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RESEARCH ARTICLE

Contribution of 99mTc-Sestamibi Scintigraphy in Primary Hyperparathyroidism to Guide Minimally Invasive Parathyroidectomy

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Abstract

Background: Primary hyperparathyroidism (PHPT) is a common endocrine disorder characterized by excessive parathyroid hormone secretion resulting in hypercalcemia. Accurate preoperative localization of hyperfunctioning parathyroid glands is essential for successful minimally invasive parathyroidectomy (MIP).

Objective: To evaluate the diagnostic performance and clinical utility of 99mTc-sestamibi scintigraphy in the preoperative localization of pathological parathyroid glands in patients with PHPT.

Methods: A retrospective observational study was conducted at Charles Nicolle Hospital, Tunis, including 134 patients who underwent surgery for PHPT between January 2011 and December 2024. All patients had preoperative cervical ultrasound and 99mTc-sestamibi scintigraphy. Demographic, biochemical, imaging, surgical, and histopathological data were analyzed. The diagnostic accuracy of scintigraphy was assessed by comparison with intraoperative findings and histopathology.

Results: The study included 119 women (88.8%) and 15 men (11.2%), with a mean age of 56 years. Scintigraphy detected hyper functioning parathyroid tissue in 128 patients, yielding a sensitivity of **95.45%**. Concordance between scintigraphic localization and surgical findings was **83.6%** ($p < 0.001$). Minimally invasive parathyroidectomy was performed in **82%** of cases. Histopathology revealed solitary adenoma in **85%** and multiglandular hyperplasia in **15%** of patients. Postoperative outcomes were favorable, with transient hypocalcemia observed in **5.97%** of patients and no recurrence during follow-up.

Conclusion: 99mTc-sestamibi scintigraphy demonstrates high sensitivity and reliability in localizing hyper functioning parathyroid glands and plays a key role in guiding minimally invasive parathyroidectomy. Its effectiveness makes it particularly valuable in resource-limited healthcare settings.

Keywords: Primary hyperparathyroidism; Parathyroid scintigraphy; 99mTc-sestamibi; Minimally invasive parathyroidectomy; Endocrine surgery.

Introduction

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder after diabetes and thyroid disease [1]. It is defined by the autonomous overproduction of parathormone (PTH) by one or more parathyroid glands, leading to disturbances in calcium-phosphate homeostasis [2]. Surgical excision of the hyper functioning gland remains the only definitive cure. In recent years, minimally invasive parathyroidectomy (MIP) has emerged as the preferred surgical approach due to its benefits of reduced operative time, smaller incisions, faster recovery, and lower complication rates [3]. However, the success of MIP relies heavily on the precise preoperative localization of the pathological parathyroid tissue.

Parathyroid scintigraphy with technetium-99m sestamibi (99mTc-sestamibi) is a key imaging modality that offers functional localization of hyperactive glands, including those in ectopic or anatomically challenging locations. Its high sensitivity enhances surgical planning and enables focused, effective interventions [4]. While the utility of scintigraphy is well established in high-resource environments, its diagnostic performance and clinical value in resource-limited settings remain less thoroughly investigated.

This study aims to evaluate the diagnostic accuracy and clinical impact of 99mTc-sestamibi parathyroid scintigraphy in facilitating MIP for PHPT at a tertiary care center. The findings offer valuable insight into improving surgical strategies and optimizing outcomes in comparable healthcare contexts.

Methods

This retrospective observational study was conducted at the Department of ENT and Cervico-Facial Surgery, Charles Nicolle Hospital, Tunis. All consecutive patients who underwent surgery for primary hyperparathyroidism (PHPT) between January 2011 and December 2024 were screened for inclusion.

Inclusion criteria were:

- Biochemically confirmed PHPT (elevated serum calcium and PTH levels)
- Availability of preoperative 99mTc-sestamibi scintigraphy
- Surgical treatment with histopathological confirmation

Exclusion criteria included secondary or tertiary hyperparathyroidism and incomplete clinical or imaging records.

Data were retrospectively collected from medical records.

Collected variables included demographic data, clinical presentation, biochemical parameters (serum calcium, PTH, vitamin D) imaging findings (ultrasound, scintigraphy, and SPECT/CT where performed), surgical approach, histopathology, and postoperative outcomes.

The primary outcome was the diagnostic performance of 99mTc-sestamibi scintigraphy. Sensitivity was calculated using surgical and histopathological findings as the reference standard. Concordance between imaging and intraoperative localization was also assessed.

Statistical analysis was performed using SPSS version 27. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Pearson correlation was used to evaluate imaging-surgical agreement. A p-value < 0.05

was considered statistically significant.

Results

A total of 134 patients who underwent surgical treatment for primary hyperparathyroidism (PHPT) and met all inclusion criteria were enrolled in the study. The cohort demonstrated a marked female predominance, with 119 women (88.8%) and 15 men (11.2%), yielding a female-to-male ratio of 7.93. The mean age at diagnosis was 56 years, ranging from 12 to 86 years. No patients presented with a family history suggestive of syndromic forms such as multiple endocrine neoplasia types 1 or 2.

Comorbid conditions included hypertension (35%), type 2 diabetes mellitus (18%), thyroid disorders (6 patients), osteoporosis (14 patients), and pathological fractures (4 patients). Renal lithiasis was observed in 13% of patients, and peptic ulcer disease in 6%. Notably, none of the patients had a history of cervical irradiation.

PHPT was diagnosed incidentally in 27 patients (20%), whereas the remaining 107 patients (80%) were symptomatic. Skeletal manifestations were the most common presenting feature, affecting 86 patients (64.2%), followed by renal symptoms in 42 (31.3%), digestive symptoms in 18 (13.4%), and general symptoms such as fatigue in 36 patients (26.9%). A detailed distribution of presenting features is provided in Table 1.

Table 1: Distribution of Clinical Manifestations of Primary Hyperparathyroidism

Diagnosis Circumstance	Number of Patients	%
Incidental (Asymptomatic)	27	20.0
Bone pain	85	63.43
Fractures	4	2.98
Osteoporosis	23	17.16
Brown tumors	5	3.73
Kidney stones	31	23.13
SPUPD	11	8.2
Epigastric pain	4	2.98
Gastroduodenal ulcers	10	7.46
Constipation	5	3.73
Other	8	5.97
Fatigue (Asthenia)	36	26.86

A palpable cervical mass was noted in 24 patients (18%), while the remainder had no clinical evidence of neck swelling.

Biochemical analysis revealed a mean serum calcium level of 2.8 mmol/L and a mean parathormone (PTH) level of 377 pg/mL. Among the 77 patients with available vitamin D measurements, 47 (61%) exhibited vitamin D deficiency or insufficiency, with a mean serum level of 21 ng/mL.

All patients underwent preoperative imaging with both cervical ultrasound and dual-phase 99mTc-sestamibi parathyroid scintigraphy.

Ultrasound identified a single parathyroid adenoma in 90 cases (67.2%), multiple adenomas in 3 cases (2.2%), and parathyroid

hyperplasia in 10 cases (7.5%). No abnormality was detected in 31 patients (23.1%). Thyroid pathology was noted in 36 patients. The most frequent ultrasound-detected adenoma locations were the lower left (54 cases), lower right (34 cases), upper left (18 cases), and upper right quadrants (8 cases).

Scintigraphy revealed a single hyper functioning gland in 120 patients (89.6%) and multiple hyperactive foci in 6 patients. Two ectopic adenomas were identified in the mediastinum, and 6 patients had negative results. The most common scintigraphic localizations were the lower left (58 cases) and lower right quadrants (50 cases), followed by the upper left (12 cases) and upper right (10 cases).

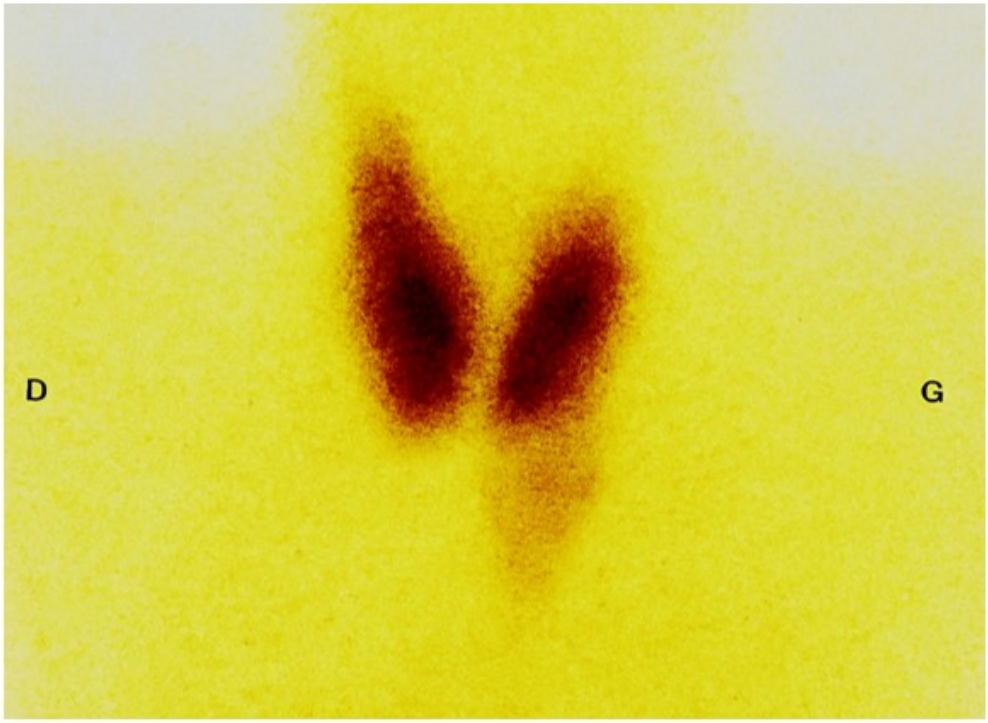

Figure 1: Dual-phase 99mTc-sestamibi scintigraphy demonstrating focal radiotracer uptake consistent with a left inferior parathyroid adenoma

Although sensitivity of 99mTc-sestamibi scintigraphy was high (95.45%), specificity and negative predictive value could not be fully assessed due to the surgical inclusion of all patients. However, the presence of six negative scintigraphic cases highlights the importance of complementary imaging in selected cases.

Among the 134 patients, 32 (23.9%) underwent additional hybrid SPECT/CT imaging. In 7 of these 32 patients (21.9%), where scintigraphy and ultrasound had been inconclusive, SPECT/CT successfully identified the pathological gland.

Twelve patients underwent cervico-thoracic computed tomography (CT) for inconclusive or discordant findings, which confirmed the presence of parathyroid adenomas in 9 cases. In two additional patients, cervical MRI identified adenomas where other modalities had failed.

All patients proceeded to surgery. A minimally invasive parathyroidectomy (MIP) was performed in 110 patients (82%), while 24 patients (18%) underwent conventional bilateral neck exploration. Intraoperative findings confirmed the adenoma locations predominantly in the lower left (58 patients) and lower right quadrants (53 patients), with additional adenomas located in the upper left (11 patients) and upper right (12). Ectopic adenomas were found in three cases (two retrosternal, one pretracheal).

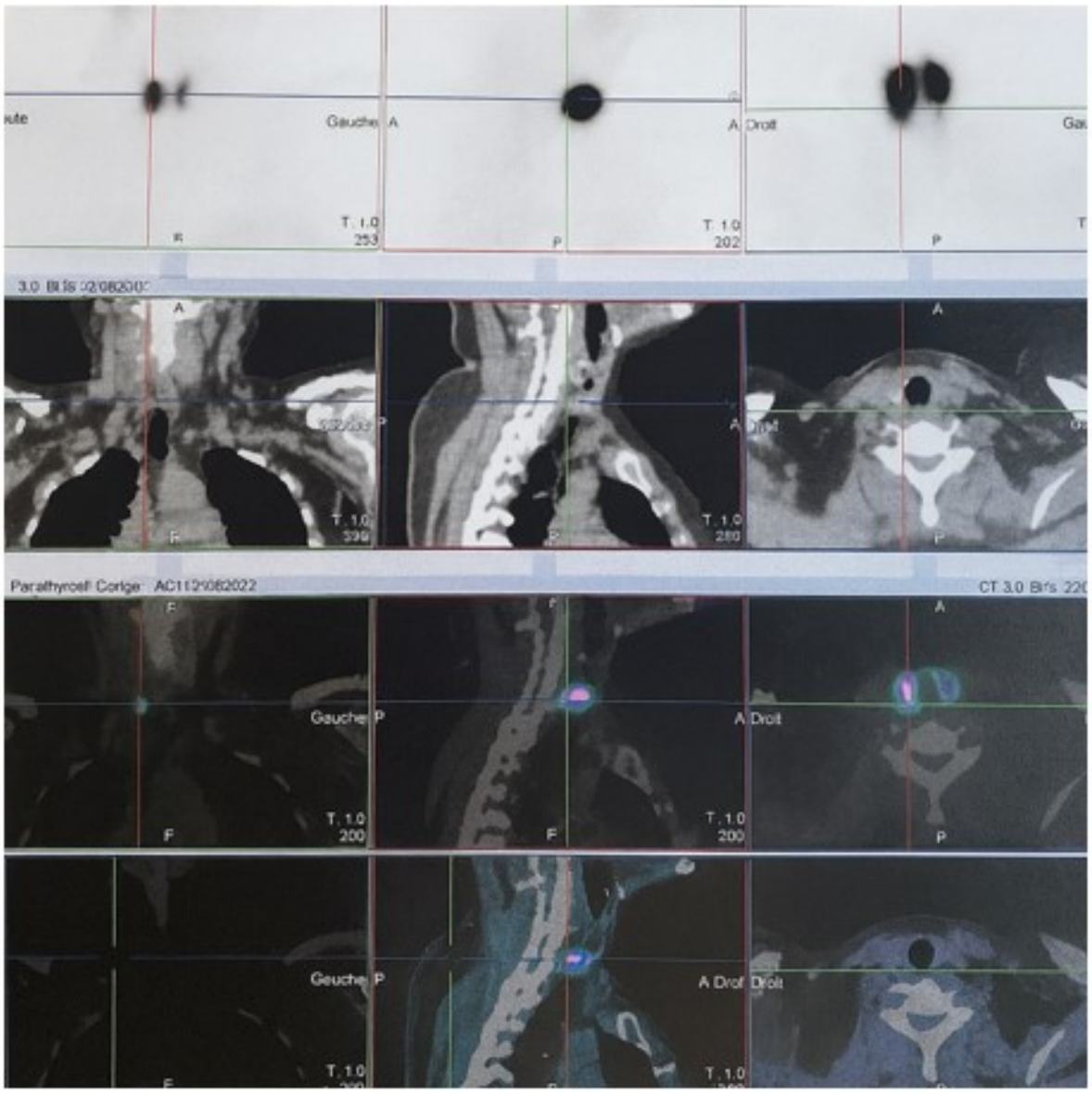

Figure 2: SPECT/CT fusion imaging demonstrating focal uptake corresponding to a right inferior parathyroid adenoma.

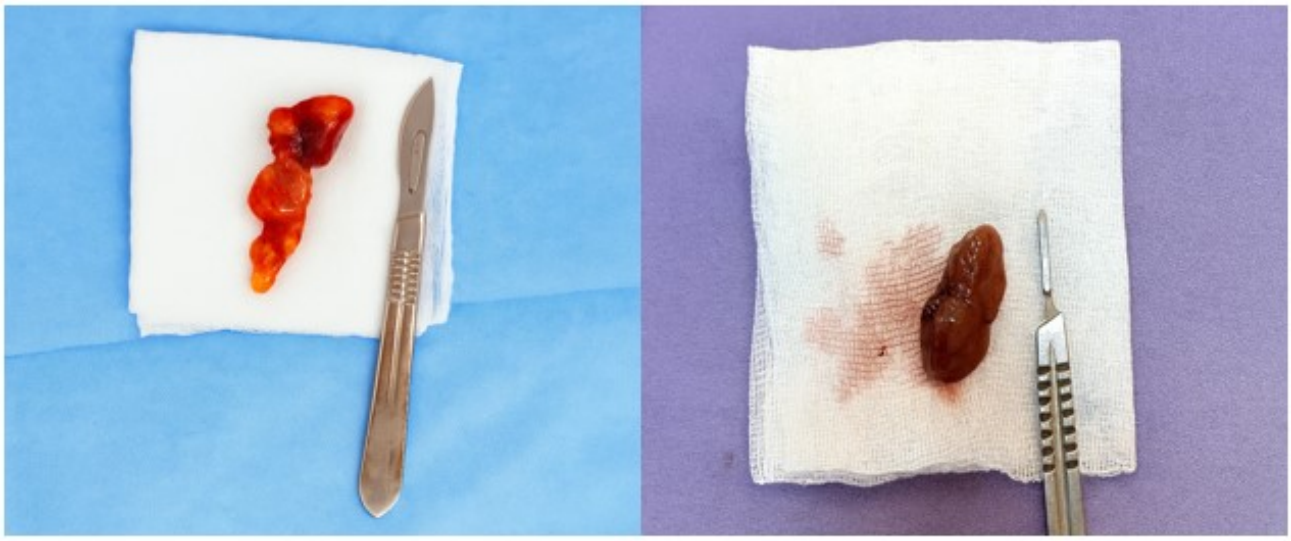

Figure 3: Intraoperative specimen of excised parathyroid adenomas

Intraoperative PTH monitoring was performed in 124 patients, all of whom exhibited a post-excision decline of more than 50% in PTH levels, confirming successful gland removal. Frozen section histology was conducted in 118 patients and confirmed parathyroid adenoma in all cases.

Concordance between preoperative scintigraphic localization and intraoperative findings was observed in 112 patients (83.6%), while 22 cases (16.4%) showed discordant results. Statistical analysis revealed a moderate but significant correlation between scintigraphy and surgical findings ($r = 0.499$, $p < 0.001$).

Histopathological examination identified a single parathyroid adenoma in 114 patients (85%) and parathyroid hyperplasia in 20 patients (15%). No parathyroid carcinomas were diagnosed.

Postoperative outcomes were favorable in all patients. Transient hypocalcemia occurred in 8 patients (5.97%), with no cases of vocal cord paralysis or surgical site infection. The mean postoperative PTH level was 65.46 pg/mL. At a minimum follow-up of six months, no cases of persistent or recurrent hyperparathyroidism were recorded.

Discussion

Primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders worldwide, surpassed only by diabetes and thyroid disease, with a global prevalence between 0.1% and 0.8% and a marked female predominance [5,6]. This predominance is often attributed to postmenopausal hormonal changes, particularly estrogen deficiency [7]. Our cohort reflects these established patterns, with 88.8% female patients and a mean age of 56 years.

All cases in this study were sporadic, consistent with existing evidence that most PHPT cases arise from solitary adenomas, whereas multiglandular disease and hereditary syndromes—such as multiple endocrine neoplasia (MEN) 1 and 2—are far less common [8,9].

In our cohort, 80% of patients were symptomatic at diagnosis, most frequently with skeletal (64.2%) and renal manifestations (31.3%). This presentation aligns with the traditional “bones, stones, abdominal groans, and psychic moans” description [8]. However, it contrasts with trends in high-income countries, where up to 80% of patients are now diagnosed incidentally due to routine serum calcium screening [10]. This likely reflects limited access to early biochemical screening in resource-constrained settings [11].

Biochemically, elevated serum calcium and PTH levels in our patients were consistent with classical PHPT[8]. Vitamin D deficiency or insufficiency was present in 61% of tested individuals, mirroring global findings that deficiency commonly coexists with PHPT and may exacerbate disease severity [11,12]. This finding underscores the importance of assessing and correcting vitamin D levels preoperatively [12,13].

The present study confirms the high diagnostic performance of 99mTc-sestamibi scintigraphy, with a sensitivity of 95.45% and strong concordance with surgical findings (83.6%). These results align with international literature reporting high sensitivity of sestamibi scintigraphy and SPECT/CT, particularly in detecting ectopic or posteriorly located glands [13,14]. Compared to ultrasound, scintigraphy demonstrated superior diagnostic accuracy in our cohort, particularly in detecting ectopic or deep-seated adenomas. Ultrasound remained a useful and accessible first-line modality, accessible tool but was limited by operator dependence and interference from thyroid pathology [14].

The statistically significant correlation between scintigraphy and intraoperative findings ($r = 0.499$, $p < 0.001$) supports its role in guiding surgical strategy. Accurate localization enabled minimally invasive parathyroidectomy (MIP) in 82% of patients. Th-

ese findings are consistent with previous studies demonstrating that reliable preoperative localization enables safe and effective MIP [15]. MIP offers advantages such as reduced operative time, lower morbidity, and improved cosmetic outcomes, which are particularly relevant in resource-limited settings[16].

Although hybrid SPECT/CT was not available for all patients throughout the study period, it improved localization accuracy in 21.9% of those with inconclusive initial imaging. This supports its role as a valuable second-line imaging modality in challenging cases [12].

When comparing imaging modalities, cervical ultrasound detected pathological glands in 76.9% of cases, whereas scintigraphy demonstrated superior detection (95.45%). Ultrasound limitations were mainly related to operator dependency, coexisting thyroid disease, and difficulty detecting deep or ectopic glands

SPECT/CT, performed in 23.9% of patients, provided additional diagnostic value, particularly in cases with discordant or inconclusive findings. It successfully localized pathological glands in 21.9% of these difficult cases, confirming its role as a problem--solving modality. Overall, these findings support a complementary imaging strategy: ultrasound and scintigraphy as first-line tools, with SPECT/CT reserved for equivocal cases.

Histopathological analysis confirmed solitary adenomas in 85% and hyperplasia in 15% of patients, consistent with established epidemiology [17]. Intraoperative PTH monitoring further confirmed surgical success, with all monitored patients demonstrating an appropriate postoperative decline.

Postoperative outcomes were excellent. Transient hypocalcemia occurred in only 5.97% of patients, and no recurrent laryngeal nerve injuries or infections were recorded. No cases of persistent or recurrent PHPT were observed during follow-up, confirming the long-term effectiveness of scintigraphy-guided MIP [18].

Overall, our findings demonstrate that 99mTc-sestamibi scintigraphy provides accurate preoperative localization that facilitates minimally invasive surgical management, particularly in resource-limited settings.

Study Limitations

This study has several limitations. First, its retrospective design may introduce selection bias. Second, imaging modalities were not uniformly available throughout the study period, particularly SPECT/CT, which may have influenced diagnostic comparisons.

Additionally, the study primarily reports sensitivity, as all patients underwent surgery, limiting the assessment of specificity and predictive values. Future prospective studies with standardized imaging protocols and complete biochemical datasets are needed to further validate these findings.

Conclusion

This study highlights the pivotal role of parathyroid scintigraphy in the modern surgical management of primary hyperparathyroidism (PHPT). The high sensitivity and reliability of 99mTc-sestamibi scintigraphy significantly enhance the preoperative localization of hyper functioning parathyroid glands, particularly in cases of ectopic or multi-gland disease. Our findings demonstrate that accurate imaging facilitates a targeted, minimally invasive surgical approach in the majority of patients, thereby reducing operative time, surgical morbidity, and hospital stay while preserving excellent clinical outcomes. The strong correlation between scintigraphic findings and intraoperative localization, combined with intraoperative PTH monitoring, ensures a high sur-

gical success rate and minimizes the risk of recurrence. Given its diagnostic performance and clinical utility, parathyroid scintigraphy should remain a cornerstone in the preoperative assessment of PHPT. Future integration of advanced imaging modalities like SPECT/CT or 18F-choline PET/CT may further refine localization and expand the scope of minimally invasive surgery, particularly in challenging or recurrent cases. Ultimately, the synergy between precise imaging, surgical expertise, and biochemical monitoring represents the foundation of optimal patient care in PHPT.

Disclosure

The authors declare no conflicts of interest.

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