

Parathyroid surgery strategy (Surgery for primary hyperparathyroidism)

Today, we're going to discuss strategy in surgery for primary hyperparathyroidism, specifically bilateral exploration versus limited exploration. This is a very common question that patients will ask: Are you going to look at all 4 glands? I think it's really important to analyze this topic based on the available evidence.

When you choose an operative approach for primary hyperparathyroidism, there are several guiding principles to keep in mind. The criteria for limited exploration, meaning a focused or unilateral exploration, should be strict, whereas bilateral exploration should be used liberally.

There are five reasons for this:

- 1) It's easy and quick to look at the other side
- 2) Identifying 4 glands yields a definitive and unambiguous result
- 3) IOPTH is not always available!
- 4) Finding more glands will make you a better parathyroid surgeon
- 5) When in doubt, a subtotal parathyroidectomy is a great operation

Remember that the leading cause of failed parathyroidectomy is a missed parathyroid adenoma in a normal location. But, barring that, the second leading cause of failed parathyroidectomy is a single-gland resection in the face of multigland disease. We as surgeons must consider what an acceptable rate of failure is. We can't cure 100% of people, but a success rate of 98-99% is achievable which keeping the complication rate low.

From a technical standpoint, parathyroid surgery is an exercise in applied embryology, that is, understanding the great variability in parathyroid gland locations that arise from developmental events in utero. But, from a cognitive standpoint, parathyroid surgery is an exercise in conditional probability. Today we're going to focus more on the strategy, the cognitive exercise, the judgment and thought process that goes into parathyroid surgery.

Before the case and during the case we are continuously calculating, thinking, what is the probability of single vs multigland disease. What is the probability of multi-gland parathyroid disease...

- At baseline?
- Given biochemical severity?
- Given scan results?
- Given surgical findings?
- Given IOPTH data?

We have known since the 1960s that, in primary hyperparathyroidism, 85% of patients have single-gland disease and the remaining 15% of multigland disease, which can be either hyperplasia or double adenoma. The first modifiers to those base probabilities are genetic and environmental factors.

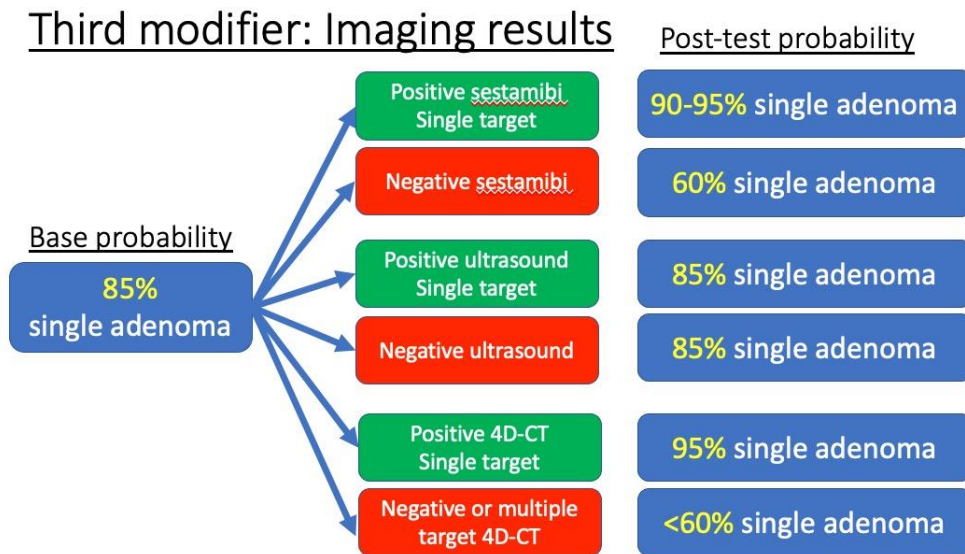
- Genetic:

- Family history of MEN-1, (MEN-2), or familial isolated primary hyperparathyroidism
- Environmental exposures:
- Lithium: ↑ incidence, ↑ multigland disease, ↑ recurrence
- Therapeutic radiation (esp. in childhood) may increase the incidence of PHPT, but likely does not influence the probability of multigland disease

The second modifier is biochemical severity:

- Biochemically mild disease: ↑ risk of multigland disease
- Calcium >12 mg/dL is almost always single adenoma
- Cases with low baseline PTH may make IOPTH difficult to interpret

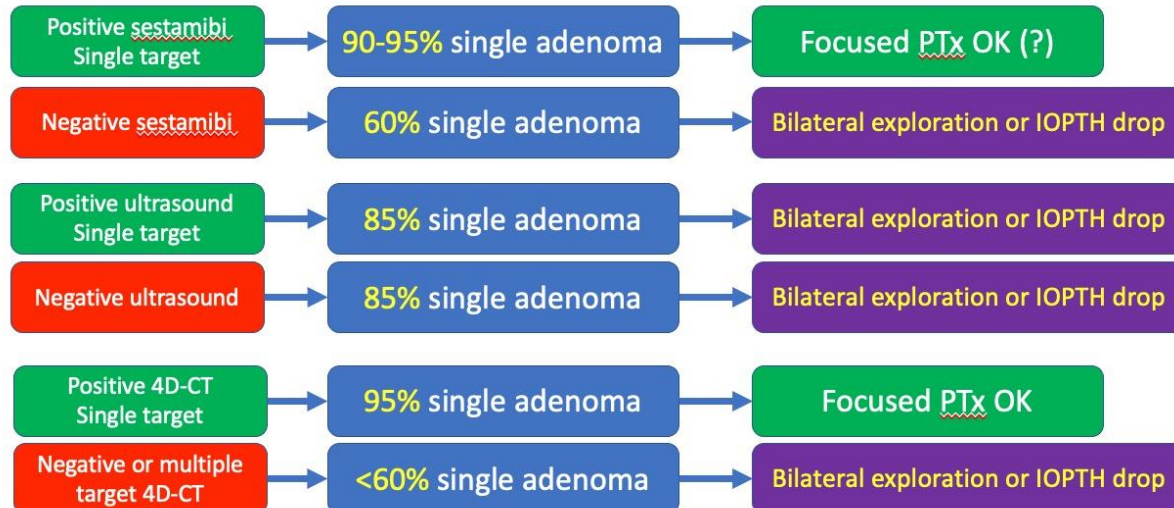
The third modifier is probably the most important one from day to day: imaging results. How do they influence the probability of single gland disease versus multi-gland disease?



Sestamibi scans represent older technology that came out around 1984, though they are still used quite often today in 2023. A positive sestamibi scan gives you a 90-95% post-test probability of single adenoma. If it's negative, then that number drops to 60%. What about ultrasound? Well, sometimes ultrasound can show you a single target, or it can be negative. But no matter what your ultrasound shows, it's not going to change the balance of single vs multigland parathyroid disease. Parathyroid 4D-CT is currently the best study. It came out around 2010. If you have a positive, single target, on 4D-CT, 95% of those patients have a single adenoma. If it's negative or shows multiple glands, that number drops below 60%.

What is your entering strategy as you scrub for these operations based on the imaging results?

Entering strategy



If you have a positive sestamibi scan with a single target, many surgeons will perform a focused or unilateral exploration, which will yield a pretty good long-term success rate of around 92%.

If you have a negative sestamibi scan, then of course you are back to either bilateral exploration or a definitive intraoperative PTH drop. Which is also true no matter what your ultrasound result is, because all ultrasound really gives you is a starting point for your operation.

What about 4D-CT? If that shows you a single target, you can probably perform a focused parathyroidectomy and have about a 95% success rate, which is pretty good. So focused parathyroidectomy is probably a reasonable option in patients with a very clear single target on 4D-CT. Remember, 4D-CT is a pretty sensitive exam, so a lot of times you might have multiple targets that show up in a subtle fashion, because the resolution of that scan is so good. If your 4D-CT is negative or shows multiple targets, then, again, you're back to bilateral exploration or an IOPTH drop.

Let's talk a little bit about interoperative PTH. Most people know about the Miami criterion, but there are several important caveats.

- Miami criterion: >50% decrease in PTH from the highest preincision or preexcision level obtained 10 minutes after removal of all abnormal parathyroid tissue
- BUT...
- Anesthesia induction can raise PTH levels
- Manipulation of parathyroid glands can cause PTH to spike
- These two factors may create a falsely elevated baseline PTH

If your baseline PTH level is falsely elevated and you fall 50% from that fake baseline, you may be misled to think you are done with the operation, when, in fact, you still have abnormal parathyroid tissue to remove.

Remember the half-life of PTH is 3 to 4 minutes. So, if you're drawing it every 5 min, it should continue to fall by half and half again. In other words, you must think about the PTH dynamics over time instead of simply threshold values.

I'm going to show you this one case. This guy had a positive system to be scan right here. You see the parathyroid adenoma. We removed one parathyroid gland. There was a little spike during the manipulation of this parathyroid adenoma, and then the PTH fell. Did it fall 50%? Yes, it did. But look, it goes 90, and then 88, and that's what I call the ominous plateau. The plateau signaled the presence of a mirror-image double adenoma. Remember that most multigland disease is bilateral. Double adenomas are not evenly distributed. Among double adenomas, double superior adenomas in a mirror-image location are the most common. In these cases, a unilateral exploration will not help you.

Here's another case. A 63 year-old woman with a calcium of 11.1, PTH of 116, and osteoporosis. On the 4D-CT scan, you can see this monster of a gland in the right superior region. But look at the mirror image location: There's another one. It's not as big as the first one, maybe it's an 8-9 mm gland. But that gland is waiting there to cause the patient a recurrence, and you don't want that patient to come back for another operation in 2 years. You'd rather nip that in the bud today. The patient would prefer that too.

What happened to that to this patient? Initially, the baseline was 219, and the PTH spiked up to 418 when the big gland on the right side was removed. And then it fell by more than half. Then we remove the second gland, and the PTH continued to fall further down to 32 post-operatively.

The post-operative PTH level, drawn when your patient is waking up in the recovery room, should ideally be between 12 and 39. That's the sweet spot. You don't want it too low, and patients with final PTH values above 40 have more problems with recurrences. Values in the teens and 20s are best, and 30s are also acceptable.

What about ambiguous results and late recurrences? One year after surgery for primary hyperparathyroidism, patients can come back with a calcium in the low 10s with a slightly elevated PTH in the double digits, or a calcium in the 9s with a triple-digit PTH level. Are these patients cured?

Most often, as long as the calcium level is normal, these patients will be fine without further intervention. Remember that up to 40% of patients will experience eucalcemic elevations in the PTH level after successful parathyroid surgery. One lingering question is whether such patients have clinical outcomes, especially with respect to long term bone mineral density

changes, that are as good as other patients whose calcium and PTH levels are both normal after surgery. It's an open question that requires further study.

The recurrence rate long term after initial surgery for primary hyperparathyroidism may be as high as 15%, with one-third of these recurrences take place after 10 years. Now, can bilateral exploration help prevent some of these suboptimal outcomes? Probably somewhat. After I transitioned to performing more bilateral explorations around 2010, I did start to see fewer of these ambiguous long-term biochemical outcomes.

To summarize when to perform a bilateral neck exploration:

- +Family history or lithium exposure
- Biochemically mild disease (Ca <10.5 mg/dL)
- Negative scan or multiple targets on scan
- IOPTH doesn't fall, not working, ambiguous, or ominous plateau
- Most multigland disease is BILATERAL (think double superior, even if mibi+)
- Subtotal parathyroidectomy is a solid operation in the face of ambiguity
- Bilateral exploration is commonly performed by experienced endocrine surgeons (40% initial approach, 11% converted to bilateral)

And some exceptions where a limited exploration might be favored:

- Known ectopic adenoma
- Prior neck surgery
- Prior parathyroid surgery
- Prior thyroid surgery
- Prior cervical spine fusion
- Concomitant thyroid resection
- Thyroid lobectomy – known or suspected thyroid cancer on the same side as parathyroid adenoma
- Total thyroidectomy – avoid HYPOparathyroidism