Improved preoperative planning for directed parathyroidectomy with 4-dimensional computed tomography

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Background. *Four-dimensional computed tomography (4D-CT) provides both functional and highly detailed anatomic information about parathyroid tumors. The purpose of this study was to compare 4D-CT with sestamibi imaging and ultrasonography as methods for the accurate preoperative localization of hyperfunctioning parathyroid glands before parathyroidectomy.*
Methods. *A study of 75 patients with primary hyperparathyroidism was performed at a tertiary-care institution. Sestamibi imaging, ultrasonography, and 4D-CT were performed on each patient preoperatively. Results of the imaging studies were compared with operative findings, pathologic data, and biochemical measurements to assess the sensitivity and specificity of each of the imaging modalities.*
Results. *4D-CT demonstrated improved sensitivity (88%) over sestamibi imaging (65%) and ultrasonography (57%), when the imaging studies were used to localize (lateralize) hyperfunctioning parathyroid glands to 1 side of the neck. Moreover, when used to localize parathyroid tumors to the correct quadrant of the neck (ie, right inferior, right superior, left inferior, or left superior), the sensitivity of 4D-CT (70%) was significantly higher than sestamibi imaging (33%) and ultrasonography (29%).*
Conclusion. *4D-CT provides significantly greater sensitivity than sestamibi imaging and ultrasonography for precise (quadrant) localization of hyperfunctioning parathyroid glands. This allows improved preoperative planning, particularly for the case of reoperation. In addition to the data that are provided, we present a novel classification scheme for use in parathyroid localization. (Surgery 2006;140:932-41.)*

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The surgical treatment of primary hyperparathyroidism (PHPT) has changed significantly over the past decade. With the advent of improved preoperative imaging and the use of intraoperative parathyroid hormone (IOPTH) monitoring, standard cervical (or "4-gland") exploration has given way to directed or "minimally invasive" parathyroidectomy (DP) for the treatment of single-gland disease. Compared with 4-gland exploratory procedures, DP results in less cervical dissection, a smaller surgical incision, decreased postoperative pain, an earlier discharge from the hospital, and decreased cost; many patients may also avoid the use of general anesthesia.[1-4]

Good quality preoperative imaging is critical to a successful DP. Currently, most institutions use Tc-99m sestamibi scanning, either alone or in combination with ultrasonography, before the surgical treatment of PHPT.[5,6] Sestamibi imaging allows identification of hyperfunctioning parathyroid glands on the basis of their increased uptake of the radiotracer. The level of anatomic detail that is provided by this technique is somewhat limited; however, the addition of single photon emission computed tomography (sestamibi-SPECT) and conventional computed

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tomography (sestamibi-SPECT/CT) has allowed improvement in the resolution of this imaging modality. In contrast, ultrasonography provides good anatomic information about masses in the neck but is less informative about function. When used together, these imaging modalities complement each other and increase the success rate of DP.[6,7] Nevertheless, sestamibi imaging and ultrasonography may still be inadequate for preoperative localization in patients with a history of previous neck surgery, in patients with coexisting thyroid disease (eg, thyroid nodules or Hashimoto's thyroiditis), and in patients with an unfavorable body habitus (eg, obesity, short neck, or kyphosis). Because we see a large number of such patients at our institution, we sought an improved method of preoperative parathyroid imaging.

We chose to evaluate 4-dimensional computed tomography (4D-CT), an imaging modality that is similar to CT angiography. The name is derived from 3-dimensional CT scanning with an added dimension from the changes in perfusion of contrast over time. Four-dimensional CT generates exquisitely detailed, multiplanar images of the neck and allows the visualization of differences in the perfusion characteristics of hyperfunctioning parathyroid glands (ie, rapid uptake and washout), compared with normal parathyroid glands and other structures in the neck (Fig 1). The images that are generated by 4D-CT provide both anatomic information and functional information (based on changes in perfusion) in a single study that the operating surgeon can interpret easily.

The aim of the current study was to compare 4D-CT with sestamibi scanning and ultrasonography as a means of preoperative parathyroid localization in patients with PHPT. With the increased level of detail that is provided by 4D-CT, we have found that the terminology that surgeons and radiologists use to describe the location of parathyroid tumors is inadequate. We therefore present a parathyroid classification scheme for use in preoperative localization.

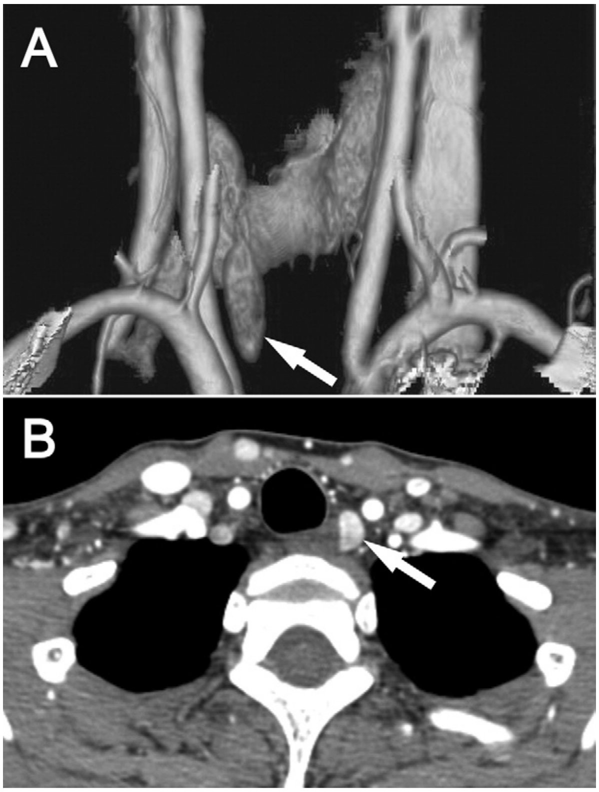

Fig 1. A, A 3-dimensional reconstruction of the neck based on 4D-CT imaging in a patient with a large (2.3 × 0.6 × 0.6 cm) left superior parathyroid adenoma (*arrow*). The bony structures and much of the soft tissue of the neck have been subtracted out, leaving only blood vessels, the thyroid gland, and the parathyroid tumor. **B,** An axial view of a 4D-CT showing the same large left superior parathyroid adenoma (*arrow*) in the tracheoesophageal groove.

METHODS

For the purposes of this paper, standard definitions of commonly used terms have been incorporated into Table I.

Patients. Data were collected on 75 patients with biochemically confirmed PHPT who underwent parathyroidectomy between August 2004 and October 2005. Forty-two patients were part of a prospective study that was approved by the Institutional Review Board of The University of Texas M.D. Anderson Cancer Center, and all of these patients provided informed consent for their participation. Institutional Review Board approval was obtained retrospectively to include an additional 33 patients who underwent 4D-CT, ultrasonography, and sestamibi scanning before parathyroidectomy.

Imaging techniques. Four-dimensional CT scanning was performed with a 16-row multidetector scanner (GE Lightspeed 16; General Electric, Fairfield, Conn) with the patient supine (head first). An 18-gauge angiocatheter was placed in an antecubital vein. Precontrast, postcontrast, and delayed images were obtained from the upper mediastinum to the lower margin of the mandible; 1.25-mm axial sections were reconstructed together with 2.5-mm sagittal, coronal, and oblique projections. Scanning parameters included a voltage of 140 kVp, a current of 220 mA, a pitch of 1.375, and a rotation time of 1 second; each patient received an injection (3 mL/sec) of 120 mL of iodinated contrast mate-

Table I. Commonly used terms for parathyroid disease

Term	*Clinical criteria*	*Biochemical criteria*	*Pathologic criteria*
PHPT	Hypercalcemia in the setting of an inappropriately elevated parathyroid hormone	Serum calcium: >10.2 mg/dL (normal 8.4-10.2 mg/dL) Parathyroid hormone: >50th percentile of the normal range[18] (normal, 10-65 pg/mL)	
Cure	IOPTH drop >50% at 5 or 10 minutes after excision of parathyroid gland(s)	Eucalcemia (≤10.2 mg/dL) 6 mo after operation	Histologic confirmation of gland hypercellularity and/or gland weight >40 mg
Single gland disease	IOPTH drop >50% at 5 or 10 minutes after excision of 1 gland	Eucalcemia (≤10.2 mg/dL) 6 mo after excision of 1 gland	Histologic confirmation of gland hypercellularity and/or gland weight >40 mg for 1 gland
Multigland disease	Multiple enlarged, hyperfunctioning glands	IOPTH drop <50% at 5 or 10 minutes after excision of only 1 gland	Hypercellularity of >1 gland
DP	Single gland excision with minimal dissection and exposure		
Precise localization	Preoperative localization of a gland to the exact position in the neck and determination of its relationship to surrounding structures		
Lateralization	Preoperative localization of a gland to the left or right of the midline		
Symptomatic PHPT	Biochemical PHPT with overt symptoms (eg, osteoporosis, nephrolithiasis, pancreatitis)	See PHPT above	
Asymptomatic PHPT	Biochemical PHPT without overt symptoms	See PHPT above	

PHPT, primary hyperparathyroidism; *IOPTH*, intraoperative parathyroid hormone; *DP*, directed parathyroidectomy.

rial (Optiray 300; Mallinckrodt, Hazelwood, Mo; 300 mg/mL), and postcontrast imaging began 25 seconds afterward.

Ultrasonography for this study was performed by the Department of Diagnostic Radiology at M.D. Anderson Cancer Center with a 7- to 13-MHz linear-array transducer (Aloka, Wallingford, Conn). Patients were imaged from the submandibular region to the clavicles. Color flow Doppler imaging was used to assess the vascularity of any suspicious lesions. Sestamibi imaging was performed by the Department of Nuclear Medicine. Patients received injections of 20 to 30 mCi of Tc-99m sestamibi; static images of the neck and chest were obtained immediately and 60 minutes after the injection. SPECT/CT was performed 30 minutes after injection.

All patients in the study underwent sestamibi scanning, ultrasonography, and 4D-CT of the neck. The sestamibi scans and ultrasonography studies were interpreted by radiologists who had access to both sets of images. However, in only a small number of cases did the radiologists who read the sestamibi scans or ultrasonography studies have access to the 4D-CT results. In 10 cases, the radiologists who interpreted the 4D-CT scans referred to the results of the sestamibi scan and/or ultrasonography. Otherwise, 4D-CT scans were interpreted independently without previous knowledge of other imaging studies. In all cases, the official reading that was provided by the radiologist in the patient's medical record was used to evaluate the accuracy of the imaging method.

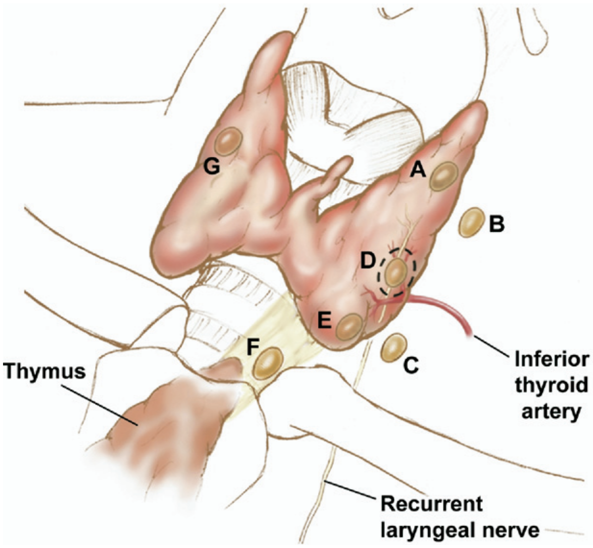

Fig 2. Schematic for categorization of the location of parathyroid glands. Type A: normal superior gland abutting the thyroid. Type B: superior gland posterior in the tracheoesophageal groove. Type C: superior gland posterior and inferior in the tracheoesophageal groove. Type D: superior or inferior gland at the junction of the recurrent laryngeal nerve and inferior thyroid artery. Type E: normal inferior gland abutting the thyroid. Type F: inferior gland in the thyrothymic ligament or superior thymus. Type G: intrathyroidal gland.

Surgical procedure. Depending on the results of preoperative imaging and the need for concomitant thyroid surgery, patients underwent either DP or a 4-gland exploration. Patients who underwent DP typically received local anesthesia with intravenous sedation, whereas patients who underwent a 4-gland exploratory procedure received general endotracheal anesthesia. For the purposes of this study, the locations of glands were recorded by the quadrant of the neck in which they were found (ie, left superior, left inferior, right superior, and right inferior). At the time of the procedure, superior and inferior parathyroid glands were defined by gland location and their relationship to the recurrent laryngeal nerve. Specifically, *superior glands* were defined as those glands with a vascular pedicle superior and lateral to the recurrent laryngeal nerve (type A through D glands; Fig 2). In some cases, a superior gland was found posterior to the recurrent laryngeal nerve in the tracheoesophageal groove (type C gland; Fig 2). *Inferior glands* were defined as those glands with a vascular pedicle inferior and medial to the recurrent laryngeal nerve (type D through F glands; Fig 2).

IOPTH monitoring was used to verify the removal of hyperfunctioning parathyroid glands. The IOPTH assay (Bayer Healthcare, Tarrytown, New York) was performed in the clinical laboratory of our hospital and required 18 minutes for completion. In most cases, the procedure was concluded when IOPTH values dropped by ≥50%, 5 minutes after excision. Hyperfunctioning glands were defined with the results of IOPTH measurements and histopathologic evaluation (eg, hypercellularity, paucity of fat, and gland weight). Biochemical cure was defined by eucalcemia 6 months after parathyroidectomy (Table I).

Statistical analysis. Results of the imaging studies, operative findings, pathologic data, and biochemical assessments were recorded for every patient. Based on a comparison between official radiologic reports and operative and histopathologic findings, true-positive, true-negative, false-positive, and false-negative results were recorded for all 75 patients for each of the 4 quadrants of the neck and for each side of the neck. The sensitivity and specificity of each imaging modality to localize hyperfunctioning parathyroid glands were calculated with conventional statistical definitions (sensitivity = [true positive/(true positive + false negative)] × 100; specificity = [true negative/(true negative + false positive)] × 100). The diagnostic units of study were the quadrant and side of the neck. The variance estimates for sensitivity and specificity were obtained with methods for clustered data, in which each cluster is a patient.[8] Data were analyzed with a *z*-test, and statistical significance was defined as a probability value of ≤.05.

Generalized linear models with generalized estimating equations were used to model single-variable effects of patient and parathyroid tumor characteristics on the probability of a true-positive result with 4D-CT. The patient and tumor characteristics that were analyzed were body mass index (BMI), history of thyroid disease, preoperative serum calcium level, preoperative intact parathyroid hormone (PTH) level, tumor size, and tumor weight. History of thyroid disease was treated as a categoric variable, whereas the remaining characteristics were treated as continuous variables. Before regression analysis, continuous variables were transformed with the natural logarithm to adjust for the significant skewness that was observed. Patient weight was not included in the regression analysis because it was highly correlated with BMI.

Parathyroid classification system. We introduce here a classification system that is based on the most frequently encountered positions of enlarged parathyroid glands (Fig 2). This classification scheme can be used both preoperatively, based on the anatomic detail provided by 4D-CT images, and in the operative record, based on intraoperative findings. In this classification scheme, a type A gland is a "normal" superior gland in proximity to the posterior surface of the thyroid parenchyma. It may be compressed within the capsule of the thyroid. A type B gland is a superior gland that has fallen posteriorly into the tracheoesophageal groove. There is minimal or no contact between the gland and the posterior surface of the thyroid tissue. On lateral views, the gland is in the plane of the superior pole of the thyroid. An undescended gland high in the neck near the carotid bifurcation or mandible may also be classified as a type B gland. A type C gland is a superior gland that has fallen posteriorly into the tracheoesophageal groove and lies at the level of or below the inferior pole of the thyroid. This places the type C gland posterior to and in many cases inferior to the recurrent laryngeal nerve. Glands in the carotid sheath are either type B or C glands, depending on their craniocaudal relationship to the thyroid. The type D gland ("difficult" or "dangerous") lies in the mid region of the posterior surface of the thyroid parenchyma, near the junction of the recurrent laryngeal nerve and the inferior thyroid artery. The type D gland may be either a superior or inferior gland, depending on its exact relationship to the nerve, which generally cannot be determined on imaging. The type E gland is an inferior gland in close proximity to the inferior pole of the thyroid parenchyma, lying in the anterior-posterior plane of the thyroid and anterior to the trachea. The type F gland is an inferior gland that has descended into the thyrothymic ligament or superior thymus. It may appear to be "ectopic" or within the mediastinum. An anterior-posterior view shows the type F gland to be anterior to and near the trachea. Finally, the type G gland is a rare intrathyroidal parathyroid gland.

RESULTS

Patients. Demographic and laboratory data are provided in Table II. The median age of patients at diagnosis was 60 years (range, 27-83 years), and the female-to-male ratio was 5.3 to 1. The median patient weight was 79.5 kg (range, 41.4-162.0 kg), and the median BMI was 29.5 kg/m^2 (range 17.8-67.4 kg/m^2). The median preoperative serum calcium level was 10.9 mg/dL (range, 9.7-16.0 mg/dL; normal, 8.4-10.2 mg/dL). The median preoperative PTH level was 118 pg/mL (range, 60-524 pg/mL; normal, 10-65 pg/mL). The median percentage drop in IOPTH level was 82% (range, 51%-99%). Twenty-two patients (29%) had a history of coexisting thyroid disease, and 12 patients (16%) had a history of previous neck surgery (8 patients had undergone thyroidectomy; 2 patients had undergone cervical laminectomy by an anterior approach; 1 patient had undergone carotid endarterectomy; and 1 patient had undergone a pre-referral parathyroidectomy). Forty-seven patients (63%) had a history of osteoporosis. Fourteen patients (19%) had a history of nephrolithiasis. The median size of parathyroid tumors that were resected was 1.5 cm (range, 0.4-5.0 cm) in greatest dimension, and the median tumor weight was 530 mg (range, 75-8330 mg). No patient had parathyroid carcinoma.

Table II. Patient and disease characteristics (n = 75)

Variable	*Measure*
Sex (n)	
Male	12 (16%)
Female	63 (84%)
Age (y)*	60 (27-83)
Weight (kg)*	79.5 (41.4-162.0)
BMI (kg/m^2)*	29.5 (17.8-67.4)
Tumor size (cm)*	1.5 (0.4-5.0)
Tumor weight (mg)*	530 (75-8,330)
Patients with thyroid disease (n)	22 (29%)
Patients with previous neck surgery (n)	12 (16%)
Peak preoperative serum calcium (mg/dL)*†	10.9 (9.7-16.0)
Peak preoperative parathyroid hormone (pg/mL)*‡	118.0 (60-524)
Drop in IOPTH (%)*	82 (51-99)

*Data are presented as median (range).
†Normal, 8.4 to 10.2 mg/dL.
‡Normal, 10-65 pg/mL.

Surgery. Of the 75 patients in this study, 61 patients underwent a planned DP. Five of these patients were converted to a standard cervical exploration. Two conversions were due to the presence of unanticipated multigland disease (see definition in Table I); 2 conversions were due to incorrect preoperative localization of an adenoma (ie, to the wrong side); and 1 conversion was due to a suspicious thyroid nodule that required thyroid lobectomy. Twelve patients underwent planned standard cervical explorations because of the suspicion of multigland disease or the need for concomitant thyroid operation. Eleven patients (15%) had multigland disease. One patient underwent a planned thoracoscopic mediastinal exploration for the removal of an intrathymic adenoma. One patient had persistent hyperparathyroidism after a DP with excision of a single parathyroid gland and required re-operation with exploration of the contralateral

Table III. Sensitivity and specificity of imaging modalities for localization of parathyroid tumors to side of the neck and quadrant of the neck

Variable	*Sensitivity (%)*	*95% CI*	*Specificity (%)*	*95% CI*
Side of the neck				
4D-CT	88	81-95	88	80-96
Ultrasonography	57	47-67	94	88-99
Sestamibi	65	55-75	88	80-96
Precise location in the neck				
4D-CT	70	59-81	89	85-93
Ultrasonography	29	20-38	86	82-90
Sestamibi	33	24-42	83	79-87

side of the neck. In this case, the pre-incision IOPTH value fell within the normal range; therefore, the percentage of the drop in IOPTH was not felt to be a reliable guide. No other patients were found to be hypercalcemic at the time of their 6-month follow-up evaluation.

Imaging findings. For all 75 patients, the sensitivity of 4D-CT, ultrasonography, and sestamibi for localization of hyperfunctioning glands to the correct side of the neck was 88%, 57%, and 65%, respectively; specificity was 88%, 94%, and 88%, respectively (Table III). In contrast, the sensitivity of 4D-CT, ultrasonography, and sestamibi for defining the precise location of all hyperfunctioning parathyroid glands was 70%, 29%, and 33%, respectively; specificity was 89%, 86%, and 83%, respectively (Table III). Differences in sensitivity between 4D-CT and the other 2 imaging modalities were statistically significant ($P < .0001$), but differences in sensitivity between ultrasonography and sestamibi were not statistically significant. With the exception of 4D-CT versus sestamibi imaging for quadrant localization of hyperfunctioning parathyroids ($P = .027$), there were no statistically significant differences in the specificity of the 3 imaging modalities.

In the 11 patients with multigland disease, 4D-CT predicted the involvement of >1 gland in 5 patients (45%). In 3 of these patients, 4D-CT correctly identified all of the diseased glands. In contrast, ultrasonography recognized >1 enlarged parathyroid gland in none of these patients (0%), whereas sestamibi predicted the involvement of >1 gland in only 1 patient (9%).

Factors that affected the accuracy of 4D-CT. Univariate analysis was performed to determine whether patient or tumor characteristics had any measurable effect on the ability of 4D-CT to localize hyperfunctioning parathyroid glands correctly. With a generalized linear model approach for univariate logistic regression analysis, only tumor size had a statistically significant effect that was sufficient to model its association with the odds of a true positive 4D-CT result with a single, linear term (odds ratio, 3.03; $P = .03$). However, with a more complex quadratic regression model, 2 additional variables (BMI and preoperative PTH level) exhibited a statistically significant relationship with the odds of a true-positive 4D-CT result ($P = .049$ and .013, respectively). In each of these cases, lower values for the variable were associated with an odds ratio >1, whereas, higher values for the variable were associated with an odds ratio <1 (Fig 3).

Parathyroid classification. Using the parathyroid classification scheme outlined earlier, we assigned a gland type (A through G) to the 64 patients in this study with single-gland adenomas. The distribution of gland types is given in Table VI.

DISCUSSION

Most studies in the literature that address parathyroid imaging report the ability of an imaging modality to localize (lateralize) parathyroid tumors to the correct side of the neck.[6,9-14] Sensitivity for lateralization by ultrasonography varies from 61% to 88%,[6,9-14] whereas sensitivity for lateralization by sestamibi varies from 68% to 86%.[6,9,10,12,13] Using lateralization to measure the performance of preoperative imaging modalities in the current study, we achieved a sensitivity of 88% for 4D-CT, 57% for ultrasonography, and 65% for sestamibi.

For a truly directed surgical approach, we believe that preoperative imaging techniques should not only identify the correct side of the neck but also should define the precise location of a parathyroid tumor within the neck. Therefore, we analyzed the ability of 4D-CT, ultrasonography, and sestamibi to localize hyperfunctioning parathyroid glands to the correct quadrant (ie, left superior, left inferior, right superior, and right inferior). With these criteria, 4D-CT had a sensitivity of 70%, whereas ultrasonography and sestamibi had sensi-

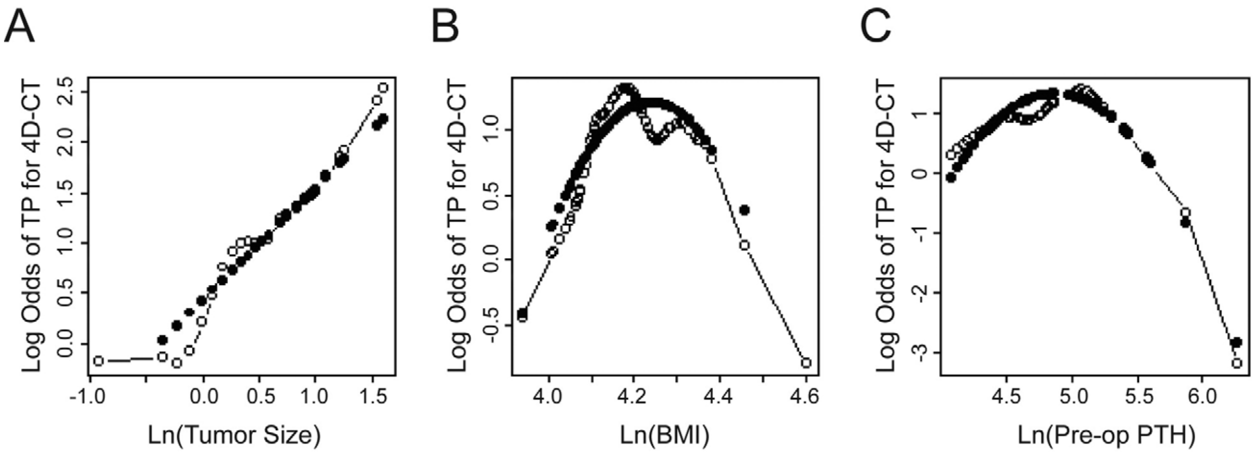

Fig 3. Comparison of patient and tumor variables with the log odds of a true-positive (*TP*) result for precise localization by 4D-CT. *Open circles* are nonparametric representations of the data. *Closed circles* represent fitted logistic regression estimates. For tumor size **(A),** a linear regression equation was adequate to model the data. For BMI **(B)** and preoperative PTH level **(C),** a quadratic term was necessary to model the data. *Ln*, Natural logarithm.

Table IV. Gland types in patients with single-gland adenomas (n = 64)

Gland type	*N (%)*
A	17 (27)
B	14 (22)
C	4 (6)
D	3 (5)
E	20 (31)
F	6 (9)
G	0

tivities of 29% and 33%, respectively. These numbers are difficult to compare with previously published results because few studies report localization to a specific quadrant of the neck and the statistical methods that were used in these studies vary.[7,15-17]

The recognition of multigland disease in patients with PHPT poses a challenge for preoperative imaging techniques. In our study, 11 of 75 patients (15%) had multigland disease. Four-dimensional CT identified ≥2 glands in 5 of these patients (45%). This was in sharp contrast to sestamibi, which identified ≥2 glands in only 1 patient (9%) from this population. Ultrasonography was not able to recognize multigland disease in any of these patients. The finding of multigland disease on preoperative 4D-CT changed the operative approach (ie, from a DP to a 4-gland exploration) in 2 cases. Such preoperative information is extremely useful for planning operative logistics, such as operating room time, type of anesthesia, anticipation of an overnight stay, and the need for IOPTH measurement.

The finding on univariate analysis that increased tumor size is associated with the ability of 4D-CT to localize hyperfunctioning parathyroid glands is not surprising. We would expect larger glands to be identified more easily on cross-sectional imaging. The complex relationships between the ability of 4D-CT to localize hyperfunctioning parathyroid glands and the variables of BMI and preoperative PTH level are more difficult to explain. The data suggest that, at lower levels, each of these variables is correlated positively with the odds of a true-positive 4D-CT result. However, at higher levels, these 2 variables are negatively correlated with the ability of 4D-CT to identify the correct quadrant of the neck. For BMI, this may represent the fact that there is an "ideal" body size for 4D-CT and that the accuracy of 4D-CT decreases for patients above or below this preferred body size.

In the current study, we provide data to support the contention that 4D-CT is superior to ultrasonography and sestamibi for preoperative localization. Furthermore, we believe that the use of 4D-CT allows the surgeon to perform a true DP and that this results in decreased operative time, reduced postoperative pain, limited dissection within the neck, and the use of a smaller incision. In this study, we were not able to assess these outcome measures for the various imaging modalities because all patients received each of the 3 imaging studies. However, a randomized comparison of 4D-CT alone to the combination of ultrasonography and sestamibi may be warranted.

Four-dimensional CT offers improved preoperative imaging because it combines in a single-study functional analysis of parathyroid glands (with perfusion as a marker of function) and detailed cross-sectional imaging. The images that are generated by 4D-CT help guide both incision placement and dissection. Additional information that can be ascertained from 4D-CT includes the location of the parathyroid gland pedicle, the presence of glands within the thyroid capsule, and the presence of glands within the carotid sheath or in the para-esophageal space. Although such information traditionally has not been thought necessary for the experienced endocrine surgeon, the addition of such data allows for better preoperative planning and a truly directed operative procedure. These advantages are particularly important in cases of reoperative surgical procedures, where scar tissue and the loss of surgical planes may increase operative morbidity. Additionally, 4D-CT images provide excellent documentation of tumor location and are interpreted more easily by surgeons, who are accustomed to reading CT-based cross-sectional imaging.

As methods of preoperative parathyroid imaging have improved, a need has arisen for a system of reproducible terminology to be used by the radiologist and the surgeon. Because of variations in the migration of parathyroid glands during embryologic development, the use of the terms *inferior* and *superior* do not provide a 3-dimensional description of parathyroid gland location. These terms are usually based on the 2-dimensional radiologic impression that an enlarged parathyroid gland is low or high in the neck. For example, ultrasonography and sestamibi reports may imply that a parathyroid gland is an inferior gland because it is "near the lower pole of the thyroid." In many cases, such a gland is a superior parathyroid gland lying posteriorly in the tracheoesophageal groove. Given a more precise description of this gland's location, the surgeon might choose to perform a DP using a lateral approach (between the lateral border of the strap muscles and the medial border of the sternocleidomastoid). In such cases, this lateral entry into the tracheoesophageal region provides a more direct approach, which often allows improved visualization of the recurrent laryngeal nerve and decreases the risk of inadvertent nerve injury.

It is our belief that the parathyroid classification scheme presented here will serve as a script for further discussion of gland location. This system eliminates the abundance of adjectives that are necessary to describe the 3-dimensional location of enlarged parathyroid glands and provides consistency in reports of preoperative imaging.

In summary, 4D-CT is a unique tool that enables precise preoperative localization of hyperfunctioning parathyroid glands. As a single study that assesses both anatomy and function, 4D-CT may serve an important role in localization before both initial and reoperative parathyroid procedures. We introduce a classification system that offers standard terminology for the description of parathyroid gland location and that may allow improved communication between the radiologist and the surgeon.

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DISCUSSION

Dr Janice L. Pasieka (Calgary, Alberta, Canada): I am quite interested by this new technology. Did the group of patients all have PHPT and all single-gland disease?

Dr Rodgers: No, no. They all had PHPT, but approximately 15% of them had multigland disease.

Dr Pasieka: You said that this 4D-CT gives us functional data. How do you really know that the gland that is seen is secreting PTH? And what were the results of the patients with multigland disease? Were all 4 glands lighting up on the scan, and can this technology really extrapolate that they are truly hyperfunctional?

Dr Rodgers: The exact reason that there are changes in perfusion of the diseased glands is unclear, but most likely it is the result of increased vascularity. Just as with ultrasonography, not at our institution, but at some institutions, they report increased vascularity and you know that that is the diseased gland. In the operating room, we are using IOPTH at least to confirm intraoperatively that we have taken out the correct gland. We find that diseased gland in the location that was identified by 4D-CT, and we see a drop in IOPTH.

Dr Pasieka: I understand that. It is just that you said that this technology is giving us functional data, and really it is telling us the most vascular gland. How do you know that this is the gland that is functioning autonomously?

Dr Rodgers: That is a good point. We have been discussing ways to figure out exactly the reason that we are seeing increased perfusion and to link that to increased function. But the assumption is that those are hyperfunctioning glands, and when we take them out, IOPTH drops.

Dr Pasieka: In the group that had multigland disease, did all 4 glands have this functional or hypervascularity on your imaging?

Dr Rodgers: No, certainly not. Just like with sestamibi and ultrasonography, I think multigland disease is the hardest to image. But what we found was that, if 3 or 4 glands were diseased, we would pick up maybe 2 on the 4D-CT, sometimes 3.

Dr Pasieka: You have not figured it out for us yet?

Dr Rodgers: Exactly. But I would say that I think we do better than sestamibi for multigland disease, certainly.

Dr Anders Bergenfelz (Sweden): I commend you really for this study, and I find the results intriguing.

We recently performed a survey over the sestamibi sensitivity all over the Scandinavian area. We actually found that the sensitivity in this setting was approximately 65%, including most of the major university hospitals. We also analyzed the way sestamibi was performed with washout technique, sestamibi-SPECT or no SPECT, and we did not find a difference. The only difference was actually the gland size.

In the future when you are reporting not only in this study but other studies, it is very important to inform the audience about the actual gland size. Because if you are operating in patients with a very large gland, you will have the high sensitivity. In Scandinavia about one-quarter of our patients had adenomas of <250 milligrams.

Is there a difference? Were the glands that you did not pick up here small glands? What is the cost for this new investigation?

Dr Rodgers: I did not present it here just in the interest of time, but we did a univariate analysis that considered patient weight, BMI, preoperative calcium level, preoperative PTH level, gland size, and gland weight. None of them were statistically significant. Although gland size had the highest odds ratio, it just was not statistically significant. So I did not present it here. That may have to do with the number of patients that we had in the study, and with more patients we would pick up those correlations.

And then the cost: the radiologists at M.D. Anderson are going to kill me, they do not like to us name numbers. The charge to the patient for the 4D-CT is approximately $2600. Every sestamibi imaging done at M.D. Anderson is sestamibi-SPECT CT and is $3500. The ultrasound imaging of the neck is the cheapest at $500 to $515.

Dr William B. Inabnet, III (New York, NY): As with ultrasound and sestamibi scanning, the quality of the CT scanning of the parathyroid glands is highly variable and varies from institution to institution. For example, regular CT scanning uses

5-mm cuts; however, to visualize the parathyroid glands adequately on CT scanning, 1.5-mm cuts are required. Also, the study must be read by a dedicated radiologist who has an interest in parathyroid imaging.

With regards to the M.D. Anderson technique, what size slices do you use during parathyroid CT scanning?

Dr Rodgers: It is exactly what you said, it was 1.5-mmcuts. For the most part, most of our scans had been led by a single radiologist, actually a small group of radiologists who were led by 1 radiologist who developed the 4D-CT.

Dr Inabnet: That is an extremely important point. Because if the audience leaves thinking they can order a CT scan of the parathyroid glands, they will be greatly disappointed. It requires a collaborative effort.

Did you find that clips from the previous operations or dental hardware affected the reading of the interpretation of your scans?

Dr Rodgers: That is a good question. I have looked at many of the scans, and I have never had a problem with artifact from clips or anything. Titanium clips, for example, have very little, if any, artifact; the older clips have some artifact.

Dr Carmen C. Solorzano (Chicago, Ill): Those are beautiful CT scans that are probably not available at many other institutions. I wish I had this technology available in a recent reoperative case because I think this is where it is going to play the biggest role.

I have a short question regarding cervical ultrasound scans. Cervical ultrasound scanning can give you very good anatomic information as to where the parathyroid is, at least in my personal experience. We recently reported our results of surgeon-performed ultrasound scans, with a sensitivity of 77%. With ultrasound scanning, we could pinpoint exactly where to go. You can even take it to the operating room.

I would like you to comment on how you use the ultrasound information that your radiologist provides and to compare it to the results of this technology. I know the M.D. Anderson radiologists are very good and very dedicated to this.

Could you also give us more information as to how this 4D-CT scan, like Dr Pasieka asked, performed in multiglandular disease, because I think that is the crux of preoperative localization problem, and how the IOPTH hormone helped or did not help you in that situation.

Dr Rodgers: Regarding your question about ultrasound scanning, we are not performing the ultrasound scanning ourselves, the radiologists are doing it. In my short time at M.D. Anderson, I have seen that the information that comes from ultrasound scanning has not been very useful. However, I think that it is getting better. But that is one of the things that led us to use 4D-CT.

I completely agree that multigland disease is an important issue. I would say again that I did not show data specifically on multigland disease, but I think that 4D-CT may prove to be a better imaging modality than the others for that entity.