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Discordant findings on preoperative imaging for primary hyperparathyroidism and thyroid disease: Choosing the path to follow

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ABSTRACT

Background: Preoperative localization of abnormal parathyroid glands in primary hyperparathyroidism is often obtained by sestamibi, and ultrasonography. We aimed to identify which modality is most accurate when laterality of abnormal glands on preoperative imaging is discordant.
Methods: A single institution retrospective review identified 112 consecutive patients with primary hyperparathyroidism who underwent successful parathyroidectomy and sestamibi with pertechnetate.
Results: Sestamibi with pertechnetate had a sensitivity of 72% and positive predictive value of 90%; ultrasonography had sensitivity of 50% and positive predictive value 80%. Patients with thyroiditis had lesser sensitivity and positive predictive value on sestamibi with pertechnetate (53% and 77%, respectively), in contrast to ultrasonography (54%, 88%, respectively). The sensitivity and positive predictive value of sestamibi with pertechnetate and ultrasonography did not differ in patients with thyroid nodules. Seventeen patients (15%) had discordant laterality on preoperative imaging. In discordant cases, sestamibi with pertechnetate was correct in 53% overall but in only 17% of those with thyroiditis ($P = .01$), whereas ultrasonography was correct in 26% overall but in 50% of those with thyroiditis ($P = .01$).
Conclusion: Thyroiditis decreased the sensitivity and positive predictive value of sestamibi with pertechnetate in primary hyperparathyroidism. In patients with discordant laterality on preoperative imaging, sestamibi with pertechnetate is the more accurate choice to guide operative planning, although ultrasonography may be a better guide in those with thyroiditis.

Introduction

Primary hyperparathyroidism (PHPT) presents most commonly as a single adenoma but is due to multiple gland disease in 10% to 20% of patients.[1–4] With advances in imaging techniques, localization of abnormal glands preoperatively has allowed for a focused, minimally invasive approach in certain patients.[1] Multiple imaging modalities are used commonly for preoperative localization, including cervical ultrasonography (US), sestamibi scintigraphy (MIBI), sestamibi-single photon emission computed tomography (SPECT), and four-dimensional computed tomography (4D-CT). Sensitivity of these modalities varies, with a recent metanalysis reporting the sensitivity of US at 76%, MIBI plus SPECT at 79%, and 4D-CT at 89%.[5]

In the setting of PHPT, thyroid disease, including thyroid nodules and parenchymal disease such as thyroiditis, has been shown to increase false positive and false negative rates with imaging.[6–9] The addition of Tc-99m pertechnetate thyroid scan is used to highlight thyroid pathology and subtract what is highlighted from MIBI, theoretically leaving only the abnormal parathyroid tissue on MIBI. This approach improves localization of abnormal parathyroid glands in the setting of thyroid disease.[10]

Imaging modalities, including US, MIBI, SPECT, and pertechnetate, are often complementary and can be used together to aid operative planning.[10–12] But when these imaging modalities are discordant, operative planning can be conflicted. The aim of the present study is to identify which imaging modality is most accurate in discordant cases and how thyroid pathology influences the results.

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Table I
Definitions of true positive, false positive, and false negative when comparing imaging localization and surgical pathology results

True laterality*	True positive	False positive	False negative	True negative	Laterality on imaging
Abnormal gland on right side only	+	-	-	+	Right
	-	+	+	-	Left
	+	+	-	-	Bilateral
	-	-	+	+	No glands
Abnormal gland on left side only	-	+	+	-	Right
	+	-	-	+	Left
	+	+	-	-	Bilateral
	-	-	+	+	No glands
Abnormal glands bilateral	+	-	+	-	Right
	+	-	+	-	Left
	+ +	-	-	-	Bilateral
	-	-	+ +	-	No glands

TP; true positive, *FP*; false positive, *FN;* false negative, *TN;* true negative
* Determined by operative resection and histopathologic confirmation of adenoma or hyperplasia. Each side of the neck was coded separately.

Table II
Sensitivity and PPV of imaging modalities in detecting correct laterality of abnormal parathyroid gland

Imaging Modality	TP	FP	FN	TN	Sensitivity	Specificity	PPV	NPV
All patients (N = 112, each with 2 lateralities)								
US*	57	14	58	57	50%	80%	80%	50%
MIBI+P	92	10	36	86	72%	90%	90%	70%
Single gland disease (n = 80, each with 2 lateralities)								
US*	38	13	26	52	59%	80%	75%	67%
MIBI+P	63	9	18	70	78%	89%	88%	80%
Multiple gland disease (n = 32, each with 2 lateralities)								
US*	19	1	30	6	39%	86%	95%	17%
MIBI+P	29	1	28	6	51%	86%	97%	18%
Thyroiditis (n = 25, each with 2 lateralities)								
US*	15	2	13	16	54%	89%	88%	55%
MIBI+P	17	5	15	13	53%	72%	77%	46%
Thyroid nodules (n = 59, each with 2 lateralities)								
US*	33	9	34	34	49%	79%	79%	50%
MIBI+P	48	5	23	42	68%	89%	91%	65%

FP, false positive; *NPV,* negative predictive value; *PPV,* positive predictive value; *TN,* true negative; *TP,* true positive.
* Not all patients underwent US. No true negatives were present because laterality was determined per patient rather than per gland.

Methods

After obtaining institutional review board approval, a single institution retrospective cohort study identified 113 consecutive patients from January 2014 through December 2015 with PHPT who underwent successful parathyroidectomy (PTX) and who had MIBI-with pertechnetate (MIBI+P) preoperatively. The use of US was surgeon dependent. All imaging studies were performed in our radiology department preoperatively. Successful PTX was defined as >50% decrease in serum parathyroid hormone levels (PTH) 10 to 20 minutes after all abnormal gland(s) were resected, as compared to baseline intraoperative levels and no documented persistent disease, defined as an normocalcemia within 6 months after PTX. Eight surgeons performed PTXs during this time, with 3 surgeons performing 88% of cases. Variables were collected from imaging reports, operative dictations, and pathology. True positives (TP), false positives (FP), false negatives (FN), and true negatives (TN) were identified for each side of the neck by comparing imaging findings to the intraoperative identification of an abnormal parathyroid gland with histologic confirmation of a parathyroid adenoma or hyperplasia, similar to previously published studies (Table I).[13,14]

Serum PTH levels were considered abnormal when >65 pg/mL and serum calcium when either total serum calcium was ≥10.5mg/dL or ionized calcium ≥5.5mg/dL. Ionized calcium was used preferentially when both total and ionized levels were available. Normocalcemia was defined as having no documented increase of either total serum and/or ionized calcium. Multiple gland disease was defined as ≥2 abnormal glands with cellular hyperplasia on surgical pathology and single gland disease was defined as 1 abnormal gland confirmed by surgical pathology. Thyroid nodules were identified on US or MIBI+P. Fine needle aspiration (FNA) was performed if nodules were >2 cm or if they exhibited other suspicious findings on US. Thyroidectomy or hemithyroidectomy were recommended after discussion with the patient if evidence of thyroid malignancy or follicular neoplasm was identified by FNA. Evidence of thyroiditis on imaging was defined as heterogenous thyroid parenchyma consistent with thyroiditis on US or impaired uptake on MIBI+P, as reported. Signs of thyroiditis on imaging were not correlated to lab work or surgical pathology. Rather, only imaging findings were used to define patients as having evidence of thyroiditis within this study.

Statistical analysis was completed using IBM SPSS Statistics (IBM Corp, Armonk, NY). Continuous variables were expressed as either mean ± standard deviation or median (interquartile range, IQR). Variables were analyzed using Kruskal-Wallis and Mann-Whitney *U* tests.

Results

Patient demographics

A total of 112 consecutive patients who underwent successful PTX and MIBI+P were identified, 93 (83%) also had US. Within the overall cohort, mean age was 59 ± 15 years, 82% (n = 92) were

Table III
Rate of negative preoperative imaging and patient characteristics

No abnormal gland detected on:	Total n (%)	SGD n (%)	MGD n (%)	Thyroid nodule n (%)	Thyroiditis n (%)	Type of surgery completed:		
						Focused n (%)	Unilateral n (%)	Bilateral n (%)
US only	25 (22%)	19 (76%)	6 (24%)	15 (60%)	6 (24%)	5 (20%)	6 (24%)	14 (56%)
MIBI+P only	9 (8%)	6 (67%)	3 (33%)	4 (44%)	3 (33%)	2 (22%)	1 (11%)	6 (67%)
Both US and MIBI+P	9 (8%)	5 (56%)	4 (44%)	6 (67%)	3 (33%)	0 (0%)	1* (11%)	8 (89%)

MGD, multiple gland disease; *SGD,* single gland disease;.
* Bilateral exploration was planned, but dissection was stopped after unilateral dissection due to recurrent laryngeal nerve traction injury. IOPTH confirmed removal of the single abnormal gland.

Table IV
Concordant imaging patient ($n = 34$) characteristics

	All concordant patients (n = 34)*	Correct laterality (n = 25)	Incorrect laterality (n = 9)	*P* value
Age	58 ± 15	55 ± 15	69 ± 10	.002
Female sex	28 (82%)	21 (84%)	7 (78%)	.675
BMI	27 ± 5	27 ± 6	28 ± 5	.818
Known thyroid disease	11 (32%)	8 (32%)	3 (33%)	.942
Thyroid nodule on imaging	20 (59%)	15 (60%)	5 (56%)	.816
Thyroiditis on imaging	6 (18%)	4 (16%)	2 (22%)	.675
Extent of operation				<.001
Unilateral or focused	20 (59%)	20 (80%)	0 (0%)	
Bilateral	14 (41%)	5 (20%)	9 (100%)	
Result of surgical pathology				<.001
Single gland disease	24 (71%)	23 (92%)	1 (11%)	
Multiple gland disease	10 (29%)	2 (8%)	8 (89%)	
Largest abnormal gland, milligram (median, IQR)	430, 267–900	510, 289–900	370, 276–650	.673

BMI, body mass index.
* This includes only patients who had glands with the same laterality identified on MIBI+P and US. Excluded are patients with discordant findings ($n = 17$), no gland on US ($n = 25$), no gland on MIBI+P ($n = 10$), no US or MIBI+P ($n = 9$), or no US performed ($n = 19$). One patient had no gland on MIBI+P and no US was performed.

Table V
Discordant imaging ($n = 17$) patient characteristics

	All discordant patients (n = 17)	US correct (n = 5)	MIBI+P correct (n = 10)	Neither correct (n = 2)	*P* value
Age	59 ± 11	60 ± 12	57 ± 11	62 ± 16	.855
Female sex	15 (88%)	5 (33%)	8 (53%)	2 (13%)	.316
BMI	30 ± 8	30 ± 6	31 ± 9	25 ± 5	.401
Known thyroid disease	6 (35%)	2 (33%)	2 (33%)	2 (33%)	.069
Thyroid nodule on imaging	11 (65%)	2 (18%)	8 (73%)	1 (13%)	.279
Thyroiditis on imaging	6 (35%)	3 (50%)	1 (17%)	2 (33%)	.012
Extent of operation					.130
Unilateral or focused	10 (59%)	3 (30%)	7 (70%)	0 (0%)	
Bilateral	7 (41%)	2 (29%)	3 (43%)	2 (29%)	
Result of surgical pathology					.025
Single gland disease	12 (71%)	3 (25%)	9 (75%)	0 (0%)	
Multiple gland disease	5 (29%)	2 (40%)	1 (20%)	2 (40%)	
Largest abnormal gland, milligram (median, IQR)	400, 234–725	400, 174–490	440, 250–1250	228, 125–228	.363

female, and the average body mass index was 31 ± 8. Overall, 82% ($n = 92$) of patients had increases in both serum calcium and PTH, 8% ($n = 9$) had inceased serum PTH but normal serum calcium concentrations, and 10% ($n = 11$) had increased serum calcium but normal serum PTH levels. Of those with normal serum calcium levels, 3/9 (33%) had low 25-OH vitamin D. Imaging detected 1 or more thyroid nodules in 52% ($n = 59$) of patients and abnormal thyroid parenchyma consistent with thyroiditis in 22% ($n = 25$). Overall, only 37% ($n = 41$) of patients had no thyroid disease, and 12% ($n = 13$) had both thyroid nodules and signs of thyroiditis. As a result of imaging, 29% ($n = 32$) underwent FNA of the thyroid nodules, 12% ($n = 13$) underwent total thyroidectomy, and 11% ($n = 12$) underwent hemi or partial thyroidectomy. Seven patients (6%) were found subsequently to have concomitant thyroid cancer on final pathology.

Within our cohort, 31 patients (28%) underwent focused, minimally invasive PTX, while 25 (22%) had unilateral and 56 (50%) had bilateral explorations. Of the 56 bilateral explorations, 13 (23%) were due to a planned, concurrent thyroidectomy and 2 (6%) were due to a planned, concurrent hemithyroidectomy on the contralateral side of the neck, compared to the parathyroid disease. Eight patients (8%) had no abnormal parathyroid glands localized on imaging preoperatively, and in 2 patients (4%) the surgeon was suspicious of bilateral disease based on preoperative imaging. Bilateral exploration was performed in 13/56 (23%) patients due to lack of PTH decrease after gland resection and in 18/56 (32%) because intraoperative appearance of the glands was concerning formultigland disease. After evaluation by pathology, 32 patients (29%) had multigland disease. Median weight of the largest abnormal gland was 375 mg (IQR 245–685 mg). The mean weight of the parathyroid glands in patients

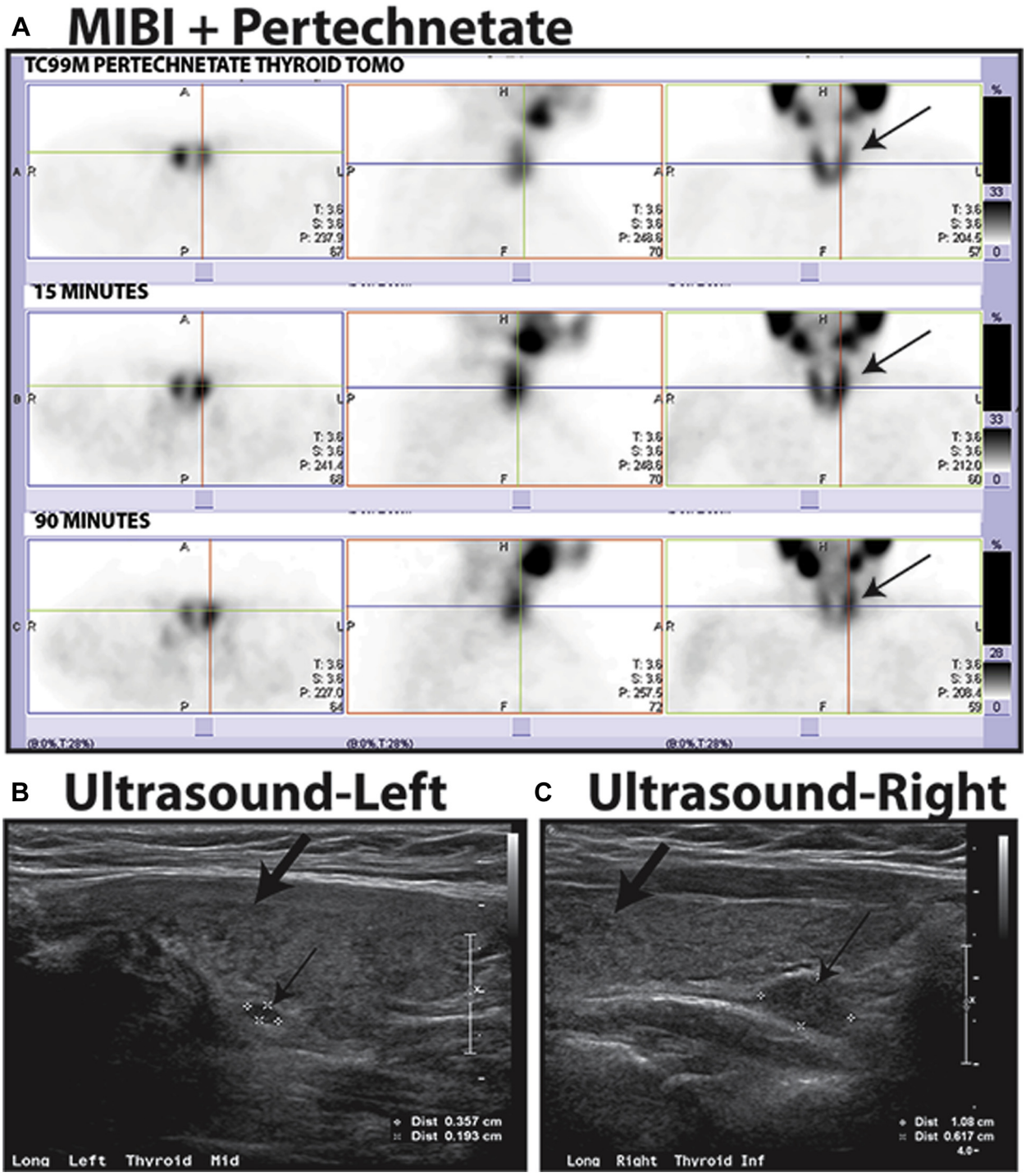

Figure. Ultrasonography (US) and MIBI+P in a patient with discordant imaging. *(A)* MIBI+P localizes the adenoma in left neck (arrows) after 90 minutes. *(B)* USof the left neck reveals a small normal parathyroid gland (small arrow) and demonstrates heterogenous parenchyma consistent with thyroiditis (large arrow). *(C)* US of the right neck reveals a large parathyroid adenoma (small arrow) and heterogenous parenchyma (large arrow).

who underwent bilateral exploration was less (276 mg, IQR 198–435) compared to those who underwent unilateral or focused PTX (480 mg, IQR 323–847) ($P < .001$).

Performance of imaging modalities

Preoperatively, 92% ($n = 103$) of patients had findings consistent with an abnormal parathyroid gland(s) localized on either US or MIBI+P. Nine patients (8%) had no gland localized on either imaging modality. No gland was localized on US in 25 patients (22%) and on MIBI+P in 10 patients (9%). US was not performed in 19 patients (17%). Of those without an US, an abnormal gland was localized on MIBI+P in 18 (95%) and MIBI+P identified the correct anatomic laterality in 16 (84%) patients.

Overall, MIBI+P had a better sensitivity (Sn) and positive predictive value (PPV) (72% and 90%, respectively) compared to US

Table VI
Discordant imaging and operative results

Patient ID	Laterality on US	Laterality on MIBI+P	Laterality surgeon started on	True laterality of abnormal glands	Thyroid nodule present	Laterality of thyroid nodule	US or MIBI+P consistent with thyroiditis
US bilateral glands, MIBI unilateral gland ($n = 9$)							
1	Bilateral	Left	Left	Left	Yes	Bilateral	Yes
2	Bilateral	Left	Left	Bilateral	Yes	Left	No
3	Bilateral	Left	Left	Bilateral	No	N/A	No
4	Bilateral	Left	Left	Left	Yes	Bilateral	No
5	Bilateral	Left	Left	Left	Yes	Right	No
6	Bilateral	Left	Left	Left	Yes	Bilateral	No
7	Bilateral	Right	Right	Right	Yes	Bilateral	No
8	Bilateral	Left	Left	Left	Yes	Bilateral	No
9	Bilateral	Right	Right	Right	No	N/A	No
MIBI bilateral glands, US unilateral gland ($n = 3$)							
10	Left	Bilateral	Left	Left	No	N/A	Yes
11	Right	Bilateral	Right	Bilateral	Yes	Bilateral	No
12	Left	Bilateral	Left	Left	Yes	Bilateral	Yes
Both MIBI and US unilateral, opposite laterality ($n = 5$)							
13	Right	Left	Right	Left	No	N/A	No
14	Left	Right	Right	Right	Yes	Right	No
15	Right	Left	Right	Right	No	N/A	Yes
16	Right	Left	Right	Bilateral	No	N/A	Yes
17	Left	Right	Right	Bilateral	Yes	Right	Yes

(50% and 80%, respectively) (Table II). In patients with single gland disease ($n = 81$, 72%), Sn and PPV improved to 78% and 88% with MIBI+P and 59% and 75% with US. Both imaging modalities were poorly sensitive in multigland disease, but highly specific (Sn 51%, PPV 97% with MIBI+P; Sn 39%, PPV 86% with US). MIBI+P and US performed similarly in patients with thyroid nodules as compared to those without nodules. In patients with thyroiditis, however, MIBI+P performed considerably worse when compared to patients without thyroiditis (Sn 53%, specificity (Sp) 72%, PPV 77% vs Sn 71%, Sp 93%, PPV 94%). Conversely, US had a better Sn and PPV in the presence of thyroiditis (Sn 54%, PPV 88% vs Sn 49%, PPV 78%).

Negative imaging results and operative findings

US was negative in 25 patients (22%), MIBI+P was negative in 9 (8%) patients, and 9 (8%) had no abnormal gland detected on either US or MIBI+P (Table III). Multigland disease was found in 4/9 (44%) of those with negative US and MIBI+P. Thyroid nodules were identified in 15/25 (60%) of patients with a negative US and in 6/9 (67%) of those with negative US and negative MIBI+P. Bilateral exploration was performed in 89% of patients with both negative US and MIBI+P, 70% of those with a negative MIBI+P, and 56% of those with a negative US.

Concordant imaging results

Of patients who had abnormal glands localized on both MIBI+P and US preoperatively ($n = 51$), both imaging modalities localized to the same side of the neck in 34 patients (67%) (Table IV). In this concordant group, 10/34 (29%) had multigland disease. In patients with concordant imaging and single gland disease, correct laterality was found in 23/24 (92%). Overall, 20/34 (59%) were able to undergo unilateral or focused exploration, and 14/34 (41%) had bilateral exploration. There was no difference in the rate of thyroid nodules or thyroiditis between patients with correct and incorrect lateralization; incorrect laterality, however, was associated with older age ($P = .002$).

Discordant imaging results

A total of 17 patients (15% of all patients) had discordant laterality reported on US and MIBI+P (Table V). Thyroid nodules were present in 11 (65%) and thyroiditis in 5 (35%). Multigland disease was found in 29%, 41% of whom underwent bilateral exploration. In this group of patients, MIBI+P was correct in 53% of patients but only in 17% of those with thyroiditis ($P = .01$). In contrast, US was correct in 26% of patients, but this increased to 50% of those with thyroiditis ($P = .01$). The Figure illustrates imaging findings in a patient with thyroiditis in whom MIBI+P and US identified glands with opposite laterality; true laterality of the abnormal gland after resection was consistent with laterality on US.

Surgical variances in discordant patients

Surgical variances in patients with discordant preoperative US and MIBI+P are detailed in Table VI. When MIBI+P localized to a single laterality and US demonstrated bilateral parathyroid disease ($n = 9$), surgeons consistently started the procedure on the side localized on MIBI+P. Similarly, when MIBI+P indicated bilateral disease but US localized to a single laterality ($n = 3$), surgeons started on the side localized by US. When US and MIBI+P identified abnormal glands with opposite laterality ($n = 5$), the side a surgeon started on did not consistently follow an imaging modality. Interestingly, the surgeons started on the right side in all 5 cases. In the 2 patients without thyroiditis, MIBI+P identified the laterality of the abnormal gland correctly. In the 3 patients with thyroiditis, US identified unilateral disease correctly in 1 patient and 2 patients had bilateral disease.

Discussion

The operative approach of focused PTX with preoperative imaging and intraoperative PTH monitoring is well established in the treatment of PHPT.[1,15] Preoperative imaging is performed most commonly with MIBI, and the additional of single-photon emission computed tomography (SPECT-CT) and pertechnetate has increased its sensitivity and specificity.[5,10,16] Adding thyroid US to MIBI allows for an additional modality to identify abnormal parathyroid glands and concomitant thyroid pathology, which may require operative intervention.[17,18] Using 2 imaging modalities, however, can lead to discordant results, impacting the operative planning and intraoperative decision-making. Our study showed that the presence of thyroiditis on either US or MIBI+P negatively impacts the Sn and

PPV of MIBI+P. In addition, our results indicate that in patients with discordant imaging results and thyroiditis, US is correct more often.

The strengths of our study include having a cohort of patients with complex imaging results and detailed correlation with intraoperative findings, as well as the inclusion of patients with negative imaging and multigland disease. Though 92% of our patients had preoperative localization of abnormal parathyroid glands, only 50% had focused or unilateral PTX. In those with negative imaging, those with a negative MIBI+P had a much greater rate of bilateral exploration than those with a negative US and positive MIBI+P. Interestingly, even in patients with concordant imaging findings, there was a 29% incidence of multigland disease and a 41% bilateral exploration rate. Other studies show 96% sensitivity when US and MIBI are concordant in single gland disease but only a 17% sensitivity with concordant imaging in multigland disease .[18,19]

In our cohort, 15% of cases had discordant findings on MIBI+P and US which affected the operative planning. The accuracy of MIBI+P was decreased in patients who had signs of thyroiditis on either US or MIBI+P, whereas thyroid nodules had no effect on the performance of either study type. Thyroiditis is common and has been reported to be as great as 27% in women and 7% of men,[19] and therefore, understanding how it effects imaging studies used commonly in parathyroid surgery is important. Previous literature has demonstrated that the interpretation of parathyroid imaging is more difficult in the setting of autoimmune thyroiditis.[6,9,20] Hwang et al demonstrated increased MIBI retention in the setting of autoimmune thyroid disease.[9] Increased retention of MIBI may lead to impaired detection of abnormal parathyroid tissue and account for the decreased performance of MIBI+P in patients with thyroiditis. Although we did not examine other imaging modalities in the present study, the utility of other imaging modalities such as 4D-CT in the setting of thyroid disease may also be altered.[21] Our study shows that an additional benefit of multimodal preoperative imaging with US is the identification of thyroiditis, which can aid surgeons in choosing which imaging modality to follow when planning the operative approach.

Limitations of our study include its retrospective nature, which limits our insight into operative planning based on the imaging modalities obtained. As a single institutional review, these findings may not be generalizable, especially given that results of imaging studies and specifically US are operator dependent. Our US was performed by US technologists and interpreted by radiologists, and therefore, these results may not apply to US at other institutions. Additionally, our study cohort represents that of a tertiary referral center with a considerably greater rate of multigland disease than other studies have described previously. Our small number of patients with discordant imaging may also limit the ability to detect statistical differences.

In conclusion, thyroiditis decreased the performance of MIBI+P, but thyroid nodules had no effect on the performance of either MIBI+P or US. When MIBI+P and US had discordant laterality, MIBI+P was most often correct, except in the case of thyroiditis when US was correct more often. This observation suggests that while MIBI+P is the more accurate choice to guide operative planning when imaging is discordant, US may be a better guide in those patients with thyroiditis.

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Conflict of interest/Disclosure

No authors have conflicts of interest or other disclosures.

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Discussion

Dr Kelly Mccoy (Pittsburgh, PA): Thank you. First, I'd like to thank the society for the opportunity to discuss this interesting paper and the authors as well for providing the manuscript in advance and for completing this very interesting study. It was very thoughtfully done and really looks at a topic that vexes endocrine surgeons on a nearly daily basis. So what do we do when the imaging is discordant? Which way to go?

So I feel like—and you probably recognize this as well—that as our imaging becomes more sensitive, we're seeing this more often. For example, in Pittsburgh, we have a grading scale for our Sestamibi scans based on the level of uptake; we have definite, probable, possible negative, and we get that in the final impression. Over the last few years, as the technology has advanced, we see more definite plus and, oh, maybe there's another one, so this has become more of an issue.

The other that I think is interesting, it sounds like your patient population is quite similar to ours in Pittsburgh where there is a lot of thyroiditis. Thyroiditis is almost endemic in Pennsylvania. We are also plagued with the difficulty of these imaging modalities in that setting.

So a couple of things that I wanted to ask about. First, in the methods that you had defined successful parathyroidectomy as your intraoperative PTH drop, I wanted to see if you had longer-term care data on these patients. As you know, it's important when looking at the accuracy of an imaging study based on anatomic data that you know what the final outcome was, whether you were really right down the road.

Did you look at six-month cure data? In that event, did you take that into consideration if there were patients who were impaired at that time point and what their subsequent findings were?

Also, I kind of alluded to the fact that sometimes these studies are becoming a little too sensitive. We also have seen that we're finding other findings beyond parathyroid entities, so did you notice that just in your review that you had other things like lung nodules and other things that came up in your review of these patients?

Dr Anna Beck: To answer your first question, since we are a tertiary referral center, a lot of patients may go back to their home institutions to have long-term follow-up. We initially did not include persistent hyperparathyroidism as our exclusion criteria because of missing data for calcium or PTH out to six months. I did review, and we did have one patient who did have persistent hyperparathyroidism after surgery, so we can certainly go back and exclude that patient. Of note, that patient did not have discordant imaging findings and they did not have thyroiditis, so this change should not alter the outcome of our study.

To answer your second question, we did look at thyroid findings after imaging for hyperparathyroidism, and we did find that 6% of our patients had a malignancy that was confirmed after final surgical pathology after a thyroidectomy, but we didn't look at findings like lung nodules. It might be something we can go back and do. Thank you.

Dr Sam Snyder (Harlingen, TX): Thank you for a very nice study that was presented very well. You are trying to answer an important question to all of us as endocrine surgeons: Which study is better? I applaud your results for Sestamibi because in my new practice location, when I surveyed their prior positivity over the previous year, Sestamibi scans were 22%. So there is a vast difference in the results. You're doing very well, and I need your protocol.

I have a question: Who is doing the ultrasound? I do my own surgeon-performed ultrasound in the office first on these patients. If I see an abnormal parathyroid gland, which I think I can see about 60% of the time, that's it. I don't go to the Sestamibi. Since I'm dealing mostly with single gland disease, it's almost always positive. So I can eliminate the Sestamibi. Do you routinely get Sestamibi and ultrasound together, or do you sequence them?

Secondly, you didn't talk about 4DCT scan, which we also include in some of our evaluations, particularly if the ultrasound is negative. Do you use that as well, and does that enter into when there is discordant imaging?

Dr Anna Beck: Thank you for your questions. I'll ask our radiologist for their protocol. In terms of who is doing the ultrasound, it is the radiology techs or the radiologists that are doing the ultrasound. We do have some patients referred to us from outside hospitals who have an ultrasound done there. If the radiologists do not feel it's a good enough study, they'll repeat the ultrasound at our institution.

Then in terms of the sequencing, we only included patients who had a Sestamibi completed. The majority of the endocrine and ENT surgeons who do parathyroidectomies at our institution do get Sestamibi. Not all patients in our cohort actually had an ultrasound. I think 19 did not have an ultrasound, and that was very much surgeon dependent as to whether they included an ultrasound. 4DCTs are used in select patients and certainly were performed in some of the patients in these cohorts, but we just did not look at that specific imaging modality.

Dr Sam Snyder (Harlingen, TX): I would advocate for surgeon-performed ultrasound. You may find your results are a little bit better than radiology.

Dr Allan Siperstein (Cleveland, OH): I enjoyed your paper. Very important topic. Dr. Snyder, of course, has preempted me with some of the important questions.

Number one, what was the timing of the Sestamibi and ultrasound scans and did one radiologist know the result of the other prior to imaging? Because I think that's very important. We often, on a scientific point of view, like to do each one independently, but in terms of patient clinical management want to know what the other one is thinking.

Also, I want to echo that surgeon-performed ultrasound is very important. But, in particular, on-table ultrasound immediately before you operate on the patient, because in that case you can do more graded compression with the ultrasound transducer and bring out findings that you normally wouldn't. In addition, not all Sestamibi scans are created equally, and we've moved entirely to doing Sestamibi iodine subtraction scans, and that will subtract out a lot of the thyroid artifacts and then co-registered with a CT scan so we get better anatomic information.

My other question for you is, you looked at laterality. Very often on the imaging studies, you can distinguish an upper from a lower gland, and that's an important hint as to whether you're dealing with single versus multiple gland disease. I'm wondering if you're able to microdissect your data in that area. Thank you

Dr Anna Beck: Thank you. In terms of looking at the quadrant localized by the imaging modality, meaning laterality and then either upper or lower, we did initially start out to specifically look at that data, but the data was just not very granular, and the numbers became too small to derive meaningful findings when we looked at the sensitivity and positive predictive value by quadrant as compared to just laterality.

Then in terms of timing of the Sestamibi and ultrasound scan, again, we didn't specifically look at if one was performed before the other, but certainly it's something we can go back to add. That would influence the results of the radiology report, certainly.

Dr Steven De Jong (Maywood, IL): During this study, did you change your criteria at the University of Iowa for bilateral cervical exploration? When and how did you make that decision? Finally, how often were you planning a unilateral approach abut then convert to bilateral exploration?

Dr Anna Beck: I do not believe any protocols were changed in terms of performing a bilateral exploration during the study period. It was a one-year study period—2014-2015. We did have a high rate of bilateral explorations: 50%. Twenty-three percent of the patients had a preoperative bilateral exploration plan because they were also undergoing a thyroidectomy, either total or hemithyroidectomy. And then 8% of those patients had a bilateral exploration planned because they had both negative Sestamibi and ultrasound preoperatively. One of those patients ended up undergoing unilateral exploration because of a retraction injury of the recurrent laryngeal nerve. That made up 30% of our patients with bilateral surgery. Really it was only 20% of our cohorts that had a bilateral exploration based on intraoperative parathyroid findings which consisted of both the intraoperative PTH not dropping after resection of the abnormal appearing glands but also if surgeons were concerned for multiple gland disease based on appearance of gland size on one side of the neck.