The Role of Nuclear Medicine in Clinical Urology and Nephrology

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The application of radionuclide studies to nephrologic and urologic practice has reached a measurable degree of maturity during the past several years. In spite of this, the utilization of these techniques in many institutions in the United States continues to be far less frequent than one would expect from the clinical advantages. The aim of this editorial is to try to place the role of nuclear medicine in urology and nephrology in perspective. For purposes of simplicity we will refer to this broad area of clinical application as renal studies. Remember that nuclear medicine offers important advantages in studying the lower urinary tract as well.

Before reviewing the specific applications of radionuclides in renal diagnosis, a brief review of its current role in nuclear medicine practice is in order. There are several ways to perform this analysis. First, consider the relative number of renal abstracts presented at the annual meeting of the Society of Nuclear Medicine. Figure 1 shows that, except for 1981, the fraction of all presentations at the annual meetings classified as renal has remained stable and quite low, at about 4%. During the early formative years of nuclear medicine, renal studies represented a far greater fraction of the work. While the total of submissions to the meeting has risen impressively during the last 3 yr (Fig. 2), the number of original works dealing with the kidney has failed to show a parallel growth. Support for the assumption that this is a reflection of lack of interest and quantity of work in this area may be found in Fig. 3. The percentage of renal abstracts accepted for presentation has risen and has actually surpassed the average for the total session since 1982. Although this is at best a crude guide, it certainly suggests that the problem in the application of renal nuclear medicine is not the quality of the work but rather a lack of volume or interest.

There are a number of alternative explanations that should be considered for this lack of utilization reflected by presentations at the national meeting. It is our belief that the overwhelming factor is not a lack of value but rather a lack of understanding on the part of the nephrologist and the urologist (the consumers), as well as of the nuclear medicine physician (the provider). Renal physiology is complex and frequently poorly understood by the average practitioner. The complexity of the subject is made even worse by the large number of agents available for renal studies (Table 1). The choice of an agent for most nuclear medicine studies is limited and usually straightforward. Not only is the choice in renal studies more complex, but also the success of the study may be completely dependent on the agent chosen. Traditional urography, on the other hand is much easier to deal with. It is basically an anatomical technique offering little or no functional information. It is the functional nature of the nuclear medicine studies that provides their tremendous potential for use in studies of the kidney, where problems are so often related to functional derangements rather than easily identified anatomic problems. A familiarity with various measures of renal function and the effects of these parameters on the handling of the commonly used radiopharmaceuticals is essential to their appropriate use. We would like to use our own experience to try to put the role of renal nuclear medicine studies in proper perspective.

At the Albert Einstein College of Medicine/Montefiore Medical Center the utilization of nuclear medicine facilities by the nephrologist and urologist has shown a very different pattern from that suggested above. Renal nuclear medicine procedures represent about 15% of all of our work, and have continued to be a significant portion, even with the expansion of total procedures by the

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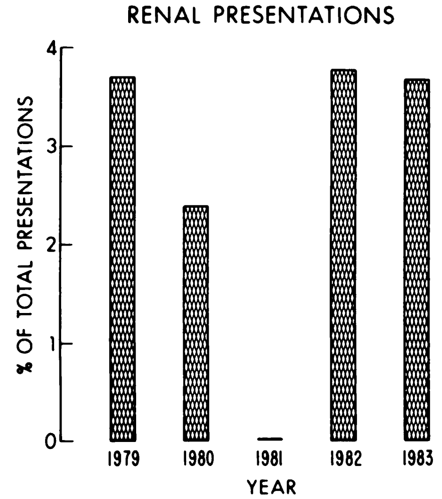

FIG. 1. Percentage of papers in renal category, relative to all presentations, at annual meetings of Society of Nuclear Medicine since 1979. Except for unexplained decrease in 1981, this has usually been near 4% (Statistics compiled by Society of Nuclear Medicine).

heavily utilized cardiovascular component (Fig. 4). It has been our experience that most institutions perform considerably fewer studies in the renal area. The overall application is illustrated in Fig. 5, which shows the number of procedures done by broad categories. Perhaps most impressive is the relation between renal nuclear

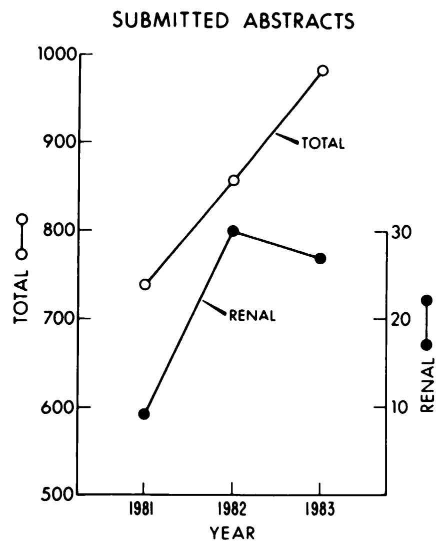

FIG. 2. Number of submissions from to annual meetings of Society of Nuclear Medicine has risen dramatically last 3 yr. Society received 14.7% more abstracts for consideration in 1983 than in 1982. Number submitted in renal category fell during this time. Small number of renal abstracts submitted in 1981 is anomaly, since considerably more were submitted in 1979 and 1980. Changing of categories in those years makes it difficult to calculate exact number, but probably renal category has been relatively stable during last 5 yr. In later years it is possible that renal category is somewhat underestimated, since some authors chose to present renal work under other related categories (statistics compiled by Society of Nuclear Medicine).

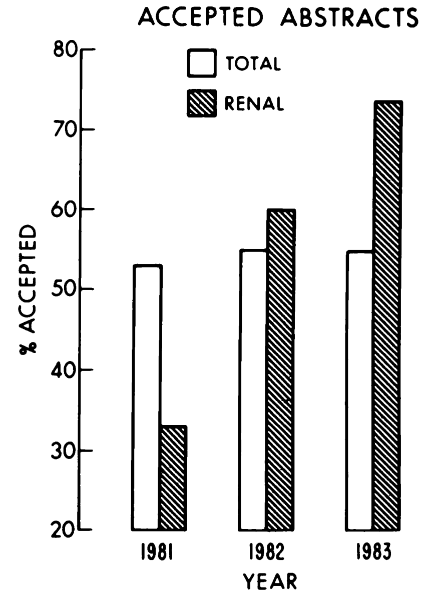

FIG. 3. In spite of small number of abstracts submitted in renal category, submissions in this area did better than general submissions in 1982 and 1983. Oral and poster presentations are included in these statistics (from Society of Nuclear Medicine). Contention is supported that small percentage of renal papers at meetings of Society of Nuclear Medicine is due to low submission rate but not lack of quality.

medicine tests and other diagnostic modalities at our institution. Intravenous urography (IVU) is the most frequent test (Fig. 6), but radiotracer studies are performed about three times as often as arteriograms (including digital subtraction angiography), and approximately one nuclear medicine test is performed for each urologic admission to the hospital or kidney discharge diagnosis.

We believe these data further support the contention of a lack of utilization rather than a lack of utility in the nuclear medicine and uro-nephrologic community. The remainder of this discussion will try to help the reader to resolve some of the obstacles to their use. The material presented here is not meant to be a comprehensive review but rather an outline of the principles of renal nuclear medicine. The references listed at the end provide a starting point for reading in this area and are highly selective.

The first thing to consider is the issue of which renal radiopharmaceutical agents should be used, and when. At the present time, in spite of the large number of renal agents that have been developed, there is no practical ideal radiopharmaceutical that can serve as a universal agent. Arbitrarily, one may reduce the chief armamentarium to only four radiopharmaceuticals; technetium-99m DTPA, I-131 OIH (orthoiodohippurate), technetium-99m glucoheptonate, and technetium-99m DMSA. These agents are listed in Table 1, with their relative advantages and disadvantages. Many other agents are available, but we have almost completely restricted our

TABLE 1. KEY RENAL AGENTS

	Advantages	Disadvantages
1. Tc-99m DTPA	1) Measures GFR 2) Low radiation dose 3) Can be used for flow and static images	1) Poor uptake in renal failure 2) About 5% aberrent behavior
2. I-131 ortho-iodohippurate	1) Measures effective renal plasma flow 2) High target-to-background ratio, even in renal failure	1) Higher radiation dose 2) Free iodide
3. Tc-99m Glucoheptonate	1) About 20% of dose bound in cortex 2) Acceptable dose when combined with flow study 3) High-resolution delayed images 4) Quantitates renal mass	1) Significant fraction filtered may cause collecting system interference 2) Hepatic excretion in renal failure
4. Tc-99m DMSA	1) About 40% bound in cortex 2) High-resolution delayed images 3) Quantitates renal mass	1) Dose unacceptable for flow study 2) Hepatic excretion in renal failure

practice to these four. Although a number of centers have abandoned the use of radiohippuran, we find that because of its very avid uptake by the kidney, its use in situations where other tests are inconclusive, or in patients with major impairment of renal function, may serve to resolve otherwise unresolvable problems.

The types of studies used include renal perfusion studies, renal imaging studies performed solely for anatomical information, and renal imaging studies combined with an estimate of renal function. We have abandoned nonimaging techniques for measurement of renal function, except in research situations. Routine clinical studies invariably include renal imaging. In most clinical situations, regardless of the need to know the level of renal function, the additional information conveyed by a renal scintigram more than warrants the small additional radiation burden. Let us first examine the potential applications of these studies and then review them from the perspective of the individual clinical indications.

Static imaging studies to gain anatomical information should be performed to complement information readily available from alternative radiographic methods. They are not usually first-line procedures. The patient who has

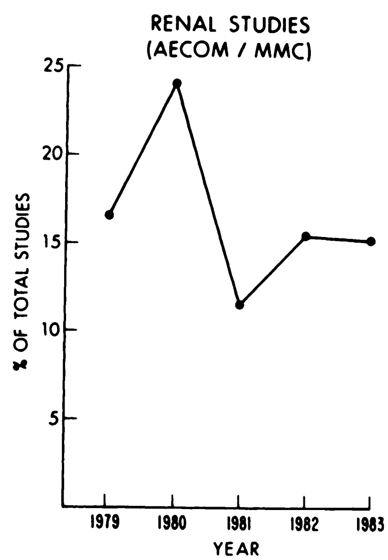

FIG. 4. Proportion of renal clinical studies, relative to total, at Albert Einstein College of Medicine/Montefiore Medical Center (AECOM/MMC) for 1979 through 1983. Fraction has consistently remained at about 15%. This represents absolute increase in renal studies performed from 1,580 in 1979 to projected 2,323 for 1983, an increase of 47%. We are experiencing continued increasing utilization and interest in this area.

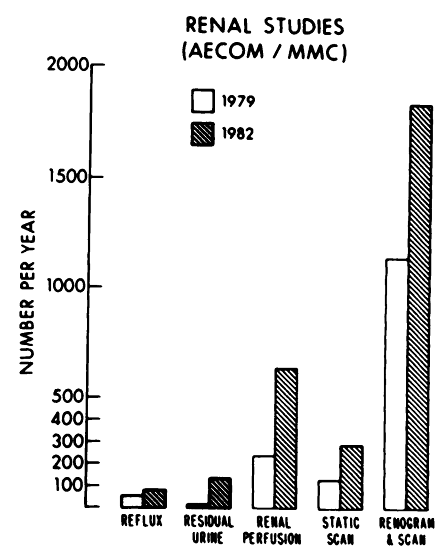

FIG. 5. Showing distribution of tests by specific procedure category. Sum of all tests in this figure is greater than in Fig. 4, in which single patient is counted as one study regardless of number of images. In Fig. 5, for example, perfusion study and static scintigram are recorded as separate procedures, even if they were combined, to reflect better the quality of work. Number of procedures done in all categories has increased.

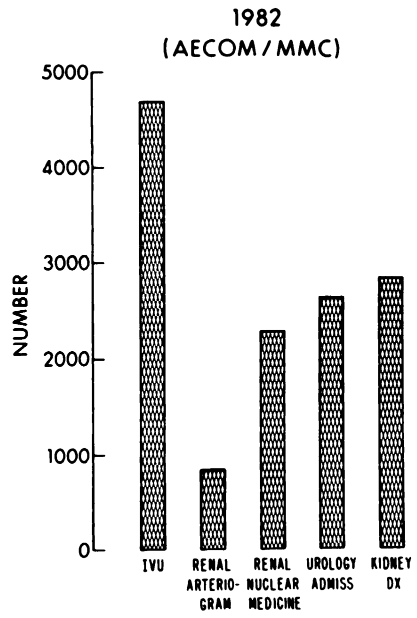

FIG. 6. Major renal procedures are shown in relation to urologic admissions and kidney diagnoses at our medical center for 1982 (total includes all primary teaching hospitals). Montefiore Medical Center performed most of renal arteriograms (803). There were 2,088 IVUs and 1,080 renal radionuclide studies done at that same hospital in 1982. Among all patients discharged from Montefiore Medical Center, 1,433 had kidney diagnosis (HUP diagnostic code numbers 580-593).

an abnormal renal configuration on intravenous urogram usually is evaluated further by ultrasonography or TCT scan before a final diagnosis is made. However, the possibility that an intrarenal mass may not be tumor can often best be excluded by the use of a glucoheptonate or DMSA study to show that this is functioning renal tissue. Similarly, static imaging can show the isthmus of the horseshoe kidney to be functioning, thereby guiding the urologist. The use of pure anatomical imaging agents is limited and usually is secondary to information that has been obtained from urography or ultrasonography; it is not definitive but may be used to precede a decision for TCT scanning or arteriography. Another situation in which this approach is occasionally helpful is in trying to determine whether a mass arises from the liver or the kidney, or whether a major renal displacement is due to renal or extrarenal tumor. So then the use of the purely anatomical agents, Tc-99m glucoheptonate or DMSA is limited, and is usually secondary to urography or echo. They may be used to help decide whether to proceed with TCT or arteriography. Technetium-99m DMSA has been advocated in special situations to estimate relative renal mass. It has an advantage over glucoheptonate in this application, since the amount of DMSA that is filtered is much smaller, reducing interference from radioactivity in the collecting system. The necessity to correct for attenuation by soft tissue of varying depths has limited accuracy and prevented this technique from gaining widespread acceptance.

There are two situations where nuclear medicine or echo should be considered primary procedures to avoid the administration of contrast material. These are in subjects with a history of sensitivity to contrast media, or in diabetics with reduced renal function who may be affected adversely by contrast material.

In our experience technetium flow studies (perfusion studies) have proven rather limited. Their sensitivity is high but their specificity is low. There are few situations, therefore, in which a flow study is of value. Patients with a diagnostic possibility of occlusion of the renal artery from thrombus or dissecting aneurysm, or with severe renal-artery stenosis, may be evaluated quickly with a flow study. However, the use of the flow study solely to determine the presence of an asymmetry of flow leads to a large number of abnormal examinations that turn out not to have clinical relevance.

The mainstay of the radionuclide study in nephrology and urology is the scintigram with I-131 OIH or Tc-99m DTPA, which provide both anatomic and functional information. In many situations adequate information is obtained from the DTPA image, but not infrequently OIH will provide the additional information necessary to arrive at a diagnosis. Neither of these tracers provides anatomic images that are competitive with glucoheptonate or DMSA, so they are really indicated when functional as well as crude structural information is needed. There is no other technique that can provide the individual functional information both in terms of glomerular filtration rate and renal plasma flow, as well as urinary flow rate, that can be obtained noninvasively with these nuclear medicine tests. The provider is faced with an overwhelming number of alternative quantitative methods from which to choose. A discussion of all of the proposed methods to estimate relative renal function and their relative merits would fill more than our entire allotted space. At our institution we rely on analysis of the 1–2 min renograms for uptake of either the DTPA or OIH to estimate relative renal function. Background subtraction is used, and we are currently studying the various techniques proposed to find the most reproducible one. Total function is routinely performed with a single-injection clearance, and we are now evaluating these techniques as well to determine their relative merits. The indications we use for these tests are outlined in Table 2.

A description of the many nephrologic and urologic conditions in which nuclear medicine procedures have a role has been reviewed many times by us and others. Table 3 lists the many clinical entities susceptible to radiotracer diagnosis where these procedures may be important.

The single most important aspect of radionuclides in studying the kidneys is, as has been stated, their functional potential, including the ability to provide quantitative information. The two most important applications

TABLE 2. CLINICAL INDICATIONS FOR EVALUATION OF RENAL FUNCTION*

1. Overall renal function (GFR, ERPF)	1. Renal transplantation 2. Chronic renal disease
2. Individual renal function (GFR, ERPF, renal mass)	1. Renal vascular hypertension 2. Unilateral renal parenchymal disease 3. Bilateral renal disease with planned surgical intervention 4. Evaluation of renal function after intervention or during growth

* These tests are most useful when used serially.

today are in urinary-tract obstruction and in serial studies of the kidney when some intervention is planned, or when there is a prospect of progressive loss of function from chronic disease. Probably the most widely accepted of all techniques is diuretic renography in the diagnosis of obstructive uropathy, but even here we do not have adequate efficacy data.

Like other techniques in nuclear medicine, virtually all renal imaging studies have a potential to yield indeterminate results. Diuretic renography is most helpful when it allows us to classify a patient clearly as obstructed or not obstructed. However, a significant percentage of studies will yield inconclusive results. This does not indicate a failure of the test, but rather a reflection of the wide spectrum of disease with which we deal and our inability to control such basic modulating factors as the patient's state of hydration. Indeterminate studies can easily be made meaningful with careful follow-up and better control of the baseline state. The single, costliest error the nuclear medicine physician makes in renal studies is an effort to convey a definitive diagnosis where the best interpretation is an indeterminate one. The nuclear medicine test, with its great sensitivity to changes in renal function, frequently makes follow-up studies in this situation extremely valuable. The most important feature of nuclear medicine is the ability it offers the physician to study the kidney serially rather than at a single point in time. Figure 7 shows this point dramatically. No other method would have allowed us to follow the consequences of the arteriovenous fistula of the patient's kidney as safely as the radiotracer technique. Similarly, with intraarterial angioplasty there is

TABLE 3. CLINICAL CONDITIONS EVALUATED BY NUCLEAR MEDICAL TECHNIQUES

Disease or condition	Test	Agent	Value
Acute renal failure	Scintigram	hippuran	Prognosis, diagnosis
Bladder-neck obstruction	Scintigram	$^{99m}TcO_4$ hippuran DTPA	Diagnosis serial changes
Chronic renal failure	Scintigram	hippuran	Location relative function serial changes
Congenital renal malfunction	Flow scintigram	glucoheptonate DMSA	Diagnosis
Interstitial nephritis	Scintigram	Ga-67	Diagnosis serial changes
Neurogenic bladder	Scintigram	hippuran DTPA $^{99m}TcO_4$	Diagnosis serial changes
Obstructive uropathy	Scintigram Renogram	DTPA hippuran	Relative function, prognosis, diagnosis serial changes
Pyelonephritis	Scintigram Renogram	DTPA hippuran glucoheptonate DMSA	Diagnosis relative function serial changes
Renal arterial embolism	Flow scintigram	DTPA hipp./gluco.	Diagnosis relative function serial changes
Renal mass	Flow scintigram	glucoheptonate DMSA	Diagnosis
Renal transplantation	Flow scintigram	DTPA hippuran	Diagnosis function serial changes
Renal trauma	Flow scintigram	DTPA hippuran	Diagnosis relative function serial changes
Renovascular hypertension	Scintigram Renogram	hippuran DTPA	Diagnosis relative function serial changes
Testicular torsion	Scintigram	$^{99m}TcO_4^-$	Diagnosis

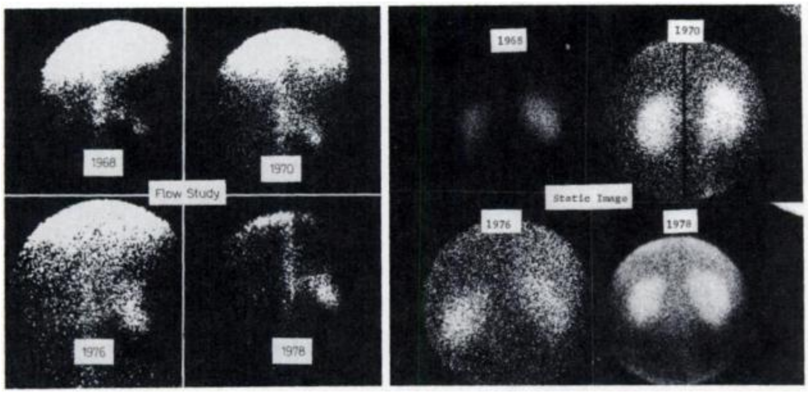

FIG. 7. Frames from Tc-99m flow study (a), and static radiohippuran image (b), from patient with arteriovenous fistula of right kidney and chronic renal disease. Radiotracer techniques permitted noninvasive follow-up since 1968. Fistula has been shown to remain stable, and function of that kidney relative to contralateral has not changed. These studies facilitated safe long-term follow-up. (From Iloreta A and Blaufox MD, Natural History of Post-Biopsy Renal Arteriovenous Fistula: A 10-Year Follow-Up, *Nephron* 24:250–253, 1979.

a need to evaluate results in a manner that only nuclear medicine makes possible. Neglect of the tracer technique has led to many reports on surgery for renal-artery stenosis in which limited follow-up information is provided about what actually happened to the kidney and its function. Were the clinicians aware of this technique's potentials, a great deal of the seemingly endless controversy over how best to treat renal-artery stenosis might have been resolved.

In some centers, patients with renal trauma are taken directly to arteriography. Why not do a perfusion and static image along with an abdominal plain film? They probably could provide all of the information needed more quickly, safely, and inexpensively.

The clinician seems to have recognized the potential of nuclear medicine in lower urinary tract and pediatric conditions better than in adult nephrology. This in some ways is akin to the thoughtless approach physicians have had in drawing blood. Long after micro methods were developed and applied in pediatrics, adult patients continue to be subjected to blood-testing patterns that may approach phlebotomy. So, too, does nuclear medicine provide a more logical and long disregarded approach to nephrologic diagnosis. Cystourethography, and studies of testicular torsion, appear to be well established at pediatric hospitals throughout the country.

Although we described a technique for measurement of residual urine at our institution 13 yr ago, it was suddenly rediscovered by the neurologists only last year, and has now become a major means of evaluation of the lower urinary tract in patients with multiple sclerosis. In 1979 we did 13 residual-urine studies, and in the first 10 mo of 1983 we performed 137.

The use of radionuclides to guide the transplant surgeon has been, and continues to be, a major area of application.

So then, what is the future for nuclear medicine in the area of renal diagnosis? The needs are easily summarized:

1. The nuclear medicine physician needs more training in renal pathophysiology.

2. The nephrologist and urologist must be better educated about the tests available and their appropriate application.

3. Renal agents need to be standardized and improved. Agents to be used clinically should have a demonstrable and reproducible relationship to known parameters of renal function such as GFR, ERPF, or renal mass. To this end, impurities of free radionuclide or nonphysiologic contaminants need to be eliminated, and more-detailed studies of the basic physiology of GHA and DMSA are needed.

4. A low-radiation-dose hippuran equivalent is needed to provide high-quality images in patients with poor renal function.

5. A single technique for measurement of total and unilateral renal function should be adopted by the nuclear medicine community. No technique should be published without clear documentation of its clinical utility in disease and superiority to existing methods. The technique-oriented research approach should be shifted to an application-oriented one.

6. Finally, there is a desperate need in this field for a study of clinical cost-effectiveness. We have no doubt that the nuclear medicine study competes favorably with intravenous urography, TCT, and arteriography. But a study similar to the classic work of McNeil (which, much to many peoples' surprise, showed the renogram to be as good as the IVU in renovascular hypertension) needs to be done for urologic and nephrologic diagnosis.

The complex events that lead to the acceptance and application of a diagnostic method are becoming increasingly better understood. In a great many instances the medical community has overlooked or ignored a valuable technique for many years because it did not fit the conservative thinking of the time. Renal nuclear medicine suffers from this fate and awaits its discovery and proper use.

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Southeastern Chapter
Society of Nuclear Medicine
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Announcement and Call for Abstracts

November 1–3, 1984 **Hyatt Regency Lexington** **Lexington, Kentucky**

The Scientific Program Committee of the 25th Annual Meeting of the Southeastern Chapter of the Society of Nuclear Medicine, chaired by Nat E. Watson, M.D., is requesting the submission of original contributions in nuclear medicine from members and nonmembers of the Society.

The program will be approved by the Subcommittee on Continuing Education and Course Accreditation of the Society of Nuclear Medicine as one which meets the criteria for AMA Category 1 credit.

Physicians and scientists are encouraged to submit abstracts as are technologists. Accepted technologist papers will be presented on the Scientific Program and will be eligible for awards.

Abstracts must be prepared in final form for direct photoreproduction on the official abstract form. For abstract forms and additional information, contact:

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Deadline for submission of abstracts is July 15, 1984.

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