

A Scintigraphic Method for the Assessment of Intraluminal Volume and Motility of Isolated Intestinal Segments

Andrew Mitchell, Dan J. Macey, and Jack Collin

Oxford University, John Radcliffe Hospital, and Churchill Hospital, Oxford, England

The isolated in vivo intestinal segment is a popular experimental preparation for the investigation of intestinal function, but its value has been limited because no method has been available for measuring changes in intraluminal volume under experimental conditions. We report a scintigraphic technique for measuring intraluminal volume and assessing intestinal motility. Between 30 and 180 ml, the volume of a 75-cm segment of canine jejunum, perfused with Tc-99m-labeled tin colloid, was found to be proportional to the recorded count rate. This method has been used to monitor the effects of the hormone vasopressin on intestinal function.

J Nucl Med 24: 571-576, 1983

Intestinal segments, isolated in vivo either surgically or by balloon occlusion, and perfused with glucose and saline solution, are widely used in the investigation of intestinal function (1-9). Effluent is collected from the segment's distal end, and absorption is calculated by subtraction of output from input. If, during such an experiment, there is an increase in the intraluminal volume and "pooling" of perfusate, there will result a fall in effluent volumes leading to a falsely high calculated absorption. Therefore, in order to validate apparent increases in absorption in such a preparation, a nonabsorbable marker is usually added to the perfusate so that absorption can also be calculated from the increase in marker concentration between perfusate and effluent (2). Though this marker technique may confirm an increase in absorption, it can provide only indirect and qualitative evidence of intraluminal volume change. Under steady-state conditions, intestinal volumes can be estimated from the mean flow rate and transit time (7), but a method for directly measuring the intraluminal volume of a perfused intestinal segment in vivo would be of value.

We have reported a fall in the volume of effluent from perfused segments of canine jejunum in response to the

intravenous administration of the peptide hormone vasopressin (8), and similar findings have been interpreted by others as an increase in absorption (9). However, our data from nonabsorbable markers suggested that there was no real increase in absorption, and therefore that the observed fall in output resulted from "pooling" of perfusate within the segment. The gamma-camera technique reported in this paper was developed in order to measure the intraluminal volume of perfused intestine under experimental conditions and to confirm and quantify the presumed increase in intestinal capacity produced by vasopressin. It has also been possible to observe changes in intestinal motility using this method.

MATERIALS AND METHODS

Phantom. A simple phantom was constructed to simulate an isolated perfused segment of intestine with its intervening and surrounding tissues. This phantom comprised 75 cm of latex tubing, 2.5 cm i.d., filled with water to which measured amounts of Tc-99m were added. The tubing was placed in a 10 × 10 × 8 cm plastic box filled with water to simulate the intra-abdominal surroundings of the experimentally prepared intestinal segments.

Animal preparation. In healthy female outbred dogs weighing 16 to 19 kg, a 75-cm segment of jejunum was

Received Dec. 6, 1982; revision accepted Feb. 28, 1983.

For reprints contact: Dr. Andrew Mitchell, Nuffield Dept. of Surgery, Oxford University, John Radcliffe Hospital, Headington, Oxford, OX39DU, UK.

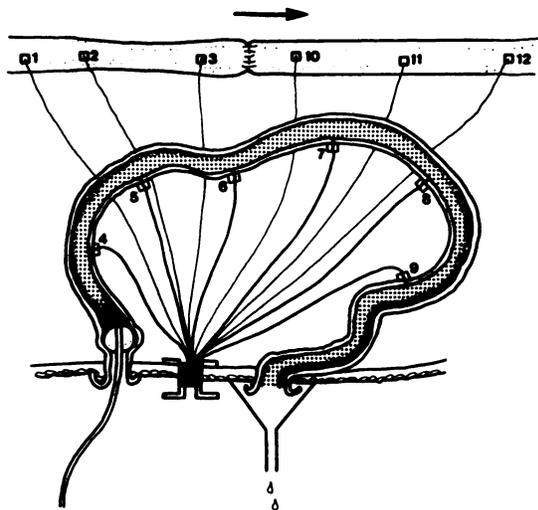


FIG. 1. Diagram of isolated, perfused jejunal segment with chronically implanted electrodes.

isolated and the continuity of the remaining bowel was restored by anastomosis. The proximal transection was made 50 cm distal to the pylorus. All measurements of gut were made after the intravenous administration of atropine 0.05 mg/kg body weight. Six monopolar silver-wire electrodes were attached to the serosal surface of the isolated segment at 10-cm intervals, and a further six at similar intervals, three above and three below the reconstituting anastomosis (Fig. 1), so that intestinal myoelectrical activity could be monitored by an external recorder. The isolated segment was placed in the left side of the abdomen and both ends brought out as stomata on the abdominal wall so that the segment could be perfused using a urinary catheter with a 5-ml retaining balloon (Fig. 1).

The dogs were allowed at least 10 days to recover from surgery. Immediately before each experiment the dog was fed a standard meal to abolish the phasic pattern of intestinal electrical activity and motility induced by fasting (10). The dog stood upright in a restraining harness throughout the experiments.

Choice of radiopharmaceutical. The radioagent used to image the intestinal segment must fulfill the following criteria:

1. It should be homogeneously distributed in the perfusion solution and remain stable during the experiment.
2. It must not be absorbed in significant quantities from the lumen of the isolated intestinal segment.
3. It should not be adsorbed onto the bowel epithelium or the perfusion apparatus.

Because of its ready availability and simple preparation, tin colloid labeled with Tc-99m was chosen as the tracer; it was found in initial perfusion experiments to meet the above criteria.

Perfusate. Net absorption from (or secretion of fluid into) the intestinal lumen would alter the concentration

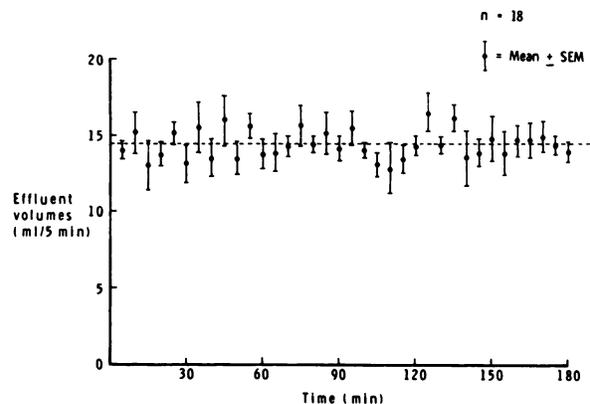


FIG. 2. Volumes of effluent recovered per 5 min using 50.7 g/l mannitol in water perfused at 2.9 ml/min.

of the tracer and thus would affect the relationship between intraluminal activity and intraluminal volume. Net fluid flux must therefore be prevented if intraluminal volume is to be measured using a radionuclide technique. Experiments were carried out using an aqueous perfusate with an osmolality of 290 mOsm/kg containing 50.7 g/l of mannitol, a poorly absorbed polyhydric alcohol. Six experiments on each of three dogs showed that there was virtually no net loss of water from, nor secretion of water into, the lumen when this solution was perfused through a 75-cm segment of canine jejunum at 2.9 ml/min (Fig. 2). The effluent volume in each experiment was within $100 \pm 2\%$ of the volume perfused. The normal pattern of intestinal myoelectrical activity was not altered by mannitol perfusion.

RESULTS

Phantom experiments. The phantom was used to test the count-rate response of the computerized gamma camera images under the following conditions:

1. The volume of the fluid in the tubing was varied, keeping the total activity constant.
2. The position of the tubing within the carton was varied.
3. The activity within the tubing was varied by adding measured volumes of fluid of a known radionuclide concentration. The results are shown in Table 1 and were interpreted as follows:

1. Increasing the volume of fluid within the tubing over the range 60 to 180 ml produced only small changes in recorded count rate when the amount of contained radioactivity was kept constant at 600 μ Ci. These changes were well within the limits of reproducibility of the measurement.

2. Altering the position of the active tubing within the carton so as to achieve the maximum possible variation in configuration and depth (Fig. 3) produced a maximum variation in recorded count rate of 6% from the mean. These variations seemed to be predominantly the result of changes in the depth of the tubing, and this

TABLE 1. VARIATION IN OBSERVED COUNT WITH CHANGES IN VOLUME, ACTIVITY, AND CONFIGURATION OF THE PHANTOM

Volume increase with constant activity		Configuration change (Fig. 3)		Volume and activity increased in parallel	
volume (ml)	cpm	frame	cpm	volume (ml)	cpm
60	125473	1	123946	30	28955
90	133842	2	139102	60	63763
120	133217	3	134578	90	97895
180	129734	4	127051	120	122398
—	—	—	—	150	154361
—	—	—	—	180	179828

factor would have little effect in the animal experiments since lateral mobility of the isolated intestinal segment is limited by stoma fixation, the attached electrodes, and intra-abdominal adhesions.

3. An increase in both the activity and volume of the fluid in the tubing, produced by adding measured volumes of fluid of the same concentration, was accompanied by a linear increase in the recorded count rate throughout the range of volumes tested (30 ml to 180 ml) (Fig. 4).

Suitability of Tc-99m-labeled tin colloid. Initial paper chromatography confirmed >99% binding of Tc-99m to the colloid. To test for absorption and adsorption, 100 ml of mannitol perfusate containing 580 μ Ci Tc-99m-labeled tin colloid was perfused through the isolated jejunal segment at 2.9 ml/min. Perfusion was continued for a further 90 min with nonradioactive mannitol perfusate. Recovery of perfused Tc-99m in the effluent was >97%, and the activity remained homogeneously distributed in the effluent. In none of the experiments was it possible to detect activity in the liver, spleen, or urinary tract of the dogs. Tc-99m-labeled tin colloid therefore meets the requirement for a nonabsorbed nonadsorbed radiopharmaceutical in this experimental preparation.

In practice the gamma image of the segment includes a left lateral view of the spleen and splenic blood pool, so that significant absorption of colloid or pertechnetate would be simple to detect.

Calibration of intestinal segment volume in vivo. Three dogs have been used in a number of experiments and an initial calibration was performed to determine the relationship between count rate and segment volume in each dog. The dog was placed immediately adjacent to the collimator of the gamma camera, so that a left lateral view of the abdomen was obtained, and the isolated segment was flushed of debris with saline and allowed to drain for 15 min. The ends of the segment were then occluded using the balloon of an No. 18 FG Foley catheter filled with water. The lumens of the catheters were occluded by cross-clamping immediately below the stomata and 15 ml of the isotonic mannitol solution containing Tc-99m-labeled tin colloid at a concentration of 650 μ Ci/l was introduced into the lumen of the intestinal segment by injection through the wall of the proximal catheter above the clamp. A 1-min count was recorded and a further 15 ml added to the segment. This process was repeated until the segment contained 120 ml of perfusion solution or until the dog showed signs of discomfort. A region of interest outlining all the perfused segment in each gamma image was defined using a 10% threshold, and this region was counted, i.e., all pixels with

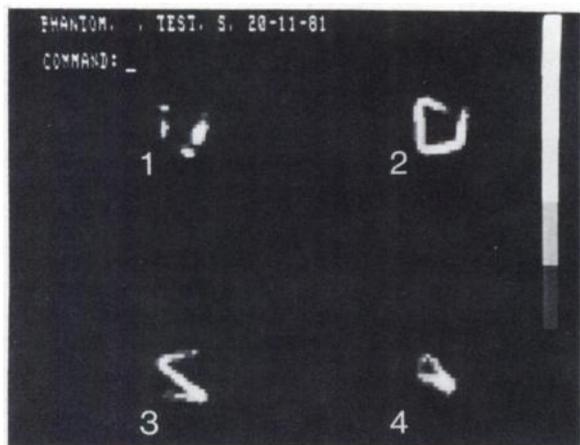


FIG. 3. Gamma camera images of the four phantom configurations.

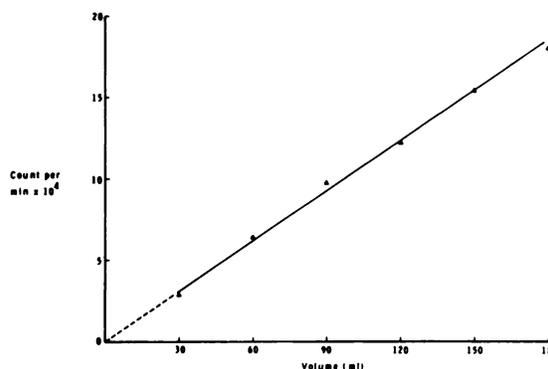


FIG. 4. Relationship between volume of active solution in phantom and recorded count rate.

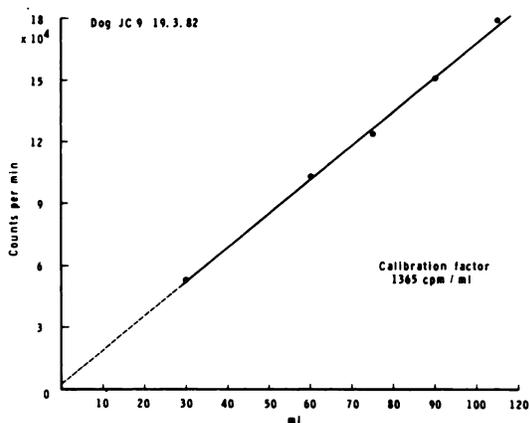


FIG. 5. Calibration of recorded count rate in vivo with increasing volume of active solution in intestinal segment.

counts less than 10% of the maximum pixel count were removed.

The recorded counts were corrected for decay and plotted against the volume of fluid in the segment. The relationship was found to be linear in vivo (Fig. 5), as it had been in the phantom experiment. The count rate obtained from this preliminary in vivo calibration was used to calculate the volume of the segment at any time during the experiment that immediately followed.

Volume measurements during intestinal perfusion. By perfusing intestinal segments with an aqueous solution of 50.7 g/l mannitol containing 650 μ Ci/l Tc-99m-labeled tin colloid, we have been able to measure steady-state intestinal volumes and changes in intestinal volume induced by hormones. Perfusion at 2.9 ml/min produces an intraluminal volume of approximately 0.45 ml/cm intestinal length in the canine jejunum. This volume varies from minute to minute about the mean because of irregular efflux of fluid from the distal stoma.

Figure 6 shows the variation in count rate and the calculated segment volume during an experiment in which a dog was given vasopressin at 0.02 pressor units/kg-min by intravenous infusion. The mean steady-state volume of 31 ml rose sharply during the first 30 min of vasopressin administration to reach a new

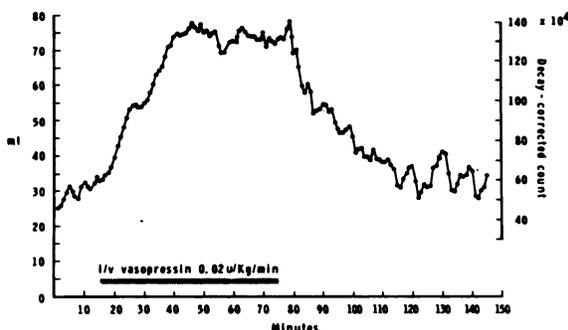
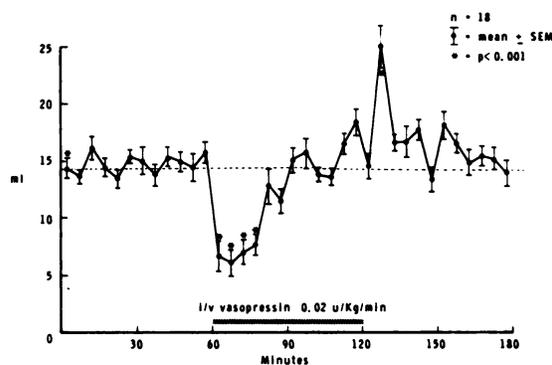
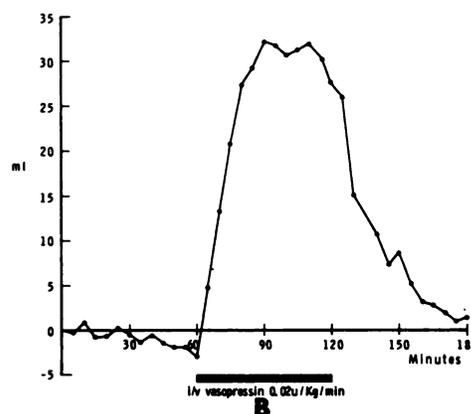


FIG. 6. Count rate and corresponding derived segment volume before, during, and after i.v. administration of vasopressin.



A



B

FIG. 7 (A). Mean volume of effluent per 5 min before, during, and after intravenous vasopressin administration while perfusing segment with isotonic mannitol solution at 2.9 ml/min. (B). Mean change in segment volume calculated by integrating data shown in (A).

plateau of 74 ml. After a further 30 min the hormone was withdrawn, and the segment volume returned to the initial level. This result is consistent with those of six experiments in each of three dogs in which mannitol perfusate was used alone. There was invariably a deficit of effluent during the first 30 min of vasopressin infusion, and this deficit was recovered after the hormone was withdrawn (Fig. 7A). Integrating the data gives a calculated mean increase in segment volume during vasopressin infusion of 32 ml (Fig. 7B). Intestinal volume has thus been shown to double in response to a hormonal stimulus.

Assessment of motility. Motility was qualitatively assessed by examining a playback buffer movie of the 180 1-min images of the segment that had been recorded during the experiment. Slight movements of the dog between images made it difficult to characterize precisely the observed changes in motility. Nevertheless, striking changes in motility of the intestinal segment were seen, and these were most marked during experiments in which intravenous vasopressin was given. Vigorous peristalsis in the segment before vasopressin administration was immediately abolished when the hormone was infused. In spite of a doubling of intralu-

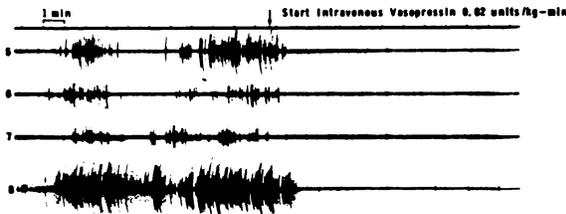


FIG. 8. Abolition of myoelectrical spike activity in four segment electrodes (see Fig. 1) by vasopressin administration.

minimal volume, the segment remained virtually motionless until the intravenous infusion was stopped, after which motility was seen to recover and segment volume fell.

These observations are consistent with the myoelectrical findings. Fast myoelectrical activity (or "spike activity") accompanies intestinal smooth-muscle contraction, and this type of activity was abolished during vasopressin infusion (Fig. 8).

DISCUSSION

This direct method of segmental volume measurement from a gamma image provides a new tool for the investigation of intestinal physiology. We emphasize, however, that its use is currently limited to the study of isolated perfused segments under conditions that prevent net flux into or out of the lumen. The linear relationship between recorded count rate and segment volume was unexpected, since the gamma camera produces a two-dimensional image of the convoluted segment, whose volume is irregularly distributed compared with that of a left ventricle, where a linear relationship also obtains (11). It seems likely that concomitant changes in the thickness of intervening and overlying tissues compensate for the changes in self-attenuation that must accompany changes in segment volume.

The magnitude of the volume changes revealed by this technique are much greater than might have been expected on a priori grounds. Intestinal volume was more than doubled by vasopressin administration. The interpretation of previous work using isolated segments of intestine to determine the effects of pharmacological and physical factors on intestinal absorption should therefore be re-examined. Volume measurements can now be made to quantify any "pooling" effect.

In particular, the suggestion that vasopressin increases intestinal absorption in the dog (9) has been refuted since the observed effects have been shown to result from volume changes. Somatostatin, a hormone with effects on intestinal myoelectrical activity and motility (12,13) similar to those of vasopressin, has been said to modify intestinal absorption in man (4). This suggestion might also be investigated by volume measurement.

Only qualitative assessment of motility was possible in this study. Characterization of motility by subtraction of successive frames, and display of positive and negative

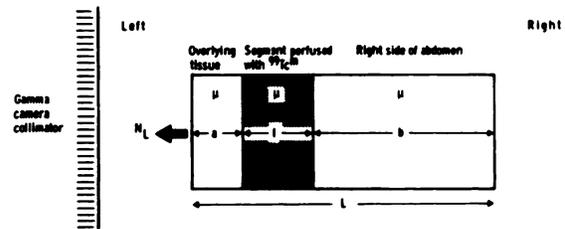


FIG. 9. Diagram of isolated segment as seen by gamma camera.

count changes, would require compensation for movement of the animal and preferably a faster frame rate. By injecting a bolus of a second tracer into the perfusate and determining the time course of its passage through the segment, simultaneous measurements of volume and transit time could be made. These would be of additional interest to intestinal physiologists.

ACKNOWLEDGMENTS

The authors thank Mr. T. G. Denton, Miss Rosemary Young, Mr. J. Hiles, and Mr. M. Beresford for their help with this work.

APPENDIX

The changes in count rate with volume and activity can be described by calculating the effect of self-attenuation in the segment and the attenuation in the overlying tissues between the segment and the camera.

Consider a segment (Fig. 9) of thickness l in an abdomen of thickness L and of unit area when seen in left lateral view. Assume that the abdominal tissues and the segment contents have the same linear attenuation coefficient (μ) and that the concentration of Tc-99m in the perfusate is A μ Ci/ml. The recorded count rate with a gamma camera and collimator system of absolute efficiency T cps/ μ Ci would be N cps/cm² where:

$$N = \frac{AT e^{-\mu a}}{\mu} \cdot (1 - e^{-\mu l})$$

In practice the concentration (A) remains constant when the segment volume increases, but both the thickness of the segment and the area seen in the gamma image increase. These changes in turn produce an increase in the observed count rate. The relationship between volume and observed count rate remains linear because changes in a and l are small compared with the half-value layer (HVL) for 140-keV photons in unit-density tissue. The calculated diameters of the segment for volumes of 30 ml and 105 ml are 0.36 and 0.67 cm, whereas the HVL is approximately 5.5 cm. Even if segment volume changes are limited, say to the proximal portion, the count rates recorded will still reflect the total volume of the segment.

REFERENCES

1. BARBEZAT GO: Triple-lumen perfusion of the canine jejunum. *Gastroenterology* 79:1243-1245, 1980
2. MODIGLIANI R, RAMBAUD JC, BERNIER JJ: Validation of the use of a tube with a proximal occlusive balloon for measurement of intestinal absorption in man. *Am J Dig Dis* 23:720-722, 1978
3. SOERGEL KH, WHALEN GE, HARRIS JA, et al: Effect of antidiuretic hormone on human small intestinal water and solute transport. *J Clin Invest* 47:1071-1082, 1969

4. KREJS GJ, BROWNE R, RASKIN P: Effect of intravenous somatostatin on jejunal absorption of glucose, amino acids, water and electrolytes. *Gastroenterology* 78:26-31, 1980
5. DA CUNHA MELO J, SUMMERS RW, THOMPSON HH, et al: Effects of intestinal secretagogues and distension on small bowel myoelectric activity in fasted and fed conscious dogs. *J Physiol* 321:483-494, 1981
6. EECKHOUT C, DEWEVER I, VANTRAPPEN G, et al: Local disorganization of interdigestive migrating complex by perfusion of a Thiry-Vella loop. *Am J Physiol* 238:G509-G513, 1980
7. SARR MG, KELLY KA, PHILLIPS SF: Canine jejunal absorption and transit during interdigestive and digestive motor states. *Am J Physiol* 239:G167-G172, 1980
8. MITCHELL A, COLLIN J: Effects of vasopressin on intestinal absorption, transit and electrical activity. *Br J Surg* 69:291, 1982
9. BLICKENSTAFF DD: Increase in intestinal absorption of water from isosmotic saline following pitressin administration. *Am J Physiol* 179:471-472, 1954
10. CODE CF, MARLETT JA: The interdigestive myoelectric complex of the stomach and small bowel of dogs. *J Physiol* 1246:289-309, 1975
11. NICKEL O, SCHAD N, ANDREWS J, et al: Scintigraphic measurement of left-ventricular volumes from the count-density distribution. *J Nucl Med* 23:404-410, 1982
12. THOR P, KRÓL R, KONTUREK SJ, et al: Effect of somatostatin on myoelectrical activity of small bowel. *Am J Physiol* 235:E249-E254, 1978
13. ORMSBEE HS, KOEHLER SL, TELFORD GL: Somatostatin inhibits motilin-induced interdigestive contractile activity in the dog. *Dig Dis Sci* 23:781-788, 1978

8th Annual Western Regional Meeting Society of Nuclear Medicine

October 6-9, 1983

Westin Hotel Seattle

Seattle, Washington

Announcement

The Annual Meeting of the Western Regional Chapter of the Society of Nuclear Medicine will be held October 6-9, 1983 at the Westin Hotel Seattle, Seattle, Washington. Dr. Raymond Marty is General Program Chairman, and Dr. John Denney is Scientific Program Chairman. The George Taplin Memorial Lecture will be given by Dr. Henry Wagner, Jr. The program will also feature eleven refresher courses, contributed papers, and an NMR minisymposium.

For information contact:

Justine J. Parker, Executive Director
PO Box 40279
San Francisco, California 94140
Tel: (415)647-0722 or 647-1668

The Western Regional Scholarship and Award Fund will make one award in the name of Norman D. Poe for the most outstanding paper in the field of pulmonary or cardiac nuclear medicine and a second award for an outstanding Technologist paper.

Commercial exhibits are invited. For information contact Becci Lynch at the above address or telephones.