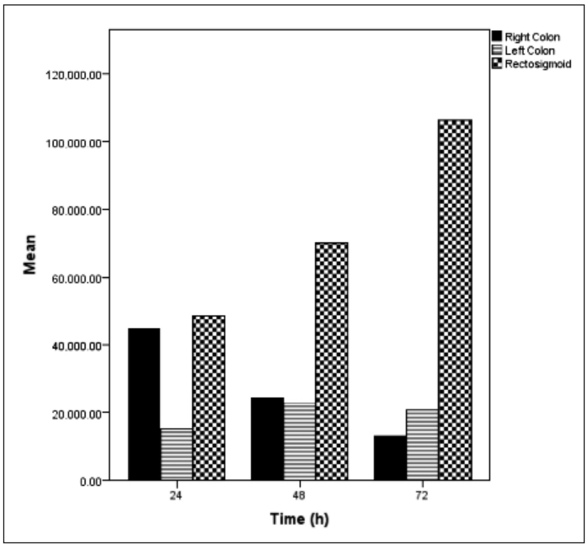

Figure 4. Activity retention profiles for three different patterns of colonic transit scintigraphy. Patient with prominent retention of activity in rectosigmoid. (ROI = right colon, ROI = left colon, ROI = rectosigmoid).

Having characterized the patients visually, we didn't find significant differences in the location of radioactivity using geometric centre analysis that supports the existence of distinct groups in this study.

Geometric mean center (GMC) determines the velocity of colonic transit up to the time points of measurement (24, 48 and 72 hr) and is calculated by adding the products of the geometric means and the segment number in each colon segment with subsequent division by the total activity.

Normal values for GMC by using ^{111}In-DTPA at 24h, 48h and 72h were 2.0- 7.0, 4.6- 7.0 and 6.2- 7.0 respectively[2]. If GMC_{48h} was less than 4.6, a diagnosis of colonic inertia was made. If GMC $\geq$ 4.6 but $GMC_{72h} < 6.2$, the scintigraphic "diagnosis" was functional rectosigmoid obstruction (FRSO).

A number of investigations have used three ROI in the analysis of the data.[3] Smart et al compared oral ^{131}I-cellulose and ^{111}In-DTPA simultaneously as tracers for colon transit scintigraphy in 11 normal and 11 constipated cases according to the 3 ROIs method of analysis. McLean et al[4] also used the 3 ROI method for analysis to evaluate colon transit in 11 normal and 29 constipated patients.

The absence of geometric mean center insignificancy in the three ROI analysis vs. the 6

Table II. Mean count activity for three groups over three time periods.

Time (hrs)	24			48			72		
ROI	R	L	RS	R	L	RS	R	L	RS
Normal	31830.50 (11186.66)	29161.50 (9610.50)	9218.71 (7660.34)	3314.28 (1362.13)	9677.42 (4693.46)	5128.85 (2402.94)	1823.800 (562.86)	4442.20 (2531.14)	2130.00 (1164.62)
Inertia	89927.83 (38197.88)	39816.83 (8214.53)	3695.66 (3686.67)	17001.33 (11883.35)	65761.67 (41554.96)	26291.00 (9702.47)	3569.66 (1535.29)	57219.67 (42716.92)	18163.67 (11445.90)
RSO	45128.50	15410.50	48648.00	25023.00	23085.00	69982.00	13387.00	20848.00	106393.00

ROI, region of interest; LT = left colon; RT = right colon; RS = rectosigmoid colon.

ROI method may be due to the use of fewer regions ; the low number of cases in each group may also explained these results. Second, when a bolus of activity is located at a junction between segments, different operators may calculate different results for segmental percent retentions, although the total percent retention will be unaltered. Therefore, it may be preferable to divide the colon into shorter units for more precise analysis.

Conversely, a number of studies focused on using a larger number of regions of interest in the analysis of the colon transit scintigraphy. Many investigations have been done using analysis methods involving 6 ROI colonic segments.[5, 6] Using counts in these regions together with calculated excreted counts, the geometric centre of the bolus of radioactivity was quantitated at time periods. The 3 ROI colon activity profile analysis has a number of advantages over the technique which uses 6 ROI. Colon shape and length are very variable from patient to patient and the geometric center analysis does not account for the length of each of the segments.

Furthermore, this analysis will be subject to inter-operator variability in the drawing of the ROI. Also, if activity moves solely within a segment or any number of segments, this will not be reflected in a change in the geometric center.

Finally, comparison of the percent retained activity with the normal range allows confirmation of the diagnosis and assessment of severity, while visual assessment of the pattern of transit may indicate the site of obstruction. However, this form of analysis is currently in the preliminary stage and will require further correlation with final diagnoses. With appropriate modifications, this technique may have a routine clinical role in Nuclear Medicine Departments that service Gastroenterological and Colorectal Units.

In addition, the proximal colonic emptying (PCE) at 24 hours was not different between groups because the proximal part of large bowel up to 24 hours seems to be unaffected in the three different subject patterns.

These scintigraphy results may help with the management of idiopathically constipated patients. First, they may facilitate the identification of the underlying cause. Second, identifying the hold-up site may guide gastrointestinal biopsy. Third, scintigraphy could help in providing effective management for patients suffering with idiopathic constipation. Differentiation between different types of constipation (colonic, inertia, or functional rectosigmoid obstruction: FRSO) is clinically useful. For instance, the prokinetic agent cisapride has been shown to be helpful in constipation due to colonic inertia, but not from anal sphincter dysfunction or functional rectosigmoid obstruction[2]. Constipation resulting from functional rectosigmoid obstruction may be treated with anal manometry biofeedback[2]. If surgery is contemplated, patients with total colonic inertia will need a colectomy, whereas patients with anorectal dysfunction may need an anorectal myomectomy[2].

The last point which must be considered is the issue of radiation dosage. In a given study, the effective dose equivalent for ^{67}Gallium citrate is 0.4 mSv/MBq for an average 10-year-old ^{67}Gallium studies[7]. On other hand, an average dose for a barium enema was 9 mSv and for abdominal radiograph was 1.5 mSv[7]. Moreover, scintigraphy provides information about the complete gastrointestinal including tract including gastric emptying and small and large bowel transit in one measurement and simultaneously allows repeated imaging with no additional radiation exposure.

Recently, wireless capsule motility using the SmartPill as a system for GI monitoring appears to be very useful in estimating gastrointestinal transit[8]. The SmartPill capsule assessment of gastric emptying and whole gut transit compares favorably with that of scintigraphy[8]. Wireless capsule motility shows promise as a useful diagnostic test to evaluate patients for GI transit disorders and to study the effect of prokinetic agents on GI transit[8,9].

Conclusions

This study demonstrates that radionuclide colon transit studies are a safe, physiological and quantitative method for evaluating the transit of fecal material from the cecum to the rectum. Although, the visual assessment of the diagnosis of subjects from the two analyses is the same, it was not completely supported by quantitative measurements and, therefore, will require further studies.

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