Commentary on: High-resolution magic angle spinning ^{1}H nuclear magnetic resonance spectroscopy metabolomics of hyperfunctioning parathyroid glands

Geoffrey B. Thompson, MD, *Rochester, MN*

From the Mayo Clinic, Rochester, MN

This significant study by Battini et al[1] of the University of Strasbourg, Strasbourg, France, examines a novel way of distinguishing single-gland primary hyperparathyroidism from multigland hyperplasia, which is present in up to 15–20% of primary hyperparathyroidism cases. We know that an operation is the only definitive curative treatment for primary hyperparathyroidism. In experienced hands, the success of operative intervention can be as great as 98% in patients with nonfamilial, nonmalignant cases of hyperparathyroidism. However, even in experienced hands, the differentiation between single-gland disease and multigland hyperplasia continues to pose a challenge in terms of diagnosis and the extent of tissue removal. Many years ago, the biggest challenge was the definitive diagnosis of primary hyperparathyroidism. Assays that looked only at fragments of parathyroid hormone were available, and these were associated with significant shortcomings. In those days, the diagnosis of primary hyperparathyroidism was based on multiple serum calcium measurements and the exclusion of all other causes of hypercalcemia. With the development of an intact immunochemiluminescent assay, the diagnosis of primary hyperparathyroidism in the presence of hypercalcemia and an inappropriate or elevated level of parathyroid hormone has become accurate and simplified. With the definitive diagnosis readily available, challenges remained for optimal localization of abnormal parathyroid glands. Preoperative localization of abnormal glands became more accurate with refinements in neck ultrasound and the development of sestamibi parathyroid nuclear medicine scans. However, multigland hyperplasia continues to be the bane of existence for even the most experienced parathyroid surgeon. Then along came the development of a rapid intraoperative parathyroid hormone assay, which in most cases could confirm successful removal of adequate amounts of parathyroid tissue to render the patient cured. This led to what we refer to today as focused or minimally invasive parathyroidectomy. However, the use of the intraoperative parathyroid hormone assay still fails to differentiate single-gland and multigland diseases in a number of instances. More recently, others have returned to 4-gland exploration. However, even in this situation, visualization by experienced surgeons and microscopic analysis by endocrine pathologists continue to avoid perfection.

The group out of Strasbourg, France has examined tissue metabolomic profiles in patients with single-gland primary hyperparathyroidism and multigland primary hyperparathyroidism and in those with secondary and tertiary renal-related hyperparathyroidism. The method used was 1H high-resolution magic angle spinning nuclear magnetic resonance spectroscopy that has the ability to assess metabolomic profiles rapidly among these various pathologic entities. The analysis, which was performed on 46 glands snap-frozen in liquid nitrogen for retrospective analysis, showed a clear

10.1016/j.surg.2016.03.002

Accepted for publication March 22, 2016.

Reprint requests: Geoffrey B. Thompson, MD, Mayo Clinic, 200 First Street SW, Rochester, MN 55902. E-mail: thompson.geoffrey@mayo.edu.

Surgery 2016;160:395-6.

0039-6060/$ - see front matter

http://dx.doi.org/10.1016/j.surg.2016.03.013

distinction between primary hyperparathyroidism and renal hyperparathyroidism and, even more importantly, was able to distinguish differences in single-gland disease from multigland hyperplasia in primary hyperparathyroidism. The authors showed this technology is reliable and fast and could be used as an intraoperative tool in the future. Very clear-cut differences were noted in the metabolomics among the various subtypes of hyperparathyroidism. This technology, at least as seen in a limited number of patients, seems to demonstrate a process that may help us to better decide intraoperatively whether a patient needs standard 4-gland cervical exploration or minimal access parathyroidectomy. The authors have demonstrated this can be done rather quickly, starting with removal of the most suspicious gland in question. Specifically, single-gland disease was predicted and was associated with significantly higher levels of phosphorylcholine, choline, glycerophosphocholine, fumarate, succinate, lactate, glucose, glutamine, and ascorbate compared with multigland disease.

The authors realize and state the limitations of the study, such as the small sample numbers, and encourage others to validate the findings. The article is extremely well written and detailed, and it is clearly something new and potentially important to the management of patients with hyperparathyroidism and multigland hyperplasia. Metabolomics or global metabolite profiling has been used for investigating metabolite changes associated with some pathologic conditions, including colorectal, breast, liver, and pancreatic cancers.[2-5] Metabolomics represents the latest in the "omics" cascade behind genomics, transcriptomics, and proteomics, generating great interest in the medical community. The technologies used in the assessment of metabolomics include nuclear magnetic resonance spectroscopy and gas or liquid chromatography. This technology is readily available in most laboratories and research institutes. With the need for accurate biomarkers to help surgeons distinguish single-gland disease and multigland disease, the current study offers a potential adjunct to the accurate identification and appropriate treatment for multigland hyperplasia. The authors point out that the potential use of this methodology as an intraoperative tool will require specific additional studies that will open an exciting avenue for future investigation.

REFERENCES

1. Battini S, Imperiale A, Taieb D, Elbayed K, Cicek EA, Sebag F, et al. High-resolution magic angle spinning ^{1}H nuclear magnetic resonance spectroscopy metabolomics of hyperfunctioning parathyroid glands. Surgery 2016;160:384-94.
2. Ritchie SA, Ahiahonu PW, Jayasinghe D, Heath D, Liu J, Lu Y, et al. Reduced levels of hydroxylated, polyunsaturated ultra long-chain fatty acids in the serum of colorectal cancer patients: Implications for early screening and detection. BMC Med 2010;8:13.
3. Denkert C, Buche E, Hilvo M, Salek R, Oresic M, Griffin J, et al. Metabolomics of human breast cancer: New approaches for tumor typing and biomarker discovery. Genome Med 2012;4:37.
4. Duarte IF, Stanley EG, Holmes E, Lindon JC, Gil AM, Tang H, et al. Metabolic assessment of human liver transplants from biopsy samples at the donor and recipient stages using high-resolution magic angle spinning 1H NMR spectroscopy. Anal Chem 2005;77:5570-8.
5. Ritchie SA, Akita I, Takemasa I, Eguchi H, Pastural E, Nagano H, et al. Metabolic system alterations in pancreatic cancer patient serum: Potential for early detection. BMC Cancer 2013;13:413.