Molecular Profiling Can Help Inform Surgical Decisions for Patients with Thyroid Nodules

Thyroid nodules are extremely common — as many as half of middle-aged adults have at least one. Although the vast majority are benign, when thyroid nodules are found (often incidentally in the doctor’s office or on imaging) they require diagnostic testing, given that 4 percent of them are malignant. The incidence of thyroid cancer is triple what it was in the 1970s.

By using molecular-profiling techniques, UCLA endocrine surgeons are bringing a new level of certainty to a significant percentage of individuals with indeterminate thyroid nodules — neither clearly malignant nor clearly benign. Protocols for assessing genetic markers in biopsy results with suspicious cytology, while continuously being refined, are nonetheless eliminating unnecessary surgeries in many cases.

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Pediatric Intestinal Transplant
UCLA’s Pediatric Intestinal Transplant Program is one of the largest such programs in the world and is regarded as a leader in achieving enteral autonomy to avoid transplantation and, when transplantation is necessary, providing among the best outcomes.

Aortic Disorders
Less-invasive endovascular techniques are more frequently being used to repair abnormalities of the aorta, but accurate diagnosis and prompt treatment are vital to achieving good patient outcomes.

Saliva Stones
Sialendoscopy is an innovative technique that uses extremely narrow endoscopes to provide a low-risk solution to saliva stones that can otherwise be difficult to manage.

Blood Clots
UCLA is the first center in California to offer a minimally invasive procedure to vacuum blood clots out of a patient’s vein and filter out solids before returning the cleansed blood to the patient. The procedure is available to many patients with blood clots in the lungs or at risk of breaking off and traveling to the heart or lungs.

Sialendoscopy allows for endoscopic removal of saliva stones.

UCLA is first center in California to offer minimally invasive procedure for removing blood clots.

Pediatric Inflammatory Bowel Disease
The pediatric IBD program at UCLA recognizes the special needs of pediatric patients and provides care in a compassionate setting, working to slow the progression of the disease and prevent operations to remove scarred intestinal tissue or the entire colon.

South Bay Endocrinology Practice
UCLA South Bay Endocrinology offers a full range of endocrinology care, continuing to serve area residents from a convenient South Bay location.

International Adoption and Travel Clinic
UCLA’s International Adoption and Travel Clinic is dedicated to the healthcare of families and children who travel internationally and assists families who are adopting with pre-adoption counseling and comprehensive evaluation of adopted children.

Pediatric Cardiology
UCLA’s comprehensive pediatric cardiology services now include a practice in the high-desert region, serving the Hesperia, Apple Valley and Victorville communities and reducing the need for patients to travel to distant centers for specialized care.

Colon Polyps
UCLA surgeons and gastroenterologists have been performing a new, minimally invasive procedure to remove large and difficult-to-reach colon polyps in cases that would normally call for bowel resection surgery.

Pediatric Asthma
UCLA pediatric pulmonologists offer comprehensive treatment options for the medical management of asthma, including advanced pulmonary function testing and a multifaceted patient-education program.

To download these and other clinical updates at UCLA Health, go to:
uclahealth.org/clinicalupdates

News from UCLA Health

Preliminary clinical trial shows great promise for new multiple sclerosis treatment
A study shows that combining estriol, a female hormone, with Copaxone, a medication currently used to treat multiple sclerosis (MS), reduced the relapse rate of MS by nearly 50 percent with only one year of treatment.
uclahealth.org/MSTreatment

Doctors issue new treatment guidelines for skin abscesses caused by MRSA
Ten years after the clinical battle began with community-acquired methicillin-resistant staphylococcus aureus (MRSA), doctors are still grappling with how to diagnose, treat and prevent this virulent form of staph infection. Now, researchers from UCLA have issued updated guidelines outlining the best ways to treat and manage these abscesses.
uclahealth.org/mRSA

Vitamin A may help boost immune system to fight tuberculosis
The rise of drug-resistant tuberculosis, called a “ticking time bomb” by the World Health Organization, and the high cost of fighting the disease highlight the need for new approaches to treatment. In recent findings, UCLA researchers investigating the role of nutrients in helping the immune system fight against major infections show that vitamin A may play an important role in combating tuberculosis.
uclahealth.org/TBandVitaminA
Broader Approach Needed to Successfully Treat Obesity

For patients with recalcitrant obesity and accompanying medical problems, simply offering bariatric surgery is not enough, says Erik Dutson, MD, surgical director of the UCLA Center for Obesity and METabolic health (COMET). “Weight-loss surgery alone can’t be expected to bring about the desired results,” Dr. Dutson explains. “It must be accompanied by radical changes in a patient’s lifestyle, which requires education about diet and exercise both before and after surgery, as well as support groups. Medical management is also very important.

The success rate for bariatric surgery is high. Approximately 85 percent of patients who undergo the Roux-en-Y gastric bypass or vertical sleeve gastrectomy (the two types of bariatric surgery offered at UCLA) experience sustained, efficacious weight loss. Nonetheless, the weight-loss strategy remains vastly underutilized. “As a field we serve less than 1 percent of patients for whom bariatric surgery is medically indicated,” Dr. Dutson says. “In many cases, patients may be fearful, or they simply see surgery as an extreme option.”

The safety of bariatric surgery has significantly improved over the years, with in-hospital mortality declining from approximately 4 percent to less than 0.1 percent. While many patients continue to be wary of the risks associated with surgery, the irony is that for patients who qualify, the risk of dying from not getting surgery is significantly higher. Studies indicate that the five-year mortality rate for patients who qualify for and receive bariatric surgery is 89 percent lower than for patients who qualify but don’t pursue the operation. “The fact that it’s much safer to get the surgery than not to if you qualify isn’t intuitive to most people,” Dr. Dutson says, “so we need to get the word out.”

The Roux-en-Y and the vertical sleeve gastrectomy are the two approaches used by COMET surgeons because they are the ones that can have significant metabolic effects in patients, Dr. Dutson explains. Of the two offered at UCLA, the Roux-en-Y is considered the gold standard, particularly for the largest patients. Those who aren’t good candidates for a gastric bypass — including patients who are on chronic nonsteroidal drugs, steroids or immunosuppressive agents — tend to be steered toward the sleeve gastrectomy.

Prior to surgery, patients are seen several times by the center’s team. “Patient education is one of the critical pieces to management that has been underemphasized in the past when you look at bariatric surgery,” Dr. Dutson says. “Patients were getting these operations without any idea of how to use them. They weren’t making good food choices; they didn’t understand the difference between carbohydrates, fats and proteins; and then they couldn’t take maximum advantage of their altered anatomy and hormones.” Postoperatively, patients are placed on a strict diet while their stomachs heal, with graded alteration of the food they eat and regular visits to the center, both for continuing education and to track metabolic parameters.

Research is also a major part of the center’s mission. “We now understand that the metabolic component of obesity is much more complex than we had ever thought,” Dr. Dutson says. “There is a tremendous amount that we don’t know.”

Under the leadership of its medical director, Simon Beaven, MD, COMET is seeking to learn more about the role of fatty liver disease in metabolic syndrome and how to better manage patients with the condition so they don’t ultimately require liver transplantation. Some clinical trials are looking at the central nervous systems of patients who don’t benefit from bariatric surgery to see how they might differ from those in the majority who do.
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Although data suggests that part of this increase is due to more frequent detection, the number of life-threatening thyroid cancers is also on the rise. “Given that so many people have thyroid nodules, 96 percent of whom don’t have cancer, the issue we have to be concerned with is how we avoid providing invasive treatment to people who don’t need it,” says Michael Yeh, MD, chief of endocrine surgery at UCLA. “As surgeons, we need to be advocates for appropriate care. Molecular profiling is contributing to our ability to better do that.”

The challenge for endocrine surgeons has been the large number of patients — about one in four — for whom ultrasound-guided biopsy, performed via fine-needle aspiration, is inconclusive. “When a biopsy reveals a benign result, which occurs in the majority of patients, we follow up with serial imaging and biopsy again later if sonographic changes are detected within the nodule,” explains UCLA endocrine surgeon Avital Harari, MD. “On the other end of the spectrum, when the biopsy gives a diagnosis of cancer, patients are treated with one definitive surgery, a total thyroidectomy. We also remove any lymph nodes associated with the cancer at the initial operation. However, in about 25 percent of patients, the initial biopsy results are inconclusive and are classified as indeterminate.”

Roughly one-fourth of indeterminate results are eventually diagnosed as thyroid cancer. The problem is that determining whether...
these patients’ nodules are malignant after an indeterminate biopsy has often required surgery. “Previously, the standard of care for determining if these nodules were cancerous was to remove the half of the thyroid with the suspicious nodule,” Dr. Harari says. “If pathology showed that it was cancer, the patient returned to the operating room within 10 days of surgery to remove the other side of the thyroid. Thus, patients who turn out to have cancer are subjected to two surgeries instead of one. That also unfortunately means that at least 70 percent of patients would end up having surgery for benign nodules.”

That’s where molecular profiling comes in. The UCLA team has been using an analysis test that they have validated through their own use with patients. The analysis uses a so-called gene-expression classifier to determine whether a nodule is benign.

“In about half of the cases where we have indeterminate cytology, the test will come back with a benign result, which means the likelihood of cancer is only 4 percent — the same likelihood as when the original biopsy comes back benign,” Dr. Yeh says. “That means these patients can avoid surgery.” If the gene-expression classifier comes back as suspicious, which it does in about half of the patients, the risk of cancer is roughly 40 percent, and those patients are recommended for surgery.

While the test is useful for its negative predictive value — determining which suspicious nodules are benign — a second test currently under study by the UCLA team is more useful for its ability to declare malignancies. The test looks for markers from among 17 mutations associated with cancer. When the test is positive, it is nearly 90-percent likely that the nodule is malignant and the patient should have a total thyroidectomy. Again, in such cases the patient is spared an initial diagnostic surgery.

Now, Dr. Yeh says, the challenge is to determine how to optimally use the two types of molecular-profiling tests to maximize value for patients with indeterminate fine-needle-aspiration biopsy results. As they continue to actively monitor how the molecular-profiling tests perform, Dr. Yeh and colleagues are looking into ways to better sort the patients with indeterminate cytology by risk. Ideally, the initial test would be used for the lower-risk patients and the second positive-marker test would be used for higher-risk patients.

“Unfortunately, we have no perfect test yet,” Dr. Yeh says. “We have some that are more sensitive and some that are more specific. In an ideal world there would be no such thing as diagnostic surgery — no patient would ever have to go through two operations, and no patient would have an unnecessary operation. We may never quite get there, but we can get closer.”

“When a biopsy reveals a benign result ... we follow up with serial imaging and biopsy again later if sonographic changes are detected within the nodule. On the other end of the spectrum, when the biopsy gives a diagnosis of cancer, patients are treated with one definitive surgery.”

— Avital Harari, MD
Ronald Reagan UCLA Medical Center is one of six Level 1 trauma centers in Los Angeles County and has received its eighth consecutive successful three-year review for excellence in both adult and pediatric trauma care from the American College of Surgeons’ Trauma Verification Committee. H. Gill Cryer, MD, chief of trauma surgery for the past 24 years, discusses UCLA’s expertise and leadership in providing care to patients with life-threatening injuries.

Describe UCLA’s role in providing trauma care within the Los Angeles County system.

Over the past decade, the Los Angeles County trauma system has become increasingly efficient in its ability to achieve the important goal of ensuring that every injured person in our county receives the right care, at the right place and at the right time. UCLA has been an important contributor to fine-tuning that process not only in our own catchment area but in the county system as a whole. In disaster situations and multi-casualty events, we have systems in place to direct the most critically injured patients to Level 1 centers by air, severe injuries to Level 1 and Level 2 centers by ground and air, and less severe injuries to local emergency departments by ground. In all situations, Level 1 trauma centers provide 24-hour access to general-trauma surgeons, emergency-room physicians and other highly specialized services such as orthopaedic surgery, neurosurgery, radiology and critical care. UCLA has been a part of the Los Angeles County trauma system since its inception in 1983. During that time, we've developed remarkable synergy among the many highly acclaimed specialties within our health system to benefit the more than 1,200 trauma patients who are admitted to our center each year. Many patients who come through our trauma center will be touched by 100-to-200 hands as they move from diagnosis and treatment to recovery and rehabilitation. We are capable of providing total care for every aspect of traumatic injuries because we have remarkable leadership and camaraderie within our team that makes it all work together.
How does UCLA ensure that trauma patients receive the highest quality of care?

As a Level 1 center, we collect specific data for every trauma patient that comes through our door and submit those data to the National Trauma Data Bank for benchmarking at the system, regional and national levels. We have a robust multidisciplinary committee at UCLA that meets monthly to compare what’s happening in our trauma center with other centers within Los Angeles County, discuss problems and outliers and initiate quality-improvement processes when necessary. We also participate in the American College of Surgeons’ National Trauma Quality Improvement Program, which is a risk-adjusted database established in the past five years that includes approximately 250 trauma centers across the country. We are proud that our results compare favorably to other leading trauma centers for a variety of outcomes — brain injuries, hemorrhagic shock, infection, fractures, etc.

What changes have you seen over time in the way trauma services are delivered?

We have been on the leading edge of trauma care both technologically and scientifically and our patients are benefiting from an evolution of small steps that have coalesced in many different areas. For example, we have immediate access to computed tomography, magnetic resonance imaging and interventional-radiology techniques that, in many circumstances, have dramatically improved our ability to very quickly determine exactly what is wrong with the patient. When we know exactly what’s wrong, we can figure out exactly what to do to fix it. We also have advanced capabilities in minimally invasive fracture management, endoscopic repair of internal organs and intravascular repairs. In the old days, we had to open the chest emergently and find the injured blood vessel and sew it up or put in a graft. Today, we can place a stent in the blood vessel using catheter-based technology and seal a hole from inside. Many patients now receive life-saving procedures and are out of the hospital in one-to-two days instead of one-to-two months. Additionally, our neuro and trauma intensive care unit is equipped with all of the most advanced technology and is staffed 24 hours per day with highly trained neurointensivists and surgical intensive care doctors.

What is your vision for UCLA’s trauma program over the next five-to-10 years?

We want to continue to work on the boundary areas between good outcomes and great outcomes, particularly after the patient leaves the hospital. Trauma is not only the leading cause of death in the United States for people ages 1-to-44 years but also a major cause of disability. Once we have saved the patient’s life and they leave the hospital, a lot of work still needs be done to get them back to normal. We want to break down some of the barriers to care and communication so that patients are returned to their pre-injury health status.

“We have been on the leading edge of trauma care both technologically and scientifically and our patients are benefiting from an evolution of small steps that have coalesced in many different areas.”
Significantly enhanced survival results are being achieved at UCLA by delaying surgery for pancreatic-cancer patients with borderline-resectable or locally advanced disease. While most centers provide preoperative treatments to this group of patients for about three months before performing surgery, the UCLA team typically waits for up to six-to-eight months — in an effort to shrink the tumor and determine which patients will benefit from the operation. For those patients who ultimately have surgery, median survival is 45 months — roughly twice as long as what is generally achieved for other patients with the same disease stage.

“We believe the longer duration of preoperative therapy is a major contributor toward that improved survival,” says Timothy R. Donahue, MD, who heads the gastrointestinal surgery team that has achieved these results, which are the best that have been reported for such patients.

Pancreatic cancer is the fourth-leading cause of cancer-related deaths in the United States, and if current incidence and survival rates continue, it is projected to be the No. 2 cancer killer in the nation, behind only lung cancer, by 2020. The median survival for all patients diagnosed with the disease is less than one year. But treatments have improved, most notably in the approach to chemotherapies that are now available.

Until recently, a single-agent therapy using gemcitabine was the standard. In the last three years, clinical trials for patients with advanced-stage disease have shown that adding albumin-
coated nanoparticle-containing paclitaxel or a multiple-drug regimen known as FOLFIRINOX significantly improves median survival. Prospective clinical trials are underway to determine whether these regimens can also bring benefits to patients with other stages of the disease. “We hope that we can improve on the chemotherapy treatment of pancreatic cancer patients even further with time,” says Dr. Donahue.

He notes that at the time of diagnosis, only 10-to-15 percent of pancreatic-cancer patients have early stage disease, for which it is clear that surgery followed by adjuvant chemotherapy is the ideal treatment approach. Of the remaining patients, about half present with metastatic disease, for which surgery is typically not considered beneficial. That leaves a group of about 40 percent of patients diagnosed with locally advanced or borderline-resectable disease. In this latter group, it’s less clear whether surgery will make a difference. “Unlike the patients with early stage disease, these patients have tumors that are just a bit too large and involve the local vasculature that surrounds the pancreas,” Dr. Donahue explains.

Rather than taking these patients directly to surgery and then resecting and reconstructing the local vasculature, the standard approach has been to treat them with chemotherapy plus or minus radiation therapy. The rationale is twofold: to shrink the tumor so that the blood vessels don’t have to be resected and to allow time to observe the tumor and ensure that no metastatic disease exists or develops that would preclude any surgical benefit.

Dr. Donahue and colleagues believe that taking a longer period to treat patients before deciding on surgery is a more optimal approach that allows for more shrinkage of the tumor to minimize the operation that needs to be performed. Waiting also allows selection of patients who will benefit from surgery by making sure no undetectable micro-metastases will soon blossom into a larger metastasis.

This approach has led to some of the best survival results ever reported for these patients. Among patients with borderline-resectable or locally advanced disease who have been treated with the longer protocol before having surgery, the median survival of 45 months is approximately two years longer than similarly staged patients typically experience in other published studies. Although the better results are in part a result of the greater selectivity concerning which patients receive surgery — those found to have metastatic disease during the pre-surgical treatment are not included in the retrospective analysis — Dr. Donahue believes the substantial improvement in survival time for these patients indicates that his team is on the right course.

As chemotherapy continues to improve, Dr. Donahue expects more patients to become surgical candidates. “Unlike in many other cancers, the majority of pancreatic-cancer patients die not from the primary tumor but from the metastasis,” Dr. Donahue explains. “Because of that, the role of surgery may not be as important. But now that we have these improvements in chemotherapy that allow us to better address the systemic lesions, local therapy — surgery — can play a more prominent role.”

“[T]he longer duration of preoperative therapy is a major contributor toward that improved survival.”

For more information about the UCLA Center for Pancreatic Cancer, go to: pancreas.ucla.edu
An innovative quality-improvement (QI) program at UCLA aims to decrease complications and reduce hospital readmissions for patients who have undergone colorectal surgery (CRS) by addressing operative risk factors prior to surgery and following up to assess potential post-operative complications before they can spiral out of control.

“We want to make it clear that everyone is important and everyone — the physicians, hospital staff and the patients — has a voice,” says Anne Lin, MD, a colorectal surgeon who pioneered the Advanced Colorectal Treatment Uniform Protocol (ACT UP!) program at UCLA. The program is one of several quality-improvement initiatives sponsored by the University of California that are designed to improve CRS outcomes. ACT UP! engages participants involved in all aspects of CRS patient care — nurses, pharmacists, anesthesiologists, surgeons, etc. — in developing team-based QI strategies. The group worked together to standardize CRS-patient-care protocols and to develop an educational booklet for CRS patients. Continual QI is facilitated through ongoing monthly meetings.

“We discuss possible changes that would improve patient care, including ways to reduce pre-operative risk factors and modifications in perioperative care of patients,” Dr. Lin says. “Our goal is to streamline our entire care process and to increase transparency.”
For example, the group improved pre-discharge pain management by working through medication-administration pathways to ensure that the transition from epidural to oral medications occurred simultaneously.

“Before, a longer delay may have occurred from the time that the epidural was turned off and oral medications were started,” Dr. Lin says. “Our team worked with pharmacists to rewrite pharmacy orders so that nurses would feel more comfortable giving additional medication to alleviate pain when necessary.” The group also standardized post-discharge medication protocols and focused on spending more time educating patients about pain management.

“When we tell patients what medications they will be on and what they should expect, they feel more comfortable because they can get on board and ask questions about it from the very start,” Dr. Lin explains.

The ACT UP! program also targets CRS complications and hospital readmissions by engaging patients in an early warning system designed to identify and report potential problems to watch for at home following hospital discharge. These signs include wound drainage, opening or redness, bowel obstruction, abdominal pain or swelling, nausea or problems with eating, high output in their ostomy pouch and problems with cognition or ambulation.

To facilitate patient-provider communication, the program is piloting the use of mobile health wireless tablets for patients to use during their postoperative hospital stay, and then later at home. “This empowers patients to participate in their own care by notifying us of any issue that seems to be outside of the norm,” Dr. Lin says. “If we’re alerted to problems sooner, we have an opportunity to see the patient in clinic and address the problem or make recommendations over the phone, before the patient ends up in the emergency department or hospital.” The program will also evaluate additional quality measures, including hospital length of stay and patient satisfaction, according to Dr. Lin.

“We want to make it clear that everyone is important and everyone — the physicians, hospital staff, and the patients — has a voice,” says Anne Lin, MD, of UCLA’s Advanced Colorectal Treatment Uniform Protocol (ACT UP!) team at UCLA.

“Minimally Invasive Procedure Provides New Option for Patients with Rectal Polyps, Tumors

Colorectal cancer strikes more than 140,000 people each year, but it may be potentially cured or even prevented if tumors or precancerous polyps are detected early and surgically removed. Transanal minimally invasive surgery (TAMIS) is a newer, less invasive surgical procedure that represents a good diagnostic or therapeutic tool for some patients with rectal polyps or tumors, according to UCLA colorectal surgeon Anne Lin, MD.

“When the tumor or polyp is larger or not amenable to removal using conventional methods or there is concern about early cancer, we can use this technique to take the polyp out in one piece as opposed to performing a piecemeal resection via colonoscope,” Dr. Lin explains. The advantage to this approach, she says, is that it allows surgeons to remove not only the specimen, but also the thick layers of tissue and fat surrounding the polyp or tumor. This helps pathologists to better determine whether early stage cancer is present, how invasive the cancer is and whether it has spread to the lymph nodes. The information can then be used to decide whether additional surgery or adjuvant therapies such as radiation or chemotherapy are required.

TAMIS is performed using laparoscopic instruments through the rectum and then removing the tumor or polyp. The surgery is associated with less pain and shorter recovery time.
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What: This four-day course provides an in-depth review for those preparing to take the vascular-board examinations as well as providing basic didactic education for vascular residents-in-training. The course recognizes four major pillars of vascular-surgery practice: conventional open operations, catheter-based intervention, the medical aspects of patient management, and diagnostic imaging and noninvasive testing.

Where: The Beverly Hilton, Beverly Hills, California

Cost: $995

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For more information about our UCLA physicians, go to: uclahealth.org/physiciandirectory

U.S. News & World Report's Best Hospital Survey ranks UCLA Psychiatry No. 9 in the nation.

UCLA Medical Group awarded Gold Level Achievement for clinical quality by the California Department of Managed Health Care.

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