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INVITED PERSPECTIVE

Will Comprehensive Assessment from Esophagus to Large Bowel Revive the Momentum for Radionuclide Gastrointestinal Transit Studies?

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In this issue of *The Journal of Nuclear Medicine,* Antoniou et al. describe a novel scintigraphic procedure designed to evaluate in a physiologic manner the transit of both the liquid and the solid components of a meal through virtually the entire gastrointestinal (GI) tract, starting with esophageal transit (*1*). Although the procedure is somewhat complex and laborious, it does offer the advantage of combining assessment of esophageal, gastric, small bowel, and colonic transit so as to obtain quantitative information on either the overall transit time and/or the separate components of transit from the esophagus to the more distal end of the gastrointestinal tract; the procedure also entails separate assessments of the liquid and of the solid components of a meal.

This scenario has always attracted the attention of nuclear physicians, and indeed the first radionuclide technique combining evaluation of gastric emptying with evaluation of the small bowel and colon transit was published in 1975 (*2*). Various approaches have subsequently been described and reference ranges for normal values in healthy subjects have been defined (*3*,*4*); nevertheless, to date there is no scintigraphic protocol univocally recognized as *the* standard adopted worldwide, even for separate assessment of transit in the different portions of the GI tract, i.e., esophagus, stomach, small bowel, large bowel – although the recent publication of guidelines jointly developed by the SNMMI and by the ESNMMI constitutes an important move in this direction (*5*).

The study by Antoniu et al. is different from others for varius reasons, the most obvious being combination in a single exam of so many components of GI pathophysiology, both region-wise (esophagus to large bowel) and meal-wise (solid and liquid). One current drawback of the study, i.e., the development of normal ranges for the various functional parameters based on a relatively small population of healthy subjects (n=18) will certainly be overcome as experience from the same group and/or from other groups stimulated by this proposal will grow. Another crucial issue addressed by Antoniu and colleagues is that their protocol for comprehensive assessment of transit from esophagus to large bowel is designed to meet the clinical demand that separate assessment of transit for single portions of the GI tract (esophagus, stomach, small bowel, large bowel) has shown not to be able to adequately meet – most likely one of the reasons why such radionuclide transit studies have never really grown to represent *the* definite solution for patients with dyspeptic syndromes.

It is important to consider that dyspeptic symptoms are common in patients with either

gastric and/or small bowel dysmotility, and constitute a common complain in patients with esophageal dysmotility as well. Moreover, although constipation and/or diarrhea are the predominant symptom directing attention to some abnormality in large bowel transit, patients with these symptoms often have additional complains that overlap with those more typical for the upper GI tract (i.e., dysphagia and/or dyspepsia). In fact, it is now well known that transit abnormalities can concomitantly affect more than one gastrointestinal region (*6*), and the assumption that dyspepsia means motility disorder of the upper GI tract while diarrhea/constipation means disorder of the lower GI tract is not systematically true. Thus, by adopting a scintigraphic protocol enabling to routinely investigate patients for small and large bowel dysmotility in addition to esophageal transit and gastric emptying, we might be able to characterize (therefore to correctly diagnose) more patients with GI dysmotility syndromes with respect to what we can achieve with separate (often incomplete) assessments of transit through the various regions of the gastrointestinal tract.

On the other hand, it should be considered that, in face of some relative inadequacy of radionuclide transit studies when performed separately and incompletely, nonradionuclide procedures that gastroenterologists can use in their own environments, such as various breath tests, ultrasound and more recently MR and wireless motility capsules, portend to yield the same diagnostic information as that derived from classical radionuclide GI transit studies. Nevertheless, it is also known that correspondence between nonradionuclide and radionuclide-based investigation modalities is less than optimal, as radionuclide procedures reflect as closely as possible the true physiology of GI motility (*7-11*). Thus, variable degrees of interaction among different specialists (gastroenterologists vis-à-vis nuclear physicians) make it difficult to standardize protocols among different clinical centers as they favour local variations that are introduced to meet specific expectations of the referring specialists. In addition to variations in clinical protocols, radionuclide GI transit studies still suffer from a considerable heterogeneity among different nuclear medicine centers, although such heterogeneity is expected to decrease after publication of the joint SNMMI/ESNMMI guidelines (*5*). These differences are related to important practical aspects not only of the procedure itself (such as preparation and composition of the radiolabelled meal, acquisition modalities, and quantitative/semiquantitative assessment of the data obtained), but also to the way in which the results are interpreted/presented.

Furthermore, standardized basic components of a radiolabelled meal are also variably available in different countries, such as the commercial preparation of egg white, which is available only in the USA. Other differences derive from country-specific variations in the balance of the basic nutrients (carbohydrates, proteins, fats), and in variable palatability and composition of food in different ethnic cultures. All the above factors probably explain why, from the nuclear medicine point of view, GI transit studies has generally remained a "niche" activity with respect to the imaging procedures most commonly performed in any nuclear medicine center. Moreover, no sufficient attention is paid to the fact that a properly performed radionuclide GI transit study is extremely useful not only in the diagnostic approach to a patient with a GI motility disorder, but also for assessing the efficacy of therapy; in this regard, it should be kept in mind that most drugs employed clinically to treat a motility disorder affecting, e.g., gastric emptying, actually interefere also with motility of other portions of the entire GI tract.

- Is it always necessary to perform a comprehensive test for GI transit/motility, including solid and liquid phases? Experience is growing that investigating motility of the entire GI tract can reduce diagnostic errors or incomplete diagnoses, leading in several instances to modify clinical management and therapy. For instance, gastroparesis can go undetected in 20%-40% of the cases (*12*)**,** while its detection can increase by about one third by extending the acquisition time from 2 to 4 hours (*13,14*); furthermore, assessing liquid gastric emptying improves the detection of gastroparesis by another third (*15,16*).
- Why do we need to standardize the comprehensive radionuclide GI transit study? Even if the joint SNMMI/ESNMMI guidelines constitute an important milestone in the process of standardization, they only concern small bowel and large bowel transit (*5*); further multidisciplinary interaction is necessary in order to develop similar guidelines, therefore standardization, also for the upper GI tract, i.e., esophageal transit and gastric emptying. In this regard, continuing discussion between the gastroenterologits and the nuclear physician on specific clinical cases encountered in the daily routine will obviously result in improved possibility of achieving a clear and complete/definite diagnosis. Diagnosis will be clear because the nuclear physician will know the diagnostic dilemma of the gastroenterologist,

and complete/definite because the nuclear physician will provide a comprehensive evaluation of the various portions of the entire GI tract. In this scenario, certainly standardization plays an important role promoting better interaction between nuclear physicians and gastroenterologists across different clinical centers.

- How can the multidisciplinary approach improve the evaluation of patients with GI motility disorders? The multidisciplinary approach is important to patients with motility disorders of the GI tract and should include a team of healthcare experts such as gastroenterologists, nutritionists, radiologists and nuclear physicians. Each of the experts listed above will contribute to some aspects in the characterization, therefore to correct diagnosis and clinical management, of patients with GI motility disorders, such overall vision of the patient being synergistically enhanced with respect to the simple arithmetic sum of each contribution.

In conclusion, based on the promise offered by a comprehensive radionuclide evaluation of GI transit, we envision a future where the clinical feedback on a patient-to-patient basis will guarantee that the information provided by such protocol is indeed of value to the specialist in gastroenterology and ultimately to the patient. Thus, we encourage the nuclear medicine and the gastroenterology communities to continue to work synergistically towards developing joint guidelines including both the upper and the lower GI tract, in the avenue opened by the work of Antoniu and colleagues and with the goal of treating all motility disorders of the GI tract as pertaining to a single organ rather than to separate portions.

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KEYWORDS: gastrointestinal transit; radionuclide evaluation; solid/liquid meal; esophagus to large bowel; comprehensive evaluation

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