

## GUEST EDITORIAL

## Controversies in Parathyroid Surgery: The Quest for a “Mini” Unilateral Parathyroid Operation Seems to Have Gone Too Far

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Primary hyperparathyroidism (pHPT) is a benign disease with malignant potential. Untreated, it is believed to carry a near twofold increase in the development of several cancers (breast, colon, and prostate) [1,2]. It is known to increase the risk of cardiac disease, hypertension, and stroke by more than double, ultimately carrying a several-year decrease in life expectancy [3]. Of course, afflicted patients will almost always develop significant if not severe osteoporosis. Thirty percent or so will get kidney stones. Aside from the damage to many organ systems, these small parathyroid tumors frequently cause chronic fatigue, memory loss, and a host of other non-specific complaints associated with a significant decreased quality of life.

Further evidence of the “malignant” potential of this disease was noted in a recent review of our last 10,000 operations [4] where we discovered that it is a very rare patient who has pHPT for 15 years. We are not sure if we have ever seen a patient who had it for 20 years or more. We suspect that they are deceased, as those patients harboring parathyroid tumors for 12 years or more typically take multiple prescription drugs (six on average), have multiple medical problems, and boast an oncologist and cardiologist among their four or five doctors.

Why then do we surgeons wring our hands so tightly when we see a patient with clear-cut biochemical pHPT and a negative (non-localizing) scan? It is troubling to see some patients categorized into those who are “good candidates” for surgery and those who can be “monitored” based solely upon whether or not their tumor has been localized on a scan. Even benign pancreatic endocrine tumors are occasionally resected in a “blind” fashion in anticipation of removing the tumor. Surely parathyroid surgery does not carry the morbidity that pancreatic surgery does. We are now denying surgery to more patients than ever before for a disease that causes considerable morbidity and deprives our patients of the joys of life. It seems to me that the quest for a “mini” or unilateral parathyroid operation has gone a bit too far.

It is possible that some of this blame lies with me. History will likely show that I played a major role in the re-thinking of parathyroid surgery, standing on my soapbox in the mid 1990’s preaching that a bilateral exploration in all people with pHPT was simply overkill and unnecessary. Our group and several others showed that advanced preoperative scanning techniques and hormone measuring adjuncts in the operating room would allow us to selectively operate only on one side of the neck in the majority of pHPT patients. This is true, but it must be kept within context. It clearly does not mean that those with a negative scan should be “monitored” until such time as the tumor can

be found on a scan. As discussed below, we have discovered that patients with negative scans are often the easiest patients to cure with a very straightforward operation.

As I look back on the past 15 years I can see that my enthusiasm for the unilateral parathyroidectomy as the panacea for patients harboring a parathyroid tumor was incorrect. We have come to understand that a unilateral parathyroid exploration—being very selective and using every intraoperative adjunct available (including examination of the ipsilateral gland)—will rarely allow long-term cure rates over 95%. When this process is managed by surgeons with lesser experience the cure rate can often drop well below 90%. Our group is troubled by the fact that we gave up on unilateral parathyroid surgery a number of years and many thousands of operations ago, yet the benefits of “focused” parathyroid surgery continues to be emphasized in the surgical literature—often using our 15-year-old observations as the standard. New reports are published regularly proclaiming the positive attributes of operating on one side of the neck. Unfortunately, most of these reports are inherently overstating the benefits of the one-sided approach by not mentioning the denominator—the actual number of patients who need to have their tumor removed. Typically the 30–35% of patients with biochemically identical disease who were not operated upon because their scan was negative are not a component of the report, and how these patients were managed is not addressed in sufficient detail. Approximately one-third of our 2000+ operations this past year were on patients who were denied surgery for no other reason than they had a negative scan—a trend other high-volume centers are seeing as well. Denying surgery to scan-negative patients is an inappropriately extrapolated message that the proponents of unilateral parathyroidectomy did not anticipate.

It is important for all of us to recognize that localizing scans are not diagnostic tools. Scans (of all types) do not correlate with the severity of clinical disease. In fact, some of the most severe, advanced cases of pHPT will have non-localizing scans. A negative scan does not mean a patient does not have pHPT. Nor does it mean they have parathyroid

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hyperplasia (as very few patients do) or a parathyroid tumor in some bizarre location. Patients with negative localizing scans have the same disease in all regards as patients with positive scans.

Our endocrinology colleagues have come along for the ride on this one. Many have come to believe—with us surgeons as their sponsors—that only patients with a localized parathyroid tumor can have a mini-parathyroid operation (or any parathyroid operation). They have been led to understand that operating on both sides of the neck can be dangerous and fraught with potential problems even though intellectually they would prefer if all four parathyroid glands were evaluated. It is an unusual endocrinologist who has ever seen a parathyroid operation (or a parathyroid gland for that matter), thus they have no choice but to listen to the surgeons about the perceived difficulties of parathyroidectomy. Even when these words are not actually verbalized, the message we send to our referring doctors when we decline to operate because the tumor has not been localized on a scan is a very loud message which is not in the best interest of our shared patients. The data would suggest that nearly a third of patients with pHPT are not being referred to a surgeon because the endocrinologist has not been able to localize the tumor on a scan. An upcoming report from our group shows that a negative sestamibi scan delays referral for surgery by an average of 2.7 years—and then it is often a secondary physician or even the patient's family who makes the eventual referral. We need to remind everyone involved in these cases that localizing scans (of all kinds) should not play a role in the diagnosis or management of pHPT and, therefore, should not be used to classify surgical from non-surgical candidates.

Giving up on the unilateral parathyroidectomy was a slow, but constant process for me and my partners who are as passionate about and committed as I am to the care of patients with parathyroid disease. We now perform the exact same bilateral operation on virtually all patients—regardless of scan results. Patients with a beautifully positive scan can expect an identical four-gland bilateral operation at our center as somebody with a negative scan. In fact, the operation that I once advocated quite strongly—unilateral parathyroidectomy—has become essentially obsolete in our practice. We have not performed a unilateral operation (as a routine first operation) in over 4,000 cases. I would not have one myself if I were diagnosed with pHPT since I want a single operation to cure me without worries of persistent disease or a recurrence a few years down the road. We have learned that there is simply no way to detect all other non-normal parathyroid glands—occurring in about 21% of patients—without examining all four. An upcoming report from our group shows that more than one gland was removed 10 times more often when we performed a bilateral operation where the activity of each gland is assessed.

For those surgeons that look for a fall in io-PTH during the operation as a determinant of the presence of additional tumors, I can assure you that it can sometimes achieve this task, but often it cannot. Large drops in io-PTH levels (far more than 50%) can be very helpful, but will not guarantee that your patient is cured. Almost daily we see surgeons putting so much faith in their io-PTH measurements that it causes them to perform maneuvers in the operating room that common sense would otherwise prevent. We do not use io-PTH assays, but for those surgeons who do it needs to be remembered that this is just a tool and it is not a perfect tool. Use this analysis with caution and sound judgment, as it will on occasion make you consider doing something you would not normally do. And remember, a large drop in io-PTH does not guarantee cure—these patients need close follow-up for years.

It was the goal of decreasing non-cures to near zero that drove us and other high-volume centers away from unilateral parathyroid surgery. As all surgeons know, a patient with an unsuccessful parathyroid operation consumes 3–5 fold the time and effort that a cured patient does (to say nothing of the anxiety and bad feelings we incur). Even a 1% failure rate would give us a failure every 2 weeks which carries responsibilities and worries that we find unacceptable.

Regardless of the hormone-measuring gymnastics that can be performed in the operating room, we have found that the only way to assure cure is to examine the physiologic state of all four parathyroid glands. To that end, we use a gamma probe to quantify the amount of hormone each gland is producing (using physiologic activity based against a standard curve) [5]. We do not use ioPTH, and do not use frozen sections. Importantly, with proper technique and a well-rehearsed surgical team, this entire operation can be completed routinely in 20 min or less regardless of scan results. High-volume surgeons are fast because they do not spend time looking for parathyroid glands in areas where they are not located, while avoiding maneuvers (like frozen section analysis) that have little or no value most of the time. Finding parathyroid glands quickly means understanding that the age-old teaching that these glands can be anywhere in the neck or chest is absolutely not true. These glands are almost always situated in very predictable locations. They cannot be “anywhere.”

The real breakthrough allowing us to perform quick, bilateral operations came literally overnight a few years ago. It was right under our nose for thousands of cases yet remained unrecognized. Like a light-bulb going off in a cartoon, we realized that the most important information provided by the sestamibi scan was the “true negative” information, not the “true positive” that everybody seeks. Even our radiology colleagues overlook the importance of the true negative aspects of these scans. We made a quantum shift in our approach to parathyroidectomy that day by realizing that a negative sestamibi scan has *more* information and is *more* helpful than a positive scan. We now *prefer* negative scans and have changed our scanning techniques such that we try to get as much pertinent negative information as possible. We do not use any scan to localize parathyroid adenomas located in the neck—that is no longer our goal. Our desire is to know definitively where the tumor is *not* located, and, therefore, we will by default know where it *is* located based on anatomy and embryology. Knowing that there is not an adenoma within the chest, in the cervical thymus, retroesophageal, within the carotid sheath, or undescended high in the neck provides the surgeon with confidence to conduct a straightforward dissection without worrying about exploring areas of the neck where “rare” tumors are located. A high-quality (in focus) scan can tell all of these things with near 100% accuracy, thereby, establishing that the tumor is where it is supposed to be: “para” to the thyroid gland.

Given this approach, the patient with a “negative” localizing study is the perfect candidate for surgery—and a mini, outpatient, bilateral operation at that. This patient's operation can be expected to be straightforward as the parathyroid tumor is almost guaranteed to be adjacent to or behind the thyroid (where it is supposed to be). A bilateral operation can easily be done through the same 1-in. incision that a unilateral operation is conducted. We would encourage all surgeons to attempt the bilateral operation through a 2.5 cm centrally placed incision (the key being a generous sub-platysmal flap). There is no need for a big incision and extensive dissection, as the negative information on the scan has already shown that there is no ectopic tissue. Be warned, however, that the scan must be high quality—fuzzy SPECT scans need not apply.

Although we no longer routinely perform unilateral parathyroidectomies, this is not to say that there is not a role for this procedure. On the contrary; the unilateral parathyroid operation is a fantastic operation for many patients and a 95% cure rate is wonderfully acceptable goal for most surgical groups. Surgeons should be comfortable offering this operation, but must keep in mind that some patients won't be cured even when the localized tumor is removed. We all need to remember that we cannot cure all patients the first time around—we all have non-cured patients. However, we need to know when to quit the operation and accept the non-cure, anticipating that the next operation can be performed quickly and safely because the limited dissection did not open unnecessary tissue planes and the normal glands still remain.

The past 15 years has seen an increasing emphasis placed on performing unilateral parathyroid operations. As one of the prime advocates of this operation it is important for us to state that too much emphasis is being put on “unilateral” and “focused,” occasionally to the detriment of our patients. As we learn more about the long-term consequences of untreated pHPT we need to make sure we are taking care of all of the patients that need our help, not denying them a curative operation because of a non-localizing scan. The primary way for this to occur, in our opinion, is to recognize the tremendous information provided by high-quality scans and the “true negative” information they contain. Realizing that parathyroid glands are almost always located where they are supposed to be (they cannot be anywhere), these operations can be safe, simple, and successful without regards to preoperative tumor localization. There are few patients as grateful as those that are cured of their pHPT. Let’s have a few more grateful patients and a few less that are being “observed.”

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practice to ever-higher standards, and whose constant goal of perfection in all aspects of patient care is a continuous inspiration.

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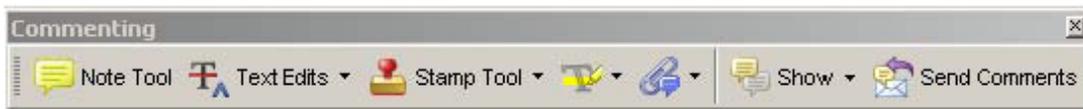
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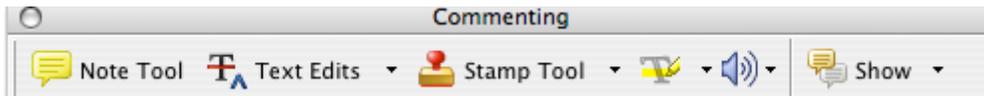
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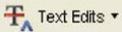
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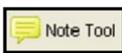
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