



GLICKMAN UROLOGICAL & KIDNEY INSTITUTE

2022 Year in Review



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ON THE COVER

Urologist Sarah Vij, MD, leads a case in the operating room.

AT A GLANCE

The Glickman Urological & Kidney Institute’s activities encompass a unique combination of high-volume and challenging clinical cases, extensive basic and translational scientific efforts, and innovative laboratory research conducted in an environment that nurtures the future leaders of its specialties.



Glickman Urological & Kidney Institute

BY THE NUMBERS

(2022)

168,670

OUTPATIENT VISITS

14,545

SURGICAL CASES

24,584

DIALYSIS TREATMENTS

2,942

ADMISSIONS

12,504

PATIENT DAYS

4.25

AVG. LENGTH OF STAY
(DAYS)

VITAL STATISTICS & RANKINGS

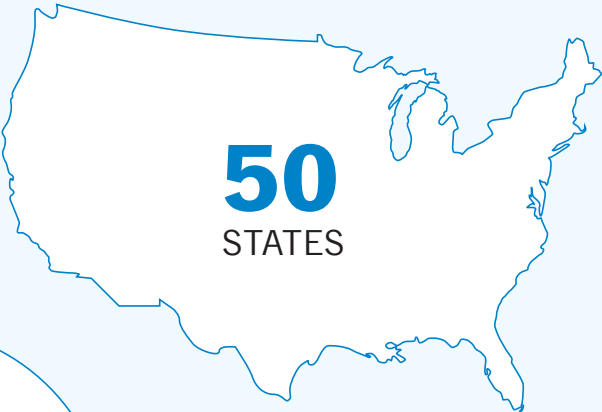
INSTITUTE VITAL STATISTICS	
64	Urologists
37	Nephrologists
32	Urology Advanced Practice Providers
21	Kidney Medicine Advanced Practice Providers
40	Urology Residents
25	Urology Fellows
11	Nephrology Fellows
472	Institute Caregivers

SURGICAL CASES	
908	Benign Prostatic Hypertrophy
1,650	Endourology and Stone Disease
1,132	Female Pelvic Medicine and Reconstructive Surgery
270	Male Fertility
527	Pediatric Urology
520	Genitourinary Reconstruction
340	Kidney and Pancreas Transplant
3,003	Urologic Oncology



U.S. News & World Report has once again ranked Cleveland Clinic urology among the top two programs in the country.

PATIENT ORIGINS



CENTERS

DEPARTMENT OF KIDNEY MEDICINE

- › Blood Pressure Disorders
- › Chronic Kidney Disease
- › Dialysis
- › Kidney and Pancreas Transplant
- › Renal Genetics

DEPARTMENT OF UROLOGY

- › Endourology and Stone Disease
- › Female Pelvic Medicine and Reconstructive Surgery
- › Genitourinary Reconstruction
- › Male Fertility
- › Men's Health
- › Minority Men's Health
- › Pediatric Urology
- › Robotic and Image-Guided Surgery
- › Urologic Oncology



DEAR COLLEAGUES,

As we reflect on 2022, I am heartened by the significant impact we continue to make as a team in the lives of our patients. Nationally, the healthcare landscape continues to change in the wake of the pandemic, but we have acted nimbly and with a growth and opportunity mindset.

Our urology program continues to be top-ranked. *U.S. News and World Report* and *Newsweek* ranked our Urology Department among the top two programs in, respectively, the country and worldwide. In addition, our residency program maintains a No. 1 ranking by Doximity. Similarly, our Kidney Medicine Department continues to garner national attention for its involvement in groundbreaking research and patient-centered initiatives.

In both disciplines, we attract trainees and faculty with exemplary clinical and academic talent. Together, we are all working to reimagine care for our patients through innovation, discovery and education.

One such example of innovation across our programs is our use of artificial intelligence, which we are leveraging to improve and personalize care across specialties. This work includes imaging-based segmentation to reduce unnecessary surgery for kidney cancers, neural networks to predict which patients with overactive bladder will respond better to specific therapies, and predictive modeling to assess the risk of acute kidney injury after cardiac surgery. Read on for more information about these projects and others.

I am exceedingly proud of what our team has accomplished despite a difficult time in healthcare. We have risen to the challenge by not only adapting but also taking the opportunity to reimagine and reinvent care to better serve our patients while training a new generation of physician leaders.

Thank you for your interest in our program.

Sincerely,



Georges-Pascal Haber, MD, PhD
Interim Chair, Glickman Urological & Kidney Institute
Chair, Department of Urology

2022 HIGHLIGHT

MACHINE LEARNING COULD CHANGE MANAGEMENT FOR PATIENTS WITH OVERACTIVE BLADDER

Urologists at Cleveland Clinic have found a new application for machine learning within their field, and they’re using it to improve shared decision making in the treatment of a common urologic diagnosis: overactive bladder (OAB).

Machine learning isn’t new to medicine or to urology, but its potential remains largely untapped, according to the authors of two new Cleveland Clinic-led studies.

“Algorithms can ‘learn’ data patterns and trends and make inferences about the relationship between input and output data and, with this knowledge, make new predictions,” explains Glenn Werneburg, MD, PhD, first author on both of the studies and a fellow in the Department of Urology.

OAB as a diagnostic target

Many patients with OAB will respond to behavioral approaches or oral medications, but for those who don’t, bladder injection of onabotulinumtoxinA (OBTX-A) and sacral neuromodulation (SNM) are two similarly effective third-line therapies. Since those treatments are invasive, it’s important to know in advance which patients are more likely to respond and, if so, to which one.

OAB is common and costly, and improved clinical management of OAB is needed. The condition currently affects about 16% of adults in the United States, and its global expenditure is expected to increase in coming years.

A novel approach with a robust data set

Dr. Werneburg, along with senior author Sandip Vasavada, MD, and co-author Howard Goldman, MD, both female pelvic medicine and reconstructive surgeons in the Department of Urology, developed neural networks using a series of novel approaches. They then applied the networks to the prediction problem in OAB using data sets from the ROSETTA study.

The ROSETTA study is one of the most complete data sets in the field. The open-label, randomized

trial included 381 women with refractory urgency incontinence across nine different U.S. centers to compare OBTX-A and SNM. These findings were published in *JAMA* in 2016.

Machine learning studies explained

The first study showed that the algorithms were extremely accurate in predicting treatment responses to both modalities; they correctly predicted who was a responder and a nonresponder about 90% of the time. In fact, the algorithms generally outperformed human experts in predictions. The study was published in 2022 in *Neurourology and Urodynamics*.

In the design of the second study, Dr. Werneburg explains, blinded expert urologists were given the same training data and this time tasked to predict patient-reported outcomes.

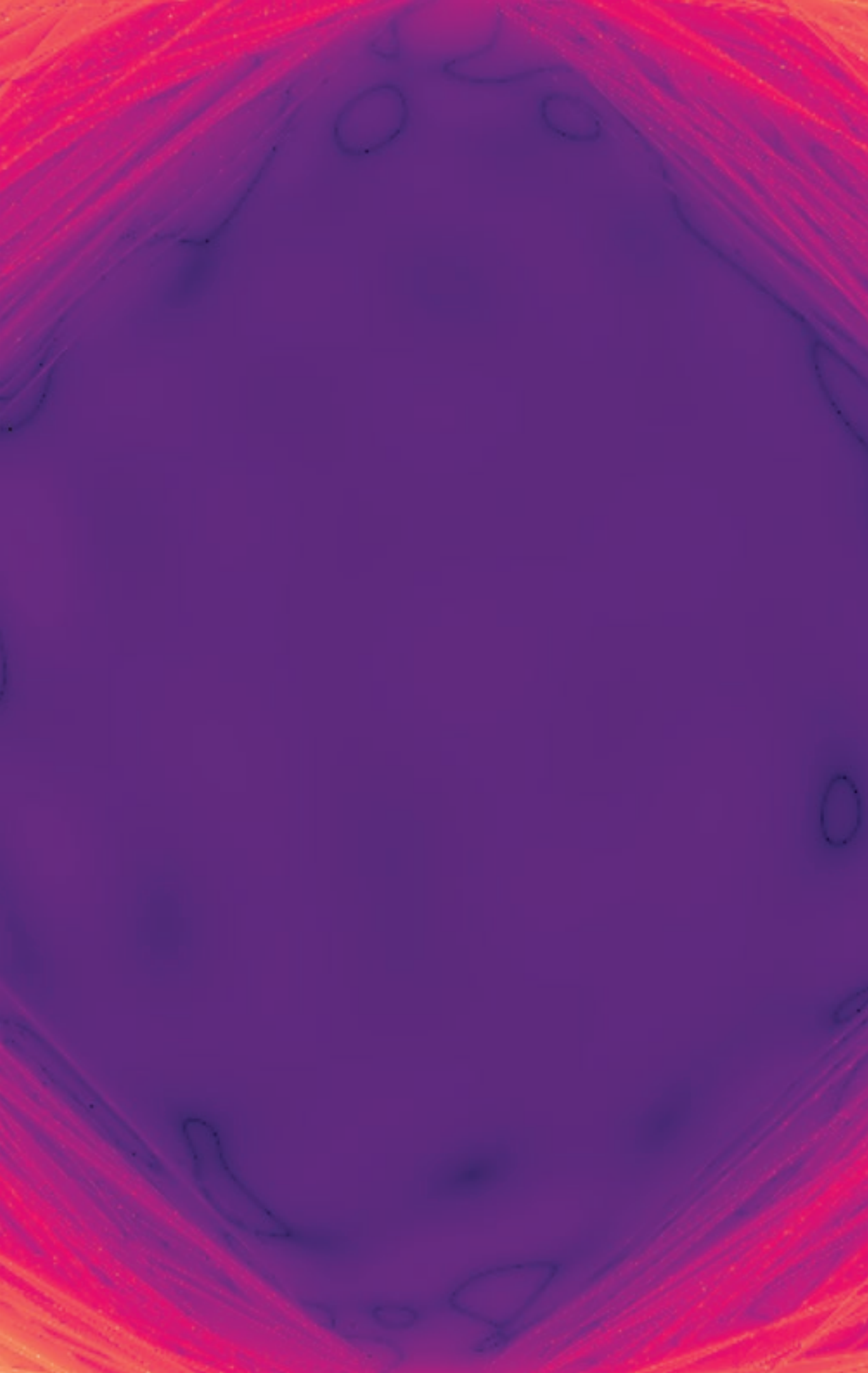
The top algorithms showed excellent predictive accuracy for patient-reported bladder function improvement for both OBTX-A and SNM and were noninferior to the predictive accuracy of expert urologists. The algorithms were also highly accurate in predicting patient-reported bladder leakage improvement for both modalities and were noninferior to experts’ predictions.

The authors presented the findings in May 2022 at the American Urological Association meeting, and the study was later published in the *International Urogynecology Journal*.

A complement to medical decision making

Despite their accuracy, the algorithms won’t replace clinician expertise, says Dr. Werneburg. “Some aspects of the physician-patient interaction are subtle and uncomputable, and thus machine learning may complement, but not replace, a physician’s judgment.”

RIGHT — The image was generated by the learning algorithm described in Werneburg et al. *Neurourology & Urodynamics* (2022) and Werneburg et al. *International Urogynecology Journal* (2022), developed by E.A. Werneburg. To generate the image, the algorithm was trained on uniform noise, and the image is the algorithm’s attempt at creating order from randomness.





2022 HIGHLIGHT

TESTICULAR TISSUE CRYOPRESERVATION FOR PREPUBESCENT MALES AT RISK FOR INFERTILITY

Fertility preservation is currently not an option for prepubescent males who are undergoing gonadotoxic treatment or who have an infertility-causing disease, as they are unable to provide a semen sample.

A team of Cleveland Clinic urologists and pediatric oncologists is hoping to change that by offering a testicular cryopreservation service — at no cost to patients.

An experimental approach with great potential

Preclinical studies have shown that autologous transplantation of spermatogonial stem cells (SSCs) from testicular tissue cryopreservation (TTC) has the potential to restore spermatogenesis in animal models. Although the approach is still in the experimental realm, clinicians and researchers are excited by its promising results.

“It’s still experimental, but the data published about its utility in primates are promising. We’re not quite there yet in humans, but I think we will be. The science is moving really quickly,” says Sarah Vij, MD, a urologist in the Department of Urology and the study’s primary investigator.

With this in mind, she and colleagues pediatric urologist Audrey Rhee, MD, and pediatric oncologists Seth Rotz, MD, and Stefanie Thomas, MD, developed a streamlined testicular tissue collection and storage process. They have enrolled and cryopreserved testicular tissue for nearly a dozen young patients so far.

Dr. Vij, who also leads Cleveland Clinic’s Center for Male Fertility, says their goal is to have the tissue available for future use when research and technologies have advanced enough to support transplantation of SSCs.

“Although we do not yet have the ability to develop sperm from spermatogonial stem cells in humans, there is hope that this will be available by the time these children are ready to grow their families,” says Dr. Vij.

The project was funded with a VeloSano Impact Award, a Cleveland Clinic cancer research grant.

In addition to obtaining and storing the tissue for potential future use and research pursuits, the team is also assessing the effect that tissue storage has on parental distress during and after treatment.

They plan to capture these data systematically to understand their association with parent experience measures and determine whether TTC plays a role in reducing parental distress and/or increasing parental hope.

“For some patients and families, having that conversation about fertility can provide some solace. You’re talking about life after treatment, which can be a hopeful dialogue and alleviate some distress, as difficult as those conversations may be,” says Dr. Rotz, who leads the Childhood Cancer Survivorship Clinic.

Improved survival has changed the conversation about future fertility

Advances in pediatric cancer treatment have led to a greater than 80% survival rate at least five years post-treatment. This has shifted the conversation among parents and providers about how to best manage the longer-term effects of cancer treatment on quality of life, which includes fertility.

“Every patient encounter is different, and age, sex and treatment are all variables that shape the fertility-preserving conversation,” emphasizes Dr. Rotz. “Regardless of the patient’s age, our goal is to have a conversation about fertility and infertility and potential fertility preservation options with all patients who have a new cancer diagnosis, before we start therapy. It’s never too early.”

Dr. Vij acknowledges that TTC is not inexpensive; it’s novel and still experimental. So to be able to offer it to all patients at no cost is significant.

“We are trying to remove all barriers to entry for interested patients and families,” she says.

2022 HIGHLIGHT

MOVING TOWARD PREVENTION AND PRECISION IN KIDNEY MEDICINE

Efforts over the past decade are contributing to a new paradigm in identifying and managing kidney diseases. Large-scale predictive modeling and new clinical trials are chipping away at traditional approaches and offering a glimpse into the future of kidney medicine.

PREDICTING RISK OF ACUTE KIDNEY INJURY FOLLOWING CARDIAC SURGERY

Earlier this year, findings from a Cleveland Clinic-led study, published in *JAMA*, showed that data from routine laboratory panels can predict risk of acute kidney injury (AKI) following cardiac surgery.

AKI and other kidney-related issues are known risks following any major surgery. Increased serum creatinine levels, a pathological hallmark of a kidney injury, can be deceptive because levels may not increase right away, and patients are at risk for serious complications if intervention isn't prompt.

In addition to serum creatinine levels, blood urea nitrogen and urine output also are components of the AKI calculation. However, this calculation does not account for events in a perioperative setting that may trigger physiologic and metabolic pathways associated with the disease.

"A patient could have been identified as low risk for developing cardiac surgery-related AKI before surgery, but unexpected perioperative events may enable progression to some form of AKI," says Sevag Demirjian, MD, lead author of the study and a nephrologist in the Department of Kidney Medicine.

With that in mind, the research team developed four multivariable models to predict moderate-to-severe AKI and AKI requiring dialysis in a post-cardiac surgery setting. They used data derived from perioperative laboratory blood tests to capture early changes in serum creatinine and immediate post-surgery laboratory parameters.

The derivation cohort (N = 58,526) was developed with clinical data extracted from Cleveland Clinic electronic health records for patients from 2000 to 2019 undergoing cardiac surgery at main campus. The external validation cohort data (N = 4,734)

included the same variables but were extracted from records at three affiliated Cleveland Clinic hospitals.

Findings from the test-train cohort show that within 72 hours of surgery, 5% of patients developed moderate-to-severe AKI, and 1% of patients developed AKI that required dialysis. Within 14 days of surgery, 5% of patients developed moderate-to-severe AKI, and 2% of patients developed AKI that required dialysis.

The models performed with "excellent predictive discrimination" across all endpoints, the authors report in the study. Models for moderate-to-severe AKI post-surgery showed areas under the curve (AUCs) of 0.88 within 72 hours and 0.85 within 14 days; and the models for AKI requiring dialysis showed AUCs of 0.92 and 0.90 at the same respective endpoints.

Operationalizing, targeting individual interventions

Although the model algorithms are computationally complex, they are based on discrete and standardized laboratory data that could be integrated with electronic medical records and are also available as a web-based calculator: [riskcalc.org /AKIpostCardiacSurgery](http://riskcalc.org/AKIpostCardiacSurgery).

"Some of the early changes in the multiple components of the blood profile are easy to overlook individually, but the models highlight patterns of changes in multiple variables better than we clinicians do," Dr. Demirjian says.

The value of flagging patients at risk for developing AKI early in the postoperative stage cannot be overstated, he explains. "It could allow for more targeted management, such as closer monitoring, hemodynamic and volume optimization, and avoidance of nephrotoxins that could be detrimental to kidney function."

“In addition to blood sugar control, blood pressure control, lipid management and lifestyle modification, the use of ACE-Is or ARBs along with SGLT2 inhibitors, GLP1 receptor agonists or newer MRAs should become the cornerstone of treating diabetic kidney disease.”

— GEORGE THOMAS, MD

More validation studies are needed

More research is needed to validate the models and their clinical utility. “The next step is proving that interventions based on early recognition of kidney issues identified by the models will actually translate to better outcomes for our patients,” concludes Dr. Demirjian.

NOVEL THERAPEUTICS USHER IN A NEW ERA OF MANAGEMENT

Over the past decade, there has been significant research investment in identifying novel therapies to manage diabetic kidney disease (DKD), with the understanding that diabetes is a major cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD).

Treatments that stop or delay the progression of DKD will have a major impact on clinical outcomes. But until only recently there were few effective medications to delay the progression of DKD other than renin-angiotensin-aldosterone system (RAAS) blockade with angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers (ARBs).

George Thomas, MD, nephrologist in the Department of Kidney Medicine, says this momentum is paying off for patients.

“We are now in a new era of DKD management with randomized controlled trials showing the efficacy of newer classes of medications, including sodium-glucose transport protein 2 inhibitors (SGLT2i), glucagon-like peptide-1 (GLP1) receptor agonists and newer mineralocorticoid receptor antagonists (MRAs), which have shown potential to surpass the benefits of ACE-Is or ARBs alone,” he explains.

And with the availability of these new treatment options, there can be a renewed focus on the preservation of kidney function.

The evidence is practice changing

Multiple landmark studies have shown the value of adding these new therapeutic agents to an ACE-I or ARB to preserve kidney function.

Recently, findings from the landmark EMPA-Kidney trial, the largest to date examining SGLT2i in patients with CKD, showed the safety and efficacy of empagliflozin in patients with both diabetic and nondiabetic CKD. Dr. Thomas was Cleveland Clinic's principal investigator for the trial.

He asserts, “In addition to blood sugar control, blood pressure control, lipid management and lifestyle modification, the use of ACE-Is or ARBs along with SGLT2 inhibitors, GLP1 receptor agonists or newer MRAs should become the cornerstone of treating diabetic kidney disease.”

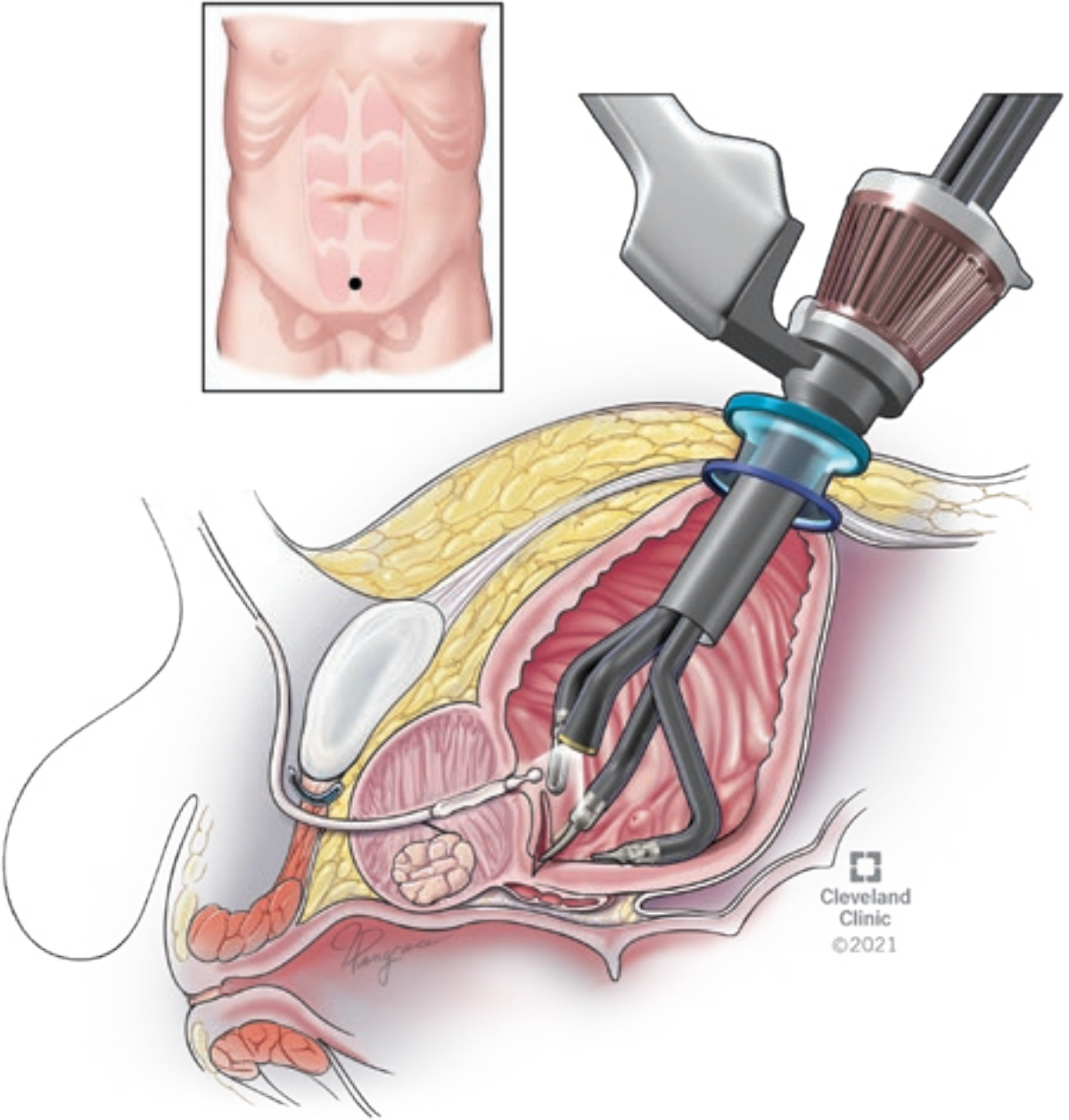
Kidney Disease: Improving Global Outcomes (KDIGO) has updated its Clinical Practice Guideline for Diabetes Management in CKD to reflect this new evidence.

Dr. Thomas says other therapeutic options are also being explored and may increase the repertoire of management options. Advances in molecular biology and genetics may provide future avenues for personalized medicine for patients with DKD.

A multilayered approach is needed

With new medications comes the need to maximize their potential. “We will need strategies to increase the appropriate use of these medications,” says Dr. Thomas.

“This will require provider and patient education and infrastructure and collaboration across specialties to identify patients who would benefit from these therapies. We must also prioritize the availability and affordability of these medications for these patients.”



2022 HIGHLIGHT

ROBOTIC PROSTATECTOMY WITHOUT VENTILATOR GENERAL ANESTHESIA? A NEW TECHNIQUE IS MAKING IT A REALITY

Efforts to regionalize robotic prostatectomies have opened the door for another innovation in urologic surgery. Patients can now undergo prostate surgery with epidural anesthesia and light sedation, known as twilight sleep, without the need for ventilator general anesthesia.

Jihad Kaouk, MD, Director of the Center for Robotic and Image-Guided Surgery, recently completed a series of 15 single-port (SP) transvesical radical prostatectomies with an epidural anesthesia regimen. He explains how a newer technique — SP robot-assisted transvesical prostatectomy — has made this anesthesia regimen possible.

“Robotic surgery requires pumping gas into the patient’s belly to create a surgical field in a gas bubble for visualization and maneuvering. Under pressure, it expands and alters the movement of the diaphragm, preventing the patient from breathing spontaneously,” he says. “This has traditionally necessitated the use of a ventilator under general anesthesia — with or without spinal or epidural anesthesia.”

“But as we continue to regionalize the surgery (limit it to the location of the disease), as in the case of the SP transvesical prostatectomy, that gas bubble is no longer in the intraperitoneal space; it’s limited to inside the bladder, so it’s not pushing on the diaphragm,” he explains.

Initial series completed with excellent results

The patients selected for the epidural underwent prostatectomy for either prostate malignancies or enlarged prostate but had no other underlying disease or comorbidities.

The teams involved established a plan B in advance of the first case in the unlikely event that the patient moved, vocalized pain or unknowingly reached into a sterile field. “It takes a minimal amount of time to intubate and continue with the surgery, and the team was on standby in case that was required,” he says, though it was never needed.

SP transvesical prostatectomy: At a glance

The transvesical approach enables surgical access

to the prostate through the bladder, avoiding the intraperitoneal cavity entirely. As a result, patients experience less pain and postoperative ileus because the bowels stay intact. In 2021, Dr. Kaouk and colleagues were the first to report their experience and early outcomes of this technique for radical prostatectomy and pelvic node dissection. It has become a preferred option in select patients with low- to intermediate-risk prostate cancer, Dr. Kaouk says.

Early results demonstrated a significant impact on urine control (50% had immediate continence), short postoperative Foley duration (three days post-surgery), minimal perioperative complications, limited use of opioids for pain control, low risk for transfusion and fast recovery, with about 87% of patients in an outpatient setting within four hours of surgery.

Expanding options for patients

For most patients, general anesthesia is a safe and appropriate option. But in patients with underlying neurologic or respiratory disorders who may be advised to avoid general anesthesia, epidural anesthesia may be a safe alternative.

Contraindications aside, some patients simply prefer to maintain consciousness if given the option, according to Dr. Kaouk. “Going forward, an epidural for SP simple or radical transvesical prostatectomy will become an option as part of the medical decision-making process. And we will recommend it to patients when there are possible benefits.”

He continues, “I’ve had patients tell me that they want the surgery but are terrified of being intubated and completely under general anesthesia, or they have medical reasons precluding them from use of general anesthesia. So it feels great to be able to give them this option.”

2022 HIGHLIGHT

PLACING PATIENTS AT THE CENTER OF THEIR KIDNEY CARE

It's been three years since the announcement of the Advancing American Kidney Health executive order, which defined a framework for policies that aim to transform prevention, diagnosis and treatment of kidney disease.

Central to this framework is prioritizing the patient. Crystal Gadegbeku, MD, Chair of the Department of Kidney Medicine, says this means empowering and engaging patients to make decisions about treatment modalities for end-stage kidney disease (ESKD). It also means improving access and quality of life for future patients. Here's a look at what the department is doing to achieve these goals.

Establishing innovation in kidney care

In 2022, Dr. Gadegbeku launched the Optimal Transition Program, which is designed to smoothly transition patients to ESKD care. The goal is to optimize patient choice and education, and facilitate navigation through the complex process of preparation for the preferred kidney replacement therapy. This program aims to familiarize patients with all therapeutic modalities, facilitate early transplant evaluation and avoid hospitalization for unplanned initiation or "crashing" into dialysis.

Currently, Cleveland Clinic surpasses the national average for patients receiving home hemodialysis therapies at 20% (the national average is 13%), and this program will further enhance home therapeutic opportunities for patients.

Automating the kidney transplant process

Recognizing that the pathway to transplant is not straightforward, even for those who need it the most, Anne Huml, MD, a nephrologist in the Department of Kidney Medicine, launched a pilot study with the goal of simplifying the referral process. The project received funding from a Cleveland Clinic Catalyst Grant.

Patients with no contraindications to transplant and who are likely to meet clinical transplant criteria will be automatically referred for transplant evaluation in their electronic medical record, making it an opt-out rather than an opt-in process. Program staff will also track the progress of patients throughout the multistep evaluation process to pinpoint barriers

within the system and determine where the drop-off is most likely to occur.

Patient education will help manage expectations about kidney transplant referral and prepare patients for their first visit to the transplant center. Dr. Huml is hopeful the project will improve equity, promote timely evaluations, ascertain key barriers, and measure patient and provider perspectives on the process.

Accelerating breakthroughs

Efforts to accelerate therapeutics, devices and biologics to treat kidney disease continue on a national level with the help of KidneyX, a public-private partnership between the U.S. Department of Health and Human Services (HHS) and the American Society of Nephrology.

John Sedor, MD, a nephrologist in the Department of Kidney Medicine, chairs the steering committee of the competition-based program that awards prizes to high-impact, meritorious proposals. Every KidneyX prize competition defines a problem, without a preconceived notion of what the solution should be, and asks participants to find solutions.

Last year, KidneyX awarded six prizes, two to groups with novel technologies for xenotransplantation. In August 2022, HHS announced an Artificial Kidney Prize competition, which seeks bioartificial kidney prototypes or solutions that address a specific challenge in the development of a functional artificial kidney. The proposals must incorporate science from the domains of regenerative medicine, tissue engineering, systems biology or synthetic biology.

These and other innovations will catalyze the drive for better kidney disease treatments. However, Dr. Sedor says innovation with an eye on health equity is essential when developing solutions for kidney disease.

"We don't want to wait until the product or device hits the market to have that conversation. There are innovations in the pipeline, and we want to ensure they get to the people who need them."





2022 HIGHLIGHT

FROM STAGING TO SURGERY: HOW INNOVATION IS CUSTOMIZING UROLOGIC CARE

Innovation is at the cornerstone of care in Cleveland Clinic's Department of Urology, and it's enabling experts to deliver more personalized approaches to patients. From developing new ways to screen for and treat genitourinary cancers to leveraging robotic and artificial intelligence platforms, our experts are transforming how urologic conditions are diagnosed and treated.

Smart imaging for smarter staging

"In the United States, tens of thousands of patients may be unnecessarily undergoing surgery or receiving treatment for kidney cancer because their benign tumor mimics a malignant one on computed tomography (CT) imaging," explains Christopher Weight, MD, Center Director for Urologic Oncology.

To address potential overtreatment, Dr. Weight and his colleagues are utilizing artificial intelligence (AI)-based segmentation to recognize pathologic characteristics of a tumor and its surrounding anatomy. Often disease features are too complex and subjective for large-scale human interpretation. However, tapping into AI imaging technologies that integrate data from CT scan segments with nephrectomy scores could prognosticate disease at a high level.

"We hope that additional investigation into this work will provide an even more personalized approach to kidney cancer care," he says.

Measuring renal parenchymal volume

Determining whether a patient should undergo partial nephrectomy versus a more aggressive radical nephrectomy is a big question in the field. Urologic oncologist Steven Campbell, MD, PhD, and colleagues are using semi-automated imaging software to optimize management.

The technology automatically measures renal parenchymal volume in the kidney with the tumor and in the contralateral kidney. "That differential of parenchymal volume provides a split renal function that's as accurate as a nuclear renal scan, and, in our studies, has actually proved to be more accurate," he says.

A new generation of surgical robotics

Single-port (SP) robotic surgery employs a new generation of robot that is enabling further regionalization of urologic surgery. The surgeon introduces a camera and three other narrow-profile instruments through one cannula, thereby avoiding unnecessary involvement of other anatomy and leading to improved recovery outcomes.

Over the past several years, the Cleveland Clinic team has pioneered numerous applications for using the SP robotic system to assist with robotic partial nephrectomy for removal of cancerous kidney tumors through a small incision outside the peritoneum. Additional complex robotic procedures have applied the SP approach, such as extraperitoneal robotic SP kidney transplant and autotransplant; nephrectomy; pyeloplasty; prostate surgery, including transvesical and extraperitoneal prostatectomy; cystectomy; and urinary tract reconstruction.

SP is also appealing for use in pediatric patients because it requires a minimal incision site and enables a retroperitoneal approach. The incision, called the mini-Pfannenstiel is performed low in the pelvis, away from the abdominal muscle, a cosmetically appealing option for younger patients.

Jihad Kaouk, MD, Director of the Center for Robotic and Image-Guided Surgery, says there is still untapped potential for robotic surgery, adding that we can look forward to the "smart" application of the system next by "moving the robot from an extension of my hands and eyes to become a partner in the surgery under human control."

"Our focus on innovation will keep moving and evolving patient care into the future," he says.

2022 HIGHLIGHT

KIDNEY TRANSPLANTATION: ADDRESSING THE ORGAN SHORTAGE BY IMPROVING TRANSPLANT STEWARDSHIP

Approximately 90,000 patients in the United States are registered for a kidney transplant. The shortage of kidneys — and other lifesaving organs for transplantation — has led to urgent calls for improved organ utilization efforts worldwide.

Experts from Cleveland Clinic’s kidney transplant and infectious disease programs continue to put forth protocols that guide transplantation of kidneys that may have previously been deemed ineligible.

COVID-19 and kidney transplant: Leading practice-changing research

With limited guidance about best practices, transplanting extrapulmonary organs from deceased donors infected with SARS-CoV-2 has been controversial.

The Organ Procurement and Transplant Network (OPTN) Ad Hoc Disease Transmission Advisory Committee has emphasized balancing theoretical risk with potential waitlist-related complications or mortality. But with no other literature, transplant teams have had to take calculated risks.

In early 2021, the kidney transplant team, led by Alvin Wee, MD, MBA, and Emilio Poggio, MD, and their infectious disease colleagues, led by Christine Koval, MD, developed a protocol to perform kidney transplants from deceased donors who tested positive incidentally, without pulmonary issues. Continuing to monitor outcomes, they published their initial experience on 10 cases. Then they gradually expanded the criteria to include deceased donors with severe COVID-19 disease — as long as their kidney function was satisfactory.

Recently, the team published their experience of utilizing more than 100 kidneys from COVID-19-positive donors. In the *American Journal of Transplantation*, the authors reported that from Feb. 1, 2021, to Jan. 31, 2022, they safely transplanted 115 adult kidneys from deceased donors with COVID-19. In total, 115 kidneys were transplanted from 68 donors with COVID-19, and 33 of these donors died due to COVID-19.

Differences in graft performance and function were insignificant among the cohorts at a median follow-up of 5.7 months, regardless of SARS-CoV-2 status or severity. Recipients of a kidney from a deceased donor with a COVID-19-related cause of death had a lower — but still acceptable — estimated glomerular filtration rate at follow-up. Waiting time for an organ was shorter, the authors noted.

Dr. Wee remarks, “Balancing the risk of accepting an organ with dying on the waitlist is always part of the decision when it comes to transplant, and the pandemic further complicated this. But this approach has enabled transplant of more than 200 kidneys, a lifesaving intervention that may have been discounted otherwise. At the same time, this has also brought some meaning to the donor’s family from this senseless death.”

Only center in Ohio performing kidney transplant under the HOPE Act

Cleveland Clinic performed a kidney transplant from a deceased donor with HIV to a patient with end-stage kidney disease who is HIV positive, the first in Ohio performed under the HIV Organ Policy Equity (HOPE) Act.

The legislation is part of a national effort to make transplantation more accessible to patients with HIV, a patient population vulnerable to healthcare disparities, reversing a decadeslong policy that prevented people with HIV from donating organs, explains Anita Modi, MD, Associate Staff in the Department of Infectious Disease.

Dr. Wee, who performed the surgery, says now that the regulatory groundwork has been established, they are eager to offer this option to candidates who are HIV positive to improve their access to a lifesaving procedure.





2022 HIGHLIGHT

IMPLEMENTING AND EVALUATING THE NEW RACE-FREE EQUATION TO ASSESS KIDNEY FUNCTION

In early 2022, Cleveland Clinic formally adopted the recently retooled race-free estimated glomerular filtration rate (eGFR) formula for consistent use across the enterprise.

This decision followed a recommendation by the National Kidney Foundation and the American Society of Nephrology Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease to adopt a new equation: the eGFR 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

The task force engaged with nearly 100 experts from seven countries for more than a year before arriving at their decision. They evaluated 26 possible equations and published data. In addition, they spoke with patients, healthcare workers and trainees before concluding that widespread adoption of the CKD-EPI equation, a race-free formula, was the best approach.

Crystal Gadegbeku, MD, Department Chair of Kidney Medicine at Cleveland Clinic and task force member, says, “As a group, we unanimously agreed that race should not be considered as a factor in estimating GFR. We recognize what a genetic mosaic we all are. Not only is race a poor proxy for genetics, but it’s a social construct. So taking race out of the eGFR equation makes sense.”

The newly recommended formula

CKD-EPI is a creatinine-based equation that excludes race but includes age and sex.

For clinical decisions where greater accuracy is essential, the task force recommends using cystatin C combined with serum creatinine, a cystatin C alone equation, or a measured GFR test to confirm kidney function.

Although cystatin C has never required a race modifier to estimate kidney function, it’s not available at every center. “With an estimate of over 200 million measurements performed annually, we need a tool for everyday use in all clinical practice settings, not only to manage kidney disease but for assessment across the spectrum of kidney function,” says Dr. Gadegbeku.

Emphasis on estimate

While the CKD-EPI formula can estimate kidney

function, primary care physicians shouldn’t base critical medical decisions on a single number. Instead, estimates should be used as a guide in making treatment decisions. Dr. Gadegbeku advocates for reporting a GFR range so that physicians and patients understand that these are not precise measurements.

Implications for care

Emilio Poggio, MD, Medical Director of the Kidney Transplant Program at Cleveland Clinic, and colleagues are now focusing on evaluating the performance of the new equation in persons interested in kidney donation.

In a recent retrospective cohort study of nearly 300 living kidney donors, the research team examined four different equations with and without the race variable. “We found that the new formula performed very well when estimating kidney function, and even better when we included cystatin C,” he explains.

Accuracy is essential in the living kidney donor population to ensure donors’ candidacy. “We need to ensure that the function of their remaining kidney is good and able to maintain its function long term,” says Dr. Poggio.

In July 2022, the United Network for Organ Sharing announced that transplant hospitals are now required to adopt the new equation for appropriate assessment in potential kidney donors and recipients.

“The old equation may overestimate GFR in Black patients, which could inadvertently delay transplant evaluation for Black candidates compared to non-Black candidates with similar creatinine values,” explains Dr. Poggio.

He adds, “We are encouraged by the findings we’ve seen so far, but it is also important to note that while the implementation of race-free GFR reporting is a step in the right direction, the use of this equation alone will not completely solve the complex issue of racial disparity in kidney transplantation.”

2022 UPDATES

The following updates from our subspecialty centers represent just a few highlights and accomplishments from 2022.

DEPARTMENT OF KIDNEY MEDICINE

The center is a major site for seven active multicenter, NIH-funded studies in nephrology:

- 1. Caring for OutPatiEnts after Acute Kidney Injury (COPE-AKI)
- 2. Kidney Precision Medicine Project (KPMP)
- 3. Cleveland CRIC-KPMP Cohort
- 4. Regulatory T Cell Modulation in Kidney Transplantation with Biologic Blockade of Dual Effector Pathways, CD28 and IL-6 (CTOT-24)
- 5. APOL1 Long-term Kidney Transplantation Outcomes Network
- 6. Nephrotic Syndrome Study Network (NEPTUNE)
- 7. Cure Glomerulonephropathy Network (CureGN)

Cleveland Research Training Network (CREATE) Scientists in Kidney, Urology and Hematology

Cleveland Clinic's Department of Kidney Medicine is part of a consortium uniting Cleveland's six biomedical research institutions. The team received a U2C/TL1 grant that supports scientific training and professional development for trainees pursuing research in kidney medicine and benign urinary and blood conditions.



WORK LED BY CLEVELAND CLINIC NEPHROLOGISTS

was featured on the cover of the *Clinical Journal of the American Society of Nephrology* twice in 2022.

33
active clinical research projects

1,993
patients enrolled in clinical research projects



RESHAPING RENAL CURRICULUM: Georges Nakhoul, MD, Associate Director for the Nephrology and Hypertension Fellowship Program, and colleagues have continued to evaluate the novel 3D virtual reality tool to improve renal physiology education. They presented recent findings at the 2022 American Society of Nephrology Annual Meeting.

Cleveland Clinic's Department of Kidney Medicine is part of a multicenter study

awarded a two-year, \$9 million grant from the Patient-Centered Outcomes Research Institute. The research team, led by investigators at Wake Forest University, will explore potential benefits and outcomes associated with incremental introduction of hemodialysis, providing a basis for individualized hemodialysis treatment models.

20%

of patients on home dialysis therapies
(national average is 13%)



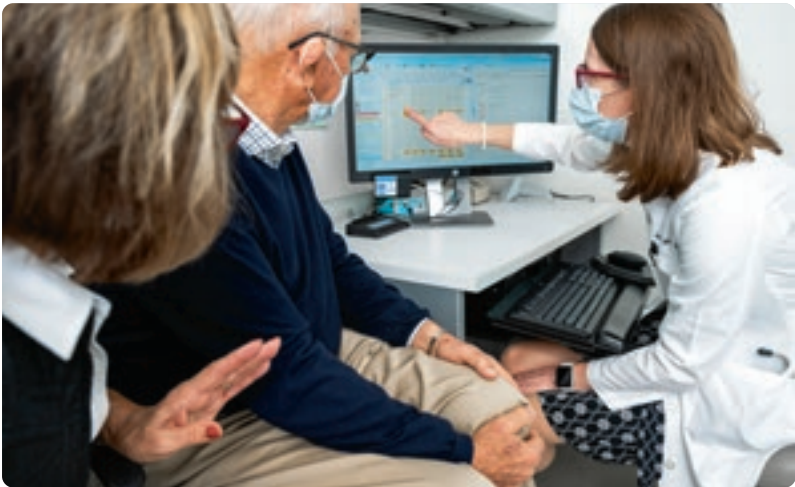
TRANSPLANT



GEOGRAPHIC HOT SPOTS LINKED TO DISPARITIES IN KIDNEY TRANSPLANT: A Cleveland Clinic study led by data scientists and nephrologists reveals subregional zones in the Southeast, Southwest, Appalachia and California with delayed listing patterns for kidney transplant.

340 Kidney and pancreas transplants in 2022

ANNE HUML, MD, was awarded a grant, in collaboration with Columbia University and the National Kidney Foundation, designed to increase kidney transplants and lower the discard of deceased donor kidneys through a patient-centered decision-making model.



DEPARTMENT OF UROLOGY

EARLIER DETECTION OF RECURRENT AND METASTATIC DISEASE

— Prostate-specific membrane antigen (PSMA) PET imaging was named a top medical innovation by Cleveland Clinic in 2022, following its FDA approval and subsequent adoption into practice in 2021. Radiation oncologists have called it a game changer, and urologic oncologists like Chris Weight, MD, say it's giving way to more opportunities to detect local recurrences that were previously believed to be systemic, leading to an increase in salvage prostatectomies.

ISOPSA IN THE REAL WORLD

— A Cleveland Clinic-led study shows the novel IsoPSA prostate cancer test is readily adopted by practitioners in various practice settings and resulted in a 55% net decrease in recommendations for prostate biopsy in men with total PSA \geq 4 ng/mL and a 9% decrease in recommendations for MRI.



**THE NEXT
GENERATION OF
UROLOGISTS**

— In an analysis of 1,814 urology residents from U.S. medical schools, Cleveland Clinic Lerner College of Medicine produced the highest percentage of medical students who elected to enter urology and match into the field (3.65%) over a five-year period (2016-2021).

15

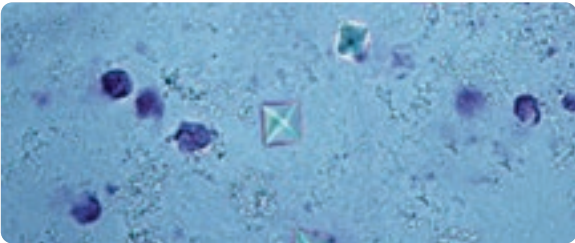
single-port transvesical radical prostatectomies with epidural anesthesia and twilight sleep. Read more on page 15 about this new anesthesia regimen appropriate for select patients.



SARAH VIJ, MD, is the first female program director for a Sexual Medicine Society of North America-endorsed fellowship.

For cancer in a solitary kidney, preserving function is almost always possible, according to an analysis by Steven Campbell, MD, PhD. It's one of the largest-ever series of renal masses in a solitary kidney (RMSK) outcomes and the first to include all RMSK patients.

UNDERSTANDING UROSYMPHYSEAL FISTULAE — Reconstructive urologists reported one of the largest series to date on urosymphyseal fistula cases, which aims to improve understanding of the condition, outline treatment approaches and raise awareness within the field.



INVESTIGATING KIDNEY STONES — Endourologists at Cleveland Clinic were awarded two Cleveland Clinic Catalyst Grants to improve use of photonic lithotripsy for treating kidney stones and explore antimicrobial nanoparticles to prevent biofilms on urologic implants.

Cleveland Clinic’s Male Infertility & Andrology Fellowship was endorsed by the Sexual Medicine Society of North America (SMSNA), along with 28 other programs in the U.S. and Canada, making it one of only six fellowships to have a dual endorsement from both the SMSNA and the Society for Male Reproduction and Urology.

NEW STAFF

Glickman Urological & Kidney Institute welcomed these new staff members in 2022.

UROLOGY

Alp Tuna Beksac, MD
Bradford Black, MD
Molly DeWitt-Foy, MD
David Heiser, MD
Ly Hoang Roberts, MD
Yi-Chia Lin, MD
Scott Lundy, MD
Steven Ochs, MD
Ruben Olivares, MD
Bechara Tabet, MD

KIDNEY MEDICINE

Korey Bartolomeo, DO
Harkanwal Dhillon, MD
Jagmeet Dhillon, MD
Niraj Karki, MD
Hanny Sawaf, MD
Yuliya Sharakova, MD
Jad Tabbara, MD

MOVING PERCUTANEOUS NEPHROLITHOTOMY (PCNL) INTO AN OUTPATIENT SETTING — PCNL is the most effective alternative for endoscopically removing kidney stones. This surgery, traditionally considered invasive, is now routinely performed as an outpatient procedure at Cleveland Clinic’s Endourology and Stone Diseases Center, without increased risk of complications or readmissions.




Connect with us at AUA2023 in Chicago. Stop by booth No. 205 and talk to us about Cleveland Clinic’s top-ranked urology program.


RESOURCES FOR PHYSICIANS


Stay Connected with Cleveland Clinic's
Glickman Urological & Kidney Institute

Consult QD Urology & Nephrology
News, research and perspectives
from Cleveland Clinic experts:
consultqd.clevelandclinic.org/urology-nephrology


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CME Opportunities
Visit ccfcme.org for offerings from
Cleveland Clinic's Center for
Continuing Education.

GLICKMAN UROLOGICAL & KIDNEY INSTITUTE

The Glickman Urological & Kidney Institute is a world leader in treating complex urologic and kidney conditions in adults and children. Our internationally recognized staff has pioneered laparoscopic and robotic surgical techniques and developed innovative procedures for urologic cancers and transplantation. We provide advanced management of kidney disease, hypertension, infertility and congenital malformations to help patients worldwide.

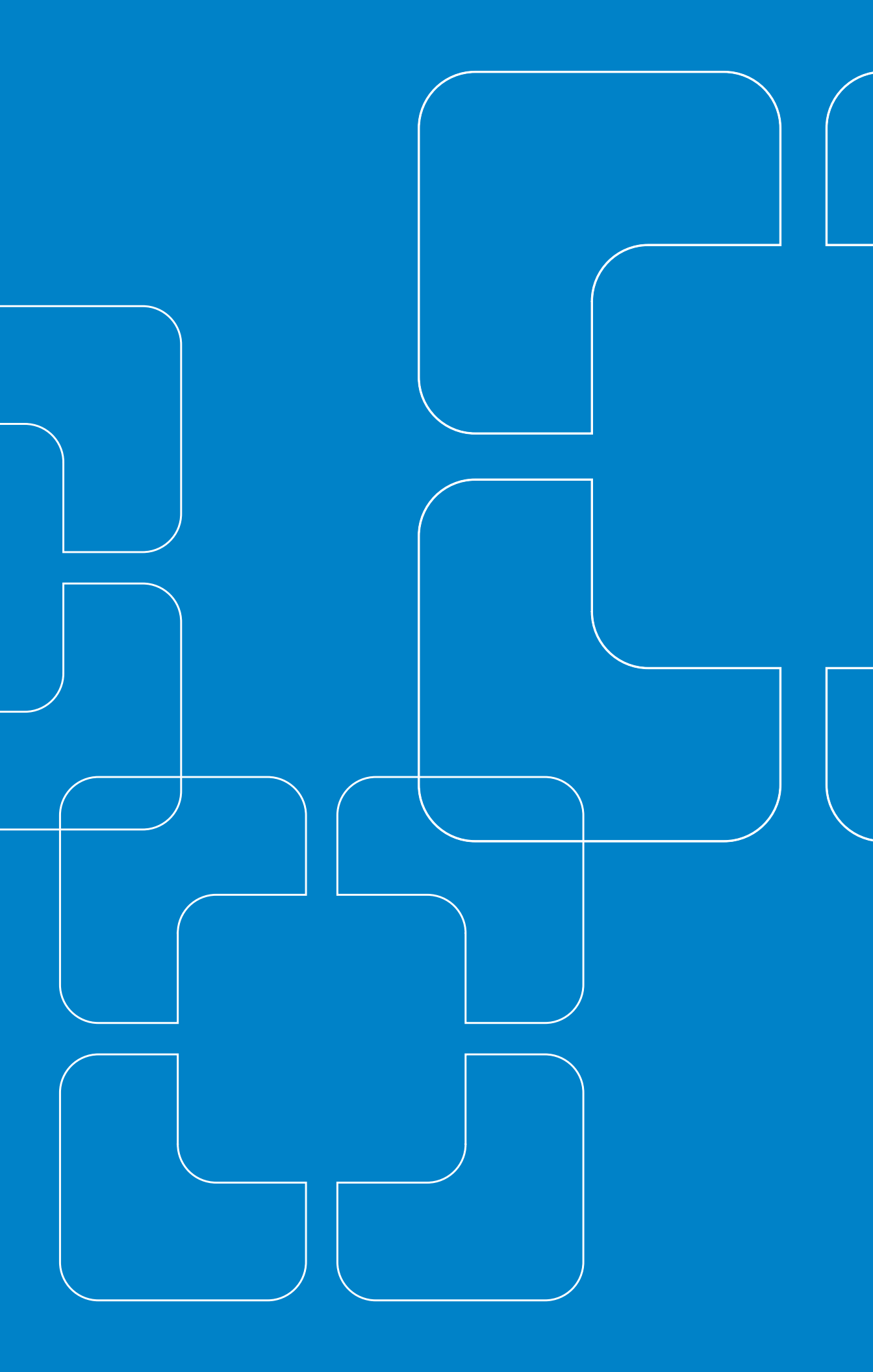
Year in Review is written for physicians and should be relied on for medical education purposes only. It does not provide a complete overview of the topics covered and should not replace the independent judgment of a physician about the appropriateness or risks of a procedure for a given patient.

Year in Review

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