



Intraoperative Ultrasound and Reoperative Parathyroid Surgery: An Initial Evaluation

Jeffrey A. Norton, M.D., Thomas H. Shawker, M.D., Bonnie L. Jones, B.S., Allen M. Spiegel, M.D., Stephen J. Marx, M.D., Lorraine Fitzpatrick, M.D., Gerald D. Aurbach, M.D., and John L. Doppman, M.D.

Surgery Branch, National Cancer Institute, Department of Radiology, Clinical Center, and Metabolic Diseases Branch, National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases; National Institutes of Health, Bethesda, Maryland, U.S.A.

We compared intraoperative ultrasound (IOUS) to preoperative high-resolution real-time ultrasound in 25 consecutive patients undergoing reoperations for primary hyperparathyroidism. Intraoperative neck scanning was performed after the platysma muscle flaps were raised, and one or both sides of the neck were opened along the medial border of the sternocleidomastoid muscle. Preoperative localization studies were used to determine which side of the neck to explore. Pathologic parathyroid glands appeared sonolucent on both pre- and intraoperative ultrasound. Glands were always imaged in 2 planes.

Neither preoperative nor intraoperative scans were able to image normal parathyroid glands. Preoperative scans were correct for abnormal tissue in 9 patients, and intraoperative scans were correct in 19 patients ($p = 0.01$). Size of a pathologic parathyroid gland was not a factor in the ability of IOUS to detect it, but location was. Intrathyroidal and inferior glands were detected reliably, but superior glands were missed (33%). If IOUS imaged the pathologic parathyroid tissue, the length of the surgical procedure was significantly reduced [5.9 hours versus 3.1 hours ($p = 0.005$)]. IOUS did not appear to impact on ultimate outcome as 5 of 6 patients in whom IOUS failed to image the pathologic gland had successful surgery without complication.

Persistent or recurrent hyperparathyroidism, following cervical or mediastinal exploration for pri-

mary hyperparathyroidism occurs in approximately 15% of initial procedures and perhaps more frequently [1-3]. The subsequent care of these patients remains a challenge for the internist, radiologist, and surgeon [2, 4, 5]. Success rates for reoperative parathyroid surgery have been reported to vary from 64% [4] to 95% [6] depending on the series and the criteria for exclusion of failures. Furthermore, parathyroid reoperations are long and tedious with higher morbidity than initial operations [7].

In 1979, high-resolution, real-time B-mode ultrasonography showed remarkable promise, when it correctly imaged the abnormal parathyroid gland location in 10 selected patients preoperatively [8]. In response to this preliminary study, Egdahl stated that preoperative localization studies might be helpful in parathyroid patients who had had a previous neck exploration [9]. However, in subsequent studies, ultrasound for preoperative parathyroid localization has not been as helpful. In studies of patients requiring reoperations for primary hyperparathyroidism, preoperative ultrasound was correct in

Table 1. Diagnosis, number of abnormal glands, and outcome of 25 patients undergoing repeat parathyroid exploration.

Diagnosis	No. of patients	No. of abnormal glands ^a	Successful outcome
Adenoma	22	22	21
Hyperplasia	3	5	3

^aTwenty-seven is believed to be the total number of abnormal parathyroid glands. Only 26 were removed; 1 suspected parathyroid adenoma is included but has not been found.

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Reprint requests: Jeffrey A. Norton, M.D., Head, Surgical Metabolism Section, Surgery Branch, National Cancer Institute, Building 10, Room 2B04, Bethesda, Maryland 20205, U.S.A.

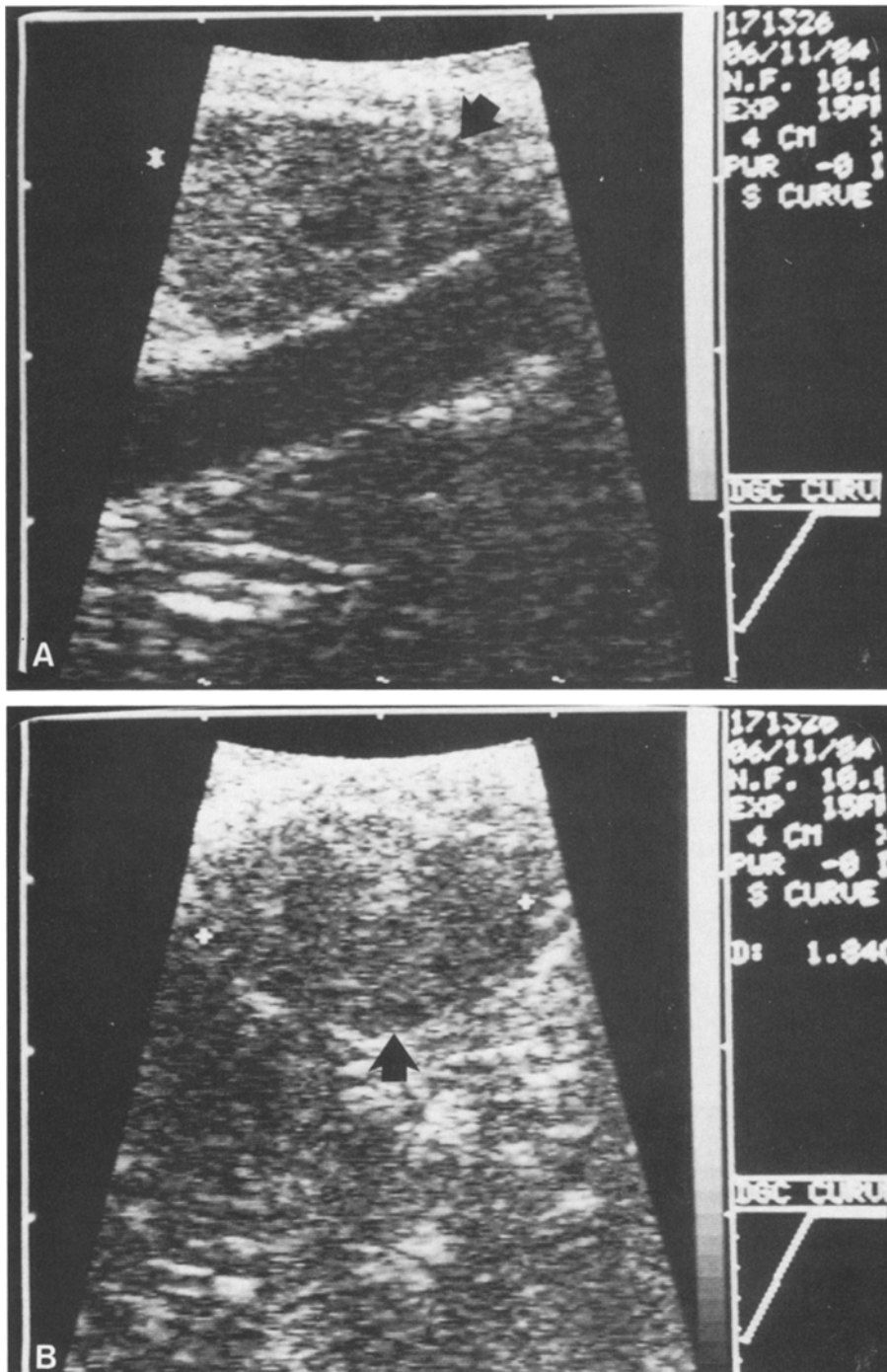


Fig. 1. Sagittal (A) and transverse (B) intraoperative ultrasound scans of an abnormal inferior gland. Scan demonstrates importance of imaging abnormal gland in 2 dimensions. Parathyroid adenoma appears sonolucent.

59% [3], 50% [10], and as low as 32% [11] in our own series.

Recently, intraoperative ultrasound (IOUS) has been used to image islet cell tumors of the pancreas [12], and it has even imaged a small insulinoma in the pancreatic head which was not palpable or seen on selective arteriography [13]. Intraoperative ultrasound successfully imaged an abnormal parathyroid gland in a patient undergoing an initial neck

exploration [14], and it successfully helped guide the resection of a parathyroid adenoma that had been missed at 2 prior neck explorations [15]. Except for a solitary patient, the use of intraoperative ultrasound has not been reported in patients undergoing reoperations for primary hyperparathyroidism.

In this study, we describe our results with IOUS in 25 consecutive patients undergoing neck

reexploration. Intraoperative ultrasound imaged more abnormal glands than preoperative ultrasound. It aided dissection and shortened operative time. It did not appear to affect ultimate outcome because 5 of 6 patients imaged with IOUS, but in whom no abnormal gland was found, still had successful procedures.

Methods

We studied 25 consecutive patients undergoing neck reexplorations for primary hyperparathyroidism from April, 1984, to August, 1985. All patients had undergone at least 1 neck and/or mediastinal exploration for primary hyperparathyroidism. The diagnosis was confirmed in all patients by serum calcium levels and parathyroid hormone levels, as well as urinary cAMP and calcium levels. Twenty-two patients had persistent postoperative disease and 3 patients had recurrent primary hyperparathyroidism meaning that they had had a 6-month period of normal or low serum calcium levels following initial exploration. Preoperative parathyroid localization studies, including computed tomography, magnetic resonance imaging, technetium-thallium scanning, ultrasound, arteriography, and venous sampling were performed. Some patients did not undergo all localization procedures.

Preoperative ultrasound scans were performed using 7.5- and 10-MHz transducer on real-time ultrasound units (ATL MK600 and Diasonics RAI). Scanning was performed with continuous visualization (real-time) in the transverse and sagittal planes. No water bag was utilized. All preoperative localization studies were reviewed and used to determine which side of the neck to explore initially. Intraoperative ultrasound scanning was performed after the platysma muscle flaps were raised, and one side of the neck was opened along the medial border of the sternocleidomastoid muscle. If the preoperative studies failed to localize abnormal parathyroid tissue to one side of the neck, intraoperative ultrasound scans were performed after opening both sides of the neck. Intraoperative scanning was performed using a real-time 10-MHz small parts unit (Diasonics). Real-time scanning was performed with continuous visualization in the transverse and sagittal planes through saline poured into the operative field. Pathologic parathyroid glands appeared sonolucent (hypoechoic) on both pre- and intraoperative studies. Glands were always imaged in 2 planes. IOUS added approximately 15 minutes to the operative procedure.

All pathologic parathyroid glands removed were measured and their location was recorded. Surgical

Table 2. Comparison of preoperative to intraoperative ultrasound.

Total no. of patients	Preoperative ultrasound imaged	Intraoperative ultrasound imaged
25	9	19 ^a

^aSignificantly greater than preoperative scans. $p = 0.01$ (chi-squared analysis).

procedure was terminated if 1 normal and 1 abnormal gland was biopsy proven (including initial exploration if pathologic slides and dimensions had been reviewed at our institution) or if intraoperative urinary cAMP levels dropped 50% from the median baseline level [16]. Length of operative procedure was recorded in hours as time from skin incision to wound closure.

Surgical outcome was defined as successful if serum calcium levels fell to normal or less for at least 14 postoperative days. Final pathologic finding was considered adenoma if only 1 abnormal gland was accounted for at all surgical procedures and outcome was successful, or hyperplasia if more than 1 abnormal parathyroid gland was accounted for. All data are presented as either absolute numbers or mean \pm SEM. Data are analyzed by independent *t*-tests, and chi-squared.

Results

Twenty-four of 25 patients underwent successful parathyroid reoperations (Table 1). Three patients had a final diagnosis of hyperplasia, and 22 patients had parathyroid adenomas. One patient presumed to have a parathyroid adenoma had an unsuccessful reexploration, and suffered an injury to the recurrent laryngeal nerve (only complication in this series). The majority (75%) of patients had pathologic parathyroid tissue localized by all the preoperative studies.

Abnormal parathyroid glands were imaged in 2 planes (sagittal and transverse) by both preoperative and intraoperative ultrasound (Fig. 1). Intraoperative ultrasound scans correctly imaged more patients with abnormal glands (76%) than preoperative scans (36%, $p = 0.01$) (Table 2). Preoperative ultrasound had a much greater false-positive rate (28%) than IOUS (4%). Neither preoperative nor intraoperative scans imaged normal parathyroid glands.

Intraoperative ultrasound was able to image small abnormal glands (Fig. 2). There was no significant difference in size between abnormal glands that were correctly imaged by intraoperative ultrasound

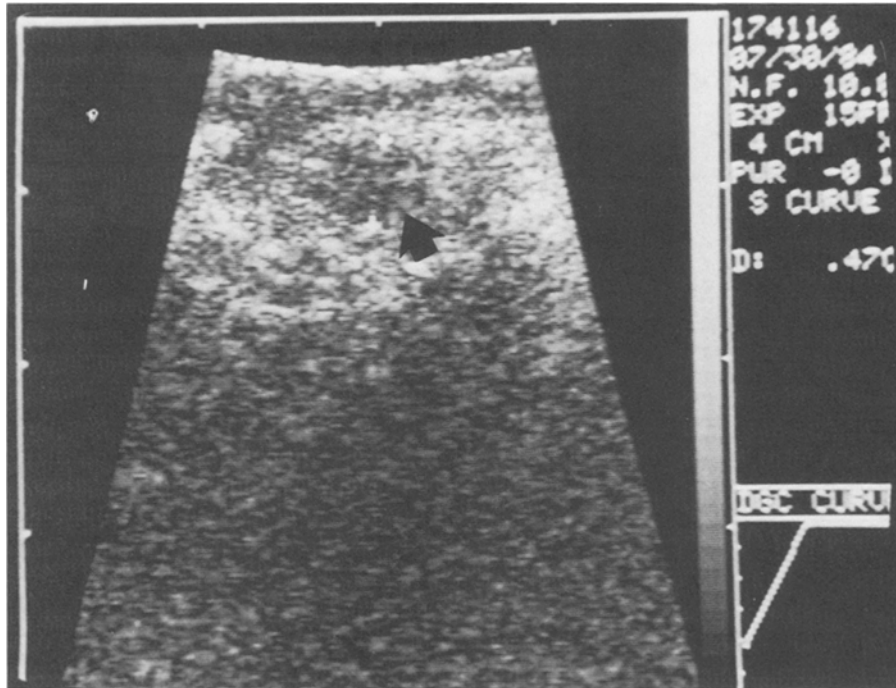


Fig. 2. Sagittal intraoperative scan of a 0.5 cm inferior parathyroid adenoma. Parathyroid adenoma appears sonolucent and scan demonstrates ability to detect small abnormal glands.

Table 3. Size and location of abnormal parathyroid gland and ability of intraoperative ultrasound to image.

Abnormal gland imaged	Size (cm ³)	Location		
		Superior	Inferior	Intrathyroid
Yes	5.7 ± 2.0 ^a	11	8	3
No	3.9 ± 2.1	5	0	0

^aData presented as mean ± SEM and no difference between 2 groups. One abnormal gland, which was not imaged, was not found.

and abnormal glands that were missed (Table 3). Inferior and intrathyroidal abnormal parathyroid glands were imaged with high specificity and sensitivity by intraoperative ultrasound. There were no incorrect images of an abnormal gland in these positions. Figure 3 demonstrates an intrathyroidal parathyroid adenoma, which was removed by incising into the thyroid and enucleating instead of performing a complete lobectomy. Figure 4 represents a remarkable intrathyroidal abnormal gland that required a complete lobectomy. After serial cross sections of the lobe at 5-mm intervals, no fresh abnormal parathyroid tissue could be recovered by the surgeon or the pathologist; however, permanent sections showed a 5-mm intrathyroidal parathyroid adenoma, and the serum calcium level fell to less than 8 mg/100 ml.

Intraoperative ultrasound had more difficulty imaging abnormal superior parathyroid glands (Table 3). All the abnormal glands missed were superior

glands, and the intraoperative study was able to detect only two-thirds of abnormal superior glands. This was even more discouraging when one found that 4 of 5 glands missed were in the usual anatomic position underneath the superior pole of the thyroid. The final one was more cephalad as an undescended parathyroid.

The total time of operation was examined as a function of whether the intraoperative ultrasound imaged an abnormal parathyroid gland or not (Table 4). If the intraoperative ultrasound correctly imaged an abnormal parathyroid gland, the length of the operative procedure was reduced by nearly 50%. This was a significant reduction in operating room time ($p = 0.005$); however, the absolute outcome was not affected by intraoperative ultrasound as 5 of 6 patients in whom intraoperative ultrasound failed to detect an abnormal gland still had a successful procedure.

Intraoperative ultrasound had a high specificity rate. Only 1 false positive was detected which was a lymph node. One would expect some intrathyroidal false positives, but that was not found. Only 1 patient with hyperplasia had more than 1 abnormal gland (3), and intraoperative ultrasound correctly imaged all 3 glands in this patient.

Discussion

In this preliminary study, high-resolution real-time ultrasonography is used primarily as a surgical tool

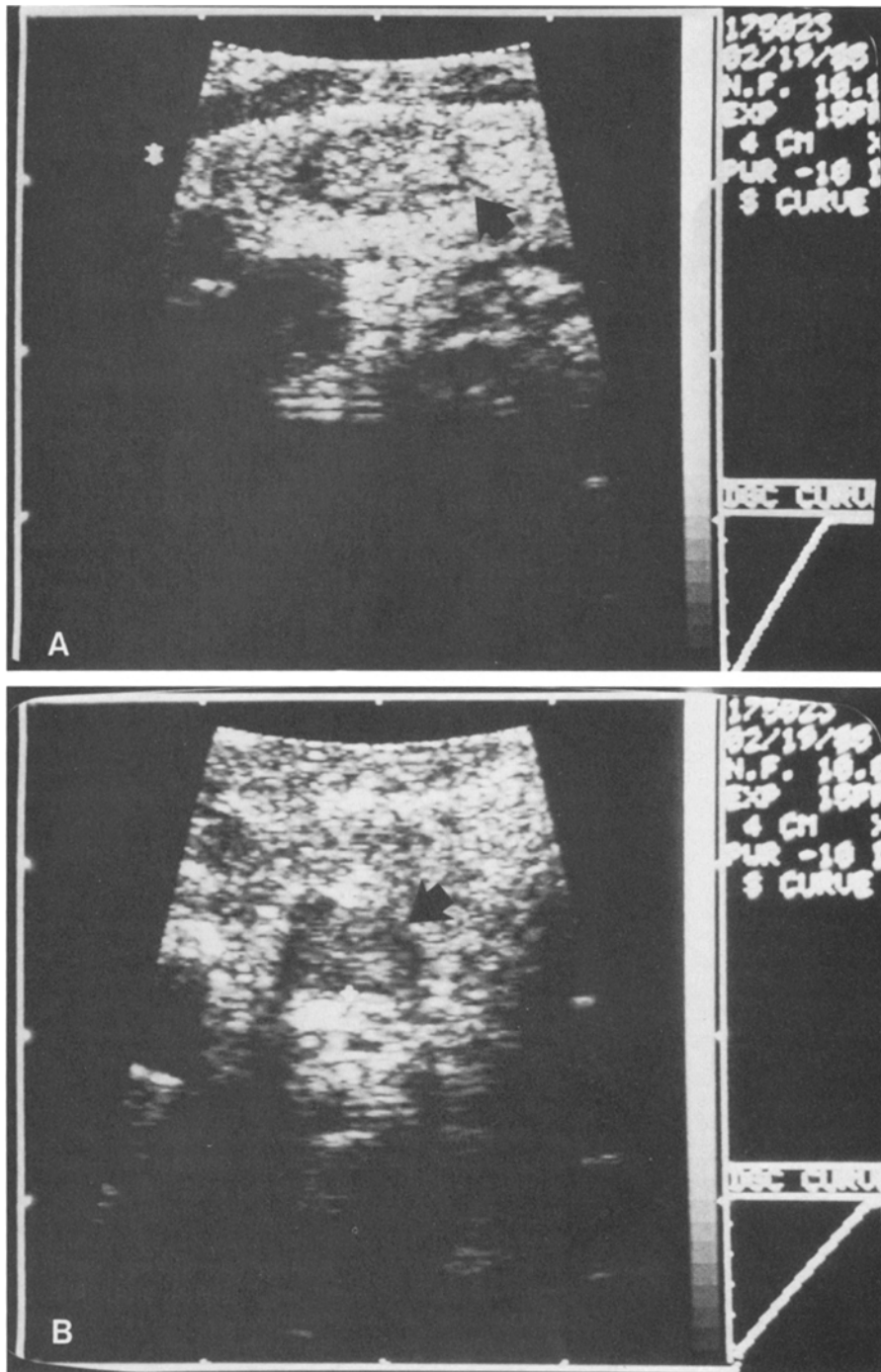


Fig. 3. Sagittal (A) and transverse (B) intraoperative scan of an intrathyroidal parathyroid adenoma. Intrathyroidal parathyroid adenoma appears sonolucent compared to the more echoic thyroid. This adenoma was enucleated instead of performing a thyroid lobectomy.

as in several other recent studies [12–15, 17]. The instrument is handled by the operating surgeon who knows the results of all the preoperative localization procedures. Since reoperations for hyperparathyroidism are extremely difficult with dense scar tissue obliterating normal planes and making dissection tedious and hazardous, the surgeon asks whether IOUS can image the abnormal parathyroid to facilitate dissection, allowing the dissection to

progress immediately to the abnormal tissue. Initial neck explorations can be performed safely and simply by experienced surgeons [18–20]; it is unlikely that IOUS would add anything to initial procedures.

In this study including only parathyroid reoperations, IOUS did appear to help facilitate dissection and more rapidly locate abnormal tissue. When compared to preoperative high-resolution

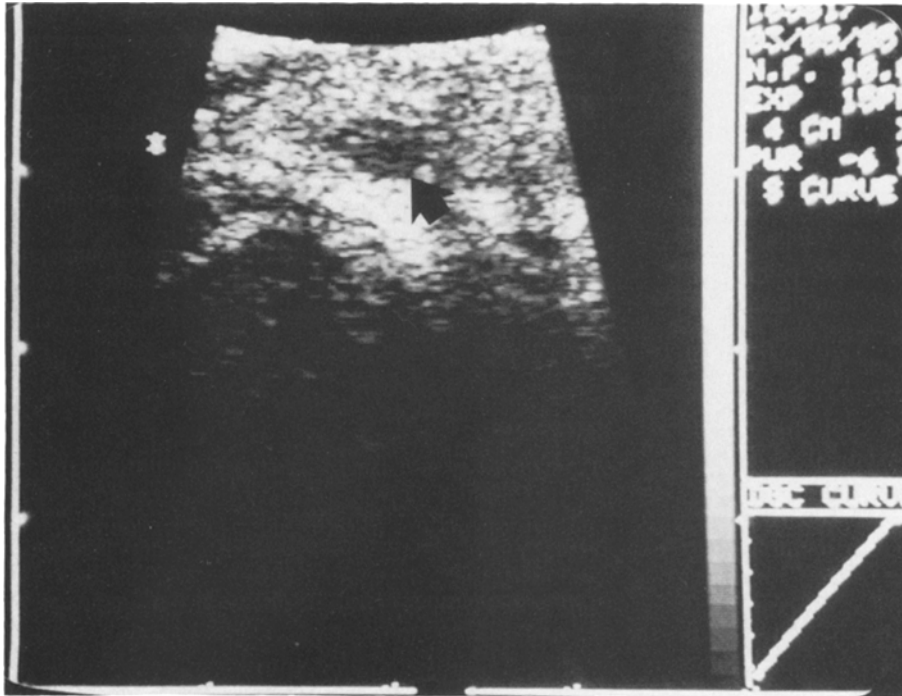


Fig. 4. Sagittal intraoperative scan of an intrathyroidal parathyroid adenoma, which was only detected subsequently on analysis of permanent sections of the resected thyroid lobe.

Table 4. Length of operation as a function of intraoperative ultrasound imaging.

Abnormal gland imaged	<i>n</i>	Length of operation (hr)
Yes	19	3.1 ± .3 ^a
No	6	5.9 ± 1.3

^aSignificantly different $p = 0.005$.

Data are presented as mean ± SEM.

real-time ultrasound, intraoperative ultrasound imaged significantly more abnormal parathyroid glands in significantly more patients. Size of the pathologic gland was not a determinant. Small abnormal glands were well imaged (Fig. 2), and no normal glands were imaged. Location of the pathologic gland did appear to be an important factor. Inferior and intrathyroidal pathologic glands were especially well imaged with 100% resolution. This instrument might eliminate blind thyroid lobectomy in reoperations that are especially hazardous to the recurrent laryngeal nerve. It correctly predicted 3 of 3 intrathyroidal pathologic glands, and there were no false-positives (Figs. 3 and 4). IOUS did poorly imaging superior pathologic glands. There was 1 false-positive, a lymph node, and 5 (33%) pathologic superior glands that went undetected. This appeared to be related to the shape of the transducer which was approximately 3 cm long. This large transducer was difficult to use posterior to the superior thyroid pole, and a high-

resolution pencil- or cigar-shaped transducer might solve this problem.

If the IOUS successfully imaged the abnormal parathyroid tissue, the length of the operation was significantly reduced from 6 to 3 hours. This has some relevance to cost. IOUS equipment used in this study costs approximately \$80,000 (U.S.) making it an expensive acquisition to any operating room. This equipment can be used for other intraoperative studies such as for examination of the pancreas, brain, and spinal cord. It is also similar to that used in general ultrasound scanning, and, therefore, use and cost of the scanner could be shared with other departments such as Diagnostic Radiology. If it can reduce parathyroid reoperation time by 50% as the data suggest, it might significantly reduce the cost of parathyroid reoperations.

The most important consideration with any new technique is outcome. IOUS had no impact on final outcome in this study. Twenty-four of 25 patients had successful reoperations. Only 1 patient had a complication. The solitary patient with the complication and unsuccessful surgery also had unsuccessful intraoperative ultrasound. However, 5 of 6 patients with negative IOUS still had successful procedures without complications, albeit their procedures took significantly longer than the others. Whether IOUS has any effect on outcome will be difficult for us to evaluate, because using other preoperative localizing methods, we have a high success rate (approximately 95%) [6], and a low complication rate (approximately 6%) [7].

From this preliminary study, it appears that intraoperative ultrasound has utility in parathyroid reoperations. Additional studies are needed to evaluate its effect on patient outcome as the equipment is further modified and the examining technique refined.

Résumé

Les auteurs ont comparé les données de l'ultrasonographie préopératoire à celles de l'ultrasonographie opératoire chez 25 malades qui atteints d'hyperparathyroïdisme primitif ont du être réopérés après échec de la première intervention. L'ultrasonographie opératoire fut pratiquée après dissection des lambeaux de platysma musculaire et abord d'un ou des deux côtés du cou par incision cervicale tracée au niveau du bord axial du sternocléido-mastoidien. Avant l'intervention l'examen du cou avait été pratiqué pour déterminer le côté à explorer. Les parathyroïdes pathologiques se sont traduites par une image anormale au cours des 2 explorations. Les images furent obtenues en 2 plans. Elles furent défaut quand les parathyroïdes étaient normales. L'ultrasonographie préopératoire fut exacte chez 9 malades qui présentaient des parathyroïdes pathologiques et l'ultrasonographie opératoire fut exacte chez 19 opérés ($p = 0.01$). L'habilité de la méthode pour déceler la lésion ne dépend pas de la taille de la parathyroïde pathologique mais de son siège. Les parathyroïdes intrathyroïdiennes et sous-thyroïdiennes anormales furent démasquées mais celles situées haut ne furent pas décelées dans 33% des cas. Lorsque l'échographie décela la lésion la durée de l'intervention fut notablement réduite (de 5.9 heures elle passa à 3.1 heures ($p = 0.005$)) mais au total elle n'intervient pas sur la destinée de l'intervention puisque dans 5 des 6 cas où ses résultats avaient été négatifs la glande anormale fut découverte par le chirurgien et extirpée avec succès et sans complication.

Resumen

Hemos comparado la ultrasonografía de alta resolución de tiempo real intraoperatoria (USIO) con la preoperatoria en 25 pacientes sometidos a reoperación por hiperparatiroidismo primario. La ultrasonografía del cuello fue realizada después de levantar los colgajos del músculo cutáneo y una vez que uno o ambos lados del cuello fueron disecados a lo largo del borde interno del esternocleidomastoideo. Los estudios preoperatorios de localización fueron utilizados para determinar qué lado del cuello debería ser explorado. Las glándulas

paratiroides anormales aparecieron sonolucientes tanto a la ultrasonografía pre- como intraoperatoria. Las imágenes de las glándulas fueron siempre obtenidas en 2 planos. No se logró visualizar glándulas paratiroides normales ni en el examen pre- ni en el intraoperatorio. Los exámenes preoperatorios dieron resultados correctos para tejido paratiroideo anormal en 9 pacientes, y los intraoperatorios en 19 pacientes ($p = 0.01$). El tamaño de la glándula paratiroidea anormal no fue un factor determinante de la capacidad de la USIO para su detección, pero sí lo fue la ubicación. Las glándulas paratiroideas en ubicación intratiroidea o inferior pudieron ser detectadas en forma confiable, pero las de ubicación superior se escaparon a la detección (33%). Cuando la USIO logró demostrar el tejido paratiroideo anormal, el procedimiento operatorio se acortó en forma significativa (5.9 horas versus 3.1 horas, $p = 0.005$). La USIO no parece determinar el resultado final de operación, puesto que 5 de 6 pacientes en quienes la USIO falló en la demostración de glándulas anormales fueron operados sin complicación.

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References

1. Brennan, M.F.: Reoperation for suspected hyperparathyroidism. *Clinical Surgery International*, vol. 4. Surgery of the Thyroid and Parathyroid Glands. New York, Churchill-Livingston, 1983, pp. 168-176
2. Wang, C.A.: Parathyroid re-exploration. *Ann. Surg.* 186:140, 1977
3. Billings, P.J., Milroy, E.J.D.: Reoperative parathyroid surgery. *Br. J. Surg.* 70:542, 1983
4. Edis, A.J., Sheedy, P.F., Behrs, O.H.: Results of reoperation for hyperparathyroidism, with evaluation of preoperative localization studies. *Surgery* 84:384, 1978
5. Saxe, A.W., Brennan, M.F.: Reoperative parathyroid surgery for primary hyperparathyroidism caused by multiple gland disease: Total parathyroidectomy and autotransplantation with cryopreserved tissue. *Surgery* 91:616, 1982
6. Brennan, M.F., Norton, J.A.: Reoperation for persistent and recurrent hyperparathyroidism. *Ann. Surg.* 201:40, 1985
7. Patow, C.A., Norton, J.A., Brennan, M.F.: Vocal cord paralysis and reoperative parathyroidectomy, a prospective study. *Surg. Forum* 35:553, 1984
8. Edis, A.J., Evans, T.C.: High-resolution, real-time

- ultrasonography in the preoperative location of parathyroid tumors, a pilot study. *N. Engl. J. Med.* 301:532, 1979
9. Egdahl, R.H.: Preoperative parathyroid localization. *N. Engl. J. Med.* 301:548, 1979
 10. Clark, O.H., Stark, D.D., Gooding, G.A., Moss, A.A., Arnaud, S.B., Newton, T.H., Norman, D., Bank, W.O., Arnaud, C.D.: Localization procedures in patients requiring reoperation for hyperparathyroidism. *World J. Surg.* 8:509, 1984
 11. Krudy, A.G., Shawker, T.H., Doppman, J.L., Horvath, K., Schneider, P.D., Norton, J.A., Marx, S.J., Spiegel, A.M.: Ultrasonic parathyroid localization in previously operated patients. *Clin. Radiol.* 35:113, 1984
 12. Sigel, B., Duarte, B., Coelho, J.C.U., Nyhus, L.M., Baker, R.J., Machi, J.: Localization of insulinomas of the pancreas at operation by real-time ultrasound scanning. *Surg. Gynecol. Obstet.* 156:145, 1983
 13. Norton, J.A., Sigel, B., Baker, A.R., Ettinghausen, S.E., Shawker, T.H., Krudy, A.G., Doppman, J.L., Taylor, S.I., Gordon, P.: Localization of an occult insulinoma by intraoperative ultrasonography. *Surgery* 97:381, 1985
 14. Sigel, B., Kraft, A.R., Nyhus, L.M., Coelho, J.C.U., Gavin, M.P., Spigos, D.G.: Identification of a parathyroid adenoma by operative ultrasonography. *Arch. Surg.* 116:234, 1981
 15. Charboneau, J.W., Grant, C.S., James, E.M., Goellner, J.R., Hodgson, S.F.: High-resolution ultrasound-guided percutaneous needle biopsy and intraoperative ultrasonography of the cervical parathyroid adenoma in a patient with persistent hyperparathyroidism. *Mayo Clin. Proc.* 58:497, 1983
 16. Norton, J.A., Brennan, M.F., Saxe, A.W., Wesley, R.A., Doppman, J.L., Krudy, A.G., Marx, S.J., Santora, A.C., Hicks, M., Aurbach, G.D., Spiegel, A.M.: Intraoperative urinary cyclic adenosine monophosphate as a guide to successful reoperative parathyroidectomy. *Ann. Surg.* 200:389, 1984
 17. Sigel, B., Coelho, J.C.U., Nyhus, L.M., Velasco, J.M., Donahue, P.E., Wood, D.K., Spigos, D.G.: Detection of pancreatic tumors by ultrasound during surgery. *Arch. Surg.* 117:1058, 1982
 18. van Heerden, J.A., James, E.M., Karsell, T.R., Charboneau, J.W., Grant, C.S., Purnell, D.C.: Small-part ultrasonography and primary hyperparathyroidism. *Ann. Surg.* 195:774, 1982
 19. Wang, C.A.: The anatomic basis of parathyroid surgery. *Ann. Surg.* 183:271, 1976
 20. Wells, S.A., Jr., Leight, G.F., Ross, A.: Primary hyperparathyroidism. *Curr. Probl. Surg.* 17:398, 1980

Invited Commentary

Matthius Rothmund, M.D.

Department of Surgery, University Hospital, Mainz, Federal Republic of Germany

Since the advent of the real-time, B-mode technique, surgeons have increasingly taken advantage of intraoperative ultrasound (IOUS), though it had already been attempted by A-mode equipment in localizing kidney stones and common duct calculi in the early 1960's [1, 2]. In endocrine surgery, IOUS was used to detect islet cell tumors [3, 4] and, casuistically, enlarged parathyroid glands as well [5, 6]. Nowadays, IOUS serves as a diagnostic tool in surgery of the liver and the biliary tree, the pancreas, and in vascular surgery [7-9].

While the benefit of IOUS in liver resections and in the detection of nonpalpable islet cell tumors is obvious, the role of this expensive method in reoperative parathyroid surgery is not clear. Norton et al. now present the first consecutive series of reoperative patients who were investigated with IOUS. As the authors conclude, the use of IOUS had no influence on the final outcome but could shorten the operation time significantly if the tumor was imaged by this method.

The authors compare the accuracy of IOUS (76%) with that of preoperative sonography (36%)

in the same patients. It is a little surprising that the accuracy of 36% is below the average range (40-60%) given for accuracy of preoperative ultrasound in reoperative patients [10], though the authors have expert radiologists at their side. Moreover, the 28% false-positive rate demonstrates that preoperative ultrasound might confuse the surgeon.

There are 2 points that might qualify the accuracy figure of 76% for IOUS given by the authors. First, it is not superior to the best results of preoperative sonography displaying a sensitivity of 82% and a specificity of 86% [11]. Second, it must be interpreted in context with all preoperative localization procedures performed.

It is obvious from the article that the patients had a variety of these procedures: computed tomography, magnetic resonance imaging, thallium-technetium scan, arteriography, venous sampling, and ultrasound. The results of these investigations were most likely already known by the surgeon. One wonders whether the ultrasound probe was guided by this knowledge in any of the patients. The question that should have been answered more precisely by the authors is how many parathyroid tumors could be localized by IOUS that have not been localized by 1 or more of the preoperative procedures. This would have elucidated the value of this method.

It is interesting to read that tumor size did not determine whether the glands could be visualized. Unfortunately, it is not easy to compare these data