10-2006

OncoLog Volume 51, Number 10, October 2006

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The University of Texas MD Anderson Cancer Center

A Publication of
M. D. Anderson Cancer Center
Making Cancer History®

REPORT TO PHYSICIANS

OCTOBER 2006 Vol. 51, No. 10

OncoLog

Robotic Surgical System Lends a Hand *(Actually, 4 Hands)*

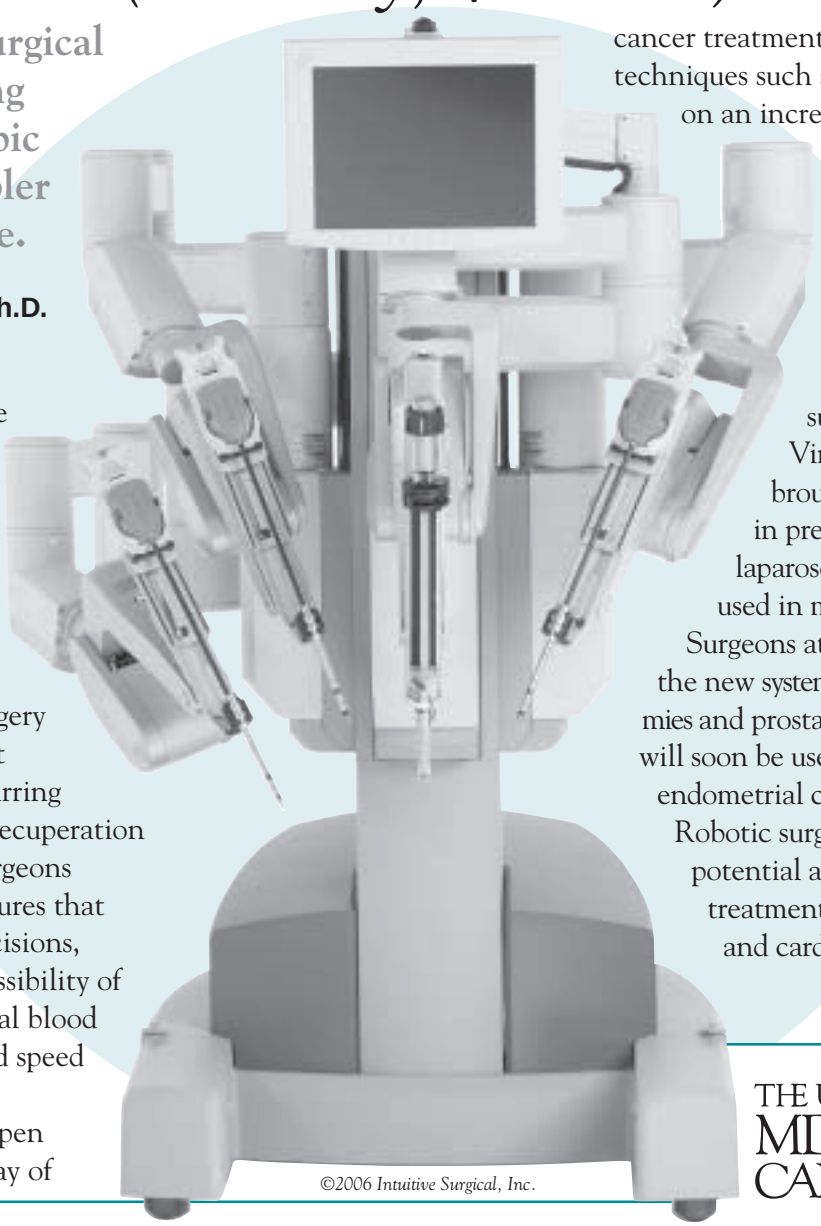
The da Vinci Surgical System is making many laparoscopic procedures simpler and more precise.

by Ellen McDonald, Ph.D.

Whether or not they are acquainted with terms like "laparoscopic radical prostatectomy" or "laparoscopic radical hysterectomy," most patients definitely know they would prefer a surgery that will cause the least amount of pain and scarring and have the shortest recuperation time. For their part, surgeons generally prefer procedures that require the smallest incisions, involve a negligible possibility of infection, cause minimal blood loss, and offer improved speed and efficiency.

While traditional, open surgery is still a mainstay of cancer treatment, minimally invasive techniques such as laparoscopy have taken on an increasingly important role in the past few years, thanks to quicker recovery times and comparable outcomes. At The University of Texas M. D. Anderson Cancer Center, robotic surgery with the new da Vinci Surgical System has brought further improvements in precision and simplicity to laparoscopy, allowing it to be used in more complex procedures. Surgeons at M. D. Anderson are using the new system in laparoscopic hysterectomies and prostatectomies now, and it will soon be used in some bladder and endometrial cancer surgeries as well. Robotic surgery has many more potential applications in cancer treatment, particularly for thoracic and cardiac procedures.

(Continued on **next page***)*



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THE UNIVERSITY OF TEXAS
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Robotic Surgical System Lends a Hand

(*Continued from* **page 1**)

Better-than-human precision

In contrast to standard laparoscopic equipment, this 1,400-pound, four-armed "robot" offers surgeons several advantages, including better control, dexterity, and visualization. At a console a short distance from the patient, the surgeon views a real-time, highly magnified three-dimensional image of the surgical site—as opposed to the two-dimensional image available with a laparoscopic television monitor. From this improved vantage point, the surgeon operates controls at the console, and those movements are replicated with better-than-human precision by the robotic arms at the bedside.

"Although it's called a robot," noted John W. Davis, M.D., an assistant professor in the Department of Urology, "the da Vinci system is actually more a flexibly wristed precision instrument that replicates what the surgeon's hands do and filters out any tremors, allowing the surgeon to make very precise motions in the patient's body.

"The da Vinci system is particularly useful for prostate surgery, which takes place low and deep in the pelvis," Dr. Davis continued. "The surgical margin between the prostate and the cancer is very small, only a few millimeters, and there are important quality-of-life outcomes associated with a technically successful surgery in terms of preserving sexual function and urinary function."

Dr. Davis noted that the system will soon be used for radical cystectomies in bladder cancer for similar reasons. "We expect it to be most useful in complex bladder procedures in which the technological precision helps with intricate reconstructive elements such as sewing the bladder to the urethra," he said. "In contrast, a procedure like kidney removal, which has no reconstructive element, can be performed very well through standard laparoscopy."

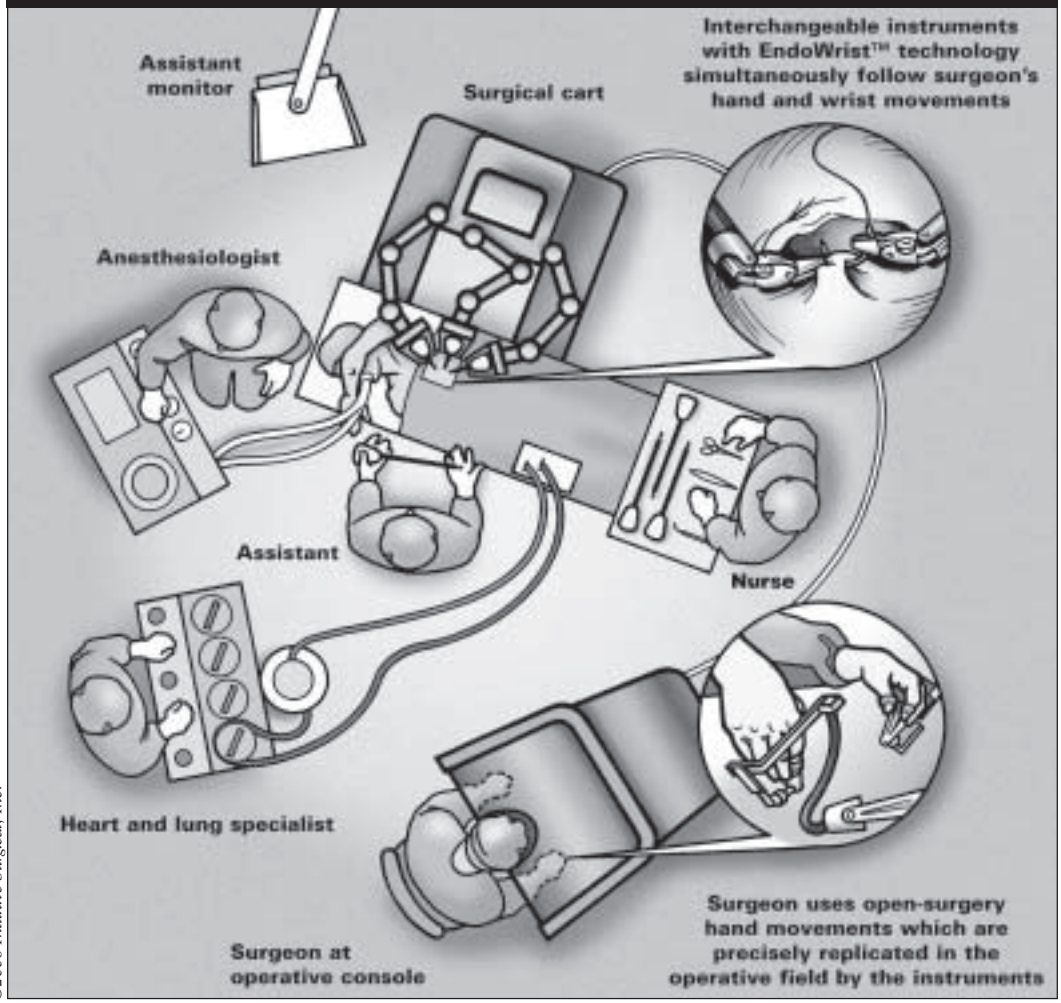
Pedro Ramirez, M.D., an associate professor in the Department of Gynecologic Oncology, is equally impressed by what he calls this "amazing" technology. "It is remarkable to see a surgeon's fingers moving in one part of the room and the instrument translating those exact movements inside the patient." He and his colleagues are currently using M. D. Anderson's da Vinci Surgical System for advanced gynecologic procedures such as laparoscopic hysterectomies for uterine cancer.

Meeting demand

The da Vinci system is expected to allow surgeons to meet the rising demand for minimally invasive procedures more rapidly, because the transition from open surgery to robotic surgery is much easier than the transition from open surgery to traditional laparoscopic surgery. "The robot basically enables surgeons to perform laparoscopy without the steep learning curve associated with standard laparoscopy," observed Surena Matin, M.D., an assistant professor in the Department of Urology.

Another advantage of the da Vinci Surgical System is the improved ability to record surgeries, thanks to the stability of the robotic arm guiding the camera into the incision. "We can videotape our cases and later refer back to a particular step when correlating pathologic outcomes with how the case went," continued Dr. Davis. "This high quality record makes it easier for surgeons to teach their techniques and skills to fellows and other faculty. In this way, I believe the robotic system will allow us to approach surgeries such as prostatectomies in a

Operating Room Set-up for the da Vinci Surgical System



A short distance from the operating table, the surgeon views a highly magnified, three-dimensional image of the surgical site at a console. Here, **Dr. Surena Matin** *demonstrates the controls which translate the surgeon's movements with better-than-human precision inside the patient.*

In contrast to standard laparoscopic equipment, this 1,400-pound, four-armed "robot" offers surgeons several advantages, including better control, dexterity, and visualization.

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very reproducible manner and achieve consistent outcomes."

Traditionally, surgery to remove a cancerous growth has meant a large incision and a lengthy recovery time. The advent of laparoscopic surgery has changed that for many cancer patients, and robotic surgery looks to be the next major step forward in the arena of minimally invasive surgery.

"Of course, promising new technologies like the robotic system don't mean the end of open surgery," said Dr. Matin. "Open surgery will continue to play an important role, particularly in advanced cancers."

"Technology changes fast, and it's hard to predict where we'll be in regard to minimally invasive procedures 20 years from now," added Dr. Ramirez. "But robotics is in its infancy, and I know for certain we aren't even close to reaching the peak potential for these procedures." Like many other surgeons, Dr. Ramirez is curious to see where robotics will ultimately fit as a tool in surgical oncology. But he points out that, from the patient's point of view, the surgeon's means aren't nearly as important as the end.

"Generally speaking, what patients want are small incisions and a good outcome," he said. "Robotic surgery is allowing us to offer that to more and more of our patients." ●

FOR MORE INFORMATION, *contact Dr. Davis at (713) 792-3250, Dr. Matin at (713) 792-3250, or Dr. Ramirez at (713) 745-5498.*

Evaluating New Surgical Technologies

With an eye toward future technological advances and new laparoscopic procedures, surgical faculty at M. D. Anderson Cancer Center formed the Minimally Invasive New Technology in Oncologic Surgery (MINTOS) program.

"The program began with a group of surgeons and other faculty from different oncologic specialties who were interested in evaluating the latest technologies for minimizing the trauma caused by traditional surgery," said Dr. Matin. "The idea was to come together as a group and evaluate promising new technologies in a randomized way, in a controlled setting, just as we evaluate new drugs. Only such scientifically grounded information can truly validate the purchase of new, and extremely expensive, equipment. The MINTOS program provides an infrastructure for such evaluations."

Although its initial focus has been on improving patient care with innovations such as the da Vinci system, the MINTOS program is also committed to improving training in minimally invasive surgery. To that end, more than 50 M. D. Anderson surgical trainees and faculty participated in a MINTOS program–sponsored training session this year that included the opportunity to hone their skills in a laboratory featuring a virtual reality surgical simulator. Plans are to further expand the training program by sponsoring courses and presentations by experts in the field and by establishing a dedicated laboratory space for training.

"We want to put M. D. Anderson at the forefront of research of minimally invasive oncologic procedures," said Dr. Matin. ●

Overweight Prostate Cancer Patients May Not Fare as Well

Obesity is an independent predictor of whether localized prostate cancer will progress after radiotherapy treatment, say researchers at M. D. Anderson Cancer Center.

In a study reported in the August 1 issue of the journal *Cancer*, researchers found that moderately and severely obese patients had a 99% greater risk of developing biochemical failure, an early marker of cancer progression, than other patients. The study also reports that obese patients had a 66% increased risk of having a tumor that recurs or becomes metastatic than did non-obese patients.

"Together, these studies confirm that a man's body mass index (BMI) can be a significant factor in how well he fares after standard treatments for prostate cancer."

– Sara Strom, Ph.D.

This finding mirrors results from a parallel study by M. D. Anderson researchers, reported last year in *Clinical Cancer Research*, that found that a history of weight gain or obesity at the time of diagnosis also played a role in how aggressive prostate cancer may become after surgery.

"Together, these studies confirm that a man's body mass index (BMI) can be a significant factor in how well he fares after standard treatments for prostate cancer," said the lead researcher of both studies, Sara Strom, Ph.D., an associate professor in the Department of Epidemiology.

Dr. Strom adds that these findings suggest that obese prostate cancer patients should be followed more closely after treatment. "When patients and their physicians are uncertain about the need for further therapy, our research indicates that a man's weight should be factored into that decision," she said.

New Tumor Suppressor Gene Identified

A single gene called BRIT1 plays a pivotal role in launching two DNA damage detection and repair pathways, suggesting that it functions as a tumor suppressor gene, researchers at M. D. Anderson Cancer Center report in the August issue of *Cancer Cell*.

Defects in BRIT1 seem to be a key pathological alteration in cancer initiation and progression, the authors note, and further understanding of its function may contribute to the development of new treatments for cancer.

"Disruption of BRIT1 function abolishes DNA damage responses and leads to genomic instability," said senior author Shiaw-Yih Lin, Ph.D., an assistant professor in the Department of Molecular Therapeutics at M. D. Anderson. Genomic instability fuels the initiation, growth, and spread of cancer.

In a series of laboratory experiments, Dr. Lin and colleagues showed that BRIT1 activates two molecular checkpoint pathways. By using small interfering RNA (siRNA) to silence the BRIT1 gene, the scientists shut down both pathways. They then used siRNA to silence the gene in normal human mammary epithelial cells. Inactivation of the gene caused chromosomal aberrations in about a quarter of the treated cells, versus none in the control group.

"We also found that BRIT1 expression is aberrant in several forms of human cancer," Dr. Lin said. The team found reduced expression of the gene in 35 out of 87 cases of advanced epithelial ovarian cancer. They also found reduced expression in breast and prostate cancer tissue compared with non-cancerous cells.

"Disruption of BRIT1 function abolishes DNA damage responses and leads to genomic instability."

– Shiaw-Yih Lin, Ph.D.

Drug Turns on Tumor Death Receptors

A clinical trial evaluating a new type of drug that activates death receptors on cancer cells has shown it to be safe and potentially beneficial, reported researchers from M. D. Anderson Cancer Center at the 42nd annual meeting of the American Society of Clinical Oncology.

In an ongoing phase I study, the drug, human Apo2L/TRAIL (Apo2L), has produced only minimal side effects in 58 patients with a variety of advanced cancers, reported Roy Herbst, M.D., Ph.D., professor and chief, Section of Thoracic Medical Oncology. The drug is designed to activate pathways inside tumor cells that lead to the destruction of these cells.

"This is an interesting new class of targeted agents, and Apo2L may well prove to be promising as we study it further."

– Roy Herbst, M.D., Ph.D.

Dr. Herbst also reported that the agent shrunk tumors in one patient with sarcoma and stabilized tumor growth in over half of the patients. He noted, however, that the potential of Apo2L cannot be established yet, especially since the maximum tolerated dose has not yet been determined.

In preclinical studies, Apo2L first caught researchers' attention when it selectively induced apoptosis in cancer cells while sparing normal cells. It showed activity in animal models of leukemia, non-small cell lung cancer, melanoma, and cancers of the colon, prostate, and breast.

"This is an interesting new class of targeted agents, and Apo2L may well prove to be promising as we study it further," said Dr. Herbst. He suspects that Apo2L and similar agents being developed will be most effective when used in combination with chemotherapy or radiation. He plans to test a combination of Apo2L and standard chemotherapy.

HOUSE•CALL

Q&A: Should You Take Part in a Clinical Trial?

Clinical trials are research studies that involve people, with the hope of finding better ways to prevent, diagnose, or treat a disease like cancer. Patients who participate in a clinical trial receive drugs or procedures that already have been researched in successful laboratory and/or animal studies.

Many of today's standard cancer treatments are based on the results of previous clinical trials.

When you've been diagnosed with cancer, deciding whether it's best for you to participate in a clinical trial is an important decision between you and your doctor. You'll want to consider all your options, weigh how likely it is that standard treatment will help, and evaluate the risks and benefits of joining a trial. All patients who take part in clinical trials are volunteers and can stop their participation at any time.

Q What are the types of clinical trials?

- *Therapeutic trials* test new drugs, surgery techniques, radiation therapy procedures, or other treatment methods on people with specific types and stages of cancer.
- *Prevention trials* study how healthy people may prevent cancer. People at high risk of getting cancer may benefit from participating.
- *Early-detection/screening trials* discover ways to find early-stage cancer.
- *Diagnostic trials* find better ways to determine if someone has cancer and, if so, where the cancer is located, how much cancer is there, and whether or not it has spread.
- *Quality of life/supportive care trials* seek to improve the comfort and quality of life of patients and their families or caregivers.

Q What are the phases of clinical trials?

Once the drug, device, or procedure enters the clinical trials process, it must go through several phases:

- *Phase I* trials determine the safety of a new treatment.
- *Phase II* trials determine whether a certain kind of cancer responds to a new treatment.
- *Phase III* trials study whether a new treatment is better than standard treatment.
- *Phase IV* trials find more information about a new treatment that has been already approved for use in patients.

FDA Approval: Researchers submit their clinical trial results to the the U. S. Food and Drug Administration (FDA), and based on the information, the FDA may approve the drug or treatment. Then it becomes available to all patients and sometimes becomes the new standard treatment.

Q What are the risks and benefits of participating in a clinical trial?

Some possible benefits of participation:

- You may have more treatment options
- If a new drug or treatment works, you may be among the first to benefit
- You may be able to help future cancer patients
- The trial sponsor may pay for some of your medical care or tests.

Some possible risks of participation include:

- Side effects may be worse than those from standard treatment
- New treatments do not always turn out to be better than, or as good as, standard treatment
- The new treatment may not work for you even if it works for other patients
- Your health insurance company may not pay for your clinical trial care or tests.

Q Where can I find more information?

- *National Cancer Institute:* www.cancer.gov/clinicaltrials, (800) 4-CANCER.
- *M. D. Anderson Cancer Center:* www.clinicaltrials.org, (800) 392-1611, option 3.
- *CenterWatch: Clinical Trials Listing Service:* www.centerwatch.com. This site lists trials for all types of health conditions.
- *Current Controlled Trials:* www.controlled-trials.com. This site lists trials from many nations and agencies, and it covers all health care areas.
- *U.S. National Institutes of Health:* www.clinicaltrials.gov.
- Finn R. *Cancer Clinical Trials: Experimental Treatments & How They Can Help You*. Sebastopol, Calif: O Reilly & Associates Inc; 1999.
- Getz K, Borfitz D. *Informed Consent: A Guide to the Risks and Benefits of Volunteering for Clinical Trials*. Boston, Mass: CenterWatch; 2002.
- Mulay, M. *Making the Decision: The Cancer Patient's Guide to Clinical Trials*. Sudbury, Mass: Jones & Bartlett; 2002.
- Researching clinical trials. In: Oster N, Thomas L, Joseff D. *Making Informed Medical Decisions*. Sebastopol, Calif: O Reilly & Associates Inc; 2000:148-180.

For more information, talk to your physician, or:

- *call the M. D. Anderson Cancer Center Information Line at (800) 392-1611 (option 3) within the United States.*
- *visit www.mdanderson.org.*

October 2006

OncoLog

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LUNG CANCER PROTOCOLS

November is Lung Cancer Awareness Month. Following is a sample of lung cancer clinical trials at M. D. Anderson Cancer Center. For more information and a broader listing of trials, visit www.clinicaltrials.org or call the M. D. Anderson Information Line at (800) 392-1611 or (713) 792-3245.

- Phase I study of concurrent CPT-11/cisplatin and celecoxib with radiation therapy for patients with unresectable non-small cell lung cancer (2003-0352). Physician: Ritsuko R. Komaki, M.D.
- Phase II study of ZD6474 alone and with chemotherapy in advanced non-small cell lung cancer (2003-0635). Physician: Vali Papadimitrakopoulou, M.D.
- Longitudinal study of the prevalence, severity, and interference of multiple symptoms in advanced lung cancer (2003-0701). Physician: Xin Shelley Wang, M.D.
- Celecoxib as adjuvant biologic therapy in patients with early-stage head and neck and lung cancer (2004-0104). Physician: Waun Ki Hong, M.D.
- Phase I trial of motexafin gadolinium in combination with docetaxel and cisplatin for treatment of non-small cell lung cancer (2004-0367). Physician: David J. Stewart, M.D.
- Phase II study of imatinib mesylate and docetaxel in pretreated patients with metastatic non-small cell lung cancer (2004-0726). Physician: Anne S. Tsao, M.D.
- Randomized phase III study of docetaxel or pemetrexed with or without cetuximab in patients with recurrent or progressive non-small cell lung cancer after platinum-based therapy (2004-0730). Physician: Edward Kim, M.D.
- Combined phase I and II study investigating the combination of RAD001 and erlotinib in patients with advanced non-small cell lung cancer previously treated only with chemotherapy (2004-0937). Physician: Vali Papadimitrakopoulou, M.D.
- Single agent Alimta (pemetrexed) in poor performance status non-small cell lung cancer (2004-0957). Physician: Ralph Zinner, M.D.
- Multicenter, open-label, phase II study of Velcade (bortezomib) for injection in previously treated patients with stage IIIB and IV broncholoalveolar carcinoma and adenocarcinoma with broncholoalveolar features (2004-0963). Physician: Frank V. Fossella, M.D.
- Phase II concurrent proton and chemotherapy in locally advanced stage IIIA/B non-small cell lung cancer (2004-0976). Physician: Joe Y. Chang, M.D., Ph.D.
- Phase II escalated/accelerated proton radiotherapy for inoperable stage I (T1-T2, N0, M0) non-small cell lung cancer (2004-0977). Physician: Joe Y. Chang, M.D., Ph.D.
- Phase II trial of Cloretazine (VNP40101M) for patients with relapsed or refractory small cell lung cancer (2005-0066). Physician: George Blumenschein, M.D.

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Made possible in part by a gift from the late Mrs. Harry C. Wiess.

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