OncoLog
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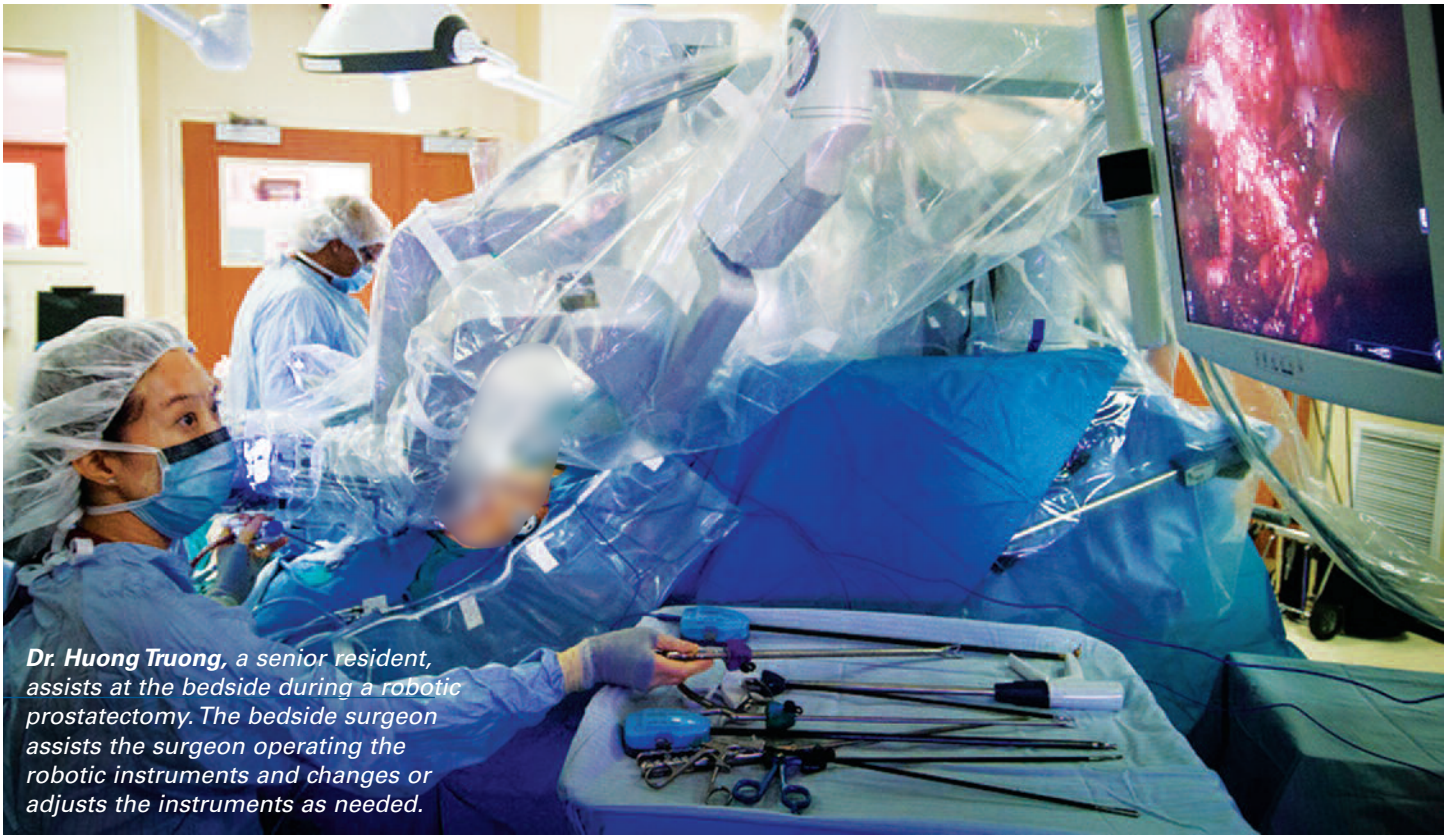
Precision Robotic Tools Facilitate Minimally Invasive Prostatectomy

By Zach Bohannan

Surgeons face a treacherous landscape when they perform a prostatectomy.

Because critical nerve bundles and blood vessels surround the prostate, prostatectomy can carry high risks of erectile dysfunction and urinary incontinence.

Today, minimally invasive robotic prostatectomies are preferred in facilities that have the necessary equipment, and these procedures often reduce the recovery times and surgeon fatigue associated with prostatectomy.



Dr. Huong Truong, *a senior resident, assists at the bedside during a robotic prostatectomy. The bedside surgeon assists the surgeon operating the robotic instruments and changes or adjusts the instruments as needed.*

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Minimally Invasive Robotic Prostatectomy

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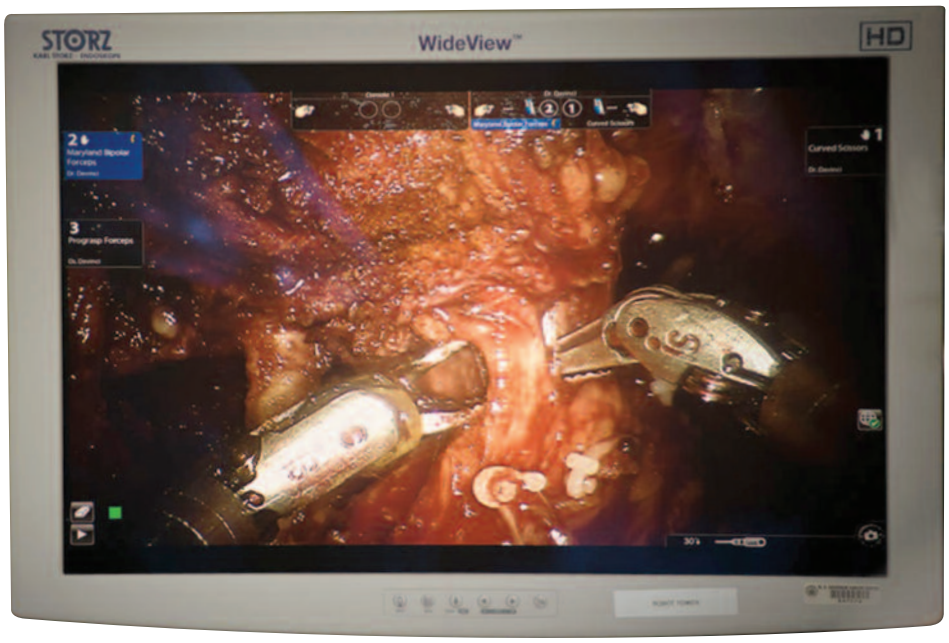

The monitors used by surgical staff during a robotic prostatectomy display in two dimensions what the surgeon sees on the three-dimensional monitor in the control booth.

Robotic advantages

Robotic prostatectomy has become the gold standard for prostate surgery in recent years. Although it has similar overall outcomes to open prostatectomy, robotic surgery limits bleeding and reduces recovery times. The size and precision of the instruments can also make it easier for surgeons to avoid sensitive structures like nerve bundles.

Because robotic surgery does not require the surgeon to remain at the operating table, performing the surgery is much less fatiguing. Adding to the comfort is the customizable nature of the control booth, which can be adjusted for the surgeon's height and personal preferences, thus reducing awkward angles and body positions. The current (third generation) robot has expanded ergonomic capabilities to accommodate surgeons of all sizes and preferences.

John W. Davis, M.D., an assistant professor in the Department of Urology at The University of Texas MD Anderson Cancer Center, said, "Because of the position of the patient, open surgery can involve a lot of reaching and leaning for the surgeon to access the area. Robotic surgery makes difficult cases easier because you don't have to reach deep into the pelvis with your arms, and you have a set vantage point."

Superficially, robotic surgery is similar to laparoscopic approaches, but the tools are vastly different. The surgical robot looks something like a spider with several arms that hover over the patient. Each arm has an interface that can connect to a wide array of modular surgical tools. Robotic surgical tools have four wheels that lock in to corresponding gears in the robot arm. These wheels move the mechanical "wrist," which is the key difference between robotic and laparoscopic tools and allows a far greater range of motion that essentially mirrors the surgeon's hand motions. Dr. Davis said, "Compared with laparoscopic tools, the robotic tools offer extra degrees of freedom that make many tasks, such as suturing, much less taxing."

> **"Robotic surgery makes difficult cases easier."**
>
> **– Dr. John Davis**

The surgeon sits several feet away from the patient in a booth that is connected to the robot by several cables and contains a pair of articulating arms that translate the surgeon's hand movements through the robot and into the tools. The interface also provides some tactile feedback: any restriction to a tool's mobility also restricts the controls. For instance, if a tool comes in contact with bone, it will prevent the tool from moving, which in turn prevents the controller arm from moving. The surgeon uses a microphone to communicate with the rest of the surgical team, who remain centered around the patient and can view the progress of the surgery via monitors.

The robotic procedure

In a typical robotic prostatectomy, the patient is first placed head-down on a slanted operating table and anesthetized. Next, the patient's abdomen is insufflated with carbon dioxide, and the surgeon places surgical ports in the abdomen. The various tools needed for the surgery are attached to the robotic arms and inserted into the ports. Once that is accomplished, the surgeon removes his or her mask and gloves and takes a seat in front of the robot control booth on the other side of the room.

Using a scissor tool and a foot pedal–activated electrocautery clamp tool, the surgeon is able to cauterize and then either cut or pull apart tissue. As in other surgeries, before any larger blood vessels are cut, surgical assistants apply clamps to the vessels using an independent laparoscopic tool. They are aided by two-dimensional monitors that project the surgeon's view. The surgeon, who has a three-dimensional monitor, helps them judge depth and gives guidance via microphone. Because the camera is physically linked to all the robotic tools, the perspective of both the surgeon's and the surgical assistants' views remains constant. This direct perspective is different than that of laparoscopy, which can

Above: ***Dr. John Davis*** *performs a robotic prostatectomy. The robotic system's three-dimensional monitor and maneuverable tools make complex tasks easier to perform compared with laparoscopic surgery. Right: Close-up of the surgeon's hands on the controls.*

involve cameras and tools at many different angles.

Patient selection

According to Dr. Davis, patient selection criteria for robotic prostatectomy are similar to those for open and laparoscopic prostatectomies. Surgeons new to the system may want to avoid complicated cases at first, but otherwise, robotic surgery can effectively replace laparoscopy for minimally invasive prostatectomies. Where robotic surgical suites are available, robotic surgery is generally preferred over laparoscopic surgery because of the advantages mentioned above. However, some surgeons still prefer to use open surgery because of their level of experience with open surgery.

Other factors that affect whether a patient is a candidate for robotic prostatectomy are similar to the considerations for open prostatectomy. If the patient has already undergone radiation therapy, later surgery may be more difficult because radiation damages the surrounding tissue and can change the anatomy of the area around the prostate. Similarly, patients treated with radiation or surgery for previous colorectal disease may not be candidates for minimally invasive prostatectomy because of scarring and anatomical changes.

There are, however, some indications that robotic surgery is advantageous for prostatectomy after radiation therapy. Dr. Davis hypothesized, "Perhaps the strength of the robotic scissors can negotiate irradiated tissue as well as, if not better than, hand-held scissors or blunt dissection. However, the surgeon will need to have a high level of expertise in dealing with irradiated tissue."

Patients who have not previously been treated with radiation must consider the different risks related to bowel control, erectile function, and other quality-of-life factors associated with radiation therapy versus surgery. Other health issues must also be taken into account. For instance, Dr. Davis said, "Some patients also have benign prostate enlargement, so they may opt for surgery to remove that obstructive element."

Future directions

Robotic surgical suites are very expensive, as are the disposables associated

Minimally Invasive Robotic Prostatectomy

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with robotic surgery, and this expense limits the technology's adoption to large or high-volume facilities. It is unclear whether the costs of robotic procedures will decrease in the near future. Dr. Davis said, "Robotic instruments have a fixed 10-use life span and then have to be replaced, which is expensive. However, many basic instruments, such as needle drivers, could be safely used many more times." Although there is currently only one manufacturer of instruments approved for patient care, the system is built to allow novel instruments that may improve vessel sealing, suction, or staple placement to be developed by other companies.

Robotic technology continues to advance. The third-generation robot has an improved high-resolution camera setup and can accommodate two surgeons working at their own consoles on the same patient. Another exciting direction is the fusion of ultrasonography and fluorescence imaging into the console such that the surgeon can view the operative field and imaging at the same time, which may allow more accurate identification of various tissue types.

Another attractive capability of the robotic surgical suite is its utility for training new surgeons in a manner similar to pilots using a flight simulator. The third-generation robot has a virtual reality surgical simulator that allows trainees to practice various skills and situations. The software also grades the trainee for time and accuracy.

Telemedicine using the robotic surgical suite is also possible, and some grants have been awarded for the development of telemedicine programs in which robotic surgery will play an important role. Dr. Davis said that telemedicine could allow surgeons at MD Anderson's main campus to collaborate on difficult robotic cases with surgeons at its regional care facilities or at other institutions, which would mean better quality of care for more patients. ■

FOR MORE INFORMATION

Dr. John Davis 713-792-3250

Fluorescence Cystoscopy

By Sarah Bronson

Fluorescence cystoscopy, although not yet widely used in the United States, has been shown to be effective for detecting tumors in the bladder that might not be visible with standard cystoscopy.

Because patients who have been treated for bladder cancer require routine monitoring over the course of long survival times and because bladder cancer recurs at a higher rate than many other cancers, this cancer is the most expensive cancer per patient from diagnosis to death. More accurate diagnostic techniques could substantially reduce this expense and improve disease management.

"Fluorescence cystoscopy has the potential to increase the number of tumors we can detect and to improve our resection of these tumors at the first go," said Ashish Kamat, M.D., an associate professor in the Department of Urology at The University of Texas MD Anderson Cancer Center. "It has the potential to decrease the number of recurrences, thus reducing the number of interventions, the number of follow-up visits, and the economic impact on society of bladder cancer."

What is fluorescence cystoscopy?

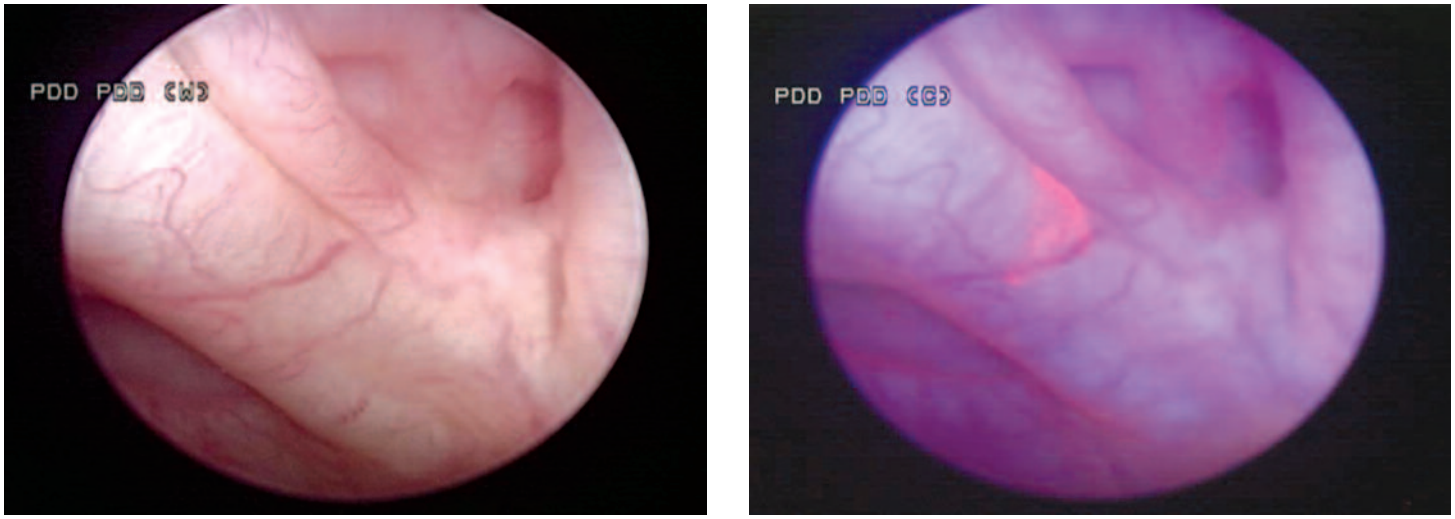
Fluorescence cystoscopy, also called blue light cystoscopy, is indicated as an adjunct to standard, white light cystoscopy for the detection of bladder tumors in patients known or suspected to have at least one bladder tumor. Using the blue light modality increases the detection rate for small or indistinct lesions that can go unseen under cystoscopy with white light alone. At MD Anderson, Dr. Kamat and H. Barton Grossman, M.D., a professor in the Department of Urology, have been using fluorescence cystoscopy since 2007, when they began doing clinical studies of the modality.

Before fluorescence cystoscopy, a urethral catheter is inserted and the bladder emptied, and hexaminolevulinate (Cysview), an inert imaging agent, is slowly instilled through the catheter and retained for at least 1 hour. The hexaminolevulinate causes photoactive porphyrins to accumulate in rapidly proliferating cells, such as neoplastic cells. The bladder is then emptied, and the patient undergoes cystoscopy, in which the bladder is filled with water or saline through the cystoscope so that the bladder wall can be clearly viewed. The bladder wall is first examined for papillary tumors using standard white light cystoscopy. Next, a photodynamic diagnostic sys-

"Fluorescence cystoscopy has the potential to increase the number of tumors we can detect and to improve our resection of these tumors at the first go."

– Dr. Ashish Kamat

Detects Hard-to-Find Bladder Tumors



The same section of a patient's bladder wall as viewed by standard (left) and fluorescence cystoscopy. In fluorescence cystoscopy, normal tissue appears blue and the tumor cells appear red.

tem that is attached to the cystoscope is activated, and the wall is examined again. Illuminated by blue light with a wavelength of 360–450 nm, normal tissue appears blue while the porphyrins that have accumulated in rapidly dividing cells appear red.

Thus, potentially malignant cells that do not visibly protrude from or contrast with the bladder wall—including any that are flattened when the bladder is filled and the wall distended—can become visible with blue light. Also, rapidly dividing cells can be detected at earlier stages, and larger areas of invasion can be revealed; consequently, malignant lesions can be resected sooner and more completely. Although sites of infection or recent biopsies also may fluoresce red, the percentage of false-positive diagnoses is comparable to that of white light cystoscopy alone.

Clinical studies

Fluorescence cystoscopy has been shown to be more sensitive than white light cystoscopy. A recent prospective, randomized study showed that blue light cystoscopy was significantly more likely to detect bladder carcinomas in situ and Ta/T1 tumors than was white light cystoscopy in patients known to have at least one such lesion, and the two modalities had similarly low false-positive rates and were similarly safe. Likewise, a phase III study showed that blue light detected more carcinomas in situ than did white light in patients with suspected or confirmed bladder cancer. Fluorescence cystoscopy was also well tolerated in this study, with hematuria as the most common adverse event.

In another study, patients examined with fluorescence cystoscopy had fewer recurrences of bladder cancer within 9 months of cystoscopy and longer disease-free intervals than did patients examined using white light only. Furthermore, some tumors classified as recurrences may actually be incipient but not observed at the time of the initial diagnosis; therefore, the more sensitive diagnostic technique may reduce the number of tumors overlooked at early stages that may remain after larger tumors have been treated.

Approval and use

Fluorescence cystoscopy is widely used in Europe, and hexaminolevulinate was approved by the U.S. Food and Drug Administration in May 2010 for use in the detection of non–muscle-invasive papillary bladder cancer. To date, only seven centers in the United States, including MD Anderson, use fluorescence cystoscopy, but Dr. Kamat expressed the hope that urologists throughout the United States will learn the technique so it can be offered to the appropriate patient populations. ■

FOR MORE INFORMATION

Dr. Ashish Kamat.....713-792-3250

FURTHER READING

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New HPV Vaccine Recommendations Could Have Multiple Benefits

By Bryan Tutt

New recommendations for vaccination against human papillomavirus (HPV) are intended to prevent cervical cancer but may also decrease the incidence rates of other cancers.

Since the first HPV vaccine was approved in 2006, the U.S. Centers for Disease Control and Prevention (CDC) has recommended that girls be vaccinated against HPV beginning at age 11 years. However, vaccination rates among teenage girls have remained low, around 30%. To further decrease the spread of HPV and thus the incidence rate of cervical cancer, the CDC recently recommended the routine vaccination of boys beginning at age 11 or 12 years.

"The reasoning for the new recommendation was to control cervical cancer by preventing the spread of the virus, but a side benefit could be a reduction in the number of oropharyngeal cancers as well," said Erich M. Sturgis, M.D., M.P.H., a professor in the Department of Head and Neck Surgery and the Department of Epidemiology at The University of Texas MD Anderson Cancer Center. This benefit occurs because HPV-16 and HPV-18, the two virus strains that cause about 70% of all cervical cancers, also have been linked to cancers of the oropharynx as well as cancers of the anus, penis, vagina, and vulva.

While the cervix remains the most common site for cancers related to HPV, Dr. Sturgis said that by 2020 there will likely be more HPV-related oropharyngeal cancers than cervical cancers. A decline in cervical cancer rates has occurred over the past 30 years in developed countries because of the implementation of routine screening with gynecological examinations and Papanicolaou tests. Such screening often detects cervical dysplasia, which can be effectively treated before it develops into cancer.

A similar decline has occurred in the incidence rates of head and neck cancers related to tobacco and alcohol use. "As we've seen less smoking in the United States over the past 40 years, over the past 20 years we've seen declines in the incidences of virtually all head and neck cancers except oropharyngeal—tonsil and base of tongue—cancer," Dr. Sturgis said. "This difference seems to be attributable to a dramatic rise in the incidence of the subgroup of oropharyngeal cancers related to HPV."

It is believed that HPV is introduced into the oropharynx principally via oral sex. "There have probably been changes in sexual behavior in the past 30-plus years that have helped cause the higher incidence of HPV-related oropharyngeal cancers," Dr. Sturgis said.

The prevention of oropharyngeal cancers is especially important because they are seldom detected in their early stages. Dr. Sturgis said that unlike cervical or anal dysplasia, premalignant oropharyngeal growths are not detectable by any current screening tests. Screening for the virus itself is unlikely to have any clinical relevance because most people are exposed to HPV without developing a chronic infection or subsequent HPV-related lesions. Instead, Dr. Sturgis said, "If a patient has symptoms like bleeding, ulceration, a neck mass, or pain in the throat that persist for 2 weeks, the patient should see an ear, nose, and throat doctor."

The two most important steps in preventing oropharyngeal cancer are avoiding tobacco products and preventing HPV infection. "I would strongly recommend that boys and girls get vaccinated against HPV as recommended by the CDC," Dr. Sturgis said. ■

What's the Difference?

Many patients know that there are two vaccines against the human papillomavirus (HPV), but most do not know the differences between the two. Physicians may find the information below useful in addressing patients' questions about the two vaccines.

Gardasil (Merck & Co.) was approved by the U.S. Food and Drug Administration (FDA) in 2006 for girls and women.

Cervarix (GlaxoSmithKline) was approved by the FDA in 2009 for girls and women.

Both vaccines protect against the two most common cancer-causing HPV strains, HPV-16 and HPV-18; Gardasil also protects against HPV-6 and HPV-11, which cause genital warts. For this reason, in 2009 the FDA approved the use of Gardasil for boys and men. Cervarix is not approved in the United States for use in boys or men.

Both vaccines are given in a series of three injections over 6 months, and both vaccines have been reported to be effective and well tolerated. ■

FOR MORE INFORMATION

Dr. Erich Sturgis.....713-792-6920

Tanning Beds Pose Health Risks

Dangers of tanning range from wrinkled skin to cancer

Tanning salons advertise a way to jump-start a tan in the winter and early spring, as consumers prepare for the summer's skin-baring clothing styles. Advertisements for tanning salons sometimes imply that indoor tanning is safer than basking in the sun. However, because indoor tanning beds give off the same harmful ultraviolet (UV) rays as the sun, they are just as dangerous as outside exposure. Exposure to UV rays can lead to skin cancer and other health and appearance problems.

Skin cancer

Skin cancer is the most common type of cancer in the United States; almost half of all cancers nationwide are skin cancers. Basal cell carcinoma accounts for 90% of skin cancers and is almost always cured with surgical intervention if caught early. Squamous cell carcinoma is the second most common type. Melanoma is the most deadly and aggressive form of skin cancer.

Studies have linked all three of these skin cancers to tanning bed use. One study found that women who used tanning beds more than once a month were 55% more likely to develop melanoma than were women who had never used tanning beds. The risk was higher for those who began using tanning beds before they were 35 years old. Another study found that, compared with those who had never used tanning beds, people who had ever used tanning beds had a 75% higher risk of developing melanoma, and frequent users faced melanoma risks as much as 200% higher.

Although the World Health Organization listed tanning beds as carcinogenic in 2009, tanning salons outnumber both Starbucks and McDonalds in more than 100 cities in the United States. And more than one-third of 17-year-old American girls have reported indoor tanning.

Legal actions against indoor tanning

State legislatures are beginning to recognize the dangers of indoor tanning and the need to regulate it, following the pattern of tobacco legislation. In 2009, Texas passed a law preventing children younger than 16 years from using tanning beds. California followed in 2011, setting the minimum age at 18 years.

Texas has also targeted tanning salon advertisements. In 2008, the Texas attorney general sued a Houston-based tanning salon chain over advertisements claiming that tanning beds reduce the risk of cancer because of the production of vitamin D. In fact, diet and outside activity usually provide plenty of the vitamin without the health risks posed by tanning beds.

Other dangers of indoor tanning

Excess exposure to UV rays can suppress the immune system, increasing vulnerability to infection and disease.

Similar to sun exposure, tanning beds can cause painful skin burns and eye damage, such as photokeratitis (sunburned corneas). Tanning beds also increase the formation of cataracts, a clouding of the eye lens that can lead to blindness.

People who tan to be more attractive often find that their pursuit of beauty has aged their skin prematurely, leaving wrinkles and dark spots. Even tanning enthusiasts who escape cancer might have to undergo surgery to remove unsightly moles, potentially leaving scars.

Indoor tanning has also been found to be addictive. A study at a northeastern college revealed that almost 40% of the students who reported indoor tanning were classified as addicts, and of that group, 78% could not kick the habit. Perhaps it is time to start thinking about tanning beds in the same way that we think about cigarettes.

Save your skin

Just as not smoking can easily prevent many cancers of the lungs and other organs, skin cancer can be prevented if you take simple precautions such as avoiding tanning beds and other unnecessary UV exposure, wearing sunscreen with a high sun protection factor (SPF) on a daily basis, and performing monthly skin checks. Follow the ABCDEs of self-screening: see your doctor immediately if you notice any moles or spots that are **A**symmetrical, have crooked **B**orders, are more than one **C**olor, increase in **D**iameter, or **E**volve in any other way.

Self-tanning lotions are far more effective than tanning beds at achieving a bronzed glow while preserving future beauty and health. Keep in mind that self-tanning lotions do not protect the skin from the sun, so a high-SPF sunscreen should also be applied. ■

– J. Delsigne

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IN BRIEF

T Cell Therapy Prolongs Survival in Dogs With Non-Hodgkin Lymphoma

T cell therapy given after the completion of standard chemotherapy has been found to prolong both overall and disease-free survival in dogs with advanced non-Hodgkin lymphoma.

In a veterinary trial conducted by researchers at The University of Texas MD Anderson Cancer Center and Texas A&M University College of Veterinary Medicine and Biomedical Sciences, eight dogs with advanced-stage non-Hodgkin lymphoma were infused with autologous T cells after receiving the standard 19-week chemotherapy regimen of cyclophosphamide, vincristine, doxorubicin, and prednisone (CHOP). The T cells were derived from peripheral blood taken from each dog at the time of trial enrollment.

While the dogs received chemotherapy at Texas A&M, their T cells were separated and expanded at MD Anderson using methods that are used to grow human T cells. The dogs were all pets whose owners wanted them to receive cancer treatment and enrolled them in the trial.

The survival data of the dogs in the trial were compared with matched historical data from dogs with non-Hodgkin lymphoma that had been treated with CHOP only. The median overall survival from the time of initial diagnosis was significantly longer in the dogs that received CHOP plus T cell therapy (392 days; range, 277–458 days) than in the dogs that received CHOP only (167 days; range, 68–413 days). Furthermore, the median disease-free survival from the time complete remission was achieved was significantly longer in the dogs that received CHOP plus T cell therapy (338 days; range, 104–369 days) than in the dogs that received CHOP only (71 days; range, 23–293 days).

The T cell treatment was well tolerated, with only one dog experiencing grade III adverse events (nausea, vomiting, and diarrhea).

"In addition to improving the dogs' health and quality of life, treating dogs with cancer provides us with a great comparative oncology model for humans," said Colleen O'Connor, Ph.D., a postdoctoral fellow in the Department of Experimental Pediatrics at MD Anderson and lead author of the study's report, which was published in February in *Scientific Reports*. "We learned important details about the interaction between chemotherapy and tumor cells that can be harnessed to improve the body's immune response. This is something we hadn't appreciated thus far from our clinical research in humans." ■

"We learned important details about the interaction between chemotherapy and tumor cells."

– Dr. Colleen O'Connor

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