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H. LEE MOFFITT CANCER CENTER & RESEARCH INSTITUTE, AN NCI COMPREHENSIVE CANCER CENTER

MOFFITT CANCER CENTER

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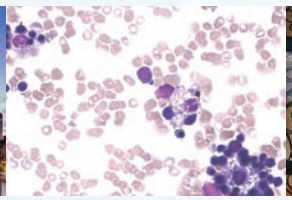


Moffitt Cancer Center is pleased to host the **4th Annual BMT Winter Workshop**, taking place in Orlando, Florida, prior to the 57th annual meeting of the American Society of Hematology. This informal meeting is formatted as previous workshops with numerous short talks on late-breaking research in BMT. Presenters will discuss recent unpublished clinical and preclinical data pertinent to hematopoietic stem cell transplantation.

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Cancer Control: Journal of the Moffitt Cancer Center is a peer-reviewed journal that is published to enhance the knowledge needed by professionals in oncology to help them minimize the impact of human malignancy. Each issue emphasizes a specific theme relating to the detection or management of cancer. The objectives of *Cancer Control* are to define the current state of cancer care, to integrate recently generated information with historical practice patterns, and to enlighten readers through critical reviews, commentaries, and analyses of recent research studies.

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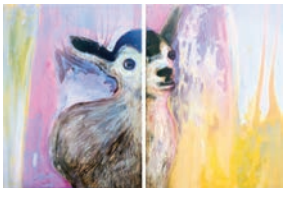

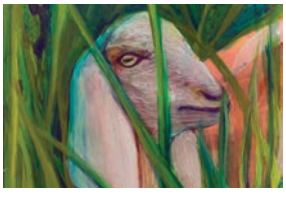

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About the art in this issue:

Sofía Cáceres Nazario is a native Puerto Rican artist who, in 2007, earned a Merit Award from the National YoungArts Foundation. In 2010, she graduated from the University of Puerto Rico and, in 2011, was awarded the Medal of Academic Distinction in drawing from the Faculty of Humanities. Sofía has participated in several local collective shows and has represented her country in various international print events. In 2013, she cofounded Finca de Rustica, a family-owned flower business located on a 10-acre farm in Naguabo, Puerto Rico. Her collection in this issue of *Cancer Control* is a pastoral mix of palatial strokes of vivid colors and hard and soft lines representative of bucolic life on that farm. Sofía can be contacted by e-mail at caceresofia@gmail.com.

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This peer-reviewed journal contains articles on the spectrum of actions and approaches needed to reduce the impact of human malignancy.

Cancer Control is sent at no charge to approximately 15,000* medical professionals, including oncologists in all subspecialties, selected primary care physicians, medical researchers who specialize in oncology, and others who have a professional interest in cancer control.

**This includes approximately 1,000 oncologists from more than 85 countries.*

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Letter From the Editors: A New Step Rather Than a New Era

Cancer Control
Journal of the Moffitt Cancer Center

Dear Readers,

Beginning with the January 2016 issue, *Cancer Control: Journal of the Moffitt Cancer Center* will be published in digital format only. With our new and improved website to be launched later this year, readers will still be able to download and print the articles they wish to keep by visiting us at cancercontroljournal.org (formerly MOFFITT.org/ccj). The new URL links to our existing webpage under MOFFITT.org and will redirect readers to the new website as soon as it is available. Reprint requests will continue to be handled by the editorial office and will be reviewed and responded to on an individual basis.

The decision to abandon the paper edition was based on considerations of cost effectiveness paramount for all fields of health care today. As the price of paper continues to rise and more and more people utilize electronic devices to read books, newspapers, and magazines, the increasing costs of printing no longer appear justified. Limited resources may be better utilized in maintaining and improving the quality and timeliness of our publication. For those of us who grew up in the pre-electronic era, who were used to waiting with anticipation for the new issue of our favorite medical journal in the mail, this change is a little disconcerting, as is the experience of seeing a daughter, now an adult, leave home and start her new family. It is disconcerting but necessary: as much as we regretted retiring our cherished stethoscope, we conceded that an echocardiogram was a more precise way to detect valvular disease or myocardial dysfunction than the human ear.

Indeed, we plan to utilize the resources of the journal to fulfill our ongoing commitment to quality and practicality. Since its inception more than 20 years ago, *Cancer Control* promised to provide practicing oncologists with exhaustive and user-friendly reviews of important issues that could not be otherwise found in the literature.

John Horton, MB, ChB, the founding editor and the quintessential clinical teacher, received universal praise for the impact *Cancer Control* had on the practice of oncology in the country and around the world. John C. Ruckdeschel, MD, the first chief executive officer of the H. Lee Moffitt Cancer Center & Research Institute and cofounder of *Cancer Control*, gave unlimited support to the educational mission of Moffitt and considered the journal to be the most effective means to fulfill this mission.

The scope of oncology is rapidly enlarging and diversifying, and the practitioner is exposed to a barrage of new information that is both incomplete and contradictory. The main challenge of oncology education is to harness the energy of this scientific upsurge into a coherent discourse that highlights scientific advances together with new clinical questions. Fully committed to guide the practitioner to a safe exit from this informational maze, *Cancer Control* will devote the next issues to novel and timely topics. These include minimally invasive surgery, prospective radiosurgery and interventional radiology, imaging techniques based on biological markers, the use of genomic testing, the interpretation of results from clinical trials of targeted therapy, the use of mathematical models to predict tumor progression, overviews of tumor immunology and signal transduction, and the new scope of palliative care. Since establishing *Cancer Control*, Moffitt has grown to be the third largest comprehensive cancer center in the country. Basic, translational, and clinical investigators working at Moffitt illustrate the array of treatments and clinical trials available at our institution for the patients of Florida, the United States, and the world.

A digital publication will allow us to focus unimpeded on the exciting and continual progress of cancer care. We would like to think that the adoption of a digital format represents a new step, rather than a new era, in the life of our journal — a step congruent with technological and scientific changes that will permit us to fulfill our mission in a rapidly changing world.

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Cancer Control
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Applications and Advances in Robotic-Assisted Oncological Surgery: Ready to Dock the 'Bot

"I have been impressed with the urgency of doing. Knowing is not enough; we must apply. Being willing is not enough; we must do."

Leonardo da Vinci

In the field of surgical oncology, the robotic surgical system is a tool that allows the surgeon to perform laparoscopic or thoracoscopic procedures by enhancing the skills of the surgeon. Thus, the robotic system provides the surgeon with magnified, 3-dimensional (3D) visualization and wristed instruments that the surgeon can remotely control. Compared with 2D visualization in conventional laparoscopic and thoracoscopic surgery, this 3D visualization heightens the depth perception of the surgeon. In addition, the wristed instrumentation enables the surgeon to precisely dissect structures — in particular, vascular structures and other deep and confined spaces, such as those of the pelvis, retroperitoneum, and mediastinum — compared with the "chopstick"-like instruments of conventional laparoscopic and thoracoscopic surgical procedures. The robotic surgical system's computer also scales down the large radius of movements and eliminates tremors from the surgeon's hands. In addition, during robotic-assisted surgery, the surgeon is sitting rather than standing and controls the movements of the robotic arm with his or her hands, with the fingers and wrists adding a very important ergonomic advantage that reduces surgeon fatigue.

Surgical specialties continue to evolve with new and improved techniques and the application of novel technologies, as has been true of surgical techniques improved upon by applying robotics in the surgical oncology specialties. "Robotic surgery" is a misnomer. Procedures assisted by robotic technology are the same as traditional laparoscopic (or thoracoscopic) surgery or minimally invasive operations in that they are still performed by a surgeon who is operating a robot. Thus, the appropriate term is robotic-*assisted* laparoscopic (or thoracoscopic) surgery.

Although robotic-assisted surgery is now widely available in the United States, the application of robotic technology in surgery became a reality 20 years ago. The robotic surgical system was first applied in surgical oncology in the setting of laparoscopic radical prostatectomy; robotic-assisted laparoscopic radical prostatectomy was initially performed in Europe in the early 2000s and then rapidly expanded into the United States.[1,2] Use of the robotic surgical system was then extended to other types of surgical oncology in the fields of gynecological surgery, thoracic surgery, and general surgical oncology.[2-4] More recently, techniques in transoral robotic-assisted surgery and robotic-assisted neurosurgery are being developed.[5] In this issue of *Cancer Control*, several authors report on both well-established and developing applications of robotics in surgical oncology.

The first article is authored by Dr Agarwal and colleagues, who review the technique and outcomes of robotic-assisted prostatectomy. Twenty years after the first robotic-assisted prostatectomy was performed, techniques continue to improve, leading to better oncological control and patient quality of life.

Dr Emtage and others review techniques for robotic-assisted oncological kidney surgery. They report that morbidity and patient satisfaction rates are potentially improved with robotic-assisted renal surgery compared with traditional open and conventional laparoscopic renal surgery without compromising oncological control, particularly for nephron-sparing partial nephrectomies.

Dr Luchey and coauthors discuss the evolving techniques and early outcomes with robotic-assisted cystectomy. Although the procedure is not widely performed, increasing numbers of centers around the world are applying robotic-assisted surgery for the management of bladder cancer.

Drs Bush and Apte review techniques and outcomes with robotic-assisted surgery in gynecological oncology. They report that robotic-assisted surgery has resulted in the increased use of minimally invasive surgical procedures for endometrial cancer and in decreased complication rates in patients who are obese.

Dr Velez-Cubian and colleagues review the benefits of adding a robotic surgical system to videothoracoscopic pulmonary resections. They report that robotic-assisted videothoracoscopic pulmonary lobectomy is as safe as conventional videothoracoscopic lobectomy, and that the robotic-assisted procedure resulted in decreased perioperative complications and shorter lengths of hospital stay than traditional open lobectomy. Mediastinal lymph node dissection and the early detection of occult mediastinal lymph node metastatic disease were also improved when using robotic-assisted videothoracoscopic approaches compared with conventional approaches to videothoracoscopy or

open thoracotomy.

Dr Straughan and others review the use of robotic-assisted videothoracoscopic surgery for mediastinal resections. They report that robotic-assisted thoracoscopic mediastinal surgery may be superior to open mediastinal approaches and has comparable patient outcomes to conventional videothoracoscopy.

Dr Burton and colleagues review the development, use, and outcomes of robotic assistance for head and neck surgery. They focus on the functional and oncological outcomes associated with the most common application of transoral robotic-assisted surgery.

In a second article, Dr Straughan and coauthors review how the advent of robotic surgical systems has revolutionized the adoption of minimally invasive approaches for managing esophageal disease. They report that robotic-assisted esophageal surgery is safe and effective for treating esophageal disorders, including gastroesophageal reflux disease, achalasia, leiomyomas, and cancer, with benefits over traditional open and conventional minimally invasive approaches.

Dr Rashid and others review the use of robotic-assisted resection of periampullary malignancies (Whipple procedure). They report that robotic-assisted techniques for managing malignant lesions of the pancreas head are safe when well-established guidelines are followed for surgical resection and that preliminary data demonstrate improved periampullary convalescence compared with the open technique.

Dr Doulgeris and colleagues review the evolution, current challenges, and compromises related to the use of robotics in neurosurgery. They explain that the majority of robotic neurosurgical systems assist in stereotactic procedures and that progress in robotic-assisted microsurgery, minimally invasive, and endoscopic neurosurgeries are challenging and hindered by the need to miniaturize current tools. In addition, they elucidate that maximizing control of those tools must be achieved so as to overcome loss of haptic feedback, proprioception, and visualization.

"Ready to dock the 'bot" is not simply the announcement given to the operating room staff of the surgeon's readiness to dock the robotic cart to the previously placed 3 or 4 ports. This declaration symbolizes the point when the surgeon has become proficient to perform robotic-assisted surgery. More importantly, it should symbolize the point when an institution has established a robust robotic surgical program, especially when multiple surgical specialties are involved.

Although controversy still exists in several surgical procedures regarding whether robotic-assisted surgery is superior to conventional laparoscopic (or thoracoscopic) or traditional open approaches, robotic-assisted surgery is here to stay, and the technology will continue to improve. Newer generations of robots will allow haptic perception, will have increased portability, and they will become more affordable.

We hope you enjoy and benefit from reading this issue of *Cancer Control*.

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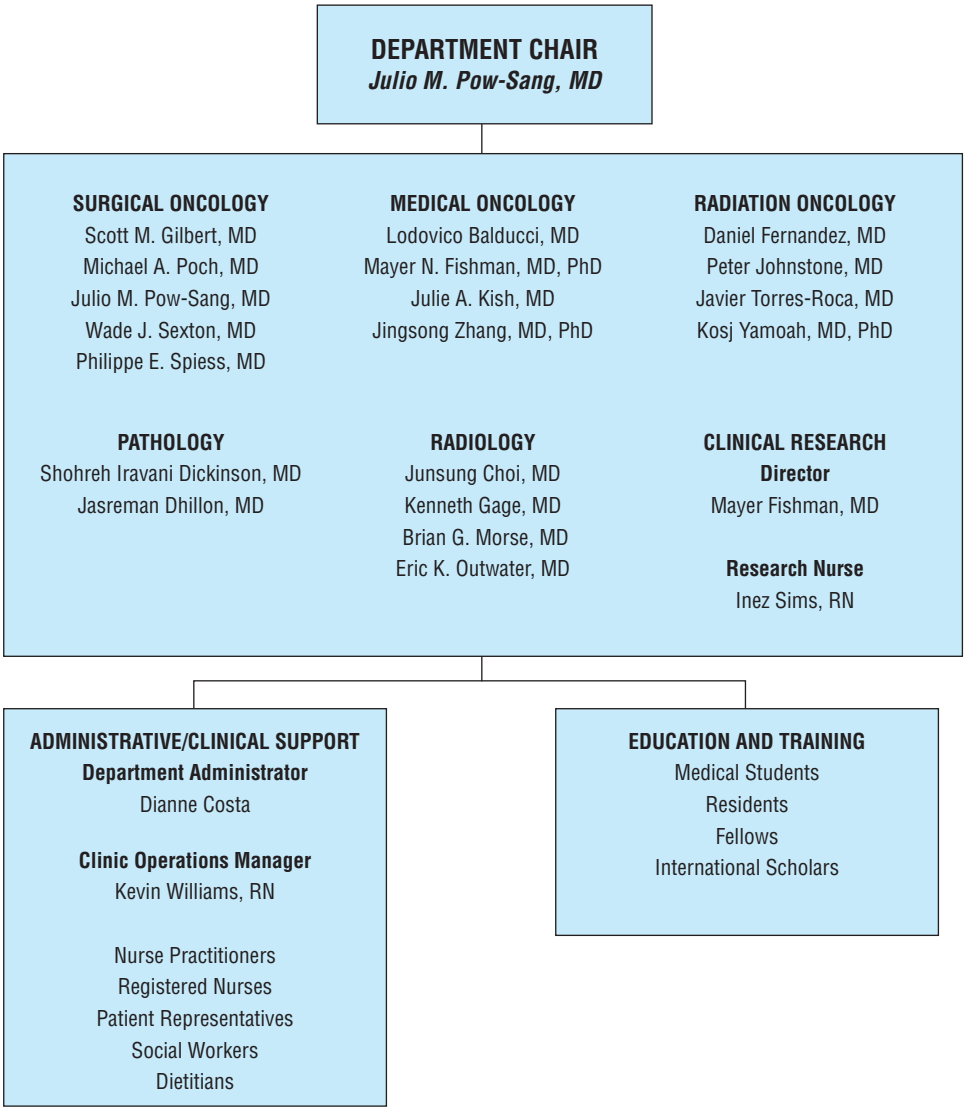
Department of Genitourinary Oncology Program

H. Lee Moffitt Cancer Center & Research Institute

The Department of Genitourinary Oncology comprises a highly specialized team of physicians from multiple fields of oncology whose expertise is treating patients with genitourinary malignancies. These include cancers of the male and female urinary systems (prostate, testicles, penis, kidneys, ureters, and bladder). The goals of the practice are to provide state-of-the-art care and develop more effective therapies for patients.



Research

Physicians in the Department of Genitourinary Oncology are actively involved in national and Moffitt Cancer Center–generated clinical studies, as well as laboratory research projects that may yield the novel, urological cancer treatments of tomorrow. When appropriate, patients can participate in clinical studies that seek to take a standard treatment and improve its tolerability or efficacy. These studies use the newest and most promising cancer treatments and drugs.

To schedule a patient appointment with a physician in the Departments of Genitourinary Oncology or Thoracic Oncology, call the New Patient Appointment Center at 813-745-3980 or 1-888-860-2778 (during normal business hours). For information about clinical trials, please call Cheryl L. Maker in the Clinical Research Department at 813-745-4106 or e-mail Cheryl.Maker@Moffitt.org.
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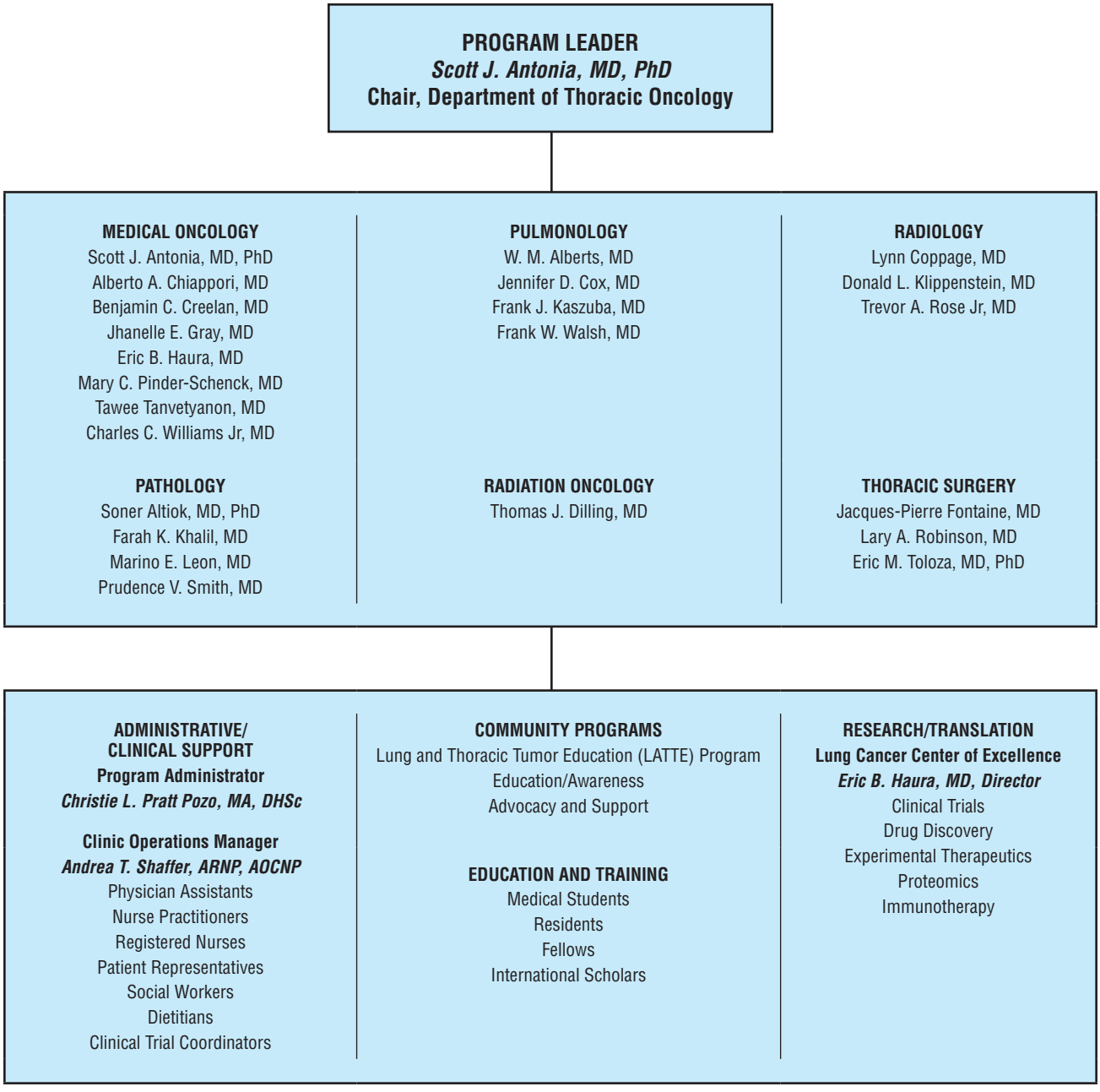
Thoracic Oncology Program

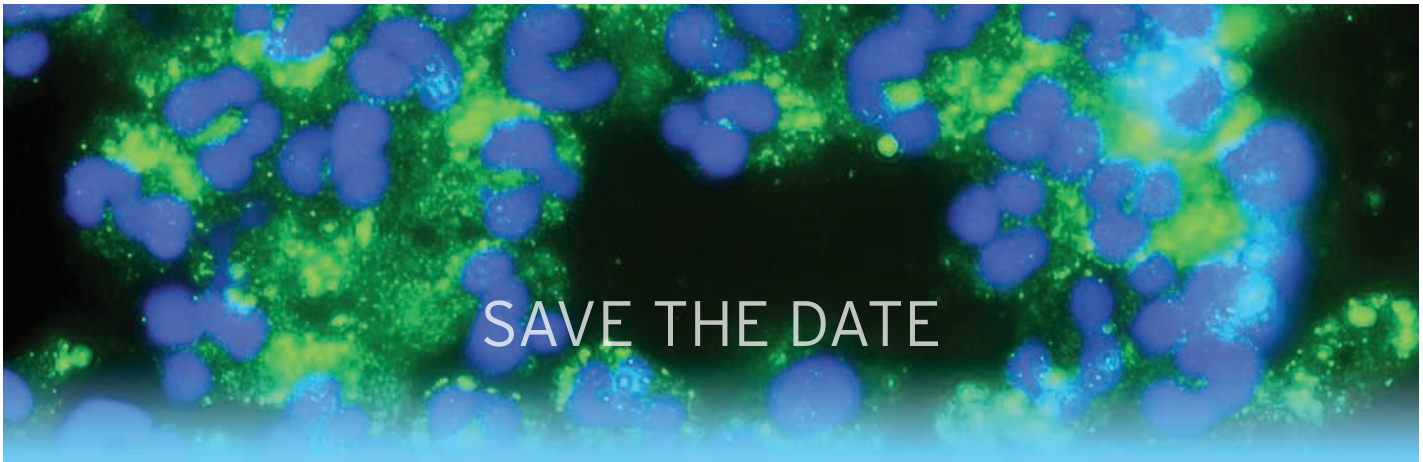
H. Lee Moffitt Cancer Center & Research Institute

Moffitt Cancer Center's Thoracic Oncology Program offers community physicians the opportunity for consultation, referral, or second opinions about patients with lung cancer, mesothelioma, lung metastases, and other cancers of the chest cavity. We are committed to serving as an important medical resource and to meeting physicians' needs through timely consults, prompt patient appointments, and ongoing communication.

Lung cancer is the leading cause of cancer deaths in the United States today. Despite advances made in the last few decades, most patients continue to be diagnosed at a late stage, making options more limited and long-term prognosis poor.

Moffitt's Thoracic Oncology Program is at the forefront of promising discoveries that will change the future for these patients. The thoracic oncology team is making great strides in innovative research, early detection, and the advance of pioneering treatments in the effort to prevent and cure lung and thoracic cancers.





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Sofía Cáceres Nazario. *Flower Gardener*, 2015 (Detail). Acrylic on canvas, 12" × 16".

RALRP is the procedure of choice when treating localized prostate cancer.

Robotic-Assisted Laparoscopic Radical Prostatectomy

Gautum Agarwal, MD, Oscar Valderrama, MD, Adam M. Luchey, MD, and Julio M. Pow-Sang, MD

Background: *The use of radical prostatectomy for the treatment of prostate cancer has been increasing during the last decade partially due to the widespread adoption of the robotic-assisted laparoscopic technique. Although no prospective, randomized controlled trials have compared open radical prostatectomy (ORP) with robotic-assisted laparoscopic radical prostatectomy (RALRP), numerous comparative studies have been retrospectively conducted.*

Methods: *A systematic review of the literature was performed to clarify the role and advancement of RALRP. Studies comparing ORP with RALRP that measured outcomes of cancer control, urinary and sexual function, and complications were included. A nonsystematic review was utilized to describe the advancements in the techniques used for RALRP.*

Results: *RALRP is the procedure of choice when treating localized prostate cancer. This preference is due to the observed improvement in morbidity rates, as evidenced by decreased rates of blood loss and postoperative pain and similar oncological outcomes when compared with ORP. Robotic assistance during surgery is continually being modified and the techniques advanced, as evidenced by improved nerve sparing for preserving potency and reconstruction of the bladder neck to help in the early recovery of urinary continence.*

Conclusions: *Morbidity rates should continue to improve with the advancement of minimally invasive techniques for radical prostatectomy. The adoption of robotic assistance during surgery will continue as the applications of robotic-assisted surgery expand into other solid organ malignancies.*

Introduction

Prostate cancer is the second leading cancer-related cause of death for men in the United States.[1] In 2015, approximately 220,800 American men will be diagnosed with prostate cancer and 27,540 will die from their disease.[1] The majority of men will present with localized disease (81%) for which multiple options for treatment exist, including radical prostatectomy, external beam radiation, brachytherapy, and active surveillance, among other less well-studied treatments.[2] During the last decade, the use of radical prostatectomy for the treatment of prostate cancer has increased, partially due to the adoption of minimally invasive surgical techniques that utilize robotic assistance.

Since the first published account of surgical treatment for prostate cancer by Young in 1905,[3] in which he described perineal prostatectomy, the disease process and goals for outcomes have changed. Walsh and Donker[4] helped to modernize the retropubic approach to include nerve sparing and preserving the external urethral sphincter to aid in potency and the maintenance of urinary continence after surgery. In 1997, Schuessler et al[5] described the first laparoscopic radical prostatectomy, but the procedure was not widely adopted because of the higher level of difficulty and advanced laparoscopic skills needed to perform the

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Submitted November 11, 2014; accepted May 14, 2015.

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No significant relationships exist between the authors and the companies/organizations whose products or services may be referenced in this article.

technique. However, despite the lack of widespread adoption, some centers of excellence exist where pure laparoscopic radical prostatectomies are performed.

To continue to incorporate the expected advantages of minimally invasive surgery into a broader base of urologic surgeons, the robotic-assisted laparoscopic radical prostatectomy (RALRP) technique was adopted, and Menon et al[6] performed the first of this procedure in the United States in 2000. Fifteen years later, RALRP is now the procedure of choice in the United States for the treatment of localized prostate cancer. More than 80% of prostatectomies are performed this way.[7]

Methods

We reviewed PubMed and the Cochrane Library for English-language studies that compared RALRP and open radical prostatectomy (ORP) in men with prostate cancer using the search terms "prostatectomy" and "comparison." We then screened 646 studies for reported outcomes of cancer control, sexual and urinary function, and complication rate. We then further narrowed our search by excluding studies that did not directly compare ORP with RALRP and had fewer than 500 patients (Fig).

No randomized controlled trials met our inclusion criteria. We included observational studies comparing ORP and RALRP in prospective, retrospective, and population studies. Two independent reviewers (GA and AML) selected the studies. The information presented on modified surgical techniques has been selected separate from the systematic review.

Of the 19 observational studies we identified and included in our review, 5 were prospective and 14 were retrospective.

Indications

Typical Candidates

Any patient with localized prostate cancer who is a candidate for open surgery is also a candidate for robotic-assisted surgery. A typical patient has T1 or T2 disease with no evidence of metastatic spread, and, similar to candidates for open surgery, the patient would be expected to have a life expectancy of more than 10 years. Patients with T3 or T4 disease should be considered for open or robotic-assisted surgery as well as those with oligometastasis in the pelvic lymph nodes (LNs). Surgery should be part of a multimodal approach to disease management in such patients.

Salvage Surgery

Patients who undergo primary treatment for localized prostate cancer with brachytherapy or external beam radiation therapy and have local recurrence within the prostate confirmed by biopsy are eligible for salvage treatment. These treatments vary in their rates of efficacy and include androgen deprivation therapy, cryoablation of the prostate, and salvage radical prostatectomy. With regard to long-term cure after salvage treatment for localized prostate cancer recurrence, salvage radical prostatectomy alone has been demonstrated to have more than 10 years of cancer control in a large proportion of patients.[8]

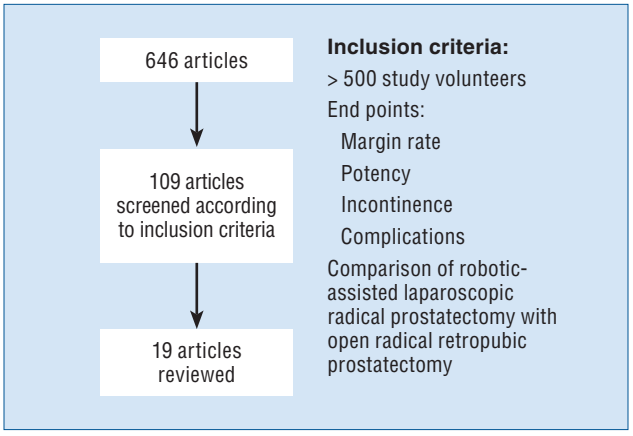

Fig. — Schematic for systematic review.

The improved magnification afforded by the laparoscopic camera is a potential benefit of the robotic technique for salvage prostatectomy because a major complication following the procedure is rectal injury as a result of the posterior dissection of the prostate. The number of overall complications encountered highlights the rate of morbidity associated with the procedure. In a review of 51 consecutive surgical candidates who underwent salvage RALRP for recurrent prostate cancer following primary radiation therapy, an overall complication rate of 47% was seen and included 2 rectal injuries; 23% of the study volunteers remained potent and 45% remained continent following treatment.[9] A total of 57% of patients remained free of biochemical recurrence at 3 years.[9] Thus, salvage surgery remains feasible; however, it should be attempted at high-volume centers alone.

Selected Contraindications

Comorbid conditions, such as chronic obstructive pulmonary disease, may disqualify a patient from robotic-assisted surgery because he or she will be in an extreme Trendelenburg position for 3 to 4 hours and pneumoperitoneum may be present with carbon dioxide, possibly resulting in hypercapnia and difficulties with ventilation. A patient with a bleeding diathesis would also not be a candidate for either robotic-assisted or laparoscopic surgery.

Surgical Techniques

Extraperitoneal vs Transperitoneal Approach

Consistent with traditional open retropubic radical prostatectomy, the extraperitoneal approach to RALRP provides the surgeon with familiar anatomy and dis-

section planes that can be assimilated with ease. Theoretical advantages to the extraperitoneal approach include the avoidance of peritoneal contents that can enter into the field of interest and cause injury to the bowel, decreased postoperative ileus, and containment of postoperative urine leaks, lymphoceles, and abscesses. In addition, avoiding adhesions by remaining in the retropubic space is advantageous in patients with a history of previous abdominal operations.

The most common approach is transperitoneal, which provides a wider space to work in and allows the surgeon to perform an extended pelvic LN dissection and posterior dissection of the prostate and seminal vesicles. In a study by Davis et al,[10] no observed differences were seen between extraperitoneal and transperitoneal RALRP with regard to length of hospital stay, complications, and positive surgical margins. Chung et al[11] found similar rates of positive surgical margins, potency, and urinary continence between the 2 techniques but a decreased incidence of bowel complications and postoperative pain in the extraperitoneal group. However, the surgeon's experience with a particular technique is the factor with the greatest effect on patient outcomes.

Anterior vs Posterior Approach

Two widely utilized approaches to dissection of the posterior prostate and seminal vesicles involve an anterior approach in which the bladder neck is opened and a posterior approach in which the plane between the rectum and posterior prostate is developed. The posterior approach is performed with a transperitoneal method alone, whereas the anterior approach can be achieved with both transperitoneal and extraperitoneal techniques. Using the posterior approach, the surgeon has direct access to the seminal vesicles and can develop the posterior plane between the prostate and the rectum to the distal extent of the apex of the prostate. Doing so allows for the dissection of the seminal vesicles in a relatively open space compared with what can sometimes be a challengingly small hole encountered in the anterior approach. The posterior approach also helps the surgeon desiring to perform robotic-assisted radical cystectomies familiarity with the technique. However, preserving the neurovascular bundles as they come into proximity with the seminal vesicles can be more readily achieved with the anterior approach. Maddox et al[12] found no differences in positive surgical margins, blood transfusions, operative times, and complication rates between the anterior and posterior approaches to RALRP.

Preservation of the Neurovascular Bundles

The morbidity from anatomic radical prostatectomy, a curative treatment for prostate cancer, has been declining. The neurovascular bundles are posterolaterally located on the prostate and contain parasympathetic and sympathetic nerve fibers. Walsh and Donker[4] initially presented their results in 1982, using the anatomical dissection of male newborns and fetuses to map the autonomic innervation of the corpora cavernosa responsible for erectile function. In their paper, the area of the pelvic plexus of nerves was most susceptible to injury during dissection of the apex and ligation of the lateral pedicles to the prostate.[4] Also reported in that manuscript were the primary predictors of postoperative potency, including age and stage of disease.[4] Men younger than 60 years of age and with cancer confined to the prostate capsule have a potency rate that nears 60%.[4]

Since the first report in 1982,[4] and with the increased magnification afforded by the laparoscopic camera utilized in RALRP, the nerves can be better visualized for preservation. In a retrospective cohort of 435 study patients who underwent nerve-sparing radical prostatectomy, Briganti et al[13] categorized patients into groups of low, intermediate, and high risk for postoperative erectile dysfunction and determined the classification system used to predict erectile function recovery. The low-risk group was composed of study patients younger than 65 years of age, those with an International Index of Erectile Function score higher than 26, and a Charlson Comorbidity Index below 1; those in the high-risk group were composed of study patients older than 70 years, those with an International Index of Erectile Function below 10, and those with a Charlson Comorbidity Index above 2.[13] In total, 89% of those in the low-risk group recovered erectile function compared with 37% in the high-risk group.[13]

Furthermore, Gandaglia et al[14] compared the open and robotic-assisted approaches to nerve-sparing radical prostatectomy and found that study patients in the low- and intermediate-risk classification of erectile function benefited the most from robotic-assisted surgery when looking at postoperative recovery rates, whereas no significant difference was seen between the open and robotic-assisted procedure in the high-risk cohort.

These studies helped determine which patients may benefit from a nerve-sparing procedure and for physicians to provide a better expectation to their patients about the surgical results. Patients with high-grade and high-volume disease seen on prostate biopsy are more likely to harbor extraprostatic disease and, thus, have an increase likelihood of experiencing positive surgical margins during a nerve-sparing procedure, resulting in poor cancer control.

Some advocate the preoperative use of magnetic resonance imaging (MRI) in such higher-risk patients to determine the extent of cancer and whether unilateral or bilateral nerve sparing can be performed. For example, Park et al[15] reviewed 353 patients who obtained preoperative MRI followed by RALRP and

found that the initial surgical plan was changed in 26% of patients following MRI. Of those patients whose surgical plans changed, 57% were changed to a plan to preserve their neurovascular bundles, and 43% were changed to a more aggressive resection of their nerves with the prostate.[15] In high-risk prostate cancer groups, MRI had a 80% sensitivity rate for detecting extracapsular extension of disease.[15]

Rifaioglu et al[16] performed a deceased donor study in which they performed prostatectomy with intrafascial and interfascial nerve-sparing techniques. They examined the tissue surrounding the prostate and found that, compared with deceased donors with interfascial nerve sparing, deceased donors with intrafascial nerve sparing had a greater amount of sympathetic fibers present in the neurovascular bundles without an increase in prostate capsular penetration. Thus, the degrees of nerve sparing can vary depending on the technique used. A large-volume comparison of retrograde and antegrade nerve-sparing techniques was conducted and the retrograde technique was shown to have an earlier recovery of potency; however, at 1 year, the potency rates were about the same between the 2 techniques.[17]

Seminal Vesicle Sparing

Included in the procedure for radical prostatectomy is en bloc resection of the seminal vesicles because they are related to the prostate and, depending on the disease risk group, may harbor disease. Huang et al[18] reviewed 7,376 patients receiving radical prostatectomy and found that those with low-risk disease have a risk of less than 2% for harboring cancer in their seminal vesicles. This risk increased with the presence of higher risk features such as a Gleason score of 7 to 10 and a prostate-specific antigen value higher than 10.

Due to the close proximity of the neurovascular bundles to the seminal vesicles, theoretically a seminal vesicle sparing approach could be performed in low-risk patients to aid in the postoperative recovery of erectile function. Sanda et al[19] measured the effect of seminal vesicle sparing during open radical prostatectomy on the recovery of erectile function in 191 study patients and found improved sexual health among those with the tips of the seminal vesicle left in situ. However, the results of seminal vesicle sparing must be prospectively validated in a larger cohort of patients before definitive conclusions can be made regarding this technique.

Posterior Reconstruction

Following the extirpation of the prostate, the surgeon must reconstruct the lower urinary system by anastomosing the bladder neck to the urethra. In 2001, Rocco et al[20] described a modification to conventional urethrovesical anastomosis by adding a step prior to this that involved restoring the posterior aspect of the rhabdosphincter. The technique involves bringing the posterior sphincter to the residual Denonvilliers fascia and posterior bladder wall. In the initial series performed in study patients undergoing radical retropubic prostatectomies, the urinary incontinence rates were significantly improved in those undergoing the "Rocco" stitch (at 90 days, the rates were 86.3% in the posterior reconstruction group and 46% in the traditional group).[20] The primary difference was seen in time to continence; at 1 year, both groups had a 90% continence rate.[20] However, in 2 randomized trials comparing study patients who received RALRP with and without posterior reconstruction, no significant difference was seen in early return of continence following catheter removal between either of the 2 groups.[21,22]

Lymph Node Dissection

The presence of LN metastasis in patients with prostate cancer portends a poor prognosis. Patients who harbor high-volume and high-grade disease are more likely to have LN metastasis present, whereas low-risk patients with prostate cancer undergoing LN dissection have a 1% rate of metastasis to the LNs.[23]

Utilizing any of the several available nomograms to predict the extent of disease at the time of radical prostatectomy makes it possible to determine which patients are likely to benefit from LN dissection at the time of surgery. A patient at risk of LN metastasis higher than 2% by nomogram should be considered for LN dissection.[24] Standard LN dissection includes the obturator and the internal and external iliac nodes. One of the most common landing sites for LN metastasis are the internal iliac nodes in which up to 50% of positive nodes in a large series were found.[25] Briganti et al[26] demonstrated an improved detection rate as the number of nodes removed increased, and they advocated for an extended LN dissection in all high-risk patients. When fewer than 10 nodes were removed, the researchers detected nearly no LN metastasis; however, when more than 30 nodes were sampled, their rate of detection was close to 100%.[26]

The number of nodes is not a marker of adequate lymphadenectomy because variability exists in this number and it depends on the sampling technique used by the pathologist. At this time, no randomized trials have demonstrated any benefit from lymphadenectomy in patients with prostate cancer. Diagnostic and therapeutic benefits may potentially exist following LN dissection; however, the procedure does have risks, including postoperative lymphocele, lymphedema, bleeding, and deep venous thrombosis; total complication rates are as high as 10% in some series.[27]

Whether LN dissection is performed or not during minimally invasive prostatectomy depends on the preference of the surgeon and has not been demonstrated to have an effect on the complication rate. In a

recent series by Liss et al,[28] the nodal yield was similar among patients undergoing open and minimally invasive surgery.

Pelvic Drain Placement

Following RALRP with or without pelvic LN dissection, placement of a pelvic drain to collect urine and lymph fluid and to detect any postoperative bleeding is a standard approach. Retrospective reviews have been performed to compare patients who did not receive a pelvic drain, because omitting this step has been theorized to aid in early postoperative discharge rates and decreased pain.[29] The conclusions from the authors of these studies is that when a properly visualized urethrovesical anastomosis is performed, omitting the pelvic drain is safe and does not result in increased complications.[29] However, the benefit from omitting the pelvic drain has not been demonstrated; thus, the diagnostic information received from recognition of a postoperative bleed, large urine, or lymph leak provide justification for its continued use, so it is still employed in our practice.

Bladder Drainage

Similar to drain placement, urethral catheter drainage following RALRP has been the standard method of bladder drainage for the majority of institutions performing this procedure. Among 184 male study patients undergoing radical prostatectomy, 45% of them reported that the urethral catheter was moderately to severely bothersome and 19% said it caused pain at the incision site.[30] Given these findings, the early removal of urethral catheters is of interest to most surgeons. The length of catheterization varies by institution, and investigations into early catheter removal at 2 to 4 days following surgery have been generally safe and no increases in incontinence or complication rates have been seen when the precatheter removal cystogram demonstrates no urinary leak; furthermore, this holds true in most series when the catheter is removed prior to 7 days.[31]

Other methods to potentially help reduce bother include the placement of a suprapubic tube at the time of prostatectomy and removal of the urethral catheter on postoperative day 1. In a randomized trial comparing early removal and placement of a suprapubic tube with traditional urethral catheter removal on postoperative day 7, no differences were seen in bother and treatment satisfaction between the 2 groups.[32]

Complications

When analyzing complications related to RALRP, a dichotomized approach is preferable in which perioperative short-term outcomes and functional effects are assessed. Short-term complications include those related to any major abdominal operation and include infection, lymphocele, deep venous thrombosis, urine leak, ileus, and bleeding. Long-term complications include impotence, urinary incontinence, penile shortening, and bladder neck contracture. Refer to Table 1 for a review of complications in the studies comparing RALRP and ORP.[33-37]

Agarwal et al[38] reported on 3,317 consecutive study patients who underwent RALRP at a single institution between 2005 and 2009 and found an overall complication rate of 10%. The majority of complications occurred within 30 days.[38] A total of 2.1% of patients received a perioperative blood transfusion, 2% had postoperative bleeding, 1% had urine leaks, and 0.3% had venous thromboembolism.[38] Nine study patients also had enterotomies during surgery that required repair.[38] These findings were confirmed in a recent meta-analysis by Novara et al[39]; the rates of blood loss and transfusions alone were significantly different between the RALRP and ORP groups, although the groups undergoing RALRP had lower values in both categories. Thus, the robotic approach to prostatectomy is a safe procedure with acceptable rates of morbidity.

Potency

Loss of erectile function is a known complication of radical prostatectomy, and extensive research into the cause, preservation, and treatment of this loss of function has been performed. The pelvic parasympathetic nerves responsible for erectile function are involved with the anatomy of the prostate, and preserving these neurovascular bundles has a beneficial impact in maintaining potency following prostatectomy; however, other factors, such as age and stage of disease, continue to have a major impact. Recovery of function utilizing phosphodiesterase (PDE) inhibitors is effective. No difference has been seen in daily PDE inhibitor use and on-demand use in recovery; however, significantly reduced function has been shown in those naive to PDE inhibitors.[40] Thus, in any potency preservation program, early use of PDE inhibitors should be encouraged because their use may reduce corporal fibro-

Table 1. — Overall Complication Rates for ORP and RALRP

Study	Complications, n (%)	
	ORP	RALRP
Sammon[33]	28,054 (11.7)	49,562 (8.3)*
Froehner[34]	2,437 (29.1)	317 (33)
Hu[35]	6,889 (23)	1,938 (22)
Krambeck[36]	588 (4.8)	294 (8)
Lowrance[37]	3,760 (24.1)	826 (21.4)

*$P < .01$.

ORP = open radical prostatectomy, RALRP = robotic-assisted laparoscopic radical prostatectomy.

sis and prevent penile shortening, an under-reported complication.[41] It is worth noting that it is important to include these sexual adverse events when counseling patients wishing to undergo the procedure.

In a review of more than 3,000 study patients who underwent RALRP between 2008 and 2011 by surgeons who had performed at least 100 cases, the potency rate at 1 year was as high as 90% in some instances.[42] However, the results from this study are retrospective, have no standardized reporting methods, and the study patients had differing clinicopathologic characteristics.[42] See Table 2 for a review of erectile function in studies comparing RALRP and ORP.[35,36,43,47]

Continence

Similar to the preservation of potency, maintaining continence following prostatectomy is a major cause of patient dissatisfaction following surgery. After removal of the prostate, the internal sphincter is no longer present, so patients must rely on their external sphincter for urinary control. By preserving the bladder neck and using modifications, such as the posterior reconstruction of the sphincter, improved rates of continence can be achieved and can reach nearly 90% in most reported series.[48] By preserving the neurovascular bundle, it may be possible to improve continence following prostatectomy.[49] Similar to potency, maintaining continence following prostatectomy depends on the surgery and the patient's clinicopathological characteristics, such as age, preoperative urinary control, and pathological stage of disease. See Table 3 for a review of continence rates in studies comparing RALRP and ORP.[50-57]

Table 2. — Urinary Function for ORP and RALRP

Study	Urinary Continence, n (%)	
	ORP	RALP
Hu[35,a]	6,889 (11.9)	1,938 (18.2)*
Krambeck[36,b]	588 (88)	294 (82)
Barry[43,c]	220 (8.9)	406 (11.7)
Kim et al[44,d]	235 (85)	528 (87)
Alemozaffar[45,e]	621 (74.4)	282 (74.4)
Malcolm[46,f]	135 (79)	447 (74)
Lowrance[47,g]	3,760 (5)	826 (6.2)

[a]Urinary function as reported in Medicare coding for incontinence.
[b]Continence defined as no pads.
[c]Urinary function reported as being a "big problem" on questionnaire.
[d]Continence described as being completely pad free.
[e]Urine function based on EPIC-26 score reporting continence.
[f]Continence reported on a health-related, quality-of-life urinary function questionnaire.
[g]Incontinence requiring a procedure.
*$P < .01$.
ORP = open radical prostatectomy, RALRP = robotic-assisted laparoscopic radical prostatectomy.

Table 3. — Rates of Positive Surgical Margins for ORP and RALRP

Study	Positive Surgical Margin Rate, n (%)	
	ORP	RALP
Smith[50]	509 (35)	1,238 (15)*
Masterson[51]	357 (18)	669 (14)
Silberstein[52]	961 (15)	493 (15)
Koo[53]	580 (21.8)	592 (19.4)
Hu[54]	5,524	5,524
Low, %	9.2	8
Intermediate, %	21	15*
High, %	21	15*
Pierorazio[55]	743 (29.4)	170 (31.8)
Park[56]	277 (21)	23% (n = 730)
Vora[57]	415	1,011
pT3, %	51.4	47.1

*$P < .01$.
ORP = open radical prostatectomy, RALRP = robotic-assisted laparoscopic radical prostatectomy.

Cancer Control

The most important outcome for patients undergoing RALRP is the presence of negative surgical margins and the removal of all prostatic disease. The positive margin rate increases with grade and stage of disease on preoperative prostate biopsy with overall rates of 27%, and, when stratified by the National Comprehensive Cancer Network, rates were 19% for low, 26% for intermediate, and 40% for high-risk prostate cancer groups.[58]

If pathology results from the final prostatectomy specimen demonstrate positive margins, seminal vesicle invasion, or extracapsular extension, then these patients are generally counseled to receive adjuvant external beam radiation, because results from randomized controlled trials have demonstrated improved metastasis and biochemical-free survival rates for those receiving adjuvant compared with salvage radiation.[59,60] No randomized controlled trial has compared RALRP with open prostatectomy, so conclusions are difficult to make regarding which approach will yield improved rates of cancer control; however, an important factor that improves outcomes is undergoing surgery at a high-volume center (> 10 prostatectomies/year).[58] See Table 4 for a review of positive surgical margin rates in studies comparing RALRP and ORP.[35,36,43-46]

Future Advancements

Adopting advanced technologies into the treatment armamentarium of the urological surgeon must be rapid and continuous, and well-designed clinical

Table 4. — Sexual Function for ORP and RALRP

Study	Sexual Function, n (%)	
	ORP	RALRP
Hu[35,a]	6,889 (18.2)	1,938 (33.8)*
Krambeck[36,b]	588 (63)	294 (70)
Barry[43,c]	220 (71.4)	406 (65.8)
Kim et al[44,d]	235 (47.5)	528 (83.8)
Alemozaffar[45,e]	621 (36.8)	282 (36.3)
Malcolm[46,f]	135 (84)	447 (81)

[a]Percentage reporting being impotent in Medicare coding.

[b]Sexual function based on potency at 1 year on a nonvalidated questionnaire.

[c]Sexual function reported as being a "big problem" on questionnaire.

[d]Sexual function reported as erection sufficient for penetration at 2 years; 34% in the ORP group received a bilateral nerve sparing procedure compared with 53% in the RALRP group.

[e]Sexual function based on the Expanded Prostate Cancer Index Composite 26-item score (reporting impotence).

[f]Health-related, quality-of-life sexual function questionnaire documenting potency.

*$P < .01$.

ORP = open radical prostatectomy, RALRP = robotic-assisted laparoscopic radical prostatectomy.

trials must be developed to test the safety and efficacy of these new techniques. The ability to better detect and preserve the neurovascular bundles involved with preserving potency using bioluminescence and sound amplification from nerve sensors as well as enhanced microscopic visualization are on the horizon. The ability of the robot to provide haptic feedback to the surgeon will allow for improved tissue discrimination, possibly reducing traction injury on the neurovascular bundles and tissue trauma. Currently, modifications of the robotic-assisted approach to prostatectomy are being performed that involve a transition to a laparoendoscopic single site. The future of prostate surgery is exciting and emphasizes patient-centered outcomes. It is our hope that robotic-assisted surgery will help reduce mortality rates from prostate cancer and morbidity rates related to treatment.

Conclusions

The diagnosis and treatment of prostate cancer have evolved during the last 20 years. The adoption of robotic-assisted laparoscopic radical prostatectomy has not been unequivocally shown to be superior to the open approach. However, continual technical advancements of prostatectomy will translate into improved patient outcomes.

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Sofía Cáceres Nazario. *Trippy Goat*, 2015 (Detail). Acrylic on canvas (diptych), 16" × 24".

Robotic-assisted surgery allows for the widespread adoption of minimally invasive techniques for patients with renal malignancies.

Robotic-Assisted Renal Surgery

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Background: *Minimally invasive surgical techniques have revolutionized the surgical management of kidney cancer. Current evidence suggests that the surgical developments gained by traditional laparoscopy have been advanced by the robotic platform, particularly as it has been applied to techniques for nephron preservation.*
Methods: *The medical literature from peer-reviewed journals was reviewed to evaluate the feasibility and efficacy of robotic-assisted surgery in the management of renal cell carcinoma. Particular attention was paid to studies comparing robotic-assisted surgery with more traditional surgical techniques. In this review, we have highlighted the evolution of robotic assistance for renal surgery as it pertains to renal oncology. The differing approaches to standard surgeries are discussed as well as current trends to improve perioperative outcomes. In addition, we have reviewed the application of robotic assistance to more complex cases and highlight technological advancements that have pushed the boundaries of surgical care.*
Results: *Robotic-assisted renal surgery is effective for appropriately selected patients. Robotic-assisted radical nephrectomy provides equivalent outcomes to traditional open and laparoscopic approaches, albeit with added financial burden. Robotic-assisted partial nephrectomy — through either transperitoneal or retroperitoneal access — can provide superior outcomes to laparoscopic approaches due to several technical advantages, including improved instrument articulation.*
Conclusions: *Robotic assistance has transformed the delivery of surgical care to the patient with renal cell carcinoma. For renal surgery, morbidity and patient satisfaction are potentially improved when using robotic platforms compared with open and traditional laparoscopic approaches without compromising oncological control, and this is particularly true for nephron-sparing surgery.*

Introduction

Sir William Osler once remarked that "the future is today," a statement that continues to be pertinent to the current practice of medicine.[1] During the last few decades, many exciting advances in medical technology have positively impacted patient care, a fact not lost in the management of renal cell carcinoma (RCC).

The incidence of kidney cancer has been rising; approximately 62,000 US patients will be diagnosed with kidney cancer in 2015 and approximately 30,000 partial and radical nephrectomies will be performed.[2,3] The incidence of RCC has been rising in part due to the incidental finding of small renal masses discovered on cross-sectional imaging for the evaluation of different abdominal pathologies.[4] As a result, most newly diagnosed renal cancers are found when confined to the kidney.[4] The prognosis of these patients primarily depends on the stage of their disease; 5-year survival rates range from 90% to 100% for T1a tumors and 0% to 10% for cases with systemic in-

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volvement.[5] These numbers highlight the aggressive nature of RCC; however, when diagnosed while the disease is organ-confined, extirpative surgery (radical or partial nephrectomy) renders a 5-year, disease-specific survival rate higher than 90%.[5-7]

Traditionally, kidney surgery is performed through larger open incisions that can result in poor cosmesis and significant pain, contributing to more prolonged patient convalescence.[8] The adoption of minimally invasive approaches to kidney surgery has been widespread with the introduction of laparoscopy, and the boundaries are continually being pushed with the type and complexity of surgeries that can be performed using robotic assistance. In the late 1980s, laparoscopic technology was routinely applied for cholecystectomies, which further advanced the knowledge base and familiarity with laparoscopic equipment and techniques until laparoscopy was adopted for renal surgery.[9,10] Clayman et al[11] performed the first laparoscopic radical nephrectomy (LRN) in 1991, and subsequent series were published showing the feasibility of laparoscopic renal surgery in larger cohorts of study patients. These studies highlighted smaller incisions, reduced rates of postoperative pain, and improved convalescence as benefits of the minimally invasive approach. Despite the advantages of laparoscopy for the patient, the ability to perform complex kidney surgery is limited to high-volume surgeons who have developed advanced laparoscopic skills.[12]

The advent of the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California) has the same advantages of open surgery without the limitations of pure laparoscopy. Specific advantages of robotic assistance include the 3-dimensional stereoscopic view with 10 times magnification, tremor attenuation, and articulating arms with 7 degrees of freedom. Given the more precise movements and shorter learning curves for surgeons, use of the robotic platform is gaining popularity. Although an open approach is arguably a more appropriate option for larger renal tumors (T2–T3), minimally invasive nephron-sparing surgery (NSS) is often utilized for smaller masses and robotic assistance is the preferred method.[12]

Robotic assistance is used for the surgical management of both malignant and benign conditions. Reports continue to be published demonstrating large series of study patients undergoing robotic-assisted surgery with positive long-term results.[13,14] Given its proven durability, this technique is likely to play a prominent role in the future of surgery.

Methods

A systematic literature search was performed of the medical literature. Original articles, editorials, and reviews were utilized. Abstracts and comments were excluded. We did not limit the date for which the reports were published, but preference was given to publications from the last 10 years and large series. Full-text articles alone were included. Manuscripts were reviewed for pertinence to the subject matter and included as available.

Radical Nephrectomy

Radical nephrectomy is the traditional benchmark management strategy for RCC to which other treatments have been compared. The laparoscopic technique was introduced in the early 1990s and initial studies defined it as a viable and effective surgical technique.[15] Since then, a natural evolution has taken place over the last several years to incorporating robotic assistance. In 2005, Klingler et al[16] provided the initial report on the viability of robotic-assisted radical nephrectomy (RARN). Although their study cohort was small (5 study patients), they showed that standard perioperative indices were acceptable; 1 study patient alone required conversion to hand-assisted laparoscopy due to bleeding.[16] More robust studies have since been published, confirming successful surgical and oncological outcomes for robotic assistance in study patients undergoing radical nephrectomy (Table 1).[16-20]

Rogers et al[18] described a series of RARN for benign and malignant renal tumors. In their series, the mean operative time was 158 minutes, the mean rate of estimated blood loss (EBL) was 223 cc, the mean tumor size was 5.1 cm, and the mean length of stay (LOS) at the hospital was 2.4 days, all of which confirmed the assertion that RARN is both safe and effective as an option for extirpative renal surgery.[18]

Exclusion criteria for RARN are no different than those for laparoscopy. RARN can be performed by either a transperitoneal or retroperitoneal approach. The initial studies describing RARN focused on the transperitoneal approach, and equivalent outcomes with LRN were demonstrated despite different port placements.[16,17] Given that earlier reports cited the feasibility of performing LRN via the retroperitoneum, robotic assistance was applied to this approach as well.[21] The largest early series was described by Patel et al,[22] in which 10 study patients underwent retroperitoneal RARN. The results showed that this was a safe and feasible alternative to transperitoneal RARN, with the authors citing direct access to the hilum and minimal bowel manipulation as potential benefits of this approach.[22] Rogers et al[18] described a cohort of 42 study patients subject to RARN, of which 39 used the transperitoneal approach and 3 used the retroperitoneal approach. Although this study was limited by its small cohort of study patients whose disease was managed through a retroperitoneal approach, the authors noted that no significant differences were seen between the outcomes of the 2 groups.[18]

Studies show a trend toward improved rates of

Table 1. — Select Perioperative Indices of Patients Undergoing Robotic-Assisted Radical Nephrectomy

Study	No. of Patients	Age, y	BMI, kg/m^2	Tumor Diameter, cm	Operative Time, min	EBL, cc	Conversion Rate, %
Klingler[16]	5	72	28	4.6	321	150	20
Nazemi[17]	6	67.5	27.6	4.5	345	125	0
Rogers[18]	35	61.5	30.5	5.1	291	221	0
Hemal[19]	15	50.3	28.3	6.7	221	210	6.7
Boger[20]	13	NR	29	4.8	168	100	7.7

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EBL, narcotic use, and LOS with minimally invasive extirpative renal surgery when compared with open radical nephrectomy (ORN).[17,23] Despite this, operative times are shorter with ORN and long-term oncological and functional outcomes are similar between the 2 approaches.[17,23] As such, both can be used for the management of renal tumors. Regarding minimally invasive renal surgery, the superiority of RARN over LRN or hand-assisted laparoscopic radical nephrectomy (HALRN) has never been demonstrated.

Rogers et al[18] acknowledged the lack of superiority but made note of several important benefits associated with robotic assistance, including a fourth robotic arm that provides renal traction to facilitate hilar dissection, the ability to suture ligate hilar vessels similar to an open approach, and the ability to more precisely place Hem-o-Lok clips (Weck Surgical Instruments, Durham, North Carolina) owing to greater degrees of freedom than pure laparoscopic instruments.[18] Other researchers have noted that case studies can be used as training for more technically challenging robotic-assisted NSS.[15,18]

Despite the noted benefits, many series have compared LRN, HALRN, and RARN and found no significant difference in perioperative characteristics and have seen a trend toward increased operative time with RARN.[17,19,20] One study suggested that RARN is not cost effective. Yang et al[24] reported data from more than 24,000 patients from the Nationwide Inpatient Sample database who underwent minimally invasive radical nephrectomy (32% of whom underwent RARN), and they found a total cost increase of nearly $12,000 per case associated with RARN over LRN or HALRN without any difference in patient morbidity.[24] Thus, even though RARN is safe and has similar outcomes to traditional laparoscopic approaches, this added cost of robotic assistance might outweigh any perceived benefit from the approach. As such, when specifically applied to renal surgery, robotic assistance may be most useful in highly complex radical nephrectomy cases and NSS.

Partial Nephrectomy

NSS is the treatment of choice for a small renal mass.[25] Although the evidence is controversial, most researchers believe that, compared with patients undergoing radical nephrectomy, NSS is associated with at least equivalent rates of survival.[26,27] An intuitive benefit also exists to preserving renal parenchyma and subsequent long-term renal function, and results from retrospective surgical series support maximizing the preservation of functioning nephrons based on lower level evidence for associated cardiovascular and metabolic benefits with NSS compared with radical nephrectomy.[28]

Laparoscopic partial nephrectomy (LPN) is a viable surgical approach for the small renal mass deemed appropriate for NSS, and early surgical series from centers of excellence have noted acceptable oncological outcomes and rapid recovery times.[29,30] However, the technical difficulty of LPN translates into increased perioperative complications compared with those seen in standard open partial nephrectomy (OPN).[25] Gill et al[31] reported outcomes from 1,800 study patients undergoing partial nephrectomy and found that patients assigned to LPN had a 2.14 times higher risk for developing postoperative complications than those assigned to OPN. Increased rates of complications appeared to be related to the limited, 2-dimensional maneuverability of laparoscopic instruments, which resulted in challenging intracorporeal suturing and a subsequent tendency toward prolonged warm ischemia times (WITs) in all but the most experienced laparoscopic surgeons.[31]

With robotic technology, improved visual optics

Table 1. — Select Perioperative Indices of Patients Undergoing Robotic-Assisted Radical Nephrectomy (cont)

Study	Transfusion Rate, %	Malignant Tumors, %	LOS, d	Mean Analgesic Need, mg[a]	Overall Complication Rate, %	Postop Rise in Serum Cr, mg/dL	Early Recurrence Rate, %
Klingler[16]	NR	80	3	28	0	0.6	NR
Nazemi[17]	16	71	3	19	18	0.3	NR
Rogers[18]	0	97	2.5	18.3	2.6	0.5	0 at 15.7 mo
Hemal[19]	13.3	100	3.5	14.3	20	NR	0 at 8.3 mo
Boger[20]	NR	NR	2	30	30	NR	NR

[a]Morphine equivalent.
BMI = body mass index, Cr = creatinine, EBL = estimated blood loss, LOS = length of stay, NR = not reported.

and articulating arms have mitigated many of the aforementioned concerns. The main advantages of RAPN are the added dexterity, which allows for more precise tumor manipulation, meticulous dissection to ensure complete tumor excision, a greater ability to rapidly control postexcisional bleeding, and more expedient renorrhaphy to maintain low ischemia times. Oncological indications for RAPN are the same as those for OPN, and technical considerations are similar to what were previously described for RARN.

Several surgical series highlight the success of RAPN (Table 2), and, by contrast to RARN, RAPN has been shown to be superior to LPN.[13,32-38] Multiple studies confirm significantly reduced or equivalent operative times, rates of EBL, WITs, and LOS when comparing RAPN with LPN. In addition, greater technical ease and a reduced likelihood of open conversion are both possible with RAPN.[36,39] The most recent of these studies was performed by Wu et al[40] in which they analyzed 146 and 91 study patients treated with LPN and RAPN, respectively. They demonstrated improved rates of EBL (158 vs 198 cc) and WIT (22.8 vs 31.0 minutes) with equivalent LOS.[40] They also noted a decreased rate of high Clavien–Dindo grade intraoperative complications (1.3% vs 11.7%) when using robotic-assisted technology.[40,41]

RAPN is frequently performed through a transperitoneal approach, which is likely secondary to surgeon preference; however, advocates for transperitoneal surgery highlight the ease of access, the large available working space resulting from the pneumoperitoneum, and more easily recognizable or established anatomical landmarks as specific benefits to their approach not readily appreciated or developed using a retroperitoneal technique.[21] High-volume robotic-assisted surgical centers commonly employ a transperitoneal approach for patients deemed appropriate candidates for RAPN. Despite this, the retroperitoneal approach is frequently used and the surgical technique performed is typically based on multiple tumor and patient characteristics, including tumor location (ie, anterior, posterior, upper pole, lower pole), tumor multifocality, relationship to vascular structures, relationship to renal pelvis and calyces, prior renal or abdominal surgery, and patient comorbidities.

Retroperitoneal Approach

The anterior transperitoneal approach to RAPN is less than ideal for posteriorly located tumors due to the extensive renal mobilization required for tumor exposure. Following extensive dissection, adequate exposure can still be suboptimal, particularly in patients with more extensive volumes of perinephric fat. In addition, patients with a history of prior abdominal surgeries may have significant adhesions difficult to manage or release with standard laparoscopic techniques, making transperitoneal access and renal exposure challenging. Approaching posterior tumors (particularly posterior–medial) and some posterior–lateral tumors via the retroperitoneum can minimize these issues.

Retroperitoneal access for minimally invasive LPN was first described in 1994.[42] Recently, robotic-assisted retroperitoneal partial nephrectomy (RARPN) has been put into use and is a proven, useful technique for appropriately selected patients and tumors. RARPN can facilitate direct access to posteriorly located tumors and early exposure and isolation of the renal vasculature. The lack of entry into the peritoneum minimizes any manipulation required to the bowel and also makes minimally invasive surgery possible in patients previously considered to be poor candidates due to significant scarring from prior abdominal procedures.

Table 2. — Select Perioperative Indices of Patients Undergoing Robotic-Assisted Partial Nephrectomy

Study	No. of Patients	Specific Inclusion Criteria	Age, y	BMI, kg/m^2	Mean Nephrometry Score	Tumor Diameter, cm	Operative Time, min	EBL, cc	WIT, min
Faria[13]	137	None	60.3	30.4	7	2.7	192.5	125	20
Dulabon[32]	446	None	59.9	30.1	NR	2.9	188.1	213.2	20.2
Kaouk[33]	400	None	58.5	30.7	7.2	3.2	190.3	260.2	19.2
Ellison[34]	108	None	59.4	30.9	NR	2.9	215	368	24.9
Khalifeh[35]	269	None	58.8	31	7.2	3.2	169.8	262.8	17.9
Masson-Lecomte[36]	220	None	59	26.4	6	3	168.1	244.8	20.4
Sammon[37]	851	None	57.1	NR	NR	NR	NR	NR	NR
Volpe[38]	44	Padua Prediction Score ≥ 10	65	26	NR	4.2	120	150	16

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Weizer et al[43] published the first series describing the retroperitoneal approach, analyzing data from 11 study patients undergoing RARPN. Their results were promising and highlighted the low rate of perioperative morbidity and the ability of the surgeon to address complex posterior tumors.[43] In a large, multiinstitutional cohort involving 227 RARPN cases, researchers compared their results with large, previously published cohorts of OPN and found a decrease in mean rate of EBL (approximately 300 mL) and shortened LOS of at least 4 days in patients undergoing RARPN when compared with OPN; significant differences in WIT were not seen.[44] In addition to these reports, other studies have assessed study patients undergoing RARPN, all of which have highlighted the feasibility of this surgical approach (Table 3).[43-50]

Access to upper-pole posterior tumors may be difficult due to interference from the eleventh and twelfth ribs. However, select upper-pole tumors can be accessed using this technique, and tumors with a high nephrometry score (greater complexity) can also be successfully treated using the retroperitoneal approach (see Table 3).[43-51] Although obesity adds to the complexity of RAPN, an elevated body mass index does not preclude acceptable patients from undergoing RARPN. In fact, data have shown the feasibility for RARN in patients who are obese.[52] Recognizing selection bias for any technique outside of a randomized clinical trial, 1 published series of RARPN included patients with a mean body mass index of 31 kg/m^2 and noted the feasibility of RARPN in select patients.[48]

Limitations

The main disadvantage associated with robotic-assisted renal surgery is centered on the cost of the technology. At the time of publication, a robotic system costs between $1.0 million and $2.5 million with an annual service agreement of about $100,000.[53] Many centers cannot afford this, a fact that has precluded the widespread, if not universal, adoption of this platform. Despite this, investigators have attempted to address whether or not increased expenditures were offset by decreased perioperative morbidities following procedures performed with robotic assistance.[54,55]

Laydner et al[56] reported a cost analysis of all partial nephrectomies performed at their institution, whether they be robotic-assisted, laparoscopic, or open procedures. They found that increased operating room costs were associated with RAPN when compared with LPN and OPN, but they noted that the total health care expenditure was less when compared with OPN, given the higher costs associated with perioperative morbidity in the OPN cohort.[56] The total cost of LPN was less than RAPN, but LPN is still arguably inferior because of the increased difficulty associated with the laparoscopic technique.[56] Although cost analyses support robotic assistance for nephron-preservation procedures, in the case of radical nephrectomy, in which LRN is rel-

Table 2. — Select Perioperative Indices of Patients Undergoing Robotic-Assisted Partial Nephrectomy (cont)

Study	Conversion Rate, %	Transfusion Rate, %	Positive Margin Rate, %	Malignant Tumors, %	LOS, d	Overall Complication Rate, %	Postop Decline in Renal Function, %	Early Recurrence Rate, %
Faria[13]	NR	2.2	1.5	86.2	NR	10.9	9	NR
Dulabon[32]	2.2	4	1.6	74.7	2.9	5.1	NR	NR
Kaouk[33]	1.5	7.3	2.3	74.5	3.6	18	11.1	NR
Ellison[34]	NR	6	7	85	2.7	33.3	0.5	NR
Khalifeh[35]	1.1	8.6	2.9	74.7	3.5	27.1	8.2	0.4 at 18 mo
Masson-Lecomte[36]	6	6	8	84	5.5	20.5	6.7	1.8 at 9.3 mo
Sammon[37]	NR	4.5	NR	NR	5	16.1	NR	NR
Volpe[38]	0	4.5	4.5	77.3	5.5	27.2	7.4	0 at 23 mo

BMI = body mass index, EBL = estimated blood loss, LOS = length of stay, NR = not reported, WIT = warm ischemic time.

atively easy to perform and costs substantially less than RARN, robotic technology affords neither the patient nor the surgeon any clinical or financial benefit.[24]

Future Directions

Standard multiport laparoscopy is safe and effective in renal surgery, and laparoendoscopic single-site (LESS) surgery has been investigated in the minimally invasive management of renal masses. Theoretical advantages over standard multiport robotics include better cosmetic results and a faster return to daily activities.[57] The LESS surgical platform has been extended to NSS, but it has not been widely adopted owing to the difficulty associated with LESS-LPN.[57] To address this, reports have emerged describing the use of robotic assistance for LESS–partial nephrectomy.[58] Tiu et al[59] reported on a series of 67 LESS-RAPN cases with good results. Their cohort included 20 study patients with tumors larger than 4 cm in diameter (mean, 5.2 cm) and a mean nephrometry score of 8.5; they highlighted the feasibility of this approach even in complex cases.[59]

A retrospective, single-center, single-surgeon comparison directly looked at RAPN and LESS-RAPN.[60] Study patients in each cohort were standardized with respect to nephrometry score, tumor size, and other characteristics. Four arms were used for LESS-RAPN, along with an optional additional 5-mm trocar for liver retraction with right-sided renal tumors.[60] The results showed significantly increased mean operative time, mean WIT, and a postoperative decline in renal function when using the LESS-RAPN technique compared with standard RAPN.[60] According to the authors, issues related to working space and collisions were significant, with the robotic arms occupying working space normally required for precise movements.[60] Such technical limitations and concerns regarding perioperative outcomes have been confirmed by other investigators.[61]

Improvements have been made to the da Vinci Xi Surgical System (Intuitive Surgical), and its robotic arms are streamlined to allow for more intimate trocar placement and reduced risk for robotic arm collision. However, whether the introduction of this system will allow for greater surgical dexterity in the context of LESS surgery remains to be seen. Regardless, LESS-RAPN may have some role in the future of minimally invasive renal surgery, but significant refinements and greater experience is required before it can be widely adopted.

In addition to the modification of surgical approaches, there has been a push toward innovative intraoperative maneuvers to improve functional outcomes associated with RAPN — in particular, the loss in renal function associated with hilar clamping and

Table 3. — Select Perioperative Indices of Patients Undergoing Robotic-Assisted Retroperitoneal Partial Nephrectomy

Study	No. of Patients	Age, y	BMI, kg/m^2	Mean Nephrometry Score	Tumor Diameter, cm	Operative Time, min	EBL, cc	WIT, min
Weizer[43]	16	57	28	7.2	2.5	185	100	27.5
Hu[44]	227	60	28	NR	2.3	165	75	19
Patel[45]	68	58.9	27.5	NA	2.5	125	97	20.7
Feliciano[46]	8	60	NR	NR	2	202	100	18
Choo[47]	50	54.5	25	6	2.8	120	100	22
Emtage[48]	18	59	31	8	2.5	225	172	30
Tanaka[49]	10	60.5	23.2	6.9	2.2	193	13.5	24.7
Hughes-Hallett[50]	44	63.3	NR	5.5	2.8	148.5	88	22.1

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warm ischemia for tumor removal.

Berg et al[62] proposed the first-assistant sparing technique, which is a method that uses intracorporeal preparation (ICP) for tumor excision and renorrhaphy. Many surgeons use this method, and it involves the pre-placement of all necessary sutures and bulldog clamps as well as a "sliding clip" method for repair of the renal defect.[62] Specifically, sutures are secured to the abdominal wall for easy access following tumor extirpation and bulldog clamps are pre-placed near the hilum. In their study, a cohort of study patients undergoing ICP-RAPN was compared with study patients assigned to consecutive standard RAPN.[62] Their results revealed reduced WITs and operative times for those undergoing ICP-RAPN.[62]

Although minimizing WIT is a desired goal, achieving cold ischemia similar to an open approach to partial nephrectomy has also been described. Rogers et al[63] reported their early experience with intracorporeal renal parenchymal cooling and the tumor extraction technique for RAPN in 7 cases. Both transperitoneal and retroperitoneal approaches for RAPN were utilized, and the researchers showed that the intracorporeal perinephric instillation of iced saline flushes resulted in significant renal cooling without lowering core body temperature above 0.5 °C.[63] Mean cold ischemia time was acceptable at 19.6 minutes and, despite no comparison of preoperative and postoperative glomerular filtration rate, this technique could hypothetically facilitate the preservation of renal function.[63] Additional prospective data with this technique are desired, but it is a reasonable option in complex cases in which more delicate work or longer clamp time is anticipated for tumor excision.

The safe duration of renal ischemia is debatable, but any reduction in ischemia is likely to yield positive results. Thus, efforts have been made to completely avoid renal ischemia for select RAPN cases. White et al[64] published one of the first series of RAPN performed without hilar clamping. The results were promising among the 8 participants studied, so the authors concluded that off-clamp partial nephrectomy was a

Table 3. — Select Perioperative Indices of Patients Undergoing Robotic-Assisted Retroperitoneal Partial Nephrectomy (cont)

Study	Conversion Rate, %	Transfusion Rate, %	Positive Margin Rate, %	Malignant Tumors, %	LOS, d	Overall Complication Rate, %	Postop Change in Renal Function, %	Early Recurrence Rate, %
Weizer[43]	12.5	0	0	94	2	37.5	Rise in Cr by 0.1 mg/dL	NR
Hu[44]	0.4	1.1	3.5	80.2	2	12.3	+1.7	0.9 at 32 mo
Patel[45]	1.5	2.9	4.4	75	2.3	7.3	N/A	NR
Feliciano[46]	NR	NR	0	87.5	2	0	NR	NR
Choo[47]	2	6	0	94	2.5	14	–11.4	NR
Emtage[48]	0	0	5	61	2.6	0	–6	NR
Tanaka[49]	10	NR	10	70	NR	10	–15.2	NR
Hughes-Hallett[50]	2.3	4.5	6.8	63	2.5	9.1	+6.8	NR

BMI = body mass index, Cr = creatinine, EBL = estimated blood loss, LOS = length of stay, NA = not applicable, NR = not reported, WIT = warm ischemic time.

feasible option for the management of small superficial tumors.

Since then, several larger series have been published describing the successes of off-clamp partial nephrectomies with tumors of increasing complexity.[65-67] One multi-institutional study evaluated the outcomes of off-clamp RAPN performed at 5 high-volume centers.[68] When the off-clamp RAPN cases were matched and compared with RAPN cases with standard hilar clamping, decreased operative time (156 vs 185 minutes), decreased decline in renal function (2% vs –6%), and increased rate of EBL (228 vs 158 cc) were seen with off-clamp RAPN.[68]

However, some theoretical concerns are associated with this technique. The rate of EBL is significantly higher than what would be expected for similar tumors managed with hilar clamping. In addition, increased bleeding in the renal parenchymal bed could lead to imprecise tumor excision, thus resulting in incomplete tumor resection or inappropriate removal or compromised perfusion of normal parenchyma. Although these concerns have not materialized in recent studies, they must be addressed through the further evaluation of larger study patient cohorts.[68] Currently, off-clamp RAPN is an evolving technique and, given more time, it may be an option that might be safely applied to properly selected patients with renal tumors.

Despite its increasing acceptance in urology, the robotic platform lacks haptic feedback.[69] Tactile sensation as provided by standard open — and even laparoscopic — surgery allows for more precise and delicate dissection. Furthermore, the lack of force recognition can negatively impact patient safety, and this is particularly true during dissection or the manipulation of tenuous anatomical structures.[69] Although haptic feedback has not yet been developed, augmented reality is a technological advance being used to assist with making robotic-assisted renal surgery more user friendly.[70] One systematic literature review examined the utility of augmented-reality techniques in

partial nephrectomy. Augmented reality involves the real-time superimposition of preoperative, cross-sectional images on 3-dimensional stereoscopic views of an organ during surgery. The goal is to allow for the early identification of important anatomical landmarks, thus aiding in complete tumor excision with negative margins while also minimizing loss of normal renal parenchyma.[70] Early studies using a variety of in vivo and ex vivo augmented-reality techniques are promising, but none has adequately superimposed preoperative images on tissue with positional changes during surgical dissection.[71,72] This is a significant factor that limits the applicability of the augmented-reality techniques, but intraoperative image guidance could address this issue in the future. Thus, augmented reality could be a promising adjunct to robotic assistance during renal surgery, but further refinement and clinical research are needed to assess its true applicability.

In addition to technical innovations, the field of robotic-assisted renal surgery has seen advancements in terms of its application to highly complex cases, including the management of RCC and associated inferior vena cava tumor thrombus. However, such patients must be highly selected due to tumor biology and the nature of the tumor thrombi. Nevertheless, small surgical series of study patients with low level 1 and 2 tumor thrombi have been described with acceptable perioperative and oncological outcomes.[73]

Conclusions

Robotic assistance has transformed surgical care for many different patients with various disease states. Compared with the open approach, robotic-assisted surgery has been shown to improve rates of morbidity and patient satisfaction in patients with renal cell carcinoma and does so without compromising oncological control — this is particularly true for nephron-sparing surgery.

The advantages of robotic-assisted partial nephrectomy compared with laparoscopic partial nephrectomy are well documented, and robotic technology allows for the more widespread adoption of minimally invasive techniques for many patients. Today, robotic-assisted partial nephrectomy is the method of choice for nephron-sparing surgery, when applicable, using either the transperitoneal or retroperitoneal approach. Although robotic-assisted radical nephrectomy is feasible, few real benefits exist to using robotic assistance in this setting, partly because of the ease and decreased cost associated with laparoscopic radical nephrectomy.

Many technical and technological advances to make robotic-assisted partial nephrectomy safer and more effective are on the horizon, but additional experience and scrutiny are necessary to gain widespread adoption. Although selected patients with locally advanced renal cell carcinoma, including inferior vena cava thrombectomy, have undergone robotic-assisted surgery, caution must still be exercised in these more complex clinical scenarios.

Despite the financial concerns associated with the robotic-assisted platform, when compared with open surgery, increased up-front medical costs might be mitigated through reduced rates of perioperative morbidity as well as the subsequent positive impact on societal costs and other factors. Such an area of focus requires added attention in the current era of value-based care.

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Sofía Cáceres Nazario. *Mallard Ducklings*, 2015 (Detail). Acrylic on canvas, 12" × 16".

The use of RARC has not been widely adopted due to lack of superiority over ORC.

Robotic-Assisted Radical Cystectomy

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Background: *The application and use of robotics during radical cystectomy for the treatment of bladder cancer are still being defined.*

Methods: *A systematic literature search was conducted, with an emphasis on studies published within the previous 5 years. Areas of interest included patient selection, outcomes, cost, and comparisons of robotic-assisted radical cystectomy to open surgery.*

Results: *Although data are lacking in this field, using robotic assistance for radical cystectomy may lead to improvements in estimated blood loss, time to bowel activity, and reduced hospital stay; however, these improvements come at the cost of increased operative time and have a learning curve.*

Conclusions: *The widespread adoption of robotic-assisted radical cystectomy has not gained acceptance due to lack of evidence and clinical trials showing superiority over open surgery.*

Introduction

The standard of care for muscle invasive or bacillus Calmette–Guérin high-grade, refractory bladder cancer is open radical cystectomy (ORC) with pelvic lymph node (LN) dissection and urinary reconstruction. ORC is associated with considerable rates of perioperative morbidity and mortality. During the past several years, the benefits of robotic assistance during minimally invasive surgery have been demonstrated for a variety of surgical techniques in urology.[1] Given the morbidity of ORC, the natural evolution of surgical practice was to attempt to incorporate robotic assistance. Robotic-assisted radical cystectomy (RARC) was first described by Menon et al[2] and has since been reported in multiple academic and large-volume centers.[3]

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The values of decreased surgical blood loss, lower incidence of ileus, quicker return to activities of daily living, and the decreased use of narcotics for pain management following surgery have fueled the arguments in favor of RARC.[4] Appropriate patient selection and understanding the learning curve, costs, and perioperative and oncological outcomes are all debated topics, and such concerns have mainly been addressed by utilizing retrospective experience, thus limiting high-quality evidence.

Methods

We performed a systematic search of the medical literature using the keywords "cystectomy," "robotics," "robotic cystectomy," and "lymph node dissection." We found that a single randomized controlled trial (RCT) had been published comparing ORC and RARC.[5] However, a thorough assessment of the details of that study is limited by lack of available published data. Aside from that study, level 1/2 evidence is lacking to evaluate the efficacy and utility of RARC. Hence, most of the studies selected were contemporary retrospective reviews.

Emphasis was placed on studies published with-

in the previous 5 years. Reports were reviewed and selected based on their scientific merit. Upon review of the initially selected manuscripts, frequently cited studies were also included.

Patient Selection

The studies that directly compare ORC with RARC are listed in Table 1.[4,6-15] Traditionally, RARC is reserved for healthy patients with minimal prior pelvic or abdominal surgeries who can tolerate pneumoperitoneum; for experienced surgeons, RARC can be performed in more complex cases. Comparative studies have demonstrated that RARC can be offered to patients presenting with locally advanced disease, a higher body mass index (BMI), or an increased American Society of Anesthesiologists (ASA) score. Among those studies that incorporated RARC, the median age of participants was between 65.5 and 70 years of age, median BMI was between 26.5 and 27.6 kg/m^2, and 14% to 78% of patients had ASA scores of 3 or higher.[6,7]

Butt et al[8] examined the effect of obesity on perioperative outcomes for robotic cystectomy. In their cohort, 71% of patients were either overweight or obese; their mean BMI was 28.0 kg/m^2. No differences were seen in the rate of estimated blood loss (EBL), complications, or operative time between those with a normal BMI and those who were overweight or obese. However, those who were obese and had pT3 to pT4 disease had an increased rate of positive margins.[8] Even though the largest cohort consisted of 227 patients, an equal distribution of patients with locally advanced bladder cancer and multiple comorbidities was represented.[8]

The preoperative routine for patients undergoing RARC should be similar to ORC. Standard contraindications apply to all patients, including uncorrected coagulopathy, severe ascites, or advanced disease. Careful consideration should be given to those patients with significant pulmonary disease, which may preclude them from tolerating a steep Trendelenburg position or prolonged pneumoperitoneum.

Perioperative Considerations

Bowel preparation similar to what is employed for ORC can be performed for RARC and is typically based on surgeon preference. Mechanical bowel preparation is usually omitted for patients undergoing an ileal conduit but can be given (eg, 1–2 bottles of magnesium citrate) prior to undergoing a continent diversion. A fleet enema should be administered for all patients regardless of urinary diversion performed should rectal injury occur.[16,17]

With the exception of urinary reconstruction,

Table 1. — Patient Demographics

Study	No. of Patients	Median Age, y	Median BMI, kg/m^2	Male/ Female, %	Clinical Stage, %	ASA Score, %
Smith[4]	227	67	27.5	78/22	≤ cT1: 31 cT2: 60 cT3–cT4: 9	3 (median)
Stegemann[12]	91	69	—	75/25	pT1: 34 pT2: 20 pT3–pT4: 46	1: 1 2: 51 3: 47 4: 1
Parekh[10]	20/20	69.5/64.5	27.6/28.3	90/10 to 80/20	≤ pT1: 35/60 pT2: 15/5 pT3: 15/10 pT4: 35/25	3/3 (median)
Khan[6]	14	65.6 (mean)	—	—	—	1: 21 2: 64 3: 14
Kader[7]	100/100	67/67	26.5/27.1	72/28 to 72/28	≤ pT2: 8/53 pT3–pT4: 30/24	1: 0/0 2: 23/27 3: 74/66 4: 4/7
Al-Daghmin[13]	272	70	28.9	75/25	—	≥ 3: 47
Nix[9]	21/20	67.4/69.2 (mean)	27.5/28.4	67/33 to 85/15	≤ cT1: 6/5 cT2: 12/14 cT3: 14/14	2.71/2.70
Pruthi[14]	100	65.5 (mean)	27.3 (mean)	73/27	≤ cT1: 30 cT2: 65 cT3–pT4: 5	2.7 (mean)
Butt[8]	49	67	28.0 (mean)	76/25	≤ pT2: 43 pT3: 37 pT4: 20	2.3
Hayn[15]	156	69	28	80/20	< pT2: 30 pT2: 19 pT3: 37 pT4: 14	≥ 3: 41
Styn[11]	50/100	66.6/65.6 (mean)	29.8/29.6 (mean)	—	—	1–2: 46/43 3–4: 54/57

ASA = American Society of Anesthesiologists, BMI = body mass index.

RARC has increased operating time compared with ORC. In their RCT, Bochner et al[5] reported mean operative times of 456 minutes for RARC and 329 minutes for ORC ($P < .001$). A recent retrospective study found similar results.[18] In a head-to-head comparison of 41 cystectomies (20 ORC and 21 RARC), Nix et al[9] found that operating times increased from 204 to 252 minutes (median). Similar operative times were also found by Kader et al[7] for a cohort of 200 patients (451 compared with 393 minutes for RARC and ORC, respectively).

All studies included in this review found a statistically significant benefit of decreased operative blood loss in favor of RARC. This is due to several reasons: (1) the increased/magnified, 3-dimensional visualization that the robot provides in identifying anatomical landmarks, structures, and vessels (including ligation of the dorsal venous complex), and (2) the ability to operate while under pneumoperitoneum. The rate of EBL ranged (median or mean) from 475 to 1351 cc for ORC and 200 to 423 cc for RARC.[7,9-11,19] Although the rate of EBL is subject to reporter variability and a learning curve is associated with RARC, improvements seen with decreased rates of EBL were substantial.

Nix et al[9] demonstrated an improvement in the required use of narcotics during patients' hospital stay to manage pain among those undergoing RARC compared with ORC. The in-hospital pain regimen, which was measured by morphine sulfate equivalents, decreased from 151.6 mg (mean) to 93.6 mg for those undergoing RARC.[9] This finding was further substantiated by Guru et al.[20] Although their cohort was small (N = 33; n = 17 ORC, n = 16 RARC), Guru et al[20] saw a decrease in morphine sulfate equivalents for each postoperative day in favor of RARC; however, the average daily pain scores reported by the patients were similar for both approaches.

Similarities and differences with regard to length of hospital stay, complications, and pathological outcomes are highlighted in Table 2.[4,6-11,13-15,21] The results from 1 RCT demonstrated no differences in hospital stays or 90-day complication rates between the 2 surgical modalities.[18] The mean hospital stay for ORC and RARC was 8 days.[18] However, the study had limitations. It consisted of a single center experience (Memorial Sloan Kettering Cancer Center, New York), open urinary reconstructions, no surgeon crossover, and patients undergoing robotic-assisted LN dissections to the aortic bifurcation and inferior mesentery artery more frequently than open surgery.[18] By contrast,

Table 2. — Perioperative Outcomes

Study	EBL (median), cc	OR Time (median), min	Time to Flatus, d	Time to Bowel Movement, d	Hospital Stay, d	Morphine for Pain Management, mg	Complications, Clavien–Dindo Grade, %	No. of LNs Removed	Positive Margins (Soft Tissue), %
Smith[4]	256	327	—	—	5.5	—	—	—	0.02
Parekh[10]	400/800[a]	300/285.5	—	Days to diet	6/6	—	≥ 2: 25/25	11/23	5/5
Khan[6]	317 (mean)	384 (mean)	—	—	12.6 (mean)	—	28.6	—	—
Kader[7]	423/986[a]	451/393[a]	—	—	—	—	Total: 35 (RARC) 57 (ORC)[a] Major: 10 (RARC) 22 (ORC)[a]	17.7/15.7 (mean)	12/11
Al-Daghmin[13]	400	369	—	—	11 (mean)	—	1–2: 58 3–5: 19	23	7
Nix[9]	200/600[a]	252/204[a]	2/3[a]	3/4[a]	4/6	87.5/121.5[a]	2 (RARC)/ 2 (ORC)	19/18 (mean)	0
Pruthi[14]	250	258	2.1 (mean)	2.8 (mean)	4.9 (mean)	—	≥ 3: 8	19 (mean)	0
Butt[8]	546	366	—	—	9.4	—	27	17	12
Hayn[15]	400	378	—	—	8	—	65	—	—
Styn[11]	350/475[a]	454.9/ 349.1[a]	—	—	9.5/10.2	—	1–2: 72/79 3–5: 28/21	14.3/15.2 (mean)	2/1
Hayn[21]	496	365	—	—	8	—	—	17	7

[a]Statistically significant.

EBL = estimated blood loss, LN = lymph node, OR = operating room, ORC = open radical cystectomy, RARC = robotic-assisted laparoscopic radical cystectomy.

data from the US Nationwide Inpatient Sample demonstrated a cumulative decrease in overall complications (49.1% for RARC and 63.8% for ORC; $P = .035$); however, differences in a particular type of complication could not be distinguished.[3] This study did cite several limitations, including the unavailability of certain patient characteristics (eg, BMI) and the inability to identify which patients received prior radiation, to distinguish readmissions, late complications, and to identify the different degree and severity of complications.[3] In an evaluation of elderly persons 75 years of age and older, Richards et al[22] retrospectively examined the data of 40 patients (20 ORC and 20 RARC) to determine perioperative outcomes. No differences were seen in patient BMI, ASA score, or number of prior abdominal surgeries between ORC and RARC.[22] Significant differences were seen in length of hospital stay (7 for RARC and 14.5 days for ORC) and Clavien–Dindo complications of grade 3 or higher (10% for RARC and 35% for ORC).[22]

Oncological Outcomes

As seen in Table 2, positive margin rates ranged from 0% to 12% and were not significantly different.[4,6-11,13-15,21] One can reasonably suspect that selection bias played a role in the margin status. It is possible that patients who received prior pelvic radiation (for prostate or bladder cancer) or those with locally advanced bladder cancer were ineligible to undergo robotic-assisted cystectomy (by surgeon preference) and, hence, may have falsely lowered the positive margin rates. Nonetheless, if key principles of the operation are followed, with meticulous dissection, positive margin rates will be optimized regardless of surgical approach.

To evaluate long-term survival rates in patients undergoing RARC, Khan et al[6] evaluated 14 patients with follow-up times of 5 years or more. Overall survival, disease-specific, and disease-free survival rates were reported to be 64%, 75%, and 50%, respectively.[6] Three of the patients died after developing distant metastasis and another 3 had disease recurrence in 44 to 77 months.[6] However, large, long-term, well-controlled studies are needed to prove that RARC has the oncological equivalency of ORC.[23]

LN dissection measured by LN yield is often considered to be a criterion for the adequacy of a surgical technique. Previous studies have demonstrated that an LN dissection has staging and therapeutic benefit. Davis et al[24] performed open pelvic LN dissection (PLND) after robotically dissecting the pelvic LNs in 11 patients. The dissection consisted of the bilateral obturator, external, and common iliac artery regions without or in combination with the presacral and para-aortic/paracaval zones. The median LN count was 43 for robotic-assisted PLNDs, with an additional 4 (median) LNs for the open dissection. Davis et al[24] concluded that robotic-assisted PLND is adequate. Abaza et al[25] found similar results when using an extended LN dissection. When comparing 120 open to 35 robotic-assisted PLNDs, they found no difference in mean LN yield (robotic, 37.5 ± 13.2; open, 36.9 ± 14.8) or positive node rate (robotic, 34%; open, 30%).[25] In a noninferior RCT comparing PLND between RARC and ORC in 41 study participants, RARC was found to be noninferior to ORC.[9] The average LNs removed were 19 for RARC and 18 for ORC.[9]

Quality of Life

Using the Convalescence and Recovery Evaluation (CARE) to assess the quality of life after RARC, Stegemann et al[12] sought to compare patient outcomes at 90 days compared with baseline (before surgery). CARE is a questionnaire that evaluates patient postoperative recovery in the areas of gastrointestinal, activity, pain, and cognitive-related symptoms following abdominal procedures.[26] The 91 study participants preoperatively and postoperatively evaluated came close to reaching their presurgical baseline levels at 90 days, except for areas related to the gastrointestinal system.[12] The average time it took for patients to reach 90% in the overall CARE difference index (ie, the time it took for patients to return to 90% of their baseline) was 63 days.[12]

Intracorporeal Diversion

One of the more controversial debates in RARC cohorts is urinary reconstruction. Intracorporeal urinary reconstruction can be the most technically challenging portion of the operation and can represent a barrier to adoption of the surgical technique.[27] Jonsson et al[28] reported on perioperative outcomes in a nonrandomized trial of 45 study participants (36 receiving an intracorporeal neobladder and 9 receiving an intracorporeal ileal conduit). Median operative times were 480 minutes for the neobladder (range, 330–760 minutes) and 460 minutes for an ileal conduit (range, 325–561 minutes).[28] The rates of EBL were 625 and 350 cc for those undergoing a neobladder and ileal conduit, respectively.[28] A total of 40% of patients had early complications (≤ 30 days) and 33% presented with late complications (> 30 days).[28] When comparing the first 18 neobladders to the second 18 neobladders, the median operative time decreased from 517 to 417 minutes.[28] The same decline was seen with early and late complications (50% to 28% and 50% to 17%, respectively).[28]

In a similar fashion, Canda et al[29] showed the feasibility of performing an intracorporeal neobladder and an ileal conduit in their first 27 cases. They

reported an average operative time of 9.9 hours (range, 7.1–12.4 hours). Of the 27 study patients, 4 experienced early (≤ 30 days) major (Clavien–Dindo grade ≥ 3) complications and 3 experienced late (> 30 days) major complications.[29] However, it is difficult to make any conclusions about long-term functional outcomes when the longest follow-up was only 12 months.[29]

Cost Analysis

Although challenging, the extrapolation of costs for adopting RARC is an important point to consider. One report concluded that the application of the robot increased direct costs for radical cystectomy by $1,600.[1] Comparing 1,444 cases of ORC to 224 cases of RARC, Yu et al[3] calculated an additional $3,797 for RARC (inpatient cost). Proponents of RARC argue that this cost is equivalent when accounting for the improved benefits in hospital course, complications, and patient quality of life.[30] In the study by Yu et al,[3] compared with ORC, patients who underwent RARC had decreased rates of inpatient complications (49.1% vs 63.8%), decreased use of parenteral nutrition (6.4% vs 13.3%), and fewer deaths (2.4% vs 0%). No difference was seen in length of hospital stay.[3]

Learning Curve

Determining the number of cases needed to become proficient with robotic-assisted cystectomy is difficult. Knowledge of pelvic anatomy and the principles of ORC are mandatory prerequisites. However, when the rate of EBL, the positive margin rate, and the number of LNs removed are used as variables to define the quality of RARC, the International Robotic Cystectomy Consortium deemed 30 cases to be the "acceptable level of proficiency" in performing RARC.[21]

Richards et al[31] evaluated the learning curve for RARC by using patient outcomes. The first 60 cases by junior faculty, under mentorship from an experienced surgeon, were retrospectively reviewed and subdivided by tertiles. Between tertiles, no statistical difference was seen with regard to total operating room time, rate of EBL, hospital stay, or soft-tissue positive margins (5%–20%).[31] However, the amount of total complications was increased (early [< 90 days] and late [> 90 days]) in the first 20 cases (70%) compared with the last 20 cases (30%).[31]

In a similar study with a single surgeon, Hayn et al[32] examined the outcomes of 164 consecutive study patients undergoing RARC. The decision to incorporate this new technique came after completing 100 prior robotic-assisted retropubic prostatectomies. To evaluate rates of improvement, cases were classified as 50 or less, 51 to 100, or more than 100.[32] No statistical differences were noted between incidence of complications, rate of positive surgical margins, or rate of EBL. A difference in operating time was seen, with operating time for cystectomy decreasing from 180 minutes to 136 minutes (mean time), and for LNs removed (from 16 to 24 [median]) between the first 50 cases compared with cases 101 to 164.[32]

Conclusions

Although it is a relatively new technique, robotic-assisted radical cystectomy (RARC) with or without intracorporeal urinary diversion in select patients may be beneficial. However, 1 randomized controlled trial demonstrated no difference in perioperative complications or hospital stay between the 2 surgical modalities. Long-term, well-designed studies examining functional and oncological outcomes are greatly anticipated and needed if RARC is to replace open radical cystectomy (ORC) as the standard of care. Results of a multi-institutional, randomized, noninferior trial of open cystectomy compared with robotic-assisted cystectomy are anticipated (NCT01157676). As of publication, 350 participants have enrolled in the study. The study researchers will examine cancer outcomes (2-year, progression-free survival rates), surgical complications, and quality-of-life issues between ORC and RARC. Accrual has been completed and the study results are expected in 2017.[33]

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Sofía Cáceres Nazario. *Red Dahlia*, 2015 (Detail). Acrylic on canvas, 16" × 12".

The use of robotic-assisted surgery is rapidly expanding into the field of gynecological oncology.

Robotic-Assisted Surgery in Gynecological Oncology

Stephen H. Bush, MD, and Sachin M. Apte, MD

Background: *Robotic-assisted surgery is a technological advancement, and its use is rapidly expanding into the field of gynecological oncology. However, a paucity of evidence exists to prove its superiority over standard laparoscopy. Its cost is also high and it lacks haptic feedback.*

Methods*: A systematic review of the relevant literature was undertaken to understand the use of robotic-assisted surgery in gynecological oncology.*

Results*: Robotic-assisted surgery is being used for select cases of endometrial cancer and has resulted in the increased utilization of minimally invasive surgery for such patients. Use of robotic-assisted surgery among patients who are obese has led to decreased complication rates. Robotic-assisted surgery appears to be more expensive than traditional laparoscopy; however, there are potential cost savings to robotic-assisted surgery, including shorter hospital stays and fewer complications, compared with laparotomy.*

Conclusions: *The gynecological oncology community is rapidly accepting the use of robotic-assisted surgery. Although randomized controlled trials are lacking, the technology appears to be safe and effective, and it has equivalent oncological outcomes in this patient population.*

Introduction

Robotic-assisted surgery is a relatively recent advancement in surgical technique. The US military planned to use a robotic system to perform surgery on injured soldiers located far from a medical center.[1] The Automated Endoscopic System for Optimal Positioning Robotic System (Computer Motion, Goleta, California) was one of the first robotic devices to operate a camera during laparoscopic surgery. The next advancement introduced was the ZEUS Robotic Surgical System (Computer Motion), which had robotic arms attached to an operating table. This device introduced the concept of removing the surgeon from the sterile operative field. Subsequently, the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California) was developed and approved in 2000 by the US Food and Drug Administration for general laparoscopic surgery.[2,3]

Since then, the da Vinci Surgical System was rapidly adopted by surgeons across many fields and received initial clearance from the US Food and Drug Administration in 2005 for gynecological conditions.[2] The adoption of this technology led to major changes in the surgical care of women with gynecological malignancies. Prior to the inception of this technology, many women with endometrial carcinoma underwent laparotomy, with relatively few receiving the traditional laparoscopic approach. However, most of these cases are now performed with robotic assistance, representing a rapid transformation in surgical practice.[4] Robotic-assisted surgery has many other benefits over traditional laparoscopy, including enhanced visualization with 3-dimensional stereoscopic vision, improved dexterity, and improved surgeon comfort. These ben-

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efits have allowed more surgeons to offer minimally invasive surgery to patients, as evidenced by the rapid change in practice patterns for the care of patients with endometrial cancer.[4] Despite these advantages, some traditional, "straight stick" expert laparoscopists believe that robotic-assisted surgery offers few, if any, benefits when compared with standard laparoscopy, citing lack of haptic feedback, lack of prospective randomized trials showing benefit, increased cost, and the impact of robotic-assisted surgery on the surgical education of medical residents and fellows.

Endometrial Cancer

In 2015, an estimated 54,870 new US cases of endometrial cancer will be diagnosed and 10,170 women are expected to die from the disease.[5] Most cases of endometrial cancers are classified as type 1, meaning that they are hormonally responsive tumors. The most common risk factor present for this disease in the United States is obesity due to the production of peripheral estrogen following steroid conversion in adipose tissue.[5] A large, open incision in a patient who is obese increases the risk of postoperative complications, such as wound infection and dehiscence, and makes the procedure more difficult. This fact made minimally invasive surgery an attractive alternative to traditional open surgery.

The Gynecologic Oncology Group conducted a large, multicenter, prospective study comparing laparoscopy with laparotomy for the surgical staging of endometrial cancers and confirmed the short-term surgical safety and the feasibility of laparoscopically conducting the procedure.[6] The trial was designed as a noninferiority study and the predetermined hazard ratio of 1.4 was not reached; however, the study was underpowered due to recurrence rates in both arms that were less than the pretrial assumptions.[6] The 5-year overall survival rates were equivalent in both arms at 89.9%.[6] These results could be confounded due to the relatively high (25%) conversion rate to laparotomy in the laparoscopic cohort.[6] Although the trial did not meet its assigned end point to confirm noninferiority, the laparoscopic staging may not have adversely affected survival rates in women with endometrial cancer.[6]

Traditional laparoscopic surgery has not been widely utilized in women with endometrial cancer due to the complexity of the procedure and the extended learning curve. Robotic-assisted surgery for endometrial cancer has become the standard in most centers across the United States. Numerous studies have evaluated robotic-assisted staging for endometrial cancer to laparotomy, the majority of which show that, when compared with open surgery, robotic-assisted surgery is associated with longer operative times, decreased rates of blood loss, decreased transfusion rates, decreased postoperative complications, and decreased length of stay; in addition, when compared with traditional laparoscopy, robotic-assisted surgery appears to decrease rates of blood loss and maintain similar lymph node (LN) counts.[7-10]

Obesity is a risk factor for endometrial cancer, and defining the optimal surgical intervention for patients at high risk is of the upmost importance.[5] Gehrig et al[11] examined 49 women (36 were obese and 13 were morbidly obese) who underwent robotic-assisted surgical staging and compared their outcomes with 32 women (25 were obese and 7 were morbidly obese) surgically staged with traditional laparoscopy. Among the women who were obese and morbidly obese, the authors found that robotic-assisted surgery was associated with shorter operative time ($P = .0004$), decreased blood loss ($P < .0001$), increased LN count ($P = .004$), and decreased length of stay ($P = .0119$).[11]

Bernardini et al[12] compared outcomes of women with stage 1 or 2 endometrial cancer and a body mass index greater than 35 kg/m^2 who were treated at a single institution with either robotic-assisted surgical staging or open surgical staging. The results from 86 women were analyzed; 45 women were assigned to the robotic-assisted cohort and 41 were assigned to the laparotomy cohort.[12] Postoperative complications were significantly higher in the patients who underwent laparotomy compared with robotic-assisted staging (44% vs 17.7%; $P = .007$).[12] Hospital stay was significantly longer in the laparotomy group compared with the robotic-assisted group (4 vs 2 days; $P < .001$).[12] No difference was seen in the rate of pelvic LN dissection, but para-aortic nodal dissection was more common in the robotic-assisted cohort.[12]

In a large study by Paley et al,[13] 377 robotic-assisted staging procedures were compared with 131 open staging procedures. No differences were seen between the groups with regard to age, body mass index, medical comorbidities, or number of prior surgeries. Operative times alone favored the open-staging group, whereas length of stay, nodal counts, and rate of blood loss were all improved in the robotic-assisted cohort; in addition, a significant decrease was seen in complications for the robotic-assisted cohort (26% vs 6.4%; $P < .001$).[13] The most significant reductions were observed in the incidence of wound separation, infectious complications, and ureteral injury or acute renal failure in the robotic-assisted cohort.[13]

Even lacking prospective randomized data to support the use of robotic-assisted staging in endometrial cancer, most of the medical literature supports the method as safe and effective.[6] Robotic-assisted surgery for endometrial cancer staging has been rapidly incorporated into the field of gynecological oncology in both academic and community settings, and the learning curve has been described by many as being faster

for robotic-assisted staging than laparoscopic staging.[14] Compared with both laparotomy and laparoscopy, robotic-assisted surgery is advantageous in patients who are obese when examining rates of blood loss, transfusions, length of stay, wound complications, and conversions to laparotomy.[11,15]

Robotic-assisted staging for endometrial cancer is an accepted surgical practice, appears to be safe and effective, and offers many advantages over laparotomy. Although its advantages over traditional laparoscopy are debatable, robotic-assisted surgery has allowed more women to have access to minimally invasive surgery for endometrial cancer.[16]

Cervical Cancer

Although safe and effective screening for cervical cancer has been available in the United States for decades, a significant number of new cases are diagnosed each year; for example, in 2015, an estimated 12,900 women will be diagnosed with cervical cancer and 4,100 will die of the disease in the United States.[5] Cervical cancer is the second leading cause of cancer death in women 20 to 39 years of age.[17] Early-stage disease is typically treated with radical hysterectomy, which has significant morbidity (eg, significant blood loss, bladder atony, lymphedema, pain, sexual dysfunction). As such, attempting to limit morbidity with a minimally invasive approach was a logical progression. Traditional laparoscopy has not been widely accepted for this procedure due to its complexity and extended learning curve.

Robotic-assisted radical hysterectomy was first reported in 2006 by Sert et al.[18] Since their initial report, subsequent publications have sought to refine the procedure and describe the safety and effectiveness associated with this approach. One case-control series compared robotic-assisted surgery with laparoscopic radical hysterectomy and bilateral pelvic lymphadenectomy and reported decreased rates of blood loss (71 vs 160 mL) and length of stay (4 vs 8 days) in the robotic-assisted group ($P < .05$), although they did not observe any differences in LN count, parametrial tissue size, or operative times.[19] Kim et al[20] confirmed the safety and feasibility of a robotic approach in a series of 10 patients with early-stage cervical cancer who had no conversions, ureteral injuries, or fistulas. They reported a mean rate of blood loss of 355 mL, an average of 28 LNs, and a median operative time of 207 minutes.[20]

Many publications have investigated the outcomes of robotic-assisted radical hysterectomy compared with traditional laparotomy. Boggess et al[7] compared 51 robotic-assisted radical hysterectomy cases with 49 open radical hysterectomy cases and reported significant improvements in rates of blood loss, operative time, and nodal counts in favor of the robotic-assisted cohort. In 2008, Magrina et al[21] compared all 3 modalities. Their mean operative times for women in the robotic-assisted, laparoscopic, and open cohorts were 190, 220, and 167 minutes, respectively; the mean rates of blood loss were 133, 208, and 443 mL, respectively; and the mean rates of length of stay were 1.7, 2.4, and 3.6 days, respectively.[21] In 2011, Soliman et al[22] also reviewed all 3 modalities. They reviewed the findings from 95 radical hysterectomies and found that minimally invasive methods offered significant benefits over the open approach, including decreased rates of blood loss and shorter hospital stays.[22] Open radical hysterectomy had shorter operative times, and the robotic approach had a shorter length of stay than traditional laparoscopy.[22]

However, all of these studies are retrospective in nature and do not describe oncological outcomes. No prospective randomized trials have addressed this issue. However, Cantrell et al[23] published a single institution, 3-year outcome report of 71 study patients undergoing robotic-assisted radical hysterectomy. They reported a progression-free survival rate of 94% and overall survival at 36 months with a median follow-up period of 12.2 months.[23] Compared with historical controls, no significant difference was seen in either of these survival rates.[23] Based on the information available in the literature, no evidence suggests that minimally invasive radical hysterectomy in general or robotic-assisted radical hysterectomy specifically is oncologically inferior to traditional open radical hysterectomy; however, no level 1 evidence suggests that the approaches are equivalent.

Given that cervical cancer is often diagnosed in women in their reproductive years,[5] fertility-sparing surgery is of great importance to these patients. This is another area in which robotic-assisted surgery is gaining traction. Radical trachelectomy, in which the cervix and parametrial tissues are removed and the uterus is left intact, is an accepted procedure for carefully selected, early stage 1 cervical cancer in women desiring to preserve their fertility. Traditional laparoscopic radical trachelectomies are rarely performed, and only select, high-volume laparoscopic centers offer them due to the complexity of the procedure and the limitations of rigid instrumentation. Nick et al[24] reported on a large series of 37 study patients undergoing radical trachelectomy. Of those, 25 underwent open trachelectomy and 12 patients underwent robotic-assisted radical trachelectomy; 1 study patient assigned to the open approach and 4 assigned to the robotic approach were converted to radical hysterectomy due to close margins.[24] The robotic-assisted cohort had a decreased rate of blood loss (62 vs 300 mL) and a shorter hospital stay (1 vs 4 days) than the open cohort, although no differences were seen in operative time or histopathological outcomes between the groups.[24]

Patients with locally advanced cervical cancer (stages 2A–4A) are at high risk for LN metastasis,

and some concern exists regarding the accuracy of positron emission tomography/computed tomography for detecting para-aortic LNs in this setting.[25] In some centers, surgically staging the para-aortic nodes is common practice in these patients, who are typically treated with concurrent chemotherapy and radiation rather than radical hysterectomy. An accurate assessment of LN status is necessary to provide optimum care for these patients. Transperitoneal lymphadenectomy is technically challenging and, when it is followed by radiation, can be associated with adverse events (eg, intestinal obstruction). Performing para-aortic lymphadenectomy using an extraperitoneal approach can avoid many of the complications associated with the transperitoneal approach, and this technique has been described using both the traditional laparoscopic and robotic approaches.[26,27] The robotic approach was first described by Vergote et al,[28] who concluded that the robotic approach was easier than traditional laparoscopy. Lambaudie et al[29] reported on a series of 39 study patients with locally advanced cervical cancer who underwent robotic-assisted para-aortic lymphadenectomy (15 underwent the extraperitoneal approach and 24 underwent the transperitoneal approach). They noted similar operative times, rates of blood loss, nodal counts, and lengths of hospital stay, but they did comment on the challenges from the limited space available that resulted in instrument collisions.[29]

For central pelvic recurrences of cervical cancer following radiation therapy, the traditional treatment offered has been pelvic exenteration in which the pelvic organs (uterus, cervix, parametria, bladder, vagina, and rectum) are removed in a highly morbid procedure. There have been reports of robotic assistance during this surgical procedure whose results suggest that the incisions used are smaller and most have also incorporated minilaparotomy.[30-33] However, these are early reports and more information is needed regarding the oncological and perioperative outcomes before the robotic approach to pelvic exenteration can be recommended.

Ovarian Cancer

Approximately 5% of cancer-related deaths among US women are due to ovarian cancer, and an estimated 21,290 new cases of ovarian cancer and 14,180 related deaths will occur in the United States this year.[5] The current standard of care for ovarian cancer in the United States is cytoreductive surgery. When ovarian cancer is debulked to microscopic residual disease, survival rates improve. Chemotherapy can either be preoperatively (neoadjuvant) or postoperatively (adjuvant) given. With the rapid growth of minimally invasive surgery — in particular, robotic-assisted surgery — interest has been growing about using the technology to benefit women with ovarian cancer. Comprehensive surgical staging in ovarian cancer requires exploration of the entire peritoneal cavity, from the diaphragm to the pelvic floor. For it to be useful, a robotic surgical system must address its limited range of motion, which requires undocking and rotation of the patient; however, such a limitation may be overcome by the fourth-generation da Vinci Xi Surgical System (Intuitive Surgical) because it eliminates the need to undock and rotate patients, thus making multiquadrant surgery easier to perform. This robotic platform also allows the camera to be attached to any arm, has a lower profile, and increases docking flexibility. However, at the time of publication, the use of robotic-assisted surgery for upfront debulking surgery in women with advanced ovarian cancer is not yet recommended.[34]

Borderline ovarian tumors are a subset of epithelial ovarian cancer with a good prognosis, although surgical staging of these tumors is still recommended due to the risk of underdiagnosis on frozen section.[35] Fauvet et al[36] compared traditional laparoscopy with surgical staging in conjunction with laparotomy for women with ovarian borderline tumors. Women in the laparoscopy group had lower rates of complete surgical staging; however, no significant difference in the recurrence rates between the laparoscopy and laparotomy groups were identified (12.1% vs 9.1%).[36] Their reported conversion rate of 28% in the laparoscopy group confirms the importance of appropriate patient selection when considering a minimally invasive approach.[36]

Early-stage ovarian cancer represents another group of patients who might benefit from robotic-assisted surgery. Tozzi and Schneider[37] reported on 24 study patients with stage 1A or 1B ovarian cancer who underwent laparoscopic staging. They showed excellent progression-free and overall survival rates of 92% and 100%, respectively.[37] The Gynecologic Oncology Group explored completion staging with laparoscopy for women with incompletely staged ovarian, fallopian tube, or primary peritoneal carcinoma.[38] Women who underwent laparoscopy had lower rates of blood loss and shorter length of hospital says than women who underwent laparotomy, whereas operative times and number of LNs removed were equivalent.[38] A 23% conversion rate was reported, thus further stressing the importance of appropriate patient selection. No follow-up survival data were provided.[38]

Magrina et al[39] reported a case-control study of 25 study patients with epithelial ovarian cancer who either underwent robotic-assisted surgical treatment or were treated by traditional laparoscopy or laparotomy. Eligibility was not limited to early disease. Patients in the robotic-assisted cohort had increased operative time, but decreased blood loss and shortened length of stay.[39] The authors concluded that laparoscopy or robotic-assisted surgery is preferred for

patients with ovarian cancer who require tumor excision alone and 1 additional major procedure; those needing more than 1 additional major procedure would fare better with laparotomy.[39]

Occasionally, recurrent ovarian cancer is amenable to surgical resection, representing another area for robotic-assisted surgery to potentially benefit patient care. Magrina et al[40] reviewed 52 study patients with recurrent ovarian cancer undergoing secondary cytoreduction by laparoscopy (n = 9), laparotomy (n = 33), or robotic assistance (n = 10) between 2006 and 2010.[40] They found decreased blood loss and decreased length of hospital stay with those assigned to the robotic-assisted procedure and laparoscopy compared with laparotomy.[40] All 3 groups were similar in regard to operating time, complications, complete debulking, and survival rates.[40]

It is important to note that robotic-assisted surgery is unlikely to replace laparotomy for primary debulking surgery in patients with ovarian cancer. For select patients with isolated recurrent disease, robotic-assisted surgery may offer benefit over laparotomy.

Cost

The increasing rate of health care expenditures in the United States is unsustainable and has resulted in significant disruption to the health care industry. As a result of the Affordable Care Act, reimbursement models, such as accountable care organizations, are evolving. Becoming cost conscious about the way in which we deliver care is increasingly important, and a major criticism of robotic-assisted surgery is its increased cost over traditional laparoscopy.[41-44] Many costs unique to robotic-assisted surgery must be taken into account, including the acquisition of the robotic system, specific robotic instruments, special drapes for the robotic arms, and increased training requirements for the entire operating room team. The robot also adds complexity and inefficiency to operating room scheduling. In 2010, Barnett et al[41] compared costs between robotic, laparoscopic, and laparotomy approaches in endometrial cancer. They calculated costs in 2 separate methods, including societal and hospital perspective models. In the societal perspective model, the least costly approach was laparoscopy ($10,128/case), followed by robotic-assisted surgery ($11,467/case) and laparotomy ($12,847/case).[41] Utilizing a hospital perspective model, the least costly approach was laparoscopy ($6,581/case), followed by laparotomy ($7,009/case) and robotic-assisted surgery ($8,770/case).[41] Venkat et al[42] and Bell et al[43] both showed that hospital charges were increased when using robotic assistance compared with traditional laparoscopy; however, hospital costs were not equitable across all of the institutions.

In a cost analysis from Memorial Sloan Kettering Cancer Center (New York), Leitao et al[44] examined direct costs for 436 patients, including 132 planned laparoscopic, 262 planned robotic-assisted, and 42 planned laparotomy cases for patients with newly diagnosed uterine cancer to assess the direct costs of the 3 surgical modalities. When accounting for the capital purchase and maintenance fees, the mean amortized cost was $3,157 more for robotic-assisted procedures than laparoscopic cases ($P < .05$) and $996 less for robotic-assisted procedures than laparotomy cases ($P = .6$).[44] When the capital costs were excluded, the robotic-assisted procedures were $178 more than laparoscopy, but they were $3,966 less for the robotic-assisted procedures than laparotomy ($P = .03$).[44] During the 3-year period of the study, the researchers found a 63% reduction in laparotomy rates, an eightfold increase in the use of robotic-assisted procedures, and a 62% decrease in traditional laparoscopy cases.[44] This shift in case selection resulted in an increased cost of $940 per patient presenting with endometrial cancer.[44] The modeling performed assumed no change in the traditional laparoscopy rates, which would have resulted in a decreased cost of $418 per patient with endometrial cancer.[44] Thus, the authors concluded that the cost of robotics must take into account how the implementation of robotic surgery affects the rate of laparotomy, rather than simply comparing successfully completed robotic-assisted procedures with laparoscopy.[44]

Lau et al[45] reported on the effect of incorporating a robotic-assisted surgical program for women with uterine cancer on patient outcomes and cost. After introducing a robotic-assisted surgical approach, 143 patients who underwent robotic-assisted procedures were compared with 160 patients (133 laparotomy cases, 27 traditional laparoscopy cases) who received treatment prior to the robotic-assisted era.[45] The rate of minimally invasive surgery improved to 98% (from 17%) in 2 years by introducing the robot, complications decreased from 42% to 13%, and mean cost decreased (and included the amortization of the robot).[45] Both a lower complication rate and a shorter length of hospital stay were thought to contribute to this cost savings, even after the authors accounted for the acquisition and maintenance costs of the robot.[45]

Reynisson and Persson[46] analyzed total hospital costs, including initial capital investment, with a depreciation time of 7 years, in a cohort of 180 consecutive cases of robotic-assisted radical hysterectomies with pelvic lymphadenectomy and compared these with a control group of 51 cases of open radical hysterectomies with pelvic lymphadenectomy. The robotic-assisted cohort was chronologically divided into smaller groups of 30 to investigate changes over time as experience was gained.[46] A break-even point was identified after 90 robotic-assisted cases.[46] Over time, the savings was mostly due to improved opera-

tive time (406 minutes for the first 30 robotic-assisted cases vs 288 minutes for the last 30 robotic-assisted cases), decreased length of stay (5.5 days for the first 30 robotic-assisted cases vs 3.5 days for the last 30 robotic-assisted cases), and decreased numbers of robotic instruments used (5 for the first 30 robotic-assisted cases vs 4 for the last 30 robotic-assisted cases).[46] Robotic-assisted radical hysterectomy and pelvic lymphadenectomy can be performed without increasing hospital costs compared with traditional open technique after an initial learning curve.[46]

Comparing robotic-assisted surgery with laparoscopic surgery is likely to show an increased cost associated with the use of robotics, but such an analysis does not capture the entire clinical situation. The robotic-assisted surgery platform increases the use of minimally invasive surgery, and it is likely that many patients undergoing robotic-assisted surgery today would not be offered traditional laparoscopic surgery.[47] As evidenced by the Lau et al[45] study, the robotic surgical system has made a dramatic impact on minimally invasive surgery in a relatively short period of time. The intent of robotic-assisted surgery should not be to replace traditional laparoscopic surgery but rather to allow more surgeons to offer minimally invasive surgery to more patients.[45]

Impact on Training Residents and Fellows

Another criticism of the robotic-assisted surgery platform is that it takes a 2-trainee case (laparoscopic hysterectomy) and turns it into a 1-trainee procedure (robotic-assisted). Other critics suggest that robotic-assisted surgery has been a root cause of the rapid decline in vaginal hysterectomies in training programs.[48] No consensus exists on how many robotic-assisted procedures during a fellowship or residency a trainee must complete to be deemed competent upon graduation. However, some institutions have incorporated skill exercises and protocols for robotic-assisted training.[49-52]

Sandadi et al[52] showed that the learning curve associated with robotic-assisted hysterectomy required a completion of 33 cases by a fellow after an initial experience of 16 cases. They suggest that 50 cases are required during a fellowship to competently perform robotic-assisted hysterectomy.[52] Soliman et al[53] showed that fellows can achieve comparable outcomes to faculty, including time and LN counts, after robotic-assisted surgery is incorporated into a fellowship program. In 2009, Brenot and Goyert[48] showed that, after the introduction of robotic-assisted surgery into a residency program, an immediate and statistically significant decrease was seen in both laparoscopic-assisted vaginal hysterectomies and total abdominal hysterectomies.

Robotic-assisted surgery has had many positive impacts in both benign gynecology and gynecological oncology. The impact on surgical training in residency programs is difficult to measure, but it is likely that residents will finish training with less experience with open and traditional laparoscopy, and the impact of this changing tide is unknown.

Conclusions

Traditional laparoscopic hysterectomies make up a small percentage of all hysterectomies performed in the United States and the rest of the world, even though the technology has been available for nearly 40 years.[54] Robotic-assisted surgery has overcome many of the limitations of traditional laparoscopy and has had a direct and measurable impact on the utilization of minimally invasive approaches.[7,45,55] Patients with endometrial cancer have seen the largest benefit from the introduction of robotic-assisted surgery, because these patients are typically obese and have a high complication rate from laparotomy; in addition, they are not appropriate candidates for traditional laparoscopy due to the limited range of motion and poor visualization related to their body habitus. Thus, robotic technology allows these high-risk patients the ability to have minimally invasive surgery, resulting in quicker recovery times and less morbidity than other traditional methods.

Although concerns about the cost of robotics remain and may potentially deter some hospitals, institutions, or health care professionals from offering this modality, potential exists for cost savings over laparotomy if the robotic surgical system is adequately utilized to make up for its initial cost and maintenance. The robotic surgical systems used in gynecological oncology are not meant to replace laparoscopy but rather to give patients who would otherwise undergo laparotomy the option of a minimally invasive approach. The financial analysis of the impact of robotics in gynecological oncology will vary between hospitals and, thus, needs must be individualized. Many factors must be considered, including all the various services using the robot (eg, urology, thoracic, gastrointestinal, head and neck). A financial analysis must include all the different types of cases that will be performed using robotic assistance, the relative impact on length of hospital stay, payer mix, and volumes. Perhaps avoiding robotic-assisted surgery for simple procedures in thin and healthy patients with no prior history of surgery may help control costs. It may also be possible to optimally develop a robotics program in gynecological oncology that is fiscally responsible, thus offering significant benefit to patients with gynecological malignancy.

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Sofía Cáceres Nazario. *Nubian Goat*, 2015. Acrylic on canvas, 16" × 12".

Robotic-assisted videothoracoscopic pulmonary lobectomy appears to be as safe as conventional videothoracoscopic surgical lobectomy.

Robotic-Assisted Videothoracoscopic Surgery of the Lung

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Background: *Despite initial concerns about the general safety of videothoracoscopic surgery, minimally invasive videothoracoscopic surgical procedures have advantages over traditional open thoracic surgery via thoracotomy. Robotic-assisted minimally invasive surgery has expanded to almost every surgical specialty, including thoracic surgery. Adding a robotic-assisted surgical system to a videothoracoscopic surgical procedure corrects several shortcomings of videothoracoscopic surgical cameras and instruments.*

Methods: *We performed a literature search on robotic-assisted pulmonary resections and compared the published robotic series data with our experience at the H. Lee Moffitt Cancer Center & Research Institute. All perioperative outcomes, such as intraoperative data, postoperative complications, chest tube duration, hospital length of stay (LOS), and in-hospital mortality rates were noted.*

Results: *Our literature search found 23 series from multiple surgical centers. We divided the literature into 2 groups based on the year published (2005–2010 and 2011–2014). Operative times from earlier studies ranged from 150 to 240 minutes compared with 90 to 242 minutes for later studies. Conversion rates (to open lung resection) from the earlier studies ranged from 0% to 19% compared with 0% to 11% in the later studies. Mortality rates for the earlier studies ranged from 0% to 5% compared with 0% to 2% for the later studies. Since 2010, our group has performed more than 600 robotic-assisted thoracic surgical procedures, including more than 200 robotic-assisted pulmonary lobectomies, which we also divided into 2 groups. Our median skin-to-skin operative time improved from 179 minutes for our early group (n = 104) to 172 minutes for our later group (n = 104). The overall conversion rate was 9.6% and the emergent conversion rate (for bleeding) was 5% for our robotic-assisted lobectomies. The most common postoperative complications in our cohort were prolonged air leak (> 7 days; 16.8%) and atrial fibrillation (12%). Hospital LOS for the early series ranged from 3 to 11 days compared with 2 to 6 days for the later series. Median hospital LOS decreased from 6 to 4 days. Our mortality rate was 1.4%; 3 in-hospital deaths occurred in the early 40 cases. Mediastinal lymph node (LN) dissection and detection of occult mediastinal LN metastases were improved during robotic-assisted lobectomy for non–small-cell lung cancer, as demonstrated by an overall 30% upstaging rate, including a 19% nodal upstaging rate, in our cohort.*

Conclusions: *Robotic-assisted videothoracoscopic pulmonary lobectomy appears to be as safe as conventional videothoracoscopic surgical lobectomy, which has decreased perioperative complications and a shorter hospital LOS than open lobectomy. Both mediastinal LN dissection and the early detection of occult mediastinal LN metastatic disease were improved by robotic-assisted videothoracoscopic surgical compared with conventional videothoracoscopic surgical or open thoracotomy.*

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Surgery for Primary and Secondary Lung Malignancies

With more than 221,000 new cases of lung cancer estimated for 2015 in the United States, lung cancer is the second most diagnosed cancer, behind only prostate and breast cancers in men and women, respectively.[1] However, with approximately 158,000 deaths from primary lung cancer in the United States estimated to occur in 2015, primary lung cancer remains the leading cause of cancer-related deaths in the United States, causing 28% and 26% of all cancer deaths in men and women, respectively, and causing more deaths than breast, prostate, and colorectal cancers combined.[1] One reason for this high mortality rate for lung cancer is that the 5-year overall survival (OS) rate for lung cancer is 17% (32% at the H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida) compared with 85% for breast cancer (88% at Moffitt Cancer Center).[1] This low OS rate for lung cancer is among the worst survival rates for any cancer, including pancreatic cancer (7.2%), mesothelioma (9.0%), liver cancer (17.4%), and esophageal cancer (17.9%).[2] Another reason for low survival rates is that most primary lung cancers (> 75%) are stage 3 or 4 at initial diagnosis.[3] The Surveillance, Epidemiology, and End Results Program of the National Cancer Institute established that all patients with lung cancer initially diagnosed with localized disease have a 5-year relative survival rate of 54%, and those initially diagnosed with regional disease or those initially diagnosed as stage 4 have 5-year relative survival rates of 27% and 4%, respectively.[2]

In 2010, the financial cost of caring for patients with lung cancer was $12.1 billion; if the 2,373,200 person-years of life lost in 2009 are added to that number, then the indirect cost was $36.1 billion.[4,5] Thus, the societal burden has prompted the need and importance of medical advancements in the prevention, screening, and treatment of lung cancer.[6]

Tobacco smoking accounts for the majority of deaths caused by lung cancer and contributes to at least 30% of all cancer deaths, which makes tobacco smoking prevention and cessation programs an integral part of any lung cancer management program.[1] Those with a relatively greater tobacco smoking history (≥ 30 pack-years), those with advanced age (55–74 years), and those who either currently smoke or recently quit (≤ 15 years) are at high risk for developing lung cancer.[6]

For this high-risk group, lung cancer screening with low-dose computed tomography (CT) of the chest has shown a 20% reduction in lung cancer mortality as well as a 6.7% reduction in deaths from any causes.[6] Results from low-dose CT screening for lung cancer revealed 8-mm solid or 10-mm ground-glass lung opacities, which led to the patients being referred to pulmonologists, interventional radiologists, thoracic surgeons, or all 3 specialists for diagnostic procedures, therapeutic procedures, or both.[6] However, of the 24.2% of low-dose lung cancer screening CT scans found to be positive for a lung abnormality, 96.4% were false-positive findings eventually diagnosed as benign lung nodules.[6]

Thus, given their lung abnormality, the patients undergoing these scans are now at risk of morbidity or mortality related to the obligate diagnostic — sometimes surgical — biopsy procedure or the deemed necessary "therapeutic" — oftentimes surgical — procedure. The subcentimeter size of these lung nodules and, oftentimes, the location of these nodules away from central airways as well as the visceral pleura made such procedures more difficult. For example, bronchoscopic biopsy procedures, risk of pneumothorax due to transthoracic needle biopsy, and risk from unnecessary lung resection (eg, lobectomy) are increased with these smaller lung nodules that, although they may be suspect for early stage lung cancer, are likely to be benign.[7-9]

Minimally Invasive Lung Surgery

Traditionally, lung surgery for suspected or confirmed primary or secondary lung malignancies was performed via a maximally invasive "open" approach through a large thoracotomy incision involving a division of the latissimus dorsi and serratus anterior muscles, and this procedure historically involved removal of the entire fifth rib for exposure. The development of endostaplers then allows for the use of slightly less-invasive muscle-sparing thoracotomy approaches that spared either or both of the latissimus and serratus muscles, thus preserving the long-term function of these muscles but without minimizing the trauma and pain associated with still relatively large incisions.

The first endoscopes were invented in the 19th century, but it was not until the early 1900s that the first laparoscopic procedures emerged; during the decades that followed, these procedures evolved into routine minimally invasive abdominal and pelvic procedures (eg, laparoscopic cholecystectomy, laparoscopic hysterectomy).[10] Jacobaeus, a Swedish internist, performed the first diagnostic thoracoscopy in 1910, leading to the development of dedicated laparoscopic and, subsequently, thoracoscopic surgical instruments in the 1960s and 1970s and performance of the first thoracoscopic lung biopsy in 1976.[11-13] During the early 1990s, improvements in laparoscopic and thoracoscopic video camera technology led to the development of videothoracoscopic surgical procedures, and the first videothoracoscopic pulmonary lobectomy was performed in 1991.[14]

Long, narrow surgical instruments were then developed so that surgeons could reach the farthest recesses of the relevant body cavities through small "keyhole" incisions; however, use of these straight,

nonarticulating instruments was akin to operating with chopsticks. Although few instruments with articulating tips had been designed, articulation often required complicated manipulation, with wheels and levers, to realize the articulation. Moreover, use of these instruments was counterintuitive, because the need to move the working internal end of the instrument in one direction required that the surgeon move the external handle of the instrument in the opposite direction. For example, to move the working internal end of the instrument up, a surgeon must move his or her hands down; to move the working internal end to the left, the surgeon must move his or her hands to the right. Other issues, such as limited visual field, 2-dimensional visualization, lack of articulating thoracoscopic instruments, and lack of scaling down of movements, have limited the widespread adoption of videothoracoscopic surgery.[15]

Despite initial concerns over the general safety of videothoracoscopic surgery, minimally invasive videothoracoscopic surgical procedures have advantages over traditional open thoracic surgery via thoracotomy that have been well-established in the medical literature, including less intraoperative bleeding, less need for perioperative blood transfusions, smaller surgical incisions, less postoperative pain, less need for postoperative narcotics, reduced exposure to internal organs, less perioperative inflammatory response, shorter length of stay (LOS) in the hospital, shorter recovery times, faster return to routine activities of daily living, reduced infection risk, and less postoperative scarring.[16-20]

In addition, initial concerns about whether videothoracoscopic lobectomy — in particular, for primary lung cancer — might result in inferior oncological outcomes due to inadequate lymph node (LN) evaluation are unwarranted. Preliminary experience supported the use of videothoracoscopic pulmonary lobectomy for patients with small peripheral lesions.[21] Since then, the debate regarding benefits, outcomes, and costs has been addressed in multiple studies. In 2009, Yan et al[22] published a systematic review and meta-analysis about the controversy and concluded that videothoracoscopic lobectomy for early-stage non–small-cell lung cancer (NSCLC) may be a valid alternative to open surgery if the procedure is performed in qualified centers. Supporters of minimally invasive surgery (MIS) now promote expanding the use of videothoracoscopic surgery to special populations, such as those with advanced age (> 70 years of age) and patients with pulmonary compromise or poor physical performance.[23]

However, videothoracoscopic lobectomy is not routinely performed. Estimates are as high as 44.7% of lobectomies, according to The Society of Thoracic Surgeons National Database; as low as 6% in the Healthcare Cost and Utilization Project's National (Nationwide) Inpatient Sample database; and 80% of these videothoracoscopic lobectomies are performed at specialized academic centers.[24-27]

Robotic-Assisted Surgical Systems

The first reported use of robotic assistance during surgery was during stereotactic neurosurgical biopsy in April 1985.[28] Since then, robotic assistance during surgery has expanded to almost every surgical specialty. The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California) was first introduced in the late 1990s and approved by the US Food and Drug Administration for general laparoscopic surgery (ie, for gallbladder disease and gastroesophageal reflux) in 2000, urological procedures in 2001, mitral valve repair in 2002, and gynecological conditions in 2005.[29] In the early 2000s, some thoracic surgeons began to adopt robotic-assisted videothoracoscopic surgery as an option for pulmonary resections. In 2001, investigators reported the first series of robotic lobectomies, including 2 right lower lobectomies and 3 left lower lobectomies, with 1 right lower lobectomy and 1 left lower lobectomy converted to an open procedure due to calcified hilar nodes in 1 case and inability to determine extent of disease in the other.[30]

With the surgeon sitting at the surgeon console (Fig 1A), the robotic system binocular cameras (Fig 2A) provide the surgeon with a high-definition, 3-dimensional view of the operating field, which provides improved depth of perception compared with the 2-dimensional image provided by conventional videothoracoscopic surgical cameras.[31] The robotic system computer translates hand movements of the surgeon at the surgeon console (Figs 1B and 2B), via cables and pulleys through the arms of the robotic patient cart (Fig 3A) and through the robotic surgical instruments inserted through port incisions through the patient's chest (Fig 3B), to equivalent movements of the robotic surgical instrument working tips within the patient (this is contrary to the popular misconception that the robot itself performs the surgery). The surgeon manipulates the hand controls within the console, just as he or she would control surgical instruments during a traditional open surgical procedure via a thoracotomy incision. When the surgeon needs to move the robotic instrument working tips up, the surgeon moves the controls up, and, when the surgeon needs to move the robotic instrument tips to the left, the surgeon moves the controls to the left. Moreover, the robotic system has the capacity to scale down the surgeon's hand movements and reduce hand-related tremors.

The articulating robotic instrument working tips have at least the same or more degrees of motion than the human hand (Fig 4), and these improve the ability of the surgeon to complete surgical procedures that require operating around and behind structures, such

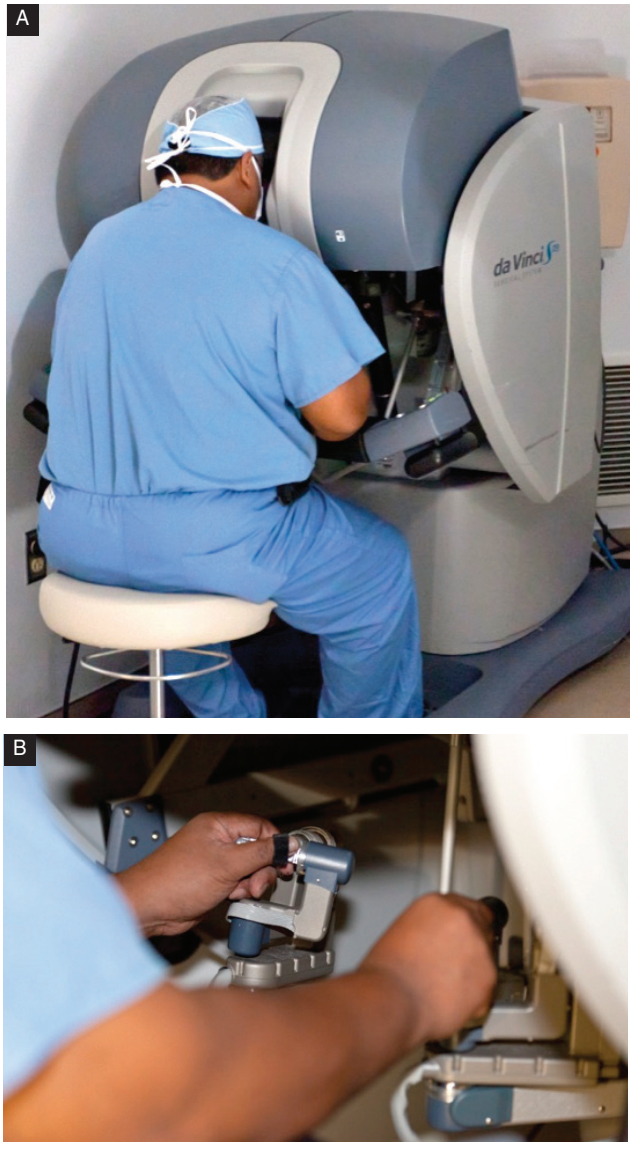

Fig 1A–B. — The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA) console. (A) Surgeon sitting at and interacting with the console using his head, hands, and feet. (B) Surgeon's hands manipulating the console master (hand) controls, which control the robotic instruments. Photography by Nicholas Gould, Moffitt Cancer Center, Tampa, FL.

as around the pulmonary artery and vein and around the bronchus within the pulmonary hilum during lung resection, as well as within deep, narrow spaces (eg, within the mediastinum during mediastinal LN dissection).

For minimally invasive thoracic procedures, such as videothoracoscopic lobectomies, these advancements in instrumentation should allow for precise hilar dissection, decreased risk of intraoperative complications, and decreased risk of conversion to open-completion lung resection via large thoracotomy — in which case, the patient will lose the benefits of MIS. Thus, robotic-assisted surgery would allow MIS procedures to be within reach of more thoracic surgeons, particularly among those primarily performing open

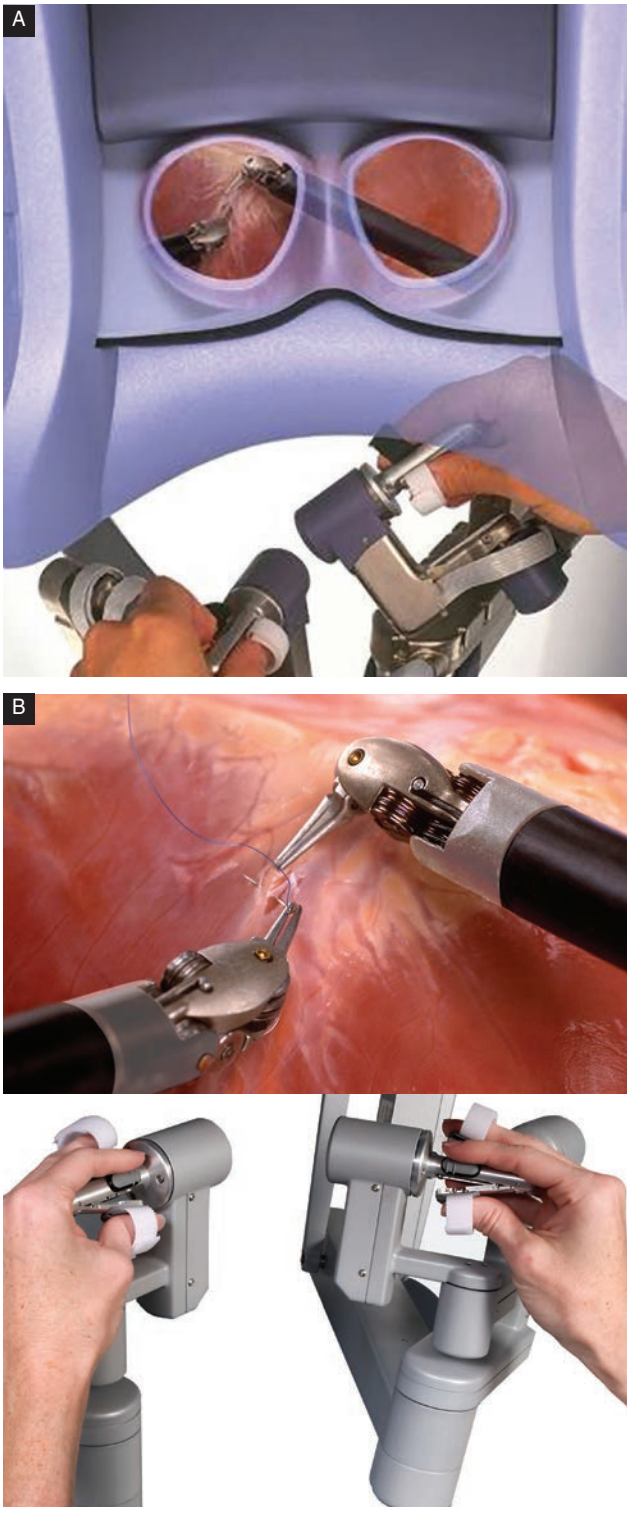

Fig 2A–B. — (A) Surgeon's binocular view and (B) hand controls at the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA) console. ©2014 Intuitive Surgical, Inc.

thoracic surgical procedures, and to be available to more patients who might benefit from the advantages of videothoracoscopic surgery.

At the time of publication, the da Vinci Surgical System is the only complete robotic system on the mar-

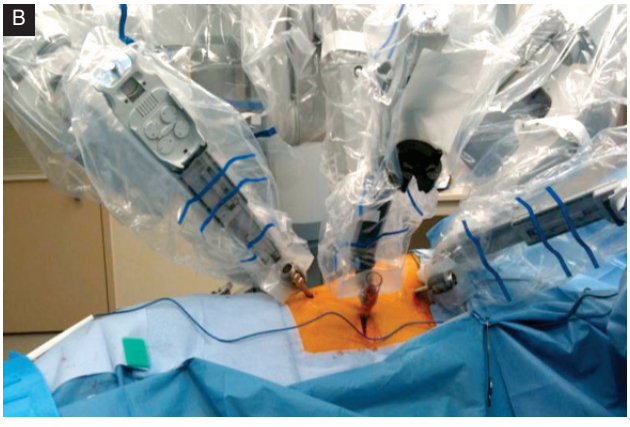

Fig 3A–B. — (A) During a typical right lung resection, the patient cart of the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA) holds up to 3 surgical instruments and a video telescope and (B) docks to the patient on the operating room table. Its robotic arms are covered with plastic sleeves for sterility. Panel A: ©2014 Intuitive Surgical, Inc. Panel B: Photography by Eric M. Toloza, Moffitt Cancer Center, Tampa, FL.

Fig 4A–B. — Typical da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA) instrument with the EndoWrist instrument (Intuitive Surgical) showing its (A) size compared with a human hand and (B) range of motion compared with a human wrist. ©2014 Intuitive Surgical, Inc.

ket, although this da Vinci robotic system has been through 4 different generations, including the original "standard" system, the second-generation S System, the third-generation Si System, and the fourth-generation Xi System. Since 2010, our group has used the S and Si systems (a typical operating room setup appears in Fig 5) to perform more than 600 robotic-assisted pulmonary resections, including wedge resections, segmentectomies, lobectomies, bilobectomies, and complete pneumonectomy after prior right lower lobectomy, via 3 small port incisions (Fig 6).

For oncological procedures, robotic-assisted thoracic surgery may improve mediastinal LN dissection and detection of mediastinal LN metastases, such that patients with clinically occult pathological stage 2 or stage 3 lung cancer may be offered adjuvant chemotherapy or adjuvant chemotherapy in combination with radiation therapy, respectively, which would, in turn, be expected to improve cancer-related survival rates.[32] Many consider robotic-assisted videothoracoscopic surgery to be the leading edge of the paradigm

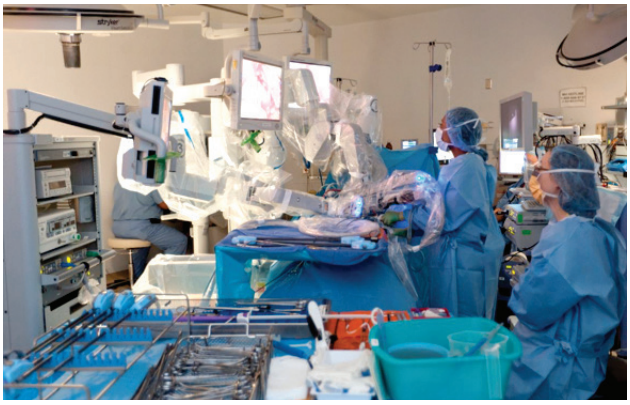

Fig 5. — Typical OR setup for robotic-assisted right lung surgery. Surgical instruments (foreground) with robotic instruments (left foreground), scrub nurse (right foreground), robotic video cart (far left), surgeon (left background, sitting at surgeon console) partially hidden by the robotic patient cart (left center) docked to patient on OR table, and surgical assistant standing by OR table (right center). OR = operating room. Photography by Nicholas Gould, Moffitt Cancer Center, Tampa, FL.

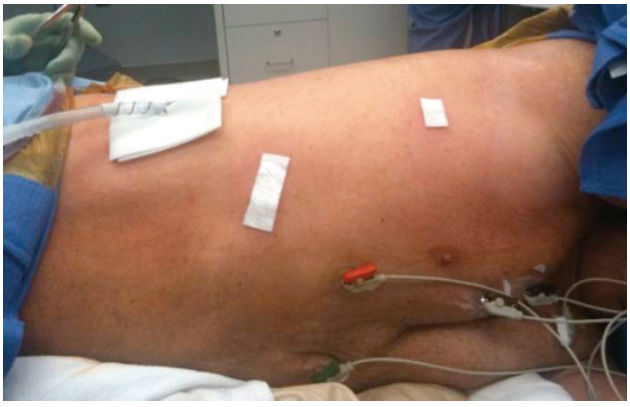

Fig 6. — Typical port incisions after 3-port robotic-assisted right lung surgery with pleural chest tube drain through the most caudal port incision. Photography by Eric M. Toloza, Moffitt Cancer Center, Tampa, FL.

shift toward minimally invasive thoracic surgery.[33]

Outcomes

Intraoperative

In 2008, Melfi et al[34] delineated and compared the advantages and disadvantages of the 2 most common MIS approaches, conventional videothoracoscopic surgery and robotic-assisted videothoracoscopic surgery. The main advantages they found for robotic-assisted surgery were 3-dimensional imaging, dexterity, 7 degrees of freedom, lack of fulcrum effect and physiological tremors, scaled-down motions, and ergonomic position. They also noted disadvantages, including lack of tactile feedback, costly equipment and maintenance, and, at the time of their review, no proven benefit.[34]

An important aspect of robotic-assisted videothoracoscopic lobectomy is the depth and accuracy of hilar and mediastinal nodal dissection.[35] As a result of 3-dimensional visualization and the "wrist-like" action of the instruments, use of the surgical robot has been hypothesized to facilitate precise dissection in a confined space, such as the mediastinal nodal dissection phase of the videothoracoscopic lobectomy procedure.[36]

During our review of the literature, we found 23 series — retrospective analyses made up the majority — that addressed the early experiences and outcomes of robotic-assisted anatomical pulmonary resection (lobectomy and segmentectomy) at multiple surgical centers. We divided these series into 2 groups based on the year of publication as follows: 2005 to 2010 and 2011 to 2014 (Table 1).[27,34-55] Operative times from the 2005–2010 series ranged from 150 to 240 minutes compared with 90 to 242 minutes for the 2011–2014 series. No significant difference in change

Table 1. — Perioperative Comparison Between Published Robotic Series

Study	No. of Patients	Resection Type	Median Operative Time, min	Conversion Rate, %	Median Hospital Stay, d	Mortality Rate, %
Louie[27]	46	Various	213	NA	4	0
Melfi[34]	107	Lobectomy	220	9	5	1
Gharagozloo[35]	61	Lobectomy	240	0	4	5
Gharagozloo[36]	100	Lobectomy	216	1	4	3
Melfi[37]	23	Lobectomy	192	9	5	4
Veronesi[38]	54	Lobectomy	235	13	4.5	0
Veronesi[39]	91	Lobectomy	239	11	5	0
Augustin[40]	26	Lobectomy	228	19	11	4
Fortes[41]	23	Various	Lobectomy: 238 Sublobar: 112	4	3	0
Giulianotti[42]	38	Various	200	16	10	3
Anderson[43]	21	Various	216	0	4	0
Ninan[44]	74	Lobectomy	150	3	3	0
Park[45]	325	Lobectomy	206	8	5	0.30
Meyer[46]	185	Lobectomy	211	2	4	2
Jang[47]	40	Lobectomy	240	0	6	0
Kent[48,a]	430	Various	NA	NA	4	0.20
Adams[49]	120	Lobectomy	242	3.3	4.7	0
Dylewski[50]	200	Various	90	3	3	2
Melfi[51,b]	69 (std)	Lobectomy	222	10	4.4	1
	160 (new)	Lobectomy	166	6	3.8	0
Lee[52]	35	Lobectomy	161	3	3	0
Nasir[53]	394	Various	107	10	2	0.25
Cerfolio[54]	168	Various	132	7.7	2	0
Pardolesi[55]	17	Segmentectomy	189	0	5	0
Present cohort	Early: 104	Lobectomy	179	7	6	3
	Later: 104	Lobectomy	172	13	4	0

[a]Data from the Healthcare Cost and Utilization Project's State Inpatient Databases.

[b]Two groups compared (standard da Vinci Surgical System [Intuitive Surgical, Sunnyvale, CA] vs da Vinci Surgical S/Si systems [Intuitive Surgical]).

NA = not applicable.

in operative times was seen, and this was most likely related to the inclusion of minor resections in the 2005–2010 series. Conversion rates from the 2005–2010 series were between 0% and 19% compared with 0% and 11% in the 2011–2014 series. Mastering of the robotic-assisted surgical technique resulted in decreased conversion rates; however, this mastery also resulted in the extension of this approach to more difficult cases, larger-sized tumors, more advanced-stage cancer, patients who received prior induction therapy, and patients with hilar adenopathy.

The major intraoperative outcomes from our cohort (N = 208) are comparable with what have been described in these previous robotic series. Comparing our early series of pulmonary lobectomies (n = 104) with our subsequent later series (n = 104), our skin-to-skin operative time improved from 179 minutes to 172 minutes. Our overall conversion rate for the entire cohort was 9.6%; a higher overall conversion rate (13.0%) was seen during the later series of robotic-assisted lobectomy cases compared with the early series (7.0%). The higher overall conversion rate in the later series can be explained by the increased level of difficulty of the cases performed. As our level of proficiency and confidence increased, pulmonary lobectomies for advanced-stage lung cancer cases and for more complex cases, such as hybrid procedures combining lung resection with chest wall resections, were performed with the robotic approach. Our emergent conversion rate for bleeding control was 2% for the early series and 5% for the later series. These higher conversion rates did not appear to affect overall postoperative outcomes. In comparison, Park[45] published a large series on robotic-assisted pulmonary lobectomy and found that the median operative time was 206 minutes and the conversion rate to open approach was 8%.

Based on operative times, rates of mortality, and surgeon comfort, the overall learning curve has been described as 18 to 20 cases.[34,46] In a case series comparing robotic-assisted lobectomies with conventional videothoracoscopic lobectomies, Jang et al[47] concluded that a robotic approach can be rapidly adapted by experienced videothoracoscopic surgeons. The outcomes for robotic-assisted videothoracoscopic lobectomy in terms of operative times, intraoperative estimated blood loss, and hospital LOS were similar to those with conventional videothoracoscopic lobectomy when surgeons had at least 2 years of experience with videothoracoscopic lobectomy.[47]

Postoperative

The 5 most commonly reported postoperative complications are atelectasis or mucous plugging (1%–22%), atrial fibrillation (3%–19%), prolonged air leak (defined as an air leak lasting > 5–7 days; 3%–13%), acute respiratory distress syndrome or respiratory failure (1%–13%), and pneumonia (1%–5%; Table 2).[27,34-38,40-55] Table 3 shows the most common postoperative complications in our cohort; prolonged air leak longer than 7 days and atrial fibrillation were the 2 most frequent complications seen in our series.

Likely related to the relatively flat learning curve for videothoracoscopic surgeons learning robotic-assisted videothoracoscopy, morbidity rates ranged from 11% to 39% in the 2005–2010 series compared with 11% to 44% in the 2011–2014 series. Morbidity rates did not change between our 2 series (43% vs 38%). In comparison, Park[45] reported an overall morbidity rate of 25% and a median hospital LOS of 5 days. Hospital LOS for the 2005–2010 series ranged from 3 to 11 days compared with 2 to 6 days for the 2011–2014 series (see Table 1).[27,34-55] The median hospital LOS for our entire cohort was 5 days, which had decreased from 6 days in our early subgroup to 4 days with our later subgroup.

A comparative study analyzing the Healthcare Cost and Utilization Project's State Inpatient Databases demonstrated the superiority of robotic-assisted lobectomy and segmentectomy compared with conventional videothoracoscopic lobectomy and open lobectomy.[48] Robotic-assisted lobectomy was associated with reductions in the overall complication rate (43.8% vs 54.1%), hospital LOS (5.9 vs 6.3 days), and overall mortality rate (0.2% vs 2.0%) when compared with open resections.[48] The overall complication rate, LOS, and mortality were also lower among the robotic group compared with videothoracoscopic surgery; however, none of these differences reached statistical significance.[48] Adams et al[49] compared their experience with The Society of Thoracic Surgeons National Database. They found that robotic-assisted surgery was equivalent to videothoracoscopic surgery on all intraoperative and postoperative outcomes and also resulted in significantly lower postoperative blood transfusion rates (0.9% vs 7.8%), air leaks for more than 5 days (5.2% vs 10.8%), and hospital LOS (4.7 vs 7.3 days) compared with open thoracotomy.[49]

Mortality also appeared to improve with surgeon experience; we found that mortality rates for the 2005–2010 series ranged from 0% to 5% compared with 0% to 2% for the 2011–2014 series (see Table 1).[27,34-55] Our in-hospital mortality rate for our entire cohort was 1.4%; 3 in-hospital deaths occurred during the early series.

Oncological

One of the main benefits of robotic-assisted techniques is the meticulous dissection that can be conducted in a nearly bloodless field.[50] Supporters of robotic surgery promote the potential superiority of the robotic approach in LN dissection, and we recently presented our LN dissection and upstaging data at the CHEST World Congress Annual Meeting.[56] Current guidelines suggest that the assessment of at least 3 mediastinal (N2) nodal

Table 2. — Frequent Postoperative Complications in Robotic-Assisted Pulmonary Lobectomies

Study	Morbidity Rate, %	AF, n (%)	Atelectasis/ Mucous Plug, n (%)	Prolonged Air Leak, n (%)	Pleural Effusion Requiring Drainage, n (%)	PE, n (%)	Pneumonia, n (%)	ARDS/ Respiratory Failure, n (%)	Chyle Leak, n (%)
Louie[27]	17/26[a]	3 (7)	1 (2)	2 (4)	1 (2)	NA	2 (4)	1 (2)	NA
Melfi[34]	NA	NA	NA	10 (9)	NA	1 (1)	NA	NA	NA
Gharagozloo[35]	22%	4 (6)	4 (6)	2 (3)	2 (3)	NA	NA	NA	NA
Gharagozloo[36]	21%	13 (13)	5 (5)	4 (4)	3 (3)	3 (3)	1 (1)	1 (1)	NA
Melfi[37]	39	1 (4)	5 (22)	2 (9)	NA	1 (4)	NA	NA	NA
Veronesi[38]	20	3 (6)	NA	2 (4)	NA	NA	NA	7 (13)	NA
Augustin[40]	15	1 (4)	NA	2 (9)	NA	NA	NA	NA	NA
Fortes[41]	39	4 (17)	NA	3 (13)	NA	NA	NA	2 (9)	NA
Giulianotti[42]	11	NA	NA	2 (5)	NA	NA	NA	1 (3)	NA
Anderson[43]	27	4 (19)	3 (14)	0 (0)	NA	NA	1 (5)	NA	NA
Ninan[44]	NA	3 (4)	NA	3 (4)	NA	NA	2 (3)	NA	NA
Park[45]	25	37 (11)	NA	NA	NA	3 (1)	NA	NA	NA
Meyer[46]	17	16 (9)	6 (3)	6 (3)	5 (3)	3 (2)	1 (1)	2 (1)	1 (1)
Jang[47]	10	NA	Yes (NA)	Yes (NA)	NA	NA	NA	NA	NA
Kent[48,b]	44	NA	NA	NA	NA	NA	NA	NA	NA
Adams[49]	NA	10 (9)	NA	6 (5)	NA	NA	2 (2)	4 (3)	NA
Dylewski[50]	26	6 (3)	NA	15 (8)	17 (9)	NA	8 (4)	NA	NA
Melfi[51,c]	NA	3 (4)	NA	9 (13)	2 (3)	NA	NA	NA	NA
	NA	7 (4)	2 (1)	11 (7)	1 (1)	NA	NA	NA	NA
Lee[52]	11	2 (6)	NA	1 (3)	1 (3)	NA	NA	NA	NA
Nasir[53]	27	26 (7)	NA	32 (8)	NA	NA	10 (3)	7 (2)	5 (1)
Cerfolio[54]	28 (27)	12 (11)	NA	10 (9)	NA	NA	NA	1 (1)	2 (2)
Pardolesi[55]	18	NA	NA	2 (12)	NA	NA	1 (6)	NA	NA
Present cohort	Early: 43	14 (13)	9 (9)	19 (18)	1 (1)	2 (2)	11 (11)	3 (3)	1 (1)
	Late: 38	11 (11)	5 (5)	16 (15)	1 (1)	1 (1)	9 (9)	1 (1)	2 (2)

[a]Divided as major and minor complications.

[b]Data from the Healthcare Cost and Utilization Project's State Inpatient Databases.

[c]Two groups compared (standard da Vinci Surgical System [Intuitive Surgical, Sunnyvale, CA] vs da Vinci Surgical S/Si systems.

AF = atrial fibrillation, ARDS = acute respiratory distress syndrome, NA = not applicable, PE = pulmonary embolus.

stations is the most important prognostic element in NSCLC staging.[57-59] A total of 98% of our robotic-assisted lobectomy cohort achieved this goal, and 89% of our cases surpassed this goal (≥ 4 N2 LN stations dissected). In comparison, a review of the National Comprehensive Cancer Network (NCCN) NSCLC Database found that 66% of videothoracoscopic surgical cases and 58% of open lobectomies had at least 3 mediastinal LN stations assessed.[60] Another study suggested that 40% to 50% of lobectomies performed for lung cancer in the United States had no mediastinal LN dissection documented at all.[61]

Our mean number of N2 LN stations dissected was 3.7 ± 0.1 stations. We had a mean number of 7.2 ± 0.3 individual N2 LNs retrieved. Our overall mean of N1 + N2 stations reported was 5.6 ± 0.1 stations, with a total of 13.4 ± 0.4 individual N1 + N2 LNs retrieved. In comparison, a review of the NCCN NSCLC Database reported that the mean number of N2 LN stations dissected via the videothoracoscopic surgical approach was 3.1 N2 LN stations and 2.9 N2 LN stations via the open approach.[60] Another study reported that the mean number of individual N2 LNs retrieved via the videothoracoscopic surgical approach was 2.5 N2 LNs and 3.7 N2 LNs via the thoracotomy approach, and the mean total number of individual N1 + N2 LNs retrieved via the videothoracoscopic surgical approach was 7.4 N1 + N2 LNs and

Table 3. — Postoperative Complications in Our Cohort

Postoperative Complication	Combined Cohort (N = 208), n (%)	First Series (n = 104), n (%)	Second Series (n = 104), n (%)
Overall minor/major complication rate	84 (40)	45 (43)	39 (38)
Prolonged air leak > 7 d[a]	35 (17)	19 (18)	16 (15)
Atrial fibrillation	25 (12)	14 (13)	11 (11)
Pneumonia	20 (10)	11 (11)	9 (9)
Mucous plugs requiring bronchoscopy	14 (7)	9 (9)	5 (5)
Aspiration pneumonitis	6 (3)	3 (3)	3 (3)
Respiratory failure	4 (2)	3 (3)	1 (1)

[a]Includes subcutaneous emphysema.

8.9 N1 + N2 LNs via the thoracotomy approach.[62]

For open lobectomies, the published clinical N0 to pathological N2 (cN0-to-pN2) upstaging rates range from 1.9% to 5%, and the cN0-to-pN1 + cN0-to-pN2 upstaging rates range from 14.3% to 14.5%; the respective upstaging rates for videothoracoscopic lobectomies are 2.1% to 4.9% and 8.8% to 15.9%.[60,62-65] In the first robotic-assisted upstaging review ever published, the rate of nodal upstaging for robotic-assisted resection (10.9%) appeared to be superior to that for videothoracoscopic surgery and was similar to thoracotomy data when analyzed by clinical tumor stage.[32,66] Park[45] reported an overall upstaging rate of 21%. Our cohort had an overall 30% upstaging rate and a 19% nodal upstaging rate, with a cN0-to-pN2 upstaging rate of 8.2% and a cN0-to-pN1 + cN0-to-pN2 upstaging rate of 16.4%, indicating the improved efficacy of LN dissection using the robotic approach.

The meticulous and detailed LN dissection provided by robotic-assisted surgery improves the early detection of metastatic disease. Robotic-assisted thoracic surgery has the potential to become the gold standard for NSCLC management, because more patients can be more accurately staged and receive appropriate adjuvant chemotherapy without or with radiation — and this is not likely to happen without an effective LN dissection.

A study by Melfi et al[51] showed a 5-year OS rate of 80% among individuals undergoing robotic-assisted lobectomy for lung cancer. A large cohort series by Park et al[67] also showed a 5-year OS rate of 80% for persons with NSCLC undergoing robotic-assisted lobectomy; 5-year survival rates were 91% and 88% for stages 1A and 1B, respectively. A meta-analysis of robotic-assisted outcomes performed by Cao et al[68] showed overall recurrence rates ranging from 0% to 9.8%, including 0% to 4.8% for local recurrence, 0% to 6% for systemic recurrence, and 0% to 3.8% for both local and systemic recurrence at the time of the latest follow-up.

Costs

Several disadvantages of robotic-assisted surgery exist, including cost (several countries cannot afford any type of robot), the need for a bedside assistant to use an endostapler across pulmonary vessels, and lack of a consistent platform, tactile feedback, standardized credentials, and training programs for surgeons and technical assistants.[69]

In a retrospective analysis by Dylewski et al,[70] lobectomies performed using a robotic-assisted approach reduced direct cost by $560 per case. The majority of cost savings occurred from reduced hospital LOS and lower overall nursing care cost.[70] However, in the Japanese health care system, for any institution willing to acquire the robotic technology, Kajiwara et al[71] notes that at least 300 robotic operations must be performed each year to avoid financial deficit with the current process of robotic surgical system management.[71]

In addition to the challenges of acquiring a robotic surgical system, Lee et al[52] analyzed intraoperative and postoperative costs between videothoracoscopic surgery and robotic-assisted videothoracoscopic surgery. Intraoperative costs include disposable instrumentation, operative time, and personnel. Compared with the videothoracoscopic surgery group, robotic-assisted cases in the series by Lee et al[52] required approximately 30 minutes of additional operative time, and no additional personnel were required. Robotic-specific instruments were an additional cost, but no difference was seen in endostapler cartridge usage.[52] The postoperative care that both groups received was identical.[52] The difference in cost was realized in the hospital LOS.[52]

The optimization of patient care and the early identification of potential complications could decrease the overall costs even further. Decreasing operating time, minimizing the number of robotic instruments needed, eradicating unnecessary laboratory work, and minimizing stays in the intensive care unit will help decrease direct hospital costs for anatomical lung resection.[72] The robotic system allows the surgeon to perform a minimally invasive operation while reducing the need for routine arterial catheters, epidural catheters, Foley catheters, and other items that impart additional fixed costs — thus resulting in a lower direct cost.[53] The most significant cost benefit to patients and their caregivers is derived from faster recovery times and a quicker return to work as well as less expenditure for the management of postoperative complications and outpatient services (eg, home health care, rehabilitation).[73]

Extended Use: Complex Surgery

Robotic-assisted surgery has been proposed to provide an MIS approach for routine lung resections,

more accurate LN dissections, and more complex surgical procedures.[74] Two robotic-assisted pneumonectomies were reported by Spaggiari and Galetta.[75] Both cases were completed in 200 minutes or less, and the patients were discharged home 6 to 7 days after uneventful hospital stays.[75] At Moffitt Cancer Center, we performed completion pneumonectomy and mediastinal LN dissection on a patient aged 57 years diagnosed with recurrent NSCLC in the right upper lobe and right hilar lymphadenopathy and a history of previous right lower lobectomy for pT1N0M0 adenocarcinoma (6 years ago) with adjuvant chemotherapy. Due to the patient's history of prior lobectomy, pleural adhesions and scar tissue were additional challenges in this procedure. He was discharged 8 days following the operation; his hospital stay was complicated by sinus tachycardia and urinary tract infection. This successful robotic-assisted completion pneumonectomy confirmed the safety of the technology, and further evaluation of this procedure should be conducted.

Chest wall resection en bloc with lung resection potentially incurs higher morbidity rates than pulmonary resection alone. One hybrid technique includes robotic-assisted pulmonary resection and LN dissection prior to freeing the chest wall through an additional incision smaller than what would be necessary had both lung and chest wall resections been performed via thoracotomy. In this setting, the goal is to minimize injury to the overlying chest wall musculature without jeopardizing the oncological element of the procedure.[76] If the tumor is higher in the chest where extensive periscapular extrathoracic musculature is present, then new minimally invasive techniques to resect the tumor with en bloc chest wall resection compared with open surgery might benefit patients because the periscapular extrathoracic muscles would be spared. At Moffitt Cancer Center, we have performed this hybrid, robotic-assisted thoracoscopic lobectomy with en bloc chest wall resection on 5 patients with primary NSCLC during a 1-year period; of those cases, 1 was converted to open lobectomy due to pulmonary artery segmental branch bleeding. Despite some complicated hospital stays, the median days for chest tube duration and hospital LOS were 5 and 7 days, respectively. Thus, from our experience, hybrid, robotic-assisted pulmonary lobectomy with en bloc chest wall resection and reconstruction is feasible and safe in select patients.

The robotic approach appears well suited for the precise dissection required for anatomical segmentectomy, and this is particularly true among patients with single-lesion, early-stage lung cancer or those whose cancer has metastasized from an extrapulmonary site and when the lung lesion is less than 2 cm in diameter.[55] A retrospective study of 35 patients showed a mean operation time of 146 minutes; 5 LN stations were sampled and there was no 60-day mortality.[77] Based on these studies, robotic-assisted surgery may be feasible for skilled and trained surgeons performing pulmonary segmentectomies. At Moffitt Cancer Center, more than 45 robotic-assisted pulmonary segmentectomies have been performed, including right and left lower lobe superior segmentectomies, right or left lower lobe basilar segmentectomies, lingulectomy, and lingula-sparing left upper lobectomy (also known as left upper lobe apical bisegmentectomies).

Conclusions

Robotic-assisted videothoracoscopic lobectomy appears to be at least as safe as traditional open and conventional videothoracoscopic lobectomy approaches. Benefits in decreased perioperative complications and shorter hospital length of stays have been demonstrated in the case series we reviewed. Based on the data provided by our experience at Moffitt Cancer Center, mediastinal lymph node (LN) dissection via robotic-assisted videothoracoscopic surgery is more effective than the conventional videothoracoscopic surgical approach and open thoracotomy. The meticulous and detailed LN dissection provided by robotic assistance during surgery improves the early detection of metastatic disease. Overall, the improved efficacy of LN dissection is the most important benefit of robotic technology. Improved intraoperative efficiency, fewer numbers of instruments used, shorter operative times, practical perioperative management, early identification of potential complications, and limiting unnecessary tests and procedures can make robotic-assisted surgery a cost-effective approach. Large multidisciplinary centers can also share the economic burden among specialties, thereby decreasing individual costs. Thus, we expect an increase in surgical procedures of the lung through the use of minimally invasive techniques (particularly robotic assistance), improved instrumentation, better understanding, and the broader acceptance of thoracoscopy among chest surgeons.[78]

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Sofía Cáceres Nazario. *Chicken*, 2015 (Detail). Acrylic on canvas, 16" × 12".

Robotic-assisted mediastinal surgery appears to be superior to the open approach and is comparable with videothoracoscopic mediastinal surgery.

Robotic-Assisted Videothoracoscopic Mediastinal Surgery

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Background: *Tumors of the mediastinum as well as normal thymus glands in patients with myasthenia gravis have traditionally been resected using large and morbid incisions. However, robotic-assisted mediastinal resections are gaining popularity because of the many advantages that the robot provides. However, few comprehensive reviews of the literature on robotic-assisted mediastinal resections exist.*

Methods: *A systemic review of the current medical literature was performed, excluding cases related to esophageal pathology. These studies were evaluated and their findings are reported in this comprehensive review. Approximately 48 papers met the inclusion criteria for review.*

Results: *Robotic-assisted surgical systems are increasingly being used in mediastinal resections. Based on the available literature, robotic-assisted thoracoscopic surgery in the mediastinum is feasible and safe. Robotic-assisted mediastinal surgery appears to be superior to open approaches of the mediastinum and is comparable with videothoracoscopic surgery when patient outcomes are considered.*

Conclusions: *Increased robotic experience and more studies, including randomized controlled trials, are needed to validate the findings of the current literature.*

Introduction

The mediastinum is the region of the thorax that lies between the 2 pleural cavities. Anatomically, the mediastinum can be divided into 3 compartments — the anterosuperior, middle, and posterior — that represent convenient subdivisions because pathology tends to be specific to a particular area of the mediastinum. Masses in the anterosuperior region are generally thymomas, teratomas, substernal thyroid/parathyroid tissue, or lymphomas. Pericardial and bronchogenic cysts are located in the middle mediastinum, and neurogenic tumors or esophageal cysts are generally found in the posterior mediastinum.[1]

The history of mediastinal resections has evolved like much of surgery. Initially, maximum exposure was necessary and was accomplished with various incisions, including median sternotomy, posterolateral thoracotomy, unilateral anterior thoracotomy with partial sternotomy (hemi-clamshell), and bilateral anterior thoracotomy with transverse sternotomy (clamshell). Secondary to the morbidity associated with these procedures, more minimally invasive approaches were developed, including videothoracoscopic surgery and combined approaches, such as subxiphoid videothoracoscopic surgery and transcervical plus subxiphoid videothoracoscopic surgery.

Although videothoracoscopic surgical access to the mediastinum decreases morbidity and hospital length of stay (LOS) when compared with the traditional open approaches, drawbacks still exist.[2]

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The mediastinum is a relatively narrow space in the thorax that contains many vital structures at risk of injury during surgery. Therefore, the 2-dimensional view afforded by a videothoracoscopic surgical approach can be less than optimal. Typically, the instruments used during videothoracoscopic surgery do not articulate, and this represents a limitation that can cause difficulty when the surgeon is trying to navigate around vital structures.

As a result of these shortcomings, new technology was developed that employed the use of robotic assistance. The benefits of the robotic system, including a high-definition, 3-dimensional view and articulating endo-wristed instruments, improve on the shortcomings of videothoracoscopic surgery while allowing for small, less-morbid incisions. Furthermore, the robotic-assisted surgical system filters hand tremors from surgeons and scales down movement, which is vital when working in small areas such as the mediastinum.[3,4]

Despite these advantages, thoracic surgeons are slow to adopt robotic assistance, typically citing the costs associated with robotic-assisted thoracoscopic surgery. Performing robotic-assisted surgery costs more than videothoracoscopic surgery, and most of the cost burden relates to instrumentation.[5] Furthermore, a paucity of literature exists on robotic-assisted mediastinal resection because it is relatively new technology compared with more established operative approaches.

Thymectomy

Surgical resection of the thymus is performed to diagnose myasthenia gravis (MG) or thymoma. Independently, Blalock et al[6] demonstrated in the early twentieth century that symptom improvement among those with MG could be accomplished with thymectomy, causing an increase in this procedure worldwide. The most common approach remained median sternotomy until the 1960s, which is when a series of 59 transcervical thymectomies was performed without significant complications or mortality.[7] However, with the results of some studies showing that thymic tissue could reside within the mediastinum or neck outside of the gland, many surgeons felt that maximum exposure techniques were more appropriate to ensure complete resection.[8] The debate between transcervical and trans-sternal thymectomies continued until a less invasive approach involving videothoracoscopic surgery was popularized in thoracic surgery.[9] Both unilateral and bilateral videothoracoscopic surgical techniques are gaining in popularity based on the benefits of shorter LOS and relatively fewer surgical complications without compromising therapeutic outcomes when compared with trans-sternal thymectomies.[2]

In an attempt to improve on these benefits, use of a robotic-assisted surgical system was implemented for the first time in the resection of a mediastinal mass in 2001 by Yoshino et al.[10] Since then, use of robotic-assisted surgery has been increasing worldwide for thymectomy. Early studies demonstrated that robotic-assisted thymectomy was a safe operation with limited morbidity and mortality.[3,11-13] These early studies identified the advantages and disadvantages of utilizing robotic assistance. Bodner et al[11] found that certain complex surgical procedures, such as dissection of the superior horns of the thymus, were technically easier to perform with robotic assistance than with traditional thoracoscopy.

Another benefit noted in a separate series is that these operations could be performed with decreased risk of postoperative wound complications.[13] This finding is an important observation because patients with MG typically take corticosteroids, and wound complications can be problematic with this patient population when undergoing median sternotomy. Total operative times varied in these early studies, ranging from 96 to 129 minutes, and some studies stated that the time needed to set up the robot was cumbersome.[3,11,12] However, multiple studies have shown that, with increased surgeon and operating room staff experience, both the times to set up the robot and the length of operation decrease.[14-16]

Cakar et al[17] published the first series comparing robotic-assisted thymectomy to median sternotomy, which is the gold standard of treatment. This group demonstrated a significant decrease in complications among those assigned to the robotic-assisted group compared with the median sternotomy group. A decrease in LOS was also established in the robotic-assisted group.[17] Balduyck et al[18] compared the same groups using quality-of-life assessment questionnaires. When compared with preoperative assessment, the median sternotomy group had a decline in general function and increased levels of fatigue at 1 month following surgery; a similar finding was not evident in the robotic-assisted group.[18] However, the robotic-assisted group had increased shoulder pain 3 months after the surgery compared with the pain level at baseline, and this finding was not seen in the median sternotomy group.[18]

Weksler et al[19] stated that robotic-assisted thymectomy was superior to median sternotomy, demonstrating decreased rates of intraoperative blood loss, complications, and LOS in the robotic group. Another series published by Seong et al[20] compared the 2 groups and showed a decrease in the number of drains used and amount of drainage at 24 hours, lower rates of hemoglobin loss, shorter duration of chest tubes, and shorter LOS in the robotic group.

Other studies have compared robotic-assisted thymectomy with videothoracoscopic surgery, and, initially, results for robotic-assisted thymectomy were compared with historical videothoracoscopic

surgery controls.[5] Augustin et al[5] demonstrated that robotic-assisted thymectomy had similar LOS (2–5 days) and overall shorter operative times than videothoracoscopic surgery thymectomies reported in the literature. They also found that robotic-assisted thymectomies cost up to 91% more than videothoracoscopic thymectomies performed in their institution, a number they attributed to instrument price (instruments can be reused in up to 10 cases before they must be replaced).[5,21]

Rückert et al[22] performed the first single institution comparison of robotic-assisted and videothoracoscopic thymectomies. Between the 2 groups, no differences were seen in rates of mortality, postoperative morbidity, operating time, or conversion rate.[22] Another study comparing these groups demonstrated decreased LOS and duration of postoperative pleural drainage in the robotic-assisted group; however, no differences were noted in operative time or intraoperative blood loss between the 2 cohorts.[23]

Because the most common indications for thymectomies are MG and thymomas, surgeons must be assured that robotic-assisted thymectomies can yield the same clinical improvements as other types of thymectomies. Thus, many series have confirmed that robotic-assisted thymectomy is a plausible treatment option for patients with MG.[24-30] Hartwich et al[30] showed that robotic-assisted thymectomy can improve symptoms in children with MG. Collectively, 82% to 92% of patients had improved symptoms of MG following robotic-assisted thymectomy, and the complete remission rate was as high as 28.5%.[29]

Reports have also shown that thymomas can be completely resected and cured using robotic-assisted thymectomy. R0 resections have been accomplished using robotic-assisted surgery for thymomas less than 4 cm.[14] Furthermore, multiple studies have shown no recurrence of thymoma in study patients followed for up to 14.5 months.[28,31] A longer study with 36 months of average follow-up time revealed 1 intrathoracic recurrence but no thymoma-related deaths.[32]

Ectopic Parathyroid Tissue in the Mediastinum

Hyperparathyroidism and its manifestations are due to the excess secretion of parathyroid hormone by the parathyroid glands. Typically, the culprit gland or glands are located in the cervical region, but they can be found in ectopic locations 15% to 20% of the time, and some of these ectopic glands are found in the mediastinum.[33] Traditionally, a cervical incision is utilized to remove such glands, but occasionally they are inferiorly or posteriorly located and require more exposure (eg, sternotomy, thoracotomy).

With improved technology, more minimally invasive approaches such as videothoracoscopic surgery are being used. Surgeons have also begun to use robotic-assisted surgery to resect ectopic parathyroid glands located in the mediastinum. To date, published data on robotic-assisted mediastinal parathyroid extirpation are limited to case reports and small case series.[34-41] Data from these series demonstrate that resection of these mediastinal parathyroid glands is feasible and safe when using the robotic-assisted system. In addition, when navigating around areas such as the aortopulmonary window, use of the robotic-assisted system has been shown to be superior to videothoracoscopic surgery.[34] Transient weakness of the left recurrent laryngeal nerve is the only postoperative complication recorded in these series, and this complication completely resolved by 8 months.[35]

One case series of 5 study patients was reported by Ismail et al.[37] No postoperative complications and no conversions to open or videothoracoscopic surgery were reported. Mean operative time was 58 minutes, and the average LOS was 3 days.[37] Case patients were followed for 41 months, at which time all 5 patients were free of symptoms and had calcium levels within the normal range, thus demonstrating that robotic-assisted mediastinal parathyroidectomy is effective.[37]

A larger series of 6 patients who underwent robotic-assisted mediastinal parathyroidectomy was published by Karagkounis et al.[42] Median operating time was 168 minutes, and nearly all study patients (all except 1) had an effective operation, as evidenced by a decreased level of intraoperative parathyroid hormone of more than 50% 10 minutes following excision.[42] The mean pain score was 7.7 out of 10 on postoperative day 1 and 1.5 out of 10 on postoperative day 10, and the average LOS was 2.2 days.[42] A complication occurred in 1 study patient (pericardial and bilateral pleural effusions requiring drainage).[42]

Posterior Mediastinum

Regarding robotic-assisted resection of tumors residing in the posterior mediastinum, few data have been published. The largest study to date comes from Cerfolio et al.[43] The researchers reviewed the data of 75 study patients with disease in the posterior or inferior mediastinum, including neurogenic-based tumors, recurrent thymomas, esophageal and bronchogenic cysts, and metastatic lymph nodes.[43] Median LOS was 1 day and conversion to open surgery secondary to stapler malfunction took place in 1 study patient.[43] The morbidity rate was 12%, and 1 major complication was noted (delayed esophageal leak following epiphrenic diverticulectomy); no mortalities were reported.[43] Thus, the researchers determined that the robotic-assisted approach used to resect these tumors is safe and practical.[43] A learning curve was evident because the median operative time decreased after both the first and second groups of

25 study patients (n = 50).[43] Specific techniques to approach these difficult-to-reach tumors were also noted to aid the surgeon and included driving the camera in from the posterior aspect of the study patient and placing ports anteriorly for better visualization. Furthermore, for tumors larger than 3 cm, the researchers recommended placing the study patient in the lateral decubitus position or tilted forward to allow the lung to fall away from the posterior mediastinum.[43]

Nakamura et al[44] published their Japanese experience with robotic-assisted resection of posterior mediastinal masses. The series included 14 study patients; the most common pathology in the study cohort was neurogenic tumor (57% of the patients).[44] The overall average operative time was 142.6 minutes; the average console time was 68.7 minutes.[44] No conversions or complications were recorded. On average, study patients were discharged on postoperative day 5.[44]

Other smaller studies have demonstrated that operating on tumors in the posterior mediastinum is feasible when using the robotic-assisted approach.[11,45-49] Results from 2 studies showed that pathology uncommon to the posterior mediastinum, such as thyroid goiters, can also be resected using robotic-assisted systems.[50,51] Chon et al[52] noted that robotic-assisted resection of double primary tumors within different areas of the mediastinum (anterior and posterior) is possible with a single-stage operation.

Other Mediastinal Pathology

Tumors occurring less frequently within the mediastinum have been resected with robotic assistance. Meehan and Sandler[53] described their experience with robotic-assisted resections of mediastinal lesions in children. Of their 5 study patients, 1 had a teratoma and another had a germ cell tumor that were both resected using the robotic-assisted system.[53] No surgical complications and no conversions to open surgery were reported.[53] Another series by Melfi et al[28] included 9 cases of pleuropericardial cysts and 3 teratoma cases. The results from both of these series demonstrate that even uncommon pathology within the mediastinal borders can be extirpated with good results.[28,53]

Conclusions

Initial operations within the mediastinum began to appear in the medical literature in the early 20th century.[6] Such operations were initially performed via large incisions and had increased rates of morbidity. Throughout the last century, less invasive surgical approaches have been developed to access the mediastinum so as to reduce morbidity. A common minimally invasive approach to the mediastinum is videothoracoscopic surgery, which has advantages when compared with traditional open approaches, including decreased rates of morbidity and postoperative pain levels as well as shorter length of hospital stays. However, its disadvantages include its 2-dimensional image projection and lack of articulating instruments — both of which are detrimental when operating in narrow spaces with vital structures (eg, mediastinum).

The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California) can be used in many different surgical specialties, including general surgery, urology, and cardiac surgery. Benefits of the robotic-assisted system include improved visualization with a 3-dimensional viewing screen and articulating instruments — both of which are useful when operating in the mediastinum and other narrow spaces. Because of these advantages, the robotic-assisted platform has been gaining popularity, and case series have demonstrated decreased rates of complications, intraoperative blood loss, chest tube duration, and length of stay when compared with the gold standard of median sternotomy for thymectomy.[19,20] In addition, when compared with videothoracoscopic thymectomy, robotic-assisted thymectomy has similar rates of morbidity and length of stay.[22] Multiple studies have demonstrated that oncological results for tumor resections from the mediastinum with robotic assistance are comparable with those of other surgical approaches.[28,31,32,53] In addition, among study patients with myasthenia gravis undergoing thymectomy, those undergoing robotic-assisted thymectomy have similar rates of symptom improvement and cure compared with those undergoing other surgical modalities.[24-30]

Despite these positive results for robotic-assisted surgery in the mediastinum, thymectomy is still the most published operation of all robotic-assisted mediastinal resections; as of 2012, approximately 3,500 cases have been registered with Intuitive Surgical.[54] In addition, median sternotomy is considered the gold standard approach for thymus gland removal — a fact that could be due to the perceived increased cost associated with robotic surgery. However, some data suggest that robotic-assisted surgery costs less than videothoracoscopic surgery because of reduced length of hospital stays and the overall nursing care required.[55]

Furthermore, some surgeons may not feel comfortable with the relatively new robotic-assisted technology because they may not have been formally trained to use the platform. The paucity of published literature on robotic-assisted mediastinal resections may also deter surgeons from using this approach. Despite the positive results previously published on the subject, in our opinion, a randomized controlled trial comparing robotic-assisted mediastinal resections with other approaches is still warranted to elucidate all of the benefits of robotic-assisted videothoracoscopic mediastinal surgery.

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Sofía Cáceres Nazario. *Golden Sunflower*, 2015 (Detail). Acrylic on canvas, 16" × 12".

Robotic surgery for use in head and neck cancer has shown promising results in numerous applications.

Robotic-Assisted Surgery in the Head and Neck

Jon Burton, MD, Robert Wong, MD, and Tapan Padhya, MD

Background: *Robotic surgery was first used in medicine in the 1980s for laparoscopic surgery. Since then, several developments have been made in the use of robotic surgery for patients with head and neck cancer.*
Methods: *A review was performed of the literature on robotic surgery in patients with head and neck cancer. The various sites of application are discussed in depth as well as the functional and oncological outcomes associated with the most common application of transoral robotic surgery (TORS).*
Results: *Robotic surgery has been used in all aspects of head and neck surgery. The results from early studies of TORS have shown at least equivalent functional and oncological outcomes.*
Conclusions: *Robotic surgery has feasible utility in patients with head and neck cancer; moreover, in several circumstances it may provide superior cosmetic, functional, and oncological outcomes than conventional methods.*

Introduction

Robotic surgery was first used in medicine in the 1980s for laparoscopic surgery.[1] The National Aeronautics and Space Administration has also played a role in the development of robotic surgery in its efforts to advance telepresence medicine.[1] The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California) was granted US Food and Drug Administration approval for select head and neck tumors after studies demonstrated the safety and feasibility of transoral robotic surgery.[2]

Using the da Vinci Surgical System, the surgeon can operate on a patient from a seated console with 3-dimensional (3-D) visualization and articulating instruments. For head and neck surgery, a 0- or 30-degree binocular endoscope is typically placed in the center with a 5-mm articulating EndoWrist instrument (Intuitive Surgical) on each side (Fig). The use of robotic surgery may help eliminate hand tremor while providing a magnified 3-D view of the surgical field. The proximity of the tip of the endoscope to the area of interest avoids line-of-sight challenges that may arise with the use of an operating microscope. Other advantages include the avoidance of external incisions through the use of transoral approaches, improved functional outcomes, a reduced need for tracheostomy and gastrostomy, decreased blood loss, and shorter hospital stays.[3,4]

Disadvantages of robotic surgery include the high financial cost and the size of the console and robotic cart. Setup time for robotic surgery can also lead to prolonged operative times; however, these times are significantly decreased with surgeon experience.[5] Few patients are not candidates for transoral robotic surgery (TORS) due to anatomical limitations. Factors such as retrognathia, a full complement of dentition, trismus, macroglossia, or a small oral stoma, may prevent the introduction of the robotic arms. Recently,

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mandibular osteotomies have been advocated to improve exposure.[6]

Robotic surgery was increasingly used during the last decade for procedures in various surgical subspecialties, including otolaryngology. With the added widespread availability in operating rooms, many studies have described novel applications of the surgical robotic system for both benign and malignant processes of the head and neck.

Applications by Anatomical Site

Oropharynx

Surgical access and visualization of the palatine tonsils, pharyngeal walls, and tongue base can be improved with robotic surgery. The Feyh–Kastenbauer retractor is commonly used to expose the oropharynx; however, the Crowe–Davis mouth gag can also provide access. A 0- or 30-degree stereoscopic endoscope is placed in combination with a 5-mm EndoWrist Schertel or Maryland grasper in the nondominant hand; a 5-mm spatula cautery is placed in the dominant hand. Radical tonsillectomy and lateral oropharyngectomy have been described for use in tumors without bone invasion, carotid involvement, prevertebral fascia invasion, or those that involve more than 50% of the tongue base.[7-9] Resection of tongue base neoplasms without the need for mandibulotomy or tracheotomy has been described with robotic surgery.[7]

Carcinoma of unknown primary origin is a challenge that may lead to increased treatment toxicities when exhaustive diagnostic efforts have failed. Transoral robotic resections of the tonsils and base of the tongue have been described as a new therapeutic and diagnostic paradigm with superior detection rates than traditional endoscopy.[10-12]

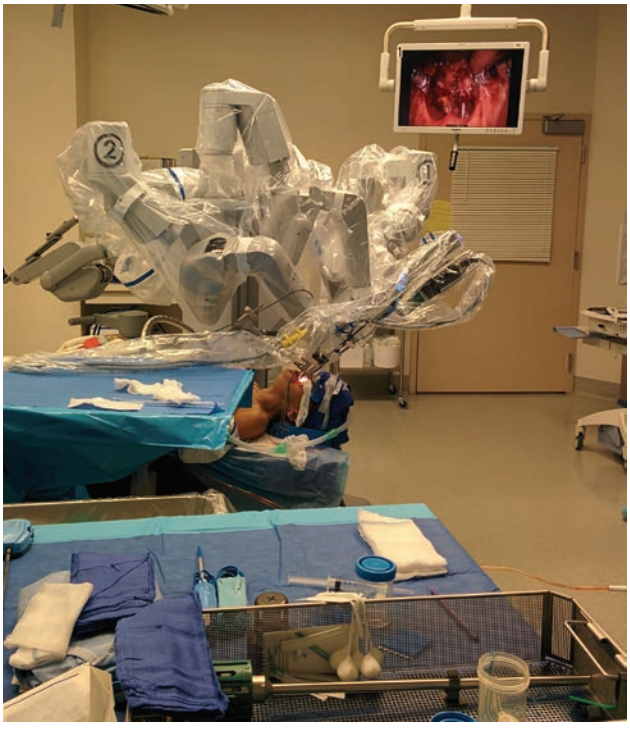

Fig. — Standard setup for transoral robotic surgery. The patient is suspended from a retractor, and the robot is positioned at a 30-degree angle to the head of the bed.

Parapharyngeal Space

Transoral robotic approaches have been used to provide direct access to the parapharyngeal space for tumors without poststyloid extension in proximity to the constrictor muscles or mucosa.[13] Although this approach may help avoid neck incisions or mandibulotomy, an increased rate of unintentional capsule violation may occur as well as pharyngeal mucosal dehiscence.[14] This can be of particular importance for recurrent pleomorphic adenomas following the transoral approach for which salvage surgery may require a wide resection of the involved mucosa, thus necessitating free-flap reconstruction.

Hypopharynx

Park et al[15] described patients with early hypopharyngeal cancer and intact vocal cord mobility who underwent transoral robotic hypopharyngectomy and had no significant complications. When TORS and conventional open surgery for hypopharyngeal cancer were compared, a trend toward improved survival rates and a significant improvement in functional outcomes were seen with TORS.[16]

Larynx

Early supraglottic and glottic larynx cancers have been removed with the surgical robotic system. The endoscope and articulating instruments of the da Vinci system can also provide the surgeon access to tumors unreachable with a CO_2 laser.[17] Transoral total laryngectomy has also been described for patients who require salvage laryngectomy to improve wound healing without violating the integrity of the strap muscles; however, prior low tracheostomy may make distal access difficult.[18]

Thyroid

Thyroidectomy can be performed with the surgical robotic system and has the added benefits of improved cosmesis, decreased sensory changes, and decreased voice and swallowing discomfort.[19] Avoiding cervical incision is possible through a transaxillary approach. However, the use of the robot for this approach is associated with increased operative times, the need for a working incision in the axilla or anterior chest wall, and the possibility of brachial plexus injuries.[20] Robotic facelift thyroidectomy offers excellent cosmetic results and relatively easier patient positioning without the significant morbidities of the transaxillary approach.[21]

Neck

Robotic selective neck dissection via the postauricular face-lift approach may be used for patients with clinically N0 tumors. Similar rates of complications and significantly improved cosmetic satisfaction rates were seen in patients undergoing the aforementioned approach compared with conventional open neck dissection.[22] Similar to robotic thyroid surgery, this procedure should be reserved for the subset of patients for whom cosmetic satisfaction is important because of its significantly increased operating time and cost.

Skull Base

Transoral robotic approaches to the skull base can be combined with endoscopic techniques to expose the posterior skull base, nasopharynx, and the infratemporal fossa.[23] The traditional endoscopic endonasal approach combined with a robotic approach complement each other due to the difficulty of endoscopic access below the hard palate and eustachian tube; in addition, the robotic system lacks a drill to remove bone.[23]

Unknown Primary Origin

Mehta et al[24] used robotic surgery in the workup of patients with unknown primary origin of head and neck cancer. They were able to identify up to 90% of primary tumors by resecting the base of the tongue following negative formal endoscopy with biopsy and tonsillectomy.[24] Using a robotic system to perform limited tongue base resection has minimal morbidity and may significantly limit the amount of radiation patients receive.

Outcomes

Functional

Definitive radiotherapy with or without chemotherapy for patients with head and neck carcinomas offers the possibility of organ preservation and obviates many of the morbidities associated with traditional surgical intervention. Organ preservation does not translate into *organ function*, which can be seen in long-term speech, swallowing, and quality-of-life scores.[25,26] Early TORS has had excellent functional outcomes.[4]

The swallowing function of most patients returns to baseline following TORS. Hurtuk et al[27] reported that all of the participants in their study returned to an oral diet on postoperative day 1. Genden et al[28] found that patients who underwent TORS had better swallowing scores 2 weeks following surgery than patients undergoing chemoradiotherapy (CRT). Twelve months after treatment, the researchers found that study volunteers assigned to the TORS group also returned to baseline function faster and had higher functional scores than those assigned to definitive CRT.[28] Moore et al[29] found that 88% of study participants returned to normal swallowing, but those who did not had advanced stage tumors and had lower preoperative function. Weintsein[30] reported that all participants in their study who had advanced oropharyngeal carcinomas returned to normal swallowing function following TORS.

The rate of gastrostomy tube dependence in patients following TORS is low compared with patients undergoing definitive CRT. Weinstein et al[30] found that patients undergoing TORS had a gastrostomy dependence rate of 2.4% following the procedure compared with rates of 9% to 38% in patients receiving CRT. Tumor stage and synchronous primaries have been correlated with the need for the placement of a gastrostomy tube prior to adjuvant treatment.[29,31]

The rate of tracheostomy dependence following TORS is low. In most cases, patients have a planned tracheostomy and are successfully decannulated.[28-30,32] The average length of time requiring tracheostomy ranges from 1.5 to 7 days.[28,29] Moore et al[29] reported that 1 patient required permanent tracheostomy, and Weinstein et al[30] reported that 2 patients underwent an unplanned tracheostomy and 1 patient required long-term tracheostomy for alcohol withdrawal.

Oncological

The oncological outcomes with TORS are excellent, but long-term follow-up has been short. Disease-specific rates are reported to be as high as 95% to 98%.[30,33] Moore et al[33] found that 17% of patients were treated with surgery alone and were able to avoid any additional adjuvant therapy. For patients with advanced-stage oropharyngeal carcinoma, Weinstein et al[30] found that 11% of patients did not require adjuvant treatment; however, the majority of patients still received definitive CRT. White et al[34] reported an overall survival rate at 2 years of 89% in a large series of patients undergoing primary TORS. All patients in the study received either adjuvant CRT or radiation alone.

An advantage to the use of TORS is the possibility of therapy deintensification, which could result in the reduced incidence of the long-term adverse events of definitive CRT. Genden et al[28] compared 30 patients undergoing TORS with a control group of 26 patients receiving CRT. Disease-free and overall survival rates at 18 months for the TORS group were 78% and 90%, respectively; the CRT group had disease-free and overall survival rates of 88% and 100%, respectively.[28] The locoregional control was comparable. Thirteen patients who, based on initial clinical staging, would have required definitive CRT had chemotherapy withheld and a reduced total radiation dose to 60 Gy. Pathological staging allowed for 24% of patients in the TORS group to avoid adjuvant chemotherapy.[28]

Future Studies

Researchers from the Radiation Therapy Oncology Group are studying TORS for the surgical intensifica-

tion of the treatment of human papillomavirus (HPV)-negative oropharyngeal tumors and the de-escalation of chemoradiation in HPV-positive oropharyngeal tumors (NCT01953952). The objective of the trial is a 15% reduction of progression-free survival in HPV-negative tumors using TORS and pathologically guided adjuvant therapy.

A trial conducted by the Eastern Cooperative Oncology Group is measuring the progression-free survival rate, locoregional recurrence, and functional outcomes of patients who are HPV positive and undergoing TORS (NCT01898494). Patients with stage N1/N2b will be observed. Those with stage 3/4 tumors undergoing TORS will be further randomized based on pathological findings. Patients with close margins, 2 to 4 positive lymph nodes, lymphovascular invasion, perineural invasion, and less than 1 mm of extracapsular spread will receive radiation doses of 50 or 60 Gy. Those with positive margins, more than 5 positive nodes, and those with more than 1 mm of extracapsular spread will receive cisplatin and a radiation dose of 66 Gy.

Conclusions

The development of robotic surgery for use in head and neck cancer has shown promising results in varied applications. The feasible use of the robotic system has been demonstrated in many aspects of head and neck surgery. Transoral robotic surgery has expanded the armamentarium of treatment modalities focused on reducing the functional deficits while also maintaining excellent oncological outcomes. Patient selection has been an important factor in initial studies as not all patients are candidates for robotic surgery.[27] Thus, the widespread adoption of the robotic system for use in patients with head and neck cancers will help clarify the indications for use of the robotic surgical system and its correlated outcomes.

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Sofía Cáceres Nazario. *African Goose*, 2015 (Detail). Acrylic on canvas, 12" × 16".

Robotic-assisted esophageal surgery is safe and feasible, but more studies are needed to assess its benefits and drawbacks.

Robotic-Assisted Esophageal Surgery

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Background: *The adoption of minimally invasive approaches to the management of esophageal disease has been slow, except for the laparoscopic management of gastroesophageal reflux disease. However, the advent of new surgical technologies — in particular, robotic-assisted surgical systems — has revolutionized esophageal surgery.*

Methods: *The literature was systematically reviewed using the keywords "robotic," "esophageal surgery," "esophagectomy," "fundoplication," and "esophageal myotomy." The reference lists from these articles were then also analyzed.*

Results: *Forty-nine studies were included in our comprehensive review of robotic-assisted esophageal surgery, and they consisted of literature reviews, case reports, retrospective and prospective case series, and randomized controlled trials.*

Conclusions: *Robotic-assisted esophageal surgery is a safe and effective way of treating esophageal disorders, including gastroesophageal reflux disease, achalasia, leiomyomas, and cancer. The use of robotic surgical systems has many benefits for managing disorders of the esophagus, but more studies, including randomized controlled trials, are necessary.*

Introduction

Surgery is a major part of esophageal pathology, and esophageal surgery is still evolving with the continuous advances seen in science and technology. Prior to the 1990s, esophageal surgery was performed through large incisions in the abdomen, the chest, or both.[1] With the advent of minimally invasive surgery (MIS), rates of morbidity and mortality related to esophageal surgery using traditional approaches were considered in part to be related to larger thoracotomy incisions, laparotomy incisions, or both. The theoretical advantages of MIS were not only "smaller incisions," but also decreased pain, decreased use of opioids, fewer complications (eg, arrhythmias), shorter hospital length of stay (LOS), shorter recovery times, and, thus, a faster return to work and other normal activities of daily living.[2-6] However, laparoscopy and thoracoscopy have drawbacks, including a 2-dimensional visual field, limited movements of instruments, and uncomfortable positioning for the surgeon. In addition, comparison of minimally invasive esophagectomy with open esophagectomy revealed higher esophagogastric anastomotic leak rates with MIS compared with the open approach.[7]

Building on the theoretical advantages of MIS,

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the use of robotic surgical systems, such as the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California), provides a 3-dimensional field of view, 7 degrees of freedom of movement with endo-wristed instruments, scaled-down movement, a 60-Hz motion filter to help eliminate tremors, and an ergonomic-seated operating position.[8-10] Although robotic-assisted surgery is relatively new, surgeons are attempting to identify its niche, including its role in surgery of the esophagus.

Fundoplication

The first robotic-assisted Nissen fundoplication was reported in 1999.[11] Following this initial report, small case series demonstrated that robotic-assisted fundoplications were safe to perform, and none of the morbidity seen was directly attributed to the use of the robotic system.[12,13] Meininger et al[14] described a robotic-assisted Nissen fundoplication in a 10-year-old girl without any change in pH, arterial oxygen pressure, arterial carbon dioxide pressure, heart rate, or mean arterial pressure, physiologically demonstrating that robotic-assisted Nissen fundoplication was a safe procedure even in the pediatric population.

The efficacy of robotic-assisted fundoplications has also been assessed for the treatment of gastroesophageal reflux disease (GERD). In a study of 9 consecutive robotic-assisted Toupet fundoplications, Wykypiel et al[15] noted that none of the study patients had symptoms of reflux 6 months following surgery. After demonstrating that robotic-assisted antireflux procedures were safe and efficacious, robotic-assisted fundoplication was then compared with the gold standard of laparoscopic fundoplication. The first such retrospective comparison was performed in Italy.[16] Average operative times were less in the robotic-assisted group (110 minutes) than those in the laparoscopic group (120 minutes).[16] The 2 groups had similar conversion rates to laparotomy, but improved morbidity rates and hospital LOS were noted in the robotic-assisted group.[16]

Following the Italian report, prospective comparison studies were performed, all of which showed that the operative times for the robotic-assisted groups were significantly longer than the laparoscopic groups.[17-19] However, Melvin et al[19] showed that robotic-assisted fundoplications might be more efficacious than laparoscopic fundoplications in the treatment of reflux disease. At the first postoperative visit, 6 of the 18 study patients (33%) from the laparoscopic group required antisecretory medications for symptoms of GERD, whereas none of the 18 of the study patients from the robotic-assisted group required further medical treatment.[19]

GERD can also be present in pediatric patients, who represent a unique population in which to study robotic-assisted fundoplication.[20] Gutt et al[21] showed that robotic-assisted fundoplication was a feasible and safe operation in children, because no conversions were made to open procedure and no complications were present in the study cohort. Another study demonstrated the efficacy of robotic-assisted Nissen fundoplication in children.[22] Following surgery, this group of 40 children had significantly decreased DeMeester scores; in addition, a significant decrease was seen in the number of study patients requiring medical treatment for reflux and asthma.[22]

The robotic surgical system also provides other specific advantages during various steps of the robotic-assisted surgical procedure. Costi et al[9] mentions some of these advantages, including easier passage behind the esophagus, better mobilization of the greater curvature of the stomach, improved suturing and knot tying, and superior visualization. Ruurda et al[23] also suggest that certain portions of fundoplication are easier with the robotic system, such as dissection behind the esophagus and suturing of the crura. The robotic system may also aid in difficult operations, such as repeat fundoplication.[24,25]

Esophageal Myotomy

Melvin et al[26] described the first case of Heller myotomy performed with the aid of a robotic system in a 76-year-old woman with achalasia, and larger studies have since reported that robotic-assisted Heller myotomy is a safe and effective treatment option for achalasia.[27,28] A multicenter, retrospective comparison of robotic-assisted and laparoscopic Heller myotomy was performed by Horgan et al.[29] Effectiveness of treating dysphagia was comparable in both groups, but a significantly decreased number of esophageal perforations were seen in the robotic-assisted group compared with the laparoscopic group (0% vs 16%, respectively).[29] Other retrospective studies have demonstrated similar results, with a 0% esophageal perforation rate in the robotic-assisted group and an 8% perforation rate in the laparoscopic group.[30,31] Iqbal et al[30] found that the robotic group also had a better long-term failure rate as judged by the lower need for reoperation. Although Huffman et al[31] demonstrated a longer average operative time in the robotic-assisted group compared with the laparoscopic group (355 vs 287 minutes, respectively), no differences were seen in the rate of estimated blood loss (EBL) and hospital LOS between the 2 groups.

The largest comparison study to date was performed by Shaligram et al[32] and included patients undergoing Heller myotomy for achalasia. The study was composed of 418 open, 2,116 laparoscopic, and 149 robotic-assisted surgical cases.[32] When comparing the robotic-assisted and laparoscopic groups, no significant differences were seen in mortality, morbid-

ity, admission rate to the intensive care unit, hospital LOS, or 30-day readmission rates.[32] The robotic-assisted operation was superior to the open technique in terms of morbidity, admission rate to the intensive care unit, and hospital LOS; however, hospital costs associated with the robotic-assisted group were significantly higher compared with the laparoscopy group ($9,415 ± 5,515 vs $7,441 ± 7,897; $P = .003$).[32] It is worth noting that the cost of hospitalization associated with the robotic-assisted group was not increased compared with the open group, as was initially expected.[32]

Esophagectomy

Surgical resection remains a key component of the multimodality treatments for esophageal cancer. However, esophagectomies — despite the type of approach employed — have been associated with high morbidity and mortality rates (60% and 14%, respectively),[33] although 1 series reports mortality rates to be as low as 4%.[34]

Minimally invasive esophagectomy was introduced and popularized by Luketich et al.[35] As surgical techniques have evolved, surgeons have begun to employ robotic assistance for esophagectomy. Initially, the robotic system was employed for thoracic dissection of the esophagus and was shown to be feasible but time consuming, with an average robotic-assisted time of 174 minutes, and, notably, the authors commented on the ability to achieve a thorough lymphadenectomy using the robotic system.[36] Another study demonstrated similar median time required for robotic-assisted thoracic esophageal dissection.[37]

As robotic technology becomes more popular, surgeons will begin to utilize it during additional steps and for other approaches to esophagectomy. Kernstine et al[38] reported their experience using a robotic system in thoracic dissection as well as in the abdominal portion of a 3-field esophagectomy and lymphadenectomy. However, they noted long mean operative and robotic-assisted times in this initial experience (11.1 and 5.0 hours, respectively).[38]

de la Fuente et al[39] published in 2013 the initial experience of robotic-assisted Ivor–Lewis esophagectomy at the H. Lee Moffitt Cancer Center & Research Institute (Tampa, Florida). The series included 50 study patients who all underwent the operation following a diagnosis of cancer.[39] All study patients received an R0 resection, and an average of 20 lymph nodes were removed.[39] Of the 50 study patients, 28% experienced a complication (the most common of which was atrial fibrillation), 1 study patient had an anastomotic leak, and 1 study patient had a gastric conduit staple-line leak.[39] The median hospital LOS was 9 days, and the average operating time was 445 minutes.[39] de la Fuente et al[39] demonstrated that a learning curve exists for the procedure, as the second half of their cases took less time than the first half (410 vs 479 minutes, respectively).

Regarding the learning curve involved with robotic-assisted esophagectomy, Hernandez et al[40] demonstrated that proficiency in performing the procedure appears to begin after 20 cases. This group recently updated their series, which now has 134 study patients, and found that study patients 70 years of age or older did not have increased median operative room time.[41] They also had lower rates of EBL, adverse events (including pneumonia, cardiac/arrhythmia, deep venous thrombosis/pulmonary embolus, wound infection, or anastomotic leak), decreased rates of intensive care unit and hospital LOS, and decreased mortality following robotic-assisted Ivor–Lewis esophagectomy.[41]

Other groups have also reported using robotic assistance during transhiatal esophagectomies.[42-44] One such study reported on 40 study patients who underwent robotic-assisted transhiatal esophagectomy.[43] The median operative time was 311 minutes and the median hospital LOS was 9 days.[43] This group accomplished an R0 resection in 95% of their study patients.[43] Recurrent laryngeal nerve paresis and anastomotic leak rates were 35% and 25%, respectively, which are higher than those reported in the literature.[43]

Coker et al[44] described a cohort of 23 study patients who underwent robotic-assisted transhiatal esophagectomy, 19 of whom had neoadjuvant chemoradiation. The results of this study showed that the robotic system could be safely and effectively used after patients underwent neoadjuvant therapy, which has now become an integral part of the treatment of locally advanced esophageal cancer.[44] Of note, this robotic-assisted transhiatal approach has also been validated in patients considered too ill to undergo single-lung ventilation, as would be necessary in the Ivor–Lewis approach.[45]

Cerfolio et al[46] demonstrated that a completely hand-sewn esophagogastric anastomosis in the chest with robotic assistance is feasible and safe. During that study, no anastomotic leaks occurred in their cohort of 16 patients.[46] Comparison studies for robotic-assisted esophagectomy are lacking at this time, but prospective, randomized controlled trials are actively accruing.[47]

Other Esophageal Pathology Treated With Robotic-Assisted Resection

Although the robotic system has been used to treat common esophageal pathology, this surgical system has also become a tool in the treatment of less-prevalent esophageal disease. For example, many case reports and small series of robotic-assisted enucleation of esophageal leiomyomas can now be found in the literature.[23,37,48-52] Although these tumors reside in the submucosa of the esophagus, resecting them requires

careful dissection of the muscular layers without perforating the mucosa. Surgeons have noted that the superior vision and dexterity provided by the robot allows for meticulous dissection and minimizes perforation during extirpation.[48]

Other rare esophageal pathology can include esophageal diverticula, for which case reports of robotic-assisted transhiatal esophageal diverticulectomies alone (for epiphrenic diverticulum) have been reported to date.[53,54] Robotic-assisted esophageal metastasectomy for primary hepatocellular carcinoma has also been reported.[55]

Discussion

Esophageal surgery has undergone a revolution from the days of large, morbid incisions in the chest and abdomen and now includes the option for MIS. The first attempts at MIS of the esophagus with laparoscopy and thoracoscopy showed benefits compared with the traditional open approaches, including lower mortality rates and shorter hospital LOS.[2-6] Although these new techniques seemed to benefit the patients, many drawbacks were evident, such as 2-dimensional vision and the limited movement of instruments.

Robotic surgical technology became popularized for general surgery after the US Food and Drug Administration approved the da Vinci Surgical System in 2000.[56] The robotic-assisted approach to surgery still affords the same benefits as laparoscopy and thoracoscopy, including small incisions, while also adding improvements, such as a high-definition, 3-dimensional view, articulating instruments, and tremor filtration.[57] Because the robotic system could be used for delicate surgery in small spaces, robotic-assisted procedures have become important for esophageal surgery.

Early on, the robotic system was shown to be safe and efficacious for esophageal surgery. However, when compared with laparoscopic fundoplication in early studies, the robotic groups tended to require longer operative times. It should be mentioned that most of the studies included in our review had fewer than 25 study volunteers and may have been the first robotic-assisted esophageal procedures performed by the respective surgeons. This qualification is important to keep in mind, because many reports have since demonstrated a learning curve associated with robotic-assisted esophageal surgery.[9,16,40,46,58] In fact, when Costi et al[9] compared the first robotic-assisted Nissen fundoplications performed by Cadiére et al[13] to their first 80 laparoscopic Nissen fundoplications, they found no difference in operative time. Therefore, the increased operative time shown in these early studies may be a reflection of each surgeon becoming accustomed to the new robotic-assisted surgical technology. However, subjecting patients to longer operations performed with robotic assistance without any obvious improved patient outcomes may not be justified.

Furthermore, aside from the multiple technical benefits afforded by the robotic system, some studies have shown that outcomes in study volunteers undergoing robotic-assisted procedures may be superior to the outcomes seen in study volunteers undergoing laparoscopic procedures. For example, Melvin et al[19] described how none of the study patients in his trial required antireflux medication following robotic-assisted fundoplication compared with 6 study patients in the laparoscopic cohort who still required medication. In addition, several studies have demonstrated a lower esophageal perforation rate following robotic-assisted Heller myotomy compared with the laparoscopic approach.[29-31] Although these results are promising, more studies are needed to better establish the advantages of robotic-assisted esophageal surgery when compared with other minimally invasive approaches.

Another criticism of robotic surgery is its increased cost. Robotic instruments used during fundoplication can cost 55% more than those used for traditional laparoscopic fundoplication.[9] However, robotic technology is relatively new and not yet widely adopted. It is possible that, with an increased supply and competition between manufacturers, cost for robotic surgical systems could decrease in the future. However, it is important to note — particularly given the present state of the US health care system — that using more costly techniques like robotic-assisted esophageal surgery without any definitive patient benefit may not be economical at the present time.

Conclusions

Robotic-assisted esophageal surgery is a young field, but its application continues to expand. Although a paucity of literature currently exists, the overall use of robotic-assisted surgical systems for esophageal surgery is associated with benefits and drawbacks. As the field expands and surgeons become comfortable with the technology, robotic-assisted surgical systems may improve the technical aspects of esophageal surgery as well as patient outcomes in the not-too-distant future.

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Sofía Cáceres Nazario. *Zinnia*, 2015 (Detail). Acrylic on canvas, 16" × 12".

The robotic Whipple procedure is a minimally invasive option for resectable pancreatic cancer and other tumors of the pancreas head, distal common bile duct, and ampulla.

Robotic Whipple Procedure for Pancreatic Cancer: The Moffitt Cancer Center Pathway

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Background: *Resection of malignancies in the head and uncinate process of the pancreas (Whipple procedure) using a robotic approach is emerging as a surgical option. Although several case series of the robotic Whipple procedure have been reported, detailed descriptions of operative techniques and a clear pathway for adopting this technology are lacking.*
Methods: *We present a focused review of the procedure as it applies to pancreatic cancer and describe our clinical pathway for the robotic Whipple procedure used in pancreatic cancer and review the outcomes of our early experience. A systematic review of the literature is provided, focusing on the indications, variations in surgical techniques, complications, and oncological results of the robotic Whipple procedure.*
Results: *A clinical pathway has been defined for preoperative training of surgeons, the requirements for hospital privileges, patient selection, and surgical techniques for the robotic Whipple procedure. The robotic technique for managing malignant lesions of the pancreas head is safe when following well-established guidelines for adopting the technology. Preliminary data demonstrate that perioperative convalescence may exceed end points when compared with the open technique.*
Conclusions: *The robotic Whipple procedure is a minimally invasive approach for select patients as part of multidisciplinary management of periampullary lesions in tertiary centers where clinicians have developed robotic surgical programs. Prospective trials are needed to define the short- and long-term benefits of the robotic Whipple procedure.*

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Introduction

Pancreatic cancer has a dismal prognosis, with annual incidence and mortality rates that are nearly equal. In 2015, nearly 49,000 Americans will be diagnosed with pancreatic cancer and 40,500 will die from the disease.[1] For the minority of patients amenable to resection at diagnosis, tumor extirpation remains the single opportunity for cure. Resection for these patients is technically demanding and fraught with intraoperative and postoperative challenges. Although the mortality rate associated with the Whipple procedure is less than 2%, the morbidity rate generally approaches 40%, even in most high-volume centers.[2]

Much of the morbidity following the Whipple procedure is secondary to the invasive nature of the operation.[2] With a large abdominal incision, patients can

have complications such as poor pulmonary function, which can lead to pneumonia.[2] In addition, due to significant intraoperative stress, patients may experience cardiac events due to fluid shifts or adrenergic demand. In the postoperative setting, surgical site infection continues to be challenging, with up to 7% of patients having a wound complication.[2] These complications may also induce stress in patients and clinicians at a time when the malignant diagnosis is still fresh in their minds. With this in mind, the identification of minimally invasive surgical techniques that can mitigate some of the physiological challenges — and, thus, morbidity — of this procedure has come to the forefront.

Prior Experience

The first report of the Whipple procedure using robotic technology was published in 2003 as part of a description about early experience with general robotic surgery by Giulianotti et al.[3] In 2011, Zureikat et al[4] published the first article dedicated to outcomes for pancreatic resection. In that report, they described 30 pancreatic operations that took place between 2008 and 2010; of those, 24 were the Whipple procedure, 4 were central pancreatectomies, and 2 were Frey procedures.[4] Initial mobilization was performed using laparoscopic techniques for some of the cases, but the resections and reconstructions were performed using the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California), and the anastomotic techniques were identical to the open approach — a fact that allows for outcome comparison.[4]

The outcomes from this early experience were encouraging. Of those undergoing the robotic Whipple procedure, the overall pancreatic leak rate was 21% (5 of 24); the majority was subclinical or grade A.[4] The overall rate of morbidity was 25% for the robotic Whipple procedure cohort and defined by Clavien–Dindo grade 3/4 complications.[4] The report focused on the safety of the robotic approach; therefore, direct benefits of the approach were not reported. Morbidity and mortality were confirmed as being noninferior to other reports of open pancreatic resection.[4]

An early report on outcome comparisons between the robotic Whipple procedure and the open Whipple procedure was published in 2012 from Lai et al.[5] Between the years 2000 and 2012, a total of 20 study patients underwent the robotic Whipple procedure and 67 underwent the open Whipple procedure.[5] End points for the comparison between groups included operative time, hospital length of stay, estimated blood loss (EBL), complication rate, perioperative mortality rate, R0 resection rate, and lymph-node harvest.[5] The group found that the study patients had decreased length of stay and EBL, but these came at the cost of increased operative time. No quality-of-life end points were used, and no conclusions could be drawn about direct patient benefits from the robotic approach.[5]

Several other experiences with pancreatic resection have since been reported,[5-12] but, to date, Zureikat et al[13] from the University of Pittsburgh has published the most recent and largest report. Of the 250 pancreatic resections completed, the authors described the outcomes for 132 robotic pancreaticoduodenectomies.[13] They found that the procedure was safe with a 30-day mortality rate of 0.8%, and 21% of their study patients experienced a Clavien–Dindo grade 3/4 complication.[13] In terms of pancreatic leak, the authors reported a total incidence of 22%, with the majority (53%) described as grade A.[13] The most common complication was fluid collection (38%), of which one-half was the result of a pancreatic leak.[13] Zureikat et al[13] also focused on feasibility in terms of conversion rate and readmission for groups seeking to expand the use of the robotic platform for the Whipple procedure. Their conversion rate was noted to be 8% and their readmission rate was 28%.[13] Both of these values suggest that the platform could be adopted at other institutions.

Benefits

Surgeons have sought to mitigate some of the complications related to pancreaticoduodenectomies through rapid advances in the field of minimally invasive surgery. Many benefits of minimally invasive surgery have been attributed to smaller incisions compared with open tumor resection. Although some of these benefits are directly related to the wounds (ie, decreased incidence of wound infection and postoperative hernia formation), many are related to the decreased intraoperative stress response.[14-16] Intuitively, these benefits are greatest for resections with significant open morbidity, such as the Whipple procedure, and, for this reason, many high-volume centers have turned toward minimally invasive approaches for this operation.

The initial experience with a minimally invasive approach to the Whipple procedure was primarily focused on the laparoscopic approach. One early international report demonstrated acceptable rates of morbidity (31%) and mortality (2%).[17] It is unclear where the cases described fell on the learning curve of the operation because there were no conversions to open resection.[17] A domestic cohort study reported favorable outcomes such as decreased length of stay and intraoperative tranfusions associated with the laparoscopic approach.[18] However, these benefits were mitigated by increased operative time.[18]

Although many benefits have been ascribed to the minimally invasive surgical approach, the technical difficulties of this operation have been highlighted by the adoption of the laparoscopic approach that has, in turn, prevented the wide-

spread adoption of this technique. The ideal minimally invasive approach to the Whipple procedure must be easily reproduced and adopted by surgeons who currently perform open resections. However, the laparoscopic approach did not meet this criterion and, thus, adoption has been generally poor.[17,18]

The robotic Whipple procedure has many benefits for both the patient and the surgeon. For the patient, the benefits previously discussed are all relevant. During resection, there is less insensible loss of fluid and manipulation of viscera through retraction, thus leading to less stress to the patient with fluid shifts and amount of medications to maintain general anesthesia. The use of smaller incisions means that patients have decreased incision-related morbidity, and, with less pain, postoperative pulmonary complications.

The benefits to the surgeon are equally demonstrable. The robotic platform is an advanced device and, like any other surgical instrument, increases the natural human ability of manual tasks in a way that no other device has achieved to this point. Performing fine dissection of crucial planes during oncological resections is fundamental to an open operation and the ease with which this can be accomplished on the robotic platform is beneficial to both the surgeon and the patient. Another benefit is the general ergonomics to the surgeon that an open resection cannot provide.

It is also worth noting that patients seek innovators, so the ability to utilize the newest technology drives referrals for resection. As multidisciplinary robotic programs are developed in tertiary centers the complication rates for these procedures should decrease over time.

Approach at the Moffitt Cancer Center

The pathway for patients with pancreatic cancer at our institution, the H. Lee Moffitt Cancer Center & Research Institute (Tampa, Florida), follows 6 key steps: (1) diagnosis, (2) staging, (3) fitness for surgery, (4) resection, (5) adjuvant therapy, and (6) surveillance. At each point along this course, the decision to proceed is predicated by the performance status and disease burden of the patient (Appendix A).[19] With this methodical approach to care, all patients have multiple points of evaluation for resection during their course of treatment.

As a referral center, most patients present to Moffitt Cancer Center with a diagnosis of pancreatic cancer. Following a review of the patient's external medical records, a medical oncologist or surgical oncologist, depending on the presumed extent of disease, sees the patient. All patients presumed to be candidates for resection are seen by a surgeon. After the patient's initial visit with a Moffitt Cancer Center physician, the pathological diagnosis is reviewed and confirmed from the original slides. Discussion of all patients then takes place during the multidisciplinary tumor board, which is composed of medical oncologists, radiation oncologists, radiologists, pathologists, gastroenterologists, and surgeons, at which point the patients are subdivided into 4 categories: (1) resectable disease, (2) borderline resectable disease, (3) unresectable disease, or (4) further evaluation needed. This classification is based on guidelines from the National Comprehensive Cancer Network and from consensus opinion of all faculty members present.[19,20]

Patients with resectable disease fit for an operation proceed to the required surgical procedure after preoperative cardiopulmonary evaluation (Appendix B). Those who have borderline resectable disease are treated with neoadjuvant chemoradiation, which includes initially gemcitabine, docetaxel, and capecitabine and then either stereotactic body radiation therapy or intensity-modulated radiation therapy with concomitant fluorouracil.[20] Following chemoradiation, patients are restaged with positron emission tomography and pancreas-protocol computed tomography. If the disease is resectable, then the patients proceed to the required surgical procedure. Those with progression or response not amenable to resection receive further systemic chemotherapy. Patients with locally advanced disease are recommended a systemic chemotherapy regimen according to performance status. The initial radiographic findings are reviewed.

Patient Selection

Appropriate patient selection for the robotic Whipple procedure is based on the characteristics of the patient and of the tumor. For patients, the most important characteristic is their fitness for general anesthesia. All patients undergoing the Whipple procedure for pancreatic cancer at Moffitt Cancer Center undergo preoperative cardiopulmonary evaluation, which is particularly important for the robotic approach because of the increased operative time — much of it spent in the reverse Trendelenburg position. Relative exclusion criteria for the robotic approach include prior intra-abdominal surgery, major abdominal wall reconstruction surgery, and a body mass index (BMI) greater than 30 kg/m^2. At this point prior chemoradiation directed to the pancreas remains a strong contraindication for the robotic approach.

Patients with a low volume of disease and no evidence of borderline characteristics, as defined by National Comprehensive Cancer Network criteria, are offered the option of robotic surgery.[19,20] Dilated biliary and pancreatic ducts facilitate the technical aspects of the ablative and reconstructive steps of the procedure and minimize the risk of complications. Specific diagnoses for which we offer the robotic Whipple proce-

dure at Moffitt Cancer Center include adenocarcinoma, pancreatic neuroendocrine tumors, duodenal cancers, bile duct cancers, periampullary cancers, cystic neoplasms of the pancreas, periampullary adenoma, and islet cell neoplasms.

Initial Operative Principles

Robotic assistance during surgery for the management of pancreatic cancer at Moffitt Cancer Center is based on the fundamental principles of surgical practice and ethics. The perioperative management involves a team of surgeons, nurses, nurse practitioners, and training staff dedicated to this procedure. During the operation, 2 surgeons are involved, along with either a complex general surgical oncology fellow or a general surgery resident. All patients receive mechanical bowel preparation with oral antibiotics and are offered an epidural catheter for pain control.

The robotic procedure is performed with the same sequence of technical maneuvers as are utilized in the open procedure. This is important for several reasons. Doing so helps us understand and compare the outcomes between both modalities. In addition, it allows the surgical team to troubleshoot, understand, and further improve the flow of the procedure. The surgeon is able to offer the open or robotic Whipple procedure to the patient while explaining that both procedures are performed in the same fashion.

A preliminary timeout is performed prior to the induction of general anesthesia and the patient is then positioned as illustrated in Fig 1. Patient positioning is performed in collaboration with the anesthesia team, with an emphasis on safety of pressure points. Special care is taken to ensure that the face, eyes, and airway are protected to prevent injury, focusing on any potential dislodgment of the endotracheal tube when docking the robot. The right arm is tucked and the left arm is left abducted for access by the anesthesia team. Once the patient is draped and all instruments are counted, a second timeout is performed with the surgeon. At that time, the team discusses the operative plan, thus following the World Health Organization timeout protocol.[21] Special emphasis is placed on the importance of communication during the procedure. The risk of bleeding during the dissection of the pancreatic head and uncinate process from the vessels is underscored. The surgeon also reviews the steps required to expeditiously convert to an open procedure in the event of uncontrolled blood loss. All instruments required for the open resection are confirmed to be available in the room during the timeout.

Initial entry to the peritoneal cavity depends on the dimensions of the patient's abdomen. The characteristics of the patient and location of the tumor allow for appropriate modification to safely and efficiently achieve the goals of the procedure (Fig 2). The procedure begins with a 3-cm midline incision in the infraumbilical position. A Veress needle is used to enter the peritoneal cavity and is confirmed by aspiration and the saline drop test in patients with no prior abdominal operations. The open Hasson technique is used for patient with prior abdominal operations. Insufflation is then initiated at low flow and an initial pressure below 10 mm Hg is targeted. After obtaining pneumoperitoneum, a 12-mm port is then placed into this incision through which an 8-mm robotic port is placed. The remaining ports include a 12-mm port for the camera to

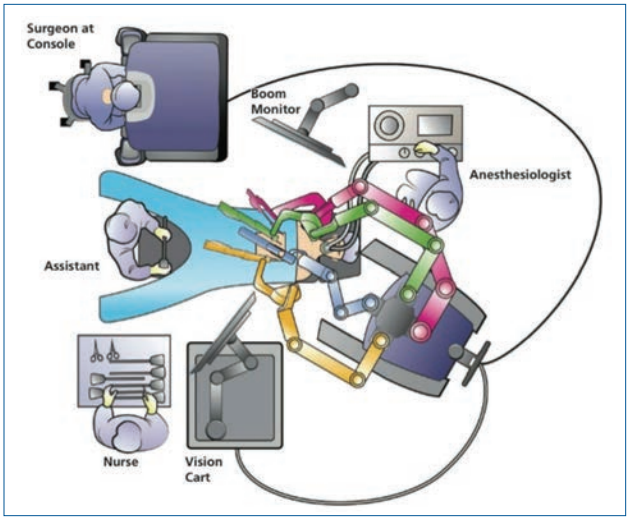

Fig 1. — da Vinci operating room schematic. © 2014 Intuitive Surgical, Inc. Used with permission.

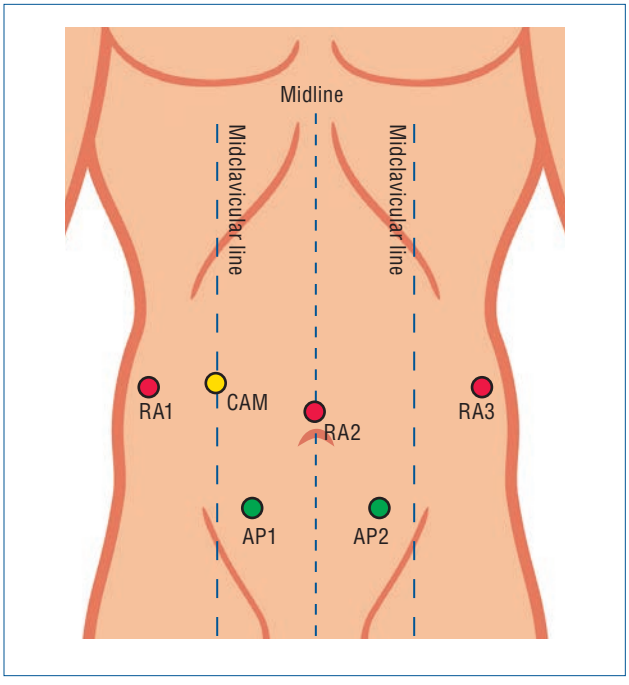

Fig 2. — Placement of ports for robotic Whipple procedure. Note: Keep a minimum of approximately 10 cm between all ports to space da Vinci (Intuitive Surgical, Sunnyvale, CA) arms appropriately to reach all anatomy. AP1 and AP2 = assistant ports, CAM = camera port, RA1 = robotic arm labeled No. 1, RA2 = robotic arm labeled No. 2, RA3 = robotic arm labeled No. 3.

the right of the umbilicus in the midclavicular line, an 8-mm port lateral and superior to that camera port at the right anterior axillary line, an 8-mm port superior to the umbilicus at the left anterior axillary line, and a 12-mm port to the right of and inferior to the umbilicus, approximately 8 cm between the camera and periumbilical port (see Fig 2). The surgeon explores the abdomen with the camera before docking the robot to determine if any obvious evidence of metastatic disease is present. At this time, the patient is placed in a reverse Trendelenburg position, the robot is brought into position, all arms are docked, and the instruments are inserted. Positioning precautions in collaboration with anesthesia are confirmed after the robot has been docked.

Ablative Steps

The ablative steps in the robotic Whipple procedure follow the same principles as the open procedure. The falciform ligament is divided from the anterior abdominal wall using the robotic vessel sealer. The gallbladder fundus is then sutured to the anterior abdominal wall (Fig 3). The second surgeon utilizes the assistant port to provide gentle, deliberate traction as needed, utilizing the suction irrigator and is in constant communication with the surgeon at the console. The gastrocolic ligament is incised with the vessel sealer to gain access to the lesser sac proximal to the planned point of gastric transection, with care not to injure the gastroepiploic vessels, short gastric, or transverse colon mesentery (Fig 4).

The dissection is then proximally carried along the transverse colon to complete a Cattell–Braasch maneuver. Attention is then turned to an extended Kocher maneuver that ends with division of the ligament of Treitz from the right side (Fig 5). Doing so results in the delivery of the proximal jejunum to the right upper quadrant — colloquially called the "ah-ha moment" (Figs 6–8). Potential pitfalls at this point include injury to the gastroepiploic vessels, colonic mesenteric vessels, duodenum, inferior vena cava, or the inferior mesenteric vein. The proximal and distal ends of the jejunum are marked with silk suture in preparation for future gastrojejunostomy. The proximal jejunum 10 cm from ligament of Trietz is divided with a stapler (see Fig 8), and the mesentery is divided proximally along the bowel wall, avoiding injuries to the superior mesenteric vein.

Attention is then turned to the safe transection and dissection of the pancreas from the surrounding ves-

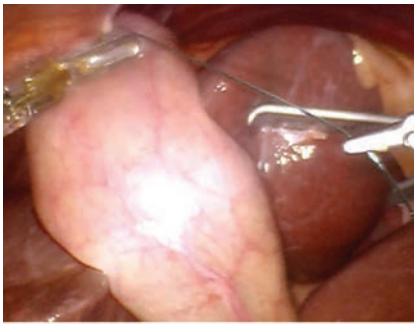

Fig 3. — Exposure is achieved by taking down the falciform ligament, placing a liver retractor under the left lobe, and tacking the gallbladder to the abdominal wall.

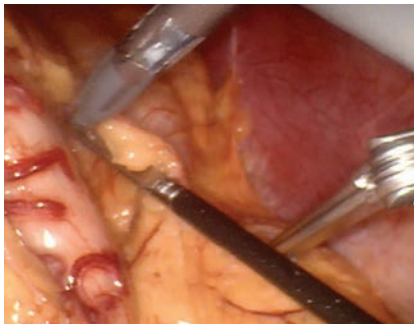

Fig 4. — The lesser sac is entered by incising the gastrocolic ligament in the avascular plane, the dissection is carried to the planned resection plane on the stomach, and then distally toward the duodenum.

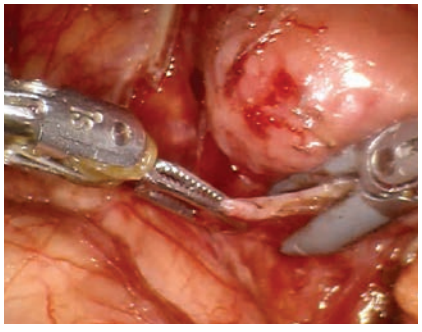

Fig 5. — The Kocher maneuver is performed by an extended mobilization of the duodenum from its retroperitoneal attachment to the ligament of Treitz, with care not to injure the duodenum or retroperitoneal structures.

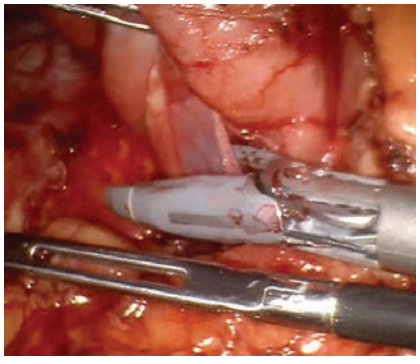

Fig 6. — The ligament of Treitz is transected with care not to injure the inferior mesenteric vein. At this point, the "ah ha" moment is reached when the proximal jejunum begins to fall into the field through the defect.

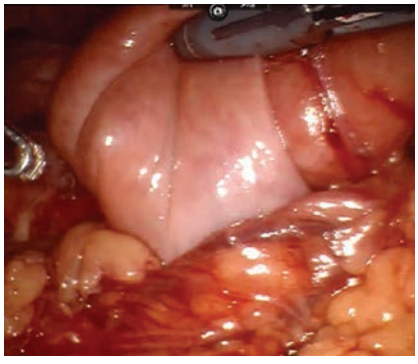

Fig 7. — The proximal jejunum is brought into the field retrograde through the transected ligament of Treitz defect.

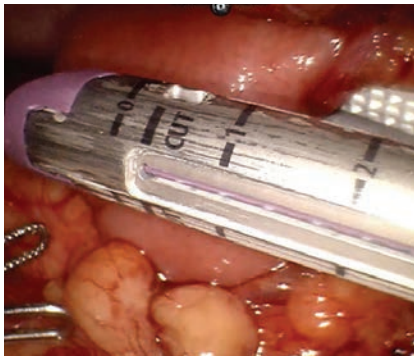

Fig 8. — The jejunum is transected with the robotic stapler and the bowel is marked with a silk suture.

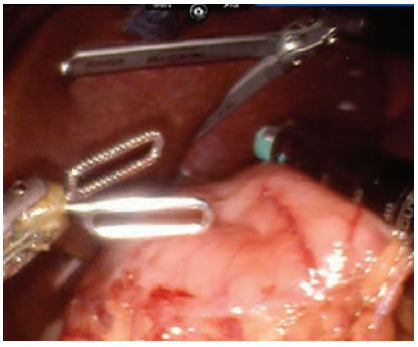

Fig 9. — The stomach is transected to include the entire antrum in the specimen using the robotic stapler.

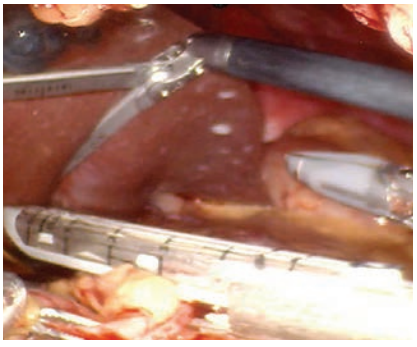

Fig 10. — The right gastric pedicle is transected with the vascular-loaded robotic stapler.

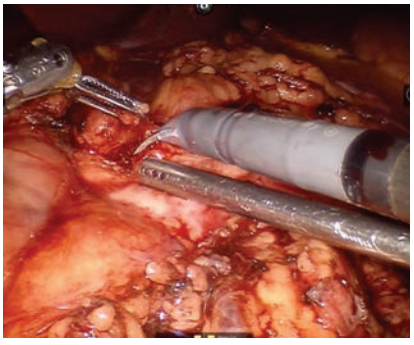

Fig 11. — The superior neck of the pancreas lymph node is dissected with the monopolar-curved robotic scissors and sent for pathology.

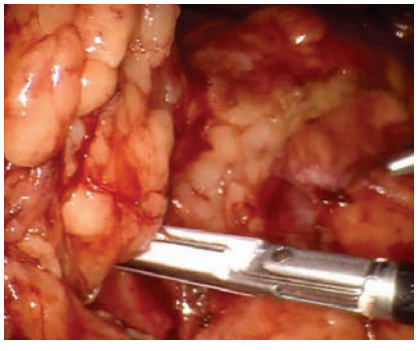

Fig 12. — The right gastroepiploic vessels are transected with bipolar robotic forceps.

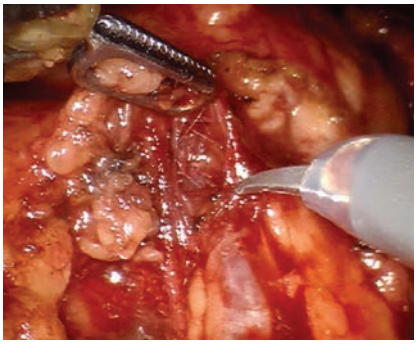

Fig 13. — The inferior edge of the pancreas is dissected with monopolar-curved robotic scissors.

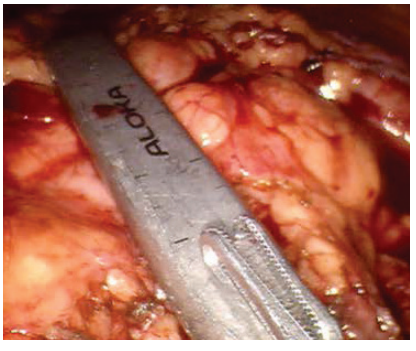

Fig 14. — Robotic-assisted ultrasonography is used to confirm the locations of the portal vein, pancreatic duct, and superior mesenteric artery.

sels. First, the stomach is transected between the body and the antrum using the robotic stapler (Fig 9), and then the right gastroepiploic vessels and right gastric vascular pedicle are transected (Fig 10). Next, the dissection of the porta hepatis superior to the neck of the pancreas begins; the hepatic artery lymph node is removed and sent to pathology for a permanent section (Fig 11). The portal vein, hepatic artery, and gastroduodenal artery are identified after meticulous dissection (Figs 12 and 13). Intraperitoneal ultrasonography helps to confirm the location and trajectory of the portal vein posterior to the pancreatic neck, which is critical for a safe and subsequent dissection (Figs 14 and 15). The superior mesenteric vein is identified inferior the pancreas, and a tunnel is then developed posterior to the neck of the pancreas, thereby connecting the previous porta hepatis dissection (Fig 16).

Extreme caution is taken because bleeding caused by an injury to the portal vein or avulsion of a portal venous branch can be life threatening. Communication between the surgical and anesthesia teams is critical prior to initiating this dissection so as to ensure that preparations are made for an expeditious conversion to laparotomy if necessary. The surgical assistant is critical to the dissection because he or she uses the laparoscopic suction irrigator to assist with exposure and the application of direct pressure to control bleeding. Should bleeding occur during the vascular dissection, the surgeon can return to the sterile field from the console while the instruments control the hemorrhage. This effectively locks the instrument in a hemostatic position and allows time to prepare for definitive repair. Hemostatic clips may also be used for quick, temporary control with subsequent suture repair after hemostasis is obtained.

After the tunnel is created anterior to the portal vein, the neck of the pancreas is transected with the robotic scissors attached to the monopolar cautery. The gastroduodenal artery is then transected with a vascular stapler after confirming pulsatile in the proper hepatic artery (Fig 17). The dissection is then carried laterally to include the porta hepatis and mobilize the bile duct. The remainder of the pancreatic head and uncinate process are then mobilized from the portal vein and superior mesenteric vein by ligating the venous branches, followed by dissection of the superior mesenteric artery and dissection of the arterial branches (Figs 18 and 19). The final retroperitoneal attachments are transected and the distal common bile duct is transected (Figs 20–22). The gallbladder is dissected from the liver bed and the cystic duct and artery are transected with robotic staplers (Fig 23). Hemostasis is confirmed and the specimen is removed from the periumbilical incision using the EndoCatch (Covidien,

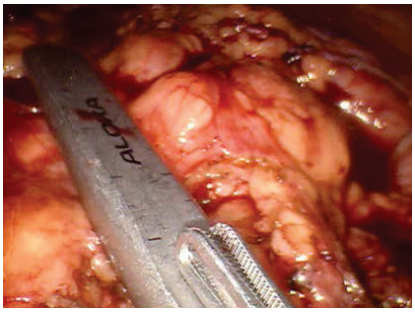

Fig 15. — Robotic-assisted ultrasonography is used to confirm the location of the tumor in relation to the planned resection margin.

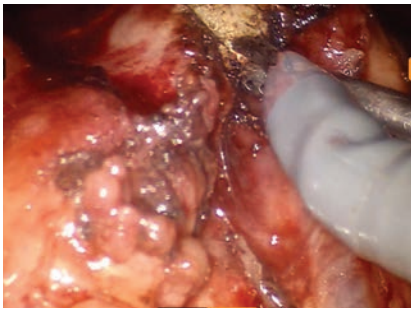

Fig 16. — The tunnel is developed under the neck of the pancreas, and the parenchyma is transected with the monopolar-curved robotic scissors.

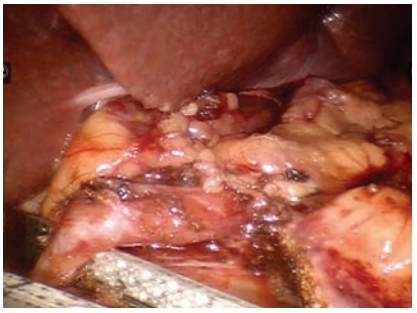

Fig 17. — The gastroduodenal artery is transected with the vascular load of the robotic stapler.

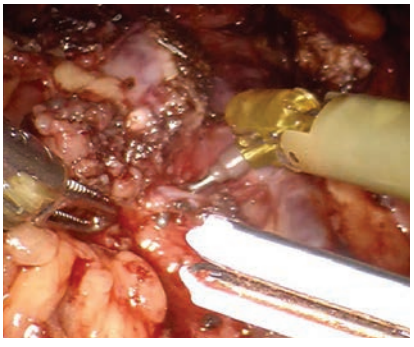

Fig 18. — The uncinate process is dissected off of the portal vein, and the venous branches are isolated with the robotic cautery hook and transected with bipolar forceps.

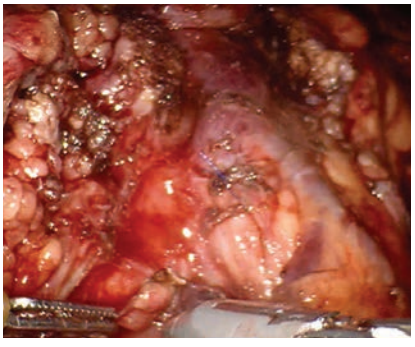

Fig 19. — The branches of the superior mesenteric artery to the pancreas are transected with the vessel sealer.

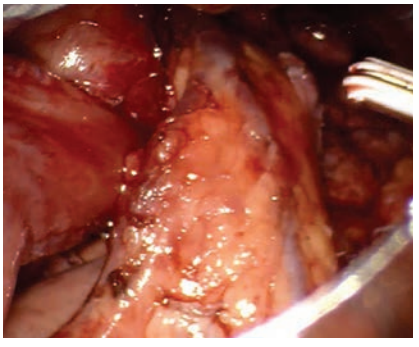

Fig 20. — The Whipple specimen is laterally retracted to facilitate identification and dissection of the remaining retroperitoneal margin.

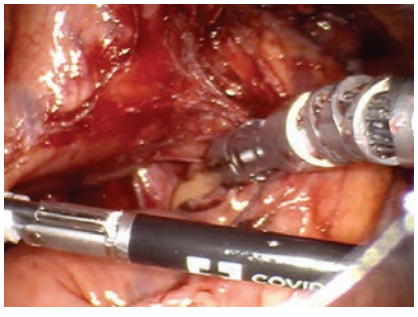

Fig 21. — The retroperitoneal margin is dissected with the robotic vessel sealer.

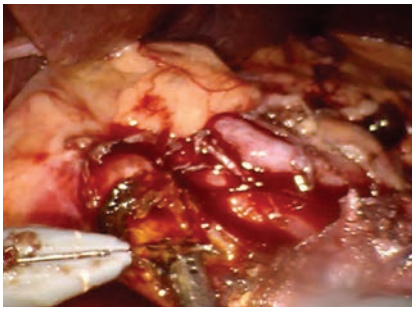

Fig 22. — The distal common bile duct is transected with the robotic monopolar-curved scissors.

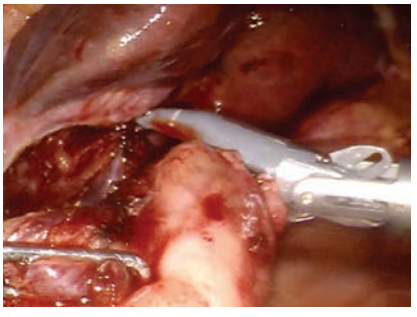

Fig 23. — Cholecystectomy is performed using the robotic vessel sealer to transect the cystic artery.

New Haven, New Jersey) device. It is marked for frozen section analysis of the margins and final pathology. Sutures are placed that will ultimately close the fascia; however, the sutures are not tied so as to allow for the continued use of the port for future reconstruction.

Reconstructive Steps

The techniques used for pancreaticobiliary anastomoses are the same for both the open and robotic Whipple procedure. The extended umbilical incision is reduced with a small wound protector and the 12-mm port is secured in place and pneumoperitonuem is achieved. The ports are placed in the same configuration for the reconstruction. The jejunum, which was previously marked with a suture, is inspected to confirm viability, orientation, or undue tension. A 2-layer, end-to-side pancreatic jejunostomy is created in the classically described duct-to-mucosa fashion. The running imbricating posterior outer layer is carefully placed so as to avoid injuring the portal vein and the main pancreatic duct (Fig 24). The duct-to-mucosa is fashioned using interrupted 4-0 dyed and undyed polyglactin 910 suture (Fig 25). Alternating dyed and undyed surtures helps orientate the surgeon. The first suture is placed in the 12-o'clock position into the pancreatic parenchyma, which is then anteriorly retracted to help with orientation and identification of the duct.

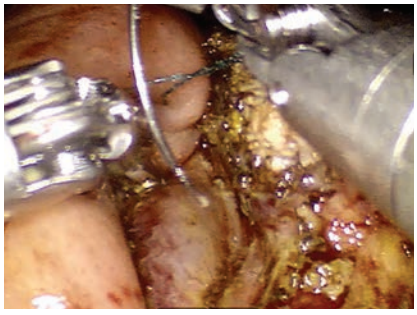

Fig 24. — The posterior outer layer of the pancreaticojejunostomy is performed with a V-Loc (Covidien, Mansfield, MA) suture.

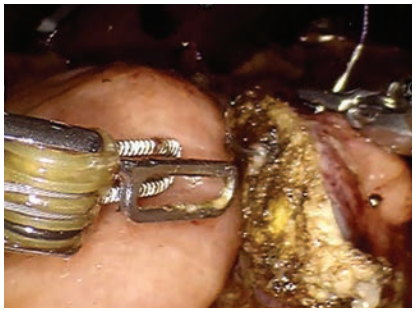

Fig 25. — The inner duct to the mucosa layer of the pancreaticojejunostomy is started at the 12-o'clock position using a polyglactin 910 suture.

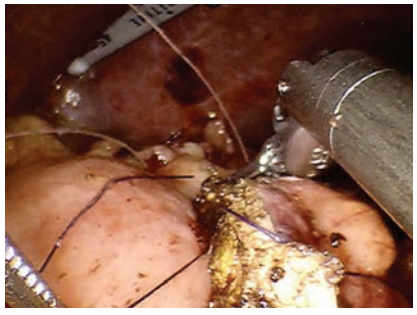

Fig 26. — The knots of the inner duct to mucosa layer are tied in line with the plane of the pancreaticojejunostomy to lay flat without tension or trauma to the delicate tissue.

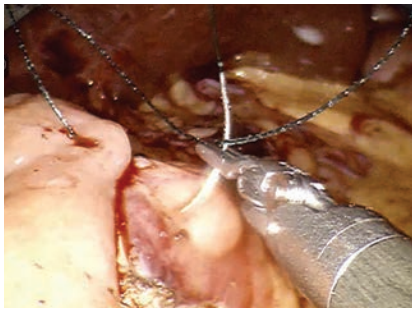

Fig 27. — The outer anterior layer of the pancreaticojejunostomy is performed with a V-Loc (Covidien, Mansfield, MA) suture.

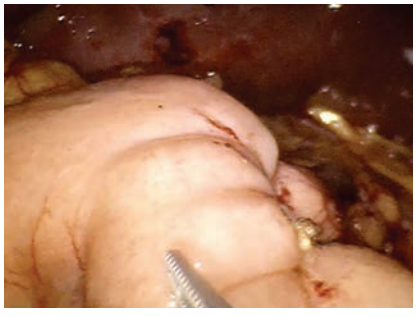

Fig 28. — Completion of the pancreaticojejunostomy demonstrates a viable, tension-free anastomosis without leak.

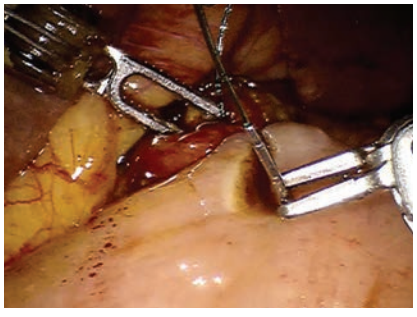

Fig 29. — Choledochojejunostomy is started by fashioning the posterior layer with a V-Loc (Covidien, Mansfield, MA) suture.

An enterotomy is created so as to avoid creating a jejunal opening concordant in size with the main pancreatic duct. The 9- and 3-o'clock sutures are then placed through the bowel, taking large serosa and small mucosal bites through the pancreatic duct; a small and large bite are made through the pancreatic parenchyma. The 6-o'clock suture is first placed through the pancreatic duct and then out of the bowel. This suture is carefully tied to place tension along the length of the pancreatic neck so that the knots lie flat (Fig 26). It is important to master intracorporeal knot tying and be facile with the visual cues of tension, utilizing the bounce technique so that adequate tension is applied without damaging tissue. In a similar fashion, the 9- and 3-o'clock sutures are tied down and are followed by the 12-o'clock suture. The anterior-running imbricating outer layer is then fashioned with a 3-0 V-loc (Covidient, Mansfield, Massachusetts) suture and tied to the posterior layer (Figs 27 and 28).

Hepaticojejunostomy is performed using 2 running 3-0 V-loc sutures. First, a site in the jejunum is identified that most naturally appears to approximate the bile duct without any tension on the pancreaticojejunostomy. Anastomosis is planned so that the surgeon would sew to himself or herself by sewing the posterior layer first. Thus, the initial suture is placed on the duct first, outside in, just on the anterior side of the 3-o'clock position so that the posterior wall is fashioned and the corner is included when the suture is cinched. Care is taken to create a jejunal defect that matches the bile duct in diameter and that the bites include a small amount of mucosa, while also avoiding surrounding structures (Figs 29 and 30). As mentioned above, familiarity with the V-loc is important, including the need to cinch between throws. After creation of the posterior layer, the anterior layer is fashioned with a second 3-0 V-loc suture so that the surgeon is sewing toward himself or herself — this time, he or she is starting on the bowel. Great caution must be taken to avoid catching the back wall with the suture. The anterior and posterior sutures are then tied to each other.

The gastrojejunostomy is created in an isoperistaltic fashion along the posterior wall of the stomach, using the jejunum approximately 20 cm from the ligament of Treitz (Fig 31). Choice of an antecolic versus retrocolic orientation depends on redundancy of the transverse colon. In cases in which retrocolic anastomosis is fashioned, a defect is made in an avascular portion of the transverse mesocolon and the stomach is tacked to the peritoneal lining of that defect to prevent herniation or twisting. The anastomosis is fashioned with the stapler after the small bowel has been marked with a suture to confirm its orientation and lack of twisting. The common channel of the gastrojejunostomy is closed with a 3-0, V-loc running suture in the Connell fashion. This completes the resection and reconstruction (Figs 32 and 33).

At this point, the health care team confirms that

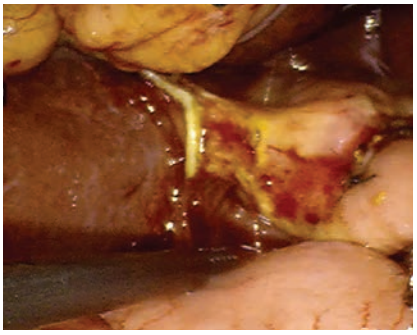

Fig 30. — Completion of the choledochojejunostomy demonstrates a viable, tension-free anastomosis without leak.

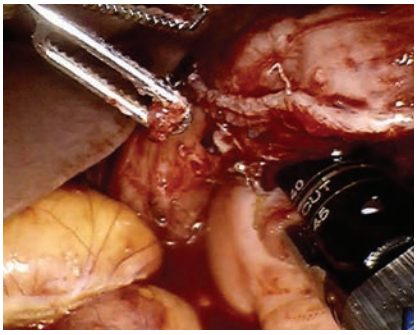

Fig 31. — Gastrojejunostomy is fashioned with the robotic stapler along the posterior wall of the stomach in an isoperistaltic orientation.

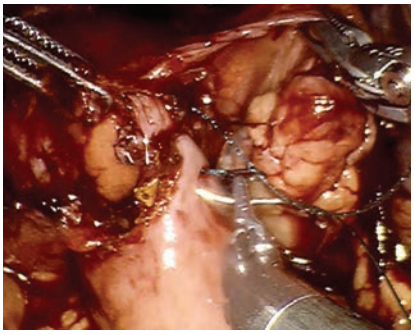

Fig 32. — Common gastrojejunostomy is closed with a V-lock suture in the Connell fashion.

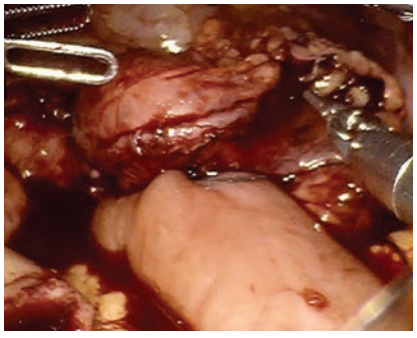

Fig 33. — Completion of the gastrojejunostomy demonstrates tension-free and viable anastomosis without twisting or leak.

the nasogastric tube has been correctly placed and inspects the abdomen again for hemostasis. A total of 9 L warm saline is used to irrigate the abdomen. A flat 15FR Jackson–Pratt drain is placed through the right lower quadrant to track behind the choledochojejunostomy and pancreaticojejunostomy and then curve anterior to the pancreaticojejunostomy. The ports are inspected for bleeding, the fascial defects of the 12-mm ports are closed, the 4-cm middline wound is closed with interrupted 0 Vicryl (Ethicon, Somerville, New Jersey) sutures, and the skin is closed.

The immediate postoperative care of the patient focuses on pain control, monitoring urine output, observation for signs of pancreatic leak, and waiting for a return of bowel function. After the patient recovers and meets the discharge criteria, he or she returns to the clinic 10 to 14 days after discharge. The staff members at the Gastrointestinal Oncology Program at the Moffitt Cancer Center communicate with all patients within 48 hours of discharge to identify any potential complications early and to address any questions or concerns. Based on the final pathological diagnosis, the patient will be offered adjuvant therapy and a surveillance regimen according to the corresponding multidisciplinary clinical pathway.

Outcomes

Our early experience with robotic Whipple procedure demonstrated comparable morbidity and perioperative outcomes to the open experience. A total of 21 patients underwent pancreatic resection in the first year (February 2012 to March 2013) using the robotic approach. Most patients were men (76.2%) with a median age of 69 years (range, 46–85 years) and a median BMI of 29.1 kg/m^2 (range, 24.3–39.2 kg/m^2), whereas 23.8% of patients were women and had a median age of 74 years (range, 24–76 years) and a BMI of 23.9 kg/m^2 (range, 20.4–26.5 kg/m^2). In terms of intraoperative end points, the median operative time was 621 minutes (range, 229–880 minutes), the median EBL was 200 mL (range, 25–800 mL), and the conversion rate was 9.5%.

The oncological principles were maintained and all resections were R0 on final pathology. The final diagnosis was adenocarcinoma in 52.4%, the median tumor size was 2.3 cm (range, 1–5 cm), and a median of 16 nodes (range, 2–23 nodes) was resected. The other diagnoses included intraductal papillary mucinous neoplasm in 19.1%, neuroendocrine tumor in 19.1%, and pseudopapillary and adenoma (both 4.7%). Postoperatively, the median length of stay was 8 days (range, 4–34 days), the overall morbidity rate was 28.5%, and the pancreatic leak rate was 14.3%.

Of the entire group of patients in our early experience, 14 underwent the Whipple procedure. For this cohort, the median operative time was 681 minutes (range, 326–880 minutes), the median EBL was 200 mL (range, 25–800 mL), and the median length of stay was 8 days (range, 4–34 days). For this group of patients, the final diagnosis was adenocarcinoma in 66.7%, the median tumor size was 2.3 cm (range, 1–4 cm), and a median of 17 nodes (range, 11–23 nodes) was resected. Postoperatively, the median length of stay was 12 days (range, 6–34 days), the overall morbidity rate was 42.8%, and the pancreatic leak rate was 21.4%. No deaths occurred perioperatively. These outcomes are similar to prior published reports.

Future Directions

Safety in the operating room and the optimization of perioperative outcomes are of paramount importance as robotic surgery becomes more accessible for patients and surgeons. Training is the only way to ensure

that surgeons can provide this service in a manner that is safe and without increased risk to the patient.

At the time of publication, training protocols still vary by institution, but nearly all are based on the Intuitive Surgical (Sunnyvale, California) pathway, which involves 4 general phases: (1) introduction to da Vinci–assisted surgery, (2) da Vinci technology training, (3) initial case series plan, and (4) continuing development. This pathway focuses on the surgeon and the operating room team during each step. The final phase is purposefully open-ended to allow for more specialized training in a particular field.

At the Moffitt Cancer Center, we have an institutional pathway for surgeons who have completed formal surgical training but seek robotic surgery privileges to treat patients with hepatobiliary malignancy. Proficiency with open complex hepatobiliary cases is required prior to training for robotic hepatobiliary surgery. Following their completion of the initial certificate training provided by Intuitive Surgical, surgeons can begin operating using the da Vinci Surgical System with a proctor, cosurgeon, or both for a continuous series of cases. At this point, the surgeon can schedule his or her own cases of escalating complexity, generally starting with distal pancreatectomy and progressing to operations requiring resection and reconstruction. We favor using a cosurgeon approach to complex resections requiring reconstruction as described above.

The training of future surgeons to use robotic surgical systems is also of paramount importance. At this time, most general surgery residency programs or surgical oncology and hepatobiliary fellowship programs do not have a training pathway for trainees. To remedy this, an effort is underway to standardize a training pathway for young surgeons who have not yet completed their formal training.[22,23] The protocol is predicated on the previous acquisition of basic open and minimally invasive surgical techniques. Through a rigorous program that relies on use of the da Vinci Skills Simulator (Intuitive Surgical), trainees are evaluated and proctored through a pathway to proficiency. The training pathway uses objective data for fine and gross motor skills built into the da Vinci Skills Simulator. Following the prospective validation of this pathway for surgical trainees, it may become the standard method used in the coming years.

Conclusions

Minimally invasive techniques offer surgeons the ability to provide complex surgical care to patients with advanced hepatobiliary malignancy — in particular, those with pancreatic cancer. Given the known morbidity and recovery rates from the open Whipple operation, the benefits of the robotic approach are proportionally greater than for other operations. The primary focus of this method must be on perioperative safety and quality outcomes for these patients. We have demonstrated a method for safely performing the operation and for training future surgeons to do the same. By adhering to rigorous academic principles and the liberal proctoring of colleagues, the benefits of this approach can be expanded to more patients with pancreatic cancer.

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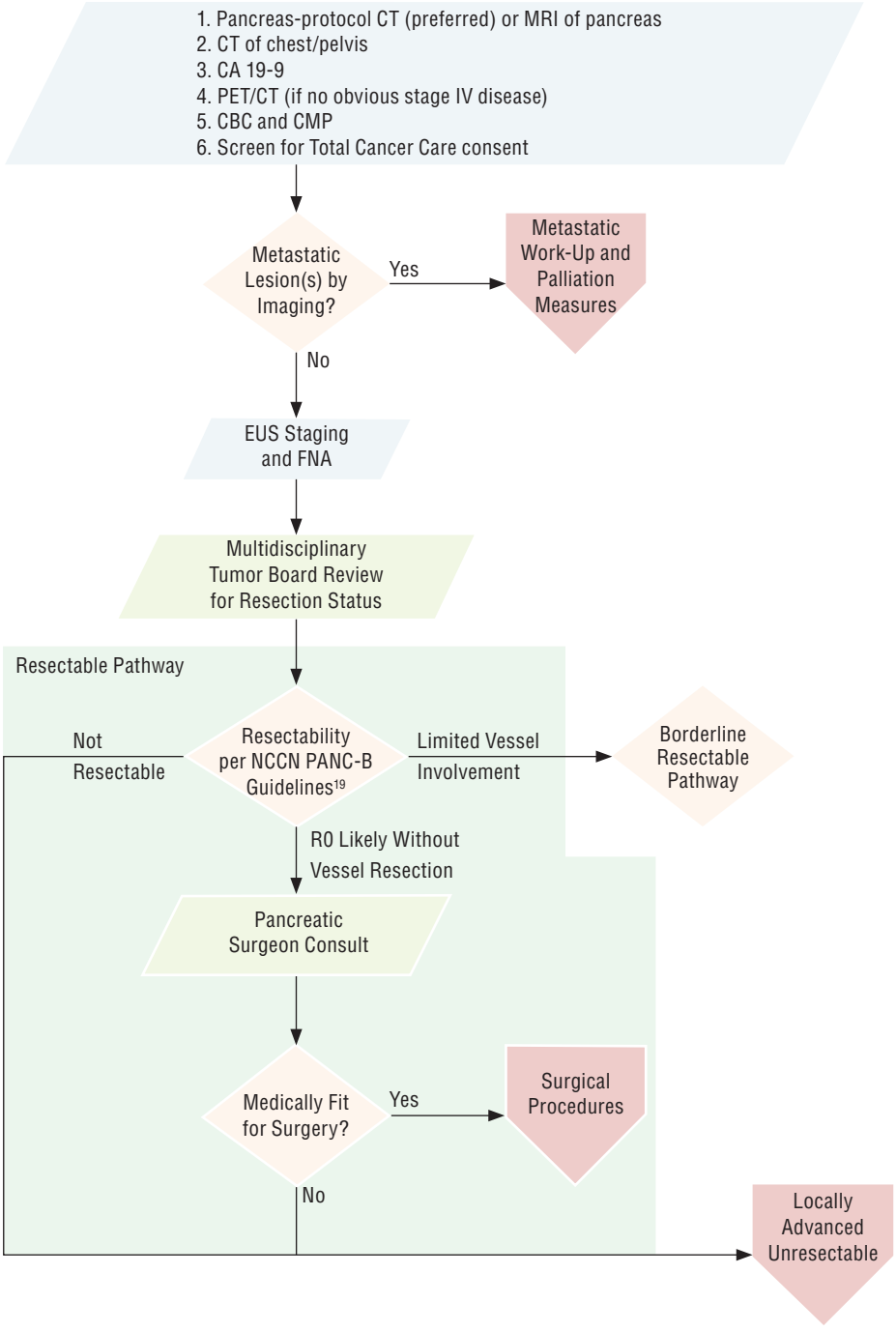
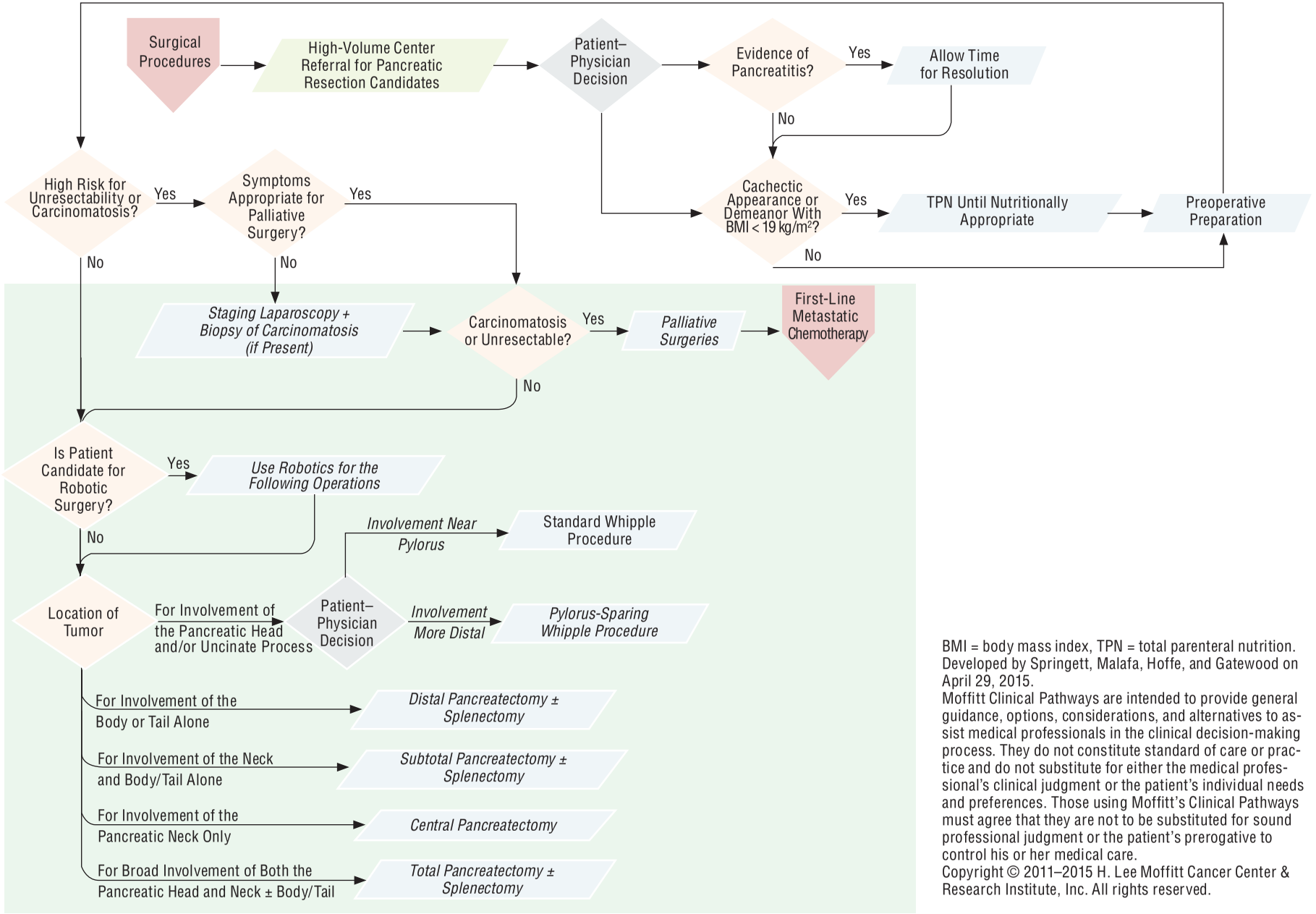
Appendix A. — Moffitt Cancer Center Clinical Pathway for Pancreatic Adenocarcinoma (Initial Care)



CA = cancer antigen, CBC = complete blood count, CMP = comprehensive metabolic panel, CT = computed tomography, EUS = endoscopic ultrasonography, FNA = fine needle aspiration, MRI = magnetic resonance imaging, NCCN = National Comprehensive Cancer Network, PET = positron emission tomography.
Developed by Springett, Malafa, Hoffe, and Gatewood on April 29, 2015.
Moffitt Clinical Pathways are intended to provide general guidance, options, considerations, and alternatives to assist medical professionals in the clinical decision-making process. They do not constitute standard of care or practice and do not substitute for either the medical professional's clinical judgment or the patient's individual needs and preferences. Those using Moffitt's Clinical Pathways must agree that they are not to be substituted for sound professional judgment or the patient's prerogative to control his or her medical care.

Appendix B. — Moffitt Cancer Center Clinical Pathway for Pancreatic Adenocarcinoma (Resectable)



BMI = body mass index, TPN = total parenteral nutrition.
Developed by Springett, Malafa, Hoffe, and Gatewood on April 29, 2015.

Moffitt Clinical Pathways are intended to provide general guidance, options, considerations, and alternatives to assist medical professionals in the clinical decision-making process. They do not constitute standard of care or practice and do not substitute for either the medical professional's clinical judgment or the patient's individual needs and preferences. Those using Moffitt's Clinical Pathways must agree that they are not to be substituted for sound professional judgment or the patient's prerogative to control his or her medical care.

Sofía Cáceres Nazario. *Muscovy Ducklings*, 2015 (Detail). Acrylic on canvas, 12" × 16".

Robotic-assisted neurosurgery may help increase accuracy and allow surgeons to perform more complicated operations.

Robotics in Neurosurgery: Evolution, Current Challenges, and Compromises

James J. Doulgeris, MSME, Sabrina A. Gonzalez-Blohm, MSBE, Andreas K. Filis, MD, Thomas M. Shea, Kamran Aghayev, MD, and Frank D. Vrionis, MD, PhD

Background: *Advances in technology have pushed the boundaries of neurosurgery. Surgeons play a major role in the neurosurgical field, but robotic systems challenge the current status quo. Robotic-assisted surgery has revolutionized several surgical fields, yet robotic-assisted neurosurgery is limited by available technology.*
Methods: *The literature on the current robotic systems in neurosurgery and the challenges and compromises of robotic design are reviewed and discussed.*
Results: *Several robotic systems are currently in use, but the application of these systems is limited in the field of neurosurgery. Most robotic systems are suited to assist in stereotactic procedures. Current research and development teams focus on robotic-assisted microsurgery and minimally invasive surgery. The tasks of miniaturizing the current tools and maximizing control challenge manufacturers and hinder progress. Furthermore, loss of haptic feedback, proprioception, and visualization increase the time it takes for users to master robotic systems.*
Conclusions: *Robotic-assisted surgery is a promising field in neurosurgery, but improvements and breakthroughs in minimally invasive and endoscopic robotic-assisted surgical systems must occur before robotic assistance becomes commonplace in the neurosurgical field.*

Introduction

The concept of robots has evolved from "human-like" machines to programmable, multifunctional specialized devices. Today robots are highly specialized machines used in a diversity of fields, particularly in industrial applications in which their speed and accuracy present recognizable advantages. In the surgical field, it was not until the mid-1980s when surgeons utilized the concept of robotics for the first time with a device used to perform precise biopsy in neurosurgery.[1] Since then, manufacturers have made efforts to improve the efficacy and reliability of their robotic systems.

The first application of robotic-assisted surgery was in the neurosurgical field, but robotic advancements in urology, gynecology, gastroenterology, and orthopedics are more common due to fewer anatomical challenges. For example, a large cavity where a robotic arm could be used to assist in spine surgery is nonexistent, and brain surgery involves delicate neural structures and approaches through narrow surgical corridors where manipulation and space are both limited.

This article provides an overview of the origin and evolution of robotic-assisted surgery, with a special

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focus on the current robotic systems in use, advancements, limitations, and future developments of neurosurgery.

Classification

A surgical robot is any reprogrammable-powered manipulator with artificial sensing that can assist in a variety of surgical tasks.[2] Since the development of this concept, others have suggested different classifications in terms of the technology, applications, and roles of the robot during surgery (Table).[2-7] The device's function/application and the degree of surgeon–robot interaction are important factors to consider in any classification, particularly because these 2 features may drive the future development of surgical robots.

The amount of interaction the surgeon receives from the robotic system during surgery is crucial. If the surgeon does not need to interact with the robotic system during surgery, then more trust is placed on the robot. In this type of situation, surgical success depends on the development of the robot, where less control can equate to increased risk if the robot is improperly programmed. Nevertheless, the amount of surgeon control determines the responsible parties, the risk in the operating room, and the classification function of the robot.

The type of function and application relies on the type of robot. In general, 3 basic types of robotic systems exist: autonomous, dependent, and shared control. Autonomous systems reproduce programmed motions or move the system to set locations by calculating the required position. The most common neurosurgical application of an autonomous system is stereotactic positioning. Dependent systems, also called master/slave systems, are the most popular type of robotic system because the surgeon maintains full control of the system at all times. These types of systems allow surgeons to perform remote surgeries, sometimes referred to as telesurgery. Shared-control systems are a hybrid between the dependent and autonomous systems. For example, a shared-control application could involve a passive arm hooked up to a surgeon's hand that moves only when permitted, but yet it can filter unwanted motions such as hand tremors.

Evolution

Although the concept of robotic surgery was first seen in the neurosurgical field less than 30 years ago, robotic technology continues to progress in the medical field. The first robot used in neurosurgery was the PUMA 200 (Unimation; manufacturer defunct) for stereotactic surgery.[3] The system allowed the placement of a biopsy needle in the brain using computed tomography (CT) guidance. The robot had the potential to deliver faster results than any other procedures available at the time that required the manual adjustment of the stereotactic frame because its computer calculated faster than humans. The device has been since discontinued, but the PUMA 200 is considered to be the pre-

Table. — Classification of Surgical Robots

Study	Type	Classification	Description
Davies[2]	Position control	Active	Interact with patient during surgery
		Passive	Can be powered off after robot achieves target position
Taylor[4]	Role based	Intern replacement	Specific surgical interns serve as role substitutes
		Telesurgical	Controlled by the surgeon throughout the procedure
		Navigational aid	Computer-assisted system integrated with imaging
		Precise positioning	Navigational aid with own motive power
		Precise path	Precise positioning that moves tool through a predetermined path
Camarillo[5]	Role based	Passive	Limited scope Low risk
		Restricted	Greater scope Higher risk than passive
		Active	Greatest involvement Highest risk
Bann[6]	Function	Dexterity enhancement	Equivalent to telesurgical method[4]
		Precision location	Equivalent to precise positioning systems[4]
		Precision manipulation	Equivalent to precise path systems[4]
	Technology	Autonomous	Performs a preoperative plan programmed by the surgeon
		Supervisory	Serves as a guide during surgery
		Teleoperated	Equivalent to telesurgical method[4] Enhanced dexterity[6]
Nathoo[7]	Technical	Active	See description in Davies[2]
		Passive	Surgeons provide motive force to achieve target position and robot is then powered off
	Interaction	Supervisory controlled	Equivalent to autonomous method[6]
		Telesurgical	Equivalent to supervisory method[6]
		Shared control	Equivalent to telesurgical method[4] Enhanced dexterity[6] Teleoperated[6]

Information from reference 3.

decessor of most surgical robots.

Some commonly used robots available for neurosurgery are the neuromate (Renishaw Mayfield, Lyon, France), Pathfinder (Prosurgics, High Wycombe, United Kingdom), the NeuroArm (University of Calgary, Calgary, Alberta, Canada), the SpineAssist (MAZOR Robotics, Orlando, Florida), and Renaissance (MAZOR Robotics). The neuromate is a stereotactic system with 6 degrees of freedom (DoF) originally developed by Integrated Surgical Systems (Sacramento, California) in 1987, and the most recent version of the neuromate from Renishaw received US Food and Drug Administration (FDA) approval and is now commercially available (Fig 1). According to the manufacturer, neuromate can be used for several neurological applications, including deep brain stimulation, endoscopy, and stereoencephalography, and it is an efficient and safe instrument for biopsies in clinical cases.[8] Similarly, the Pathfinder is a stereotactic system that has proven accuracy in clinical research.[9] These 6-DoF robotic-arm systems differ from other neurosurgical robots because they use identified reflectors attached to the head of the patient that use a camera system instead of radiological, ultrasonographic, or mechanical guidance.[9]

The NeuroArm is a magnetic resonance imaging (MRI)–compatible surgical robot developed by the University of Calgary in 2001 (Fig 2).[10] It allows the surgeon to perform skilled tasks while located in a different location than the operating room and is commonly referred to as telesurgery. The system is capable of needle insertion, cutting, cauterization, and irrigation on a microscale (microsurgery) while simultaneously obtaining MRI. In 2008, NeuroArm was used for the first time to remove a brain lesion in a 21-year-old patient.[11] Since then, early clinical reports, which include various cranial neoplastic cases, show favorable results for the NeuroArm working station.[10,12]

In the spine surgery field, the SpineAssist received FDA approval in 2011 and is considered to be the first neurorobot to incorporate a module for minimally invasive surgery.[13] This specialized device is accurate and designed to offer a less-invasive solution for spine surgery, reduced complication rates, and limited recovery time; it may also offer fluoroscopic-guided surgery.[14] Despite its advantages, clinical evidence suggests that the nonassisted conventional technique has better accuracy rates; in addition, technical difficulties with robotic-assisted surgery suggest the presence of fluoroscopy backup,[15,16] although more evidence may be needed to determine whether a difference exists between assisted and nonassisted techniques.[17]

The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California) is a robot used in urology, but its popularity is not matched in neurosurgery. The system has 4 arms, each with 7 DoF, controlled by 2 working arms and a 3-dimensional (3-D) stereoscopic view of the field that surgeons can use in a telesurgical manner (Fig 3). This robotic system has been used for transoral odontoidectomy, intrauterine repair of myelomeningocele, and spinal schwannoma

Fig 1. — The neuromate (Renishaw Mayfield, Lyon, France) is a stereotactic system used in various neurosurgical targeting applications. Image courtesy of Renishaw, Inc, Hoffman Estates, IL.

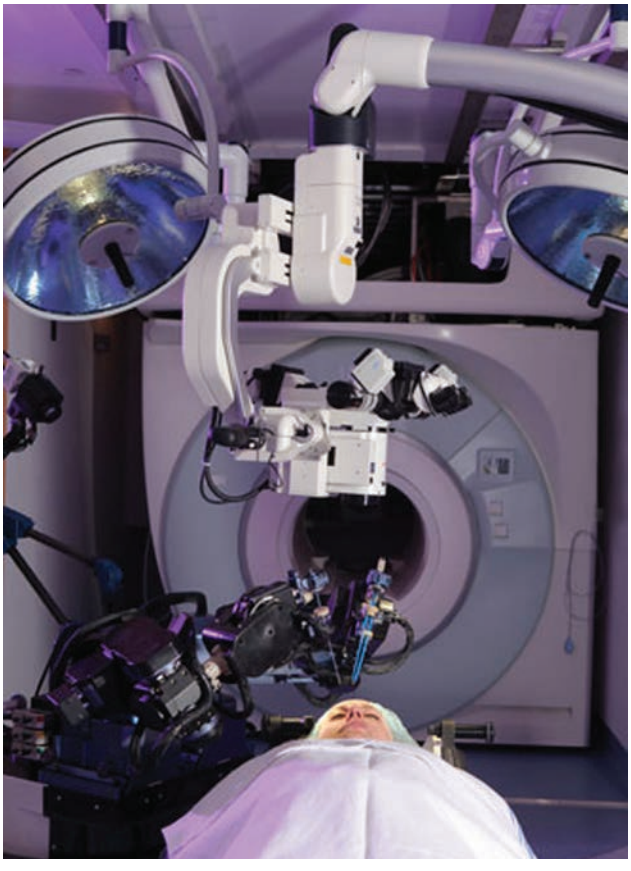

Fig 2. — NeuroArm (University of Calgary, Alberta, Canada) is a magnetic resonance imaging–computable master/slave system capable of several surgical tasks. Image courtesy of University of Calgary.

resection.[18] The feasibility of the system in a supraorbital keyhole approach for skull base tumors and aneurysms is also possible.[19] However, despite its success in various fields, the system has minimal impact in microneurosurgery because of the limited tools available, the number of ports needed, and the manipulation room and size of the system interfere with its integration into this field of neurosurgery.

According to Marcus et al,[20] the Steady Hand System (Johns Hopkins University, Baltimore, Maryland) is the only version of a shared-control system used in microneurosurgery. The main focus of this system is to filter out unwanted forces or motions, such as hand tremors, so that the surgeon can have the familiar feel of surgery with the accuracy and precision of a robotic system.[21] This system may have advantages in neurosurgery, but research on this system has been limited to retinal microsurgery.[22]

When designing a surgical robot, the features of each element depend on its specific application. Each design has an impact on the branches of neurosurgery (brain, spine, and peripheral nerve) and neuro-oncology, but the main focus of this article is endoscopic and stereotactic brain/neuro-oncology applications. Nevertheless, understanding the needs in specific fields and the anatomical constrains are crucial for optimizing the performance of the robotic system.

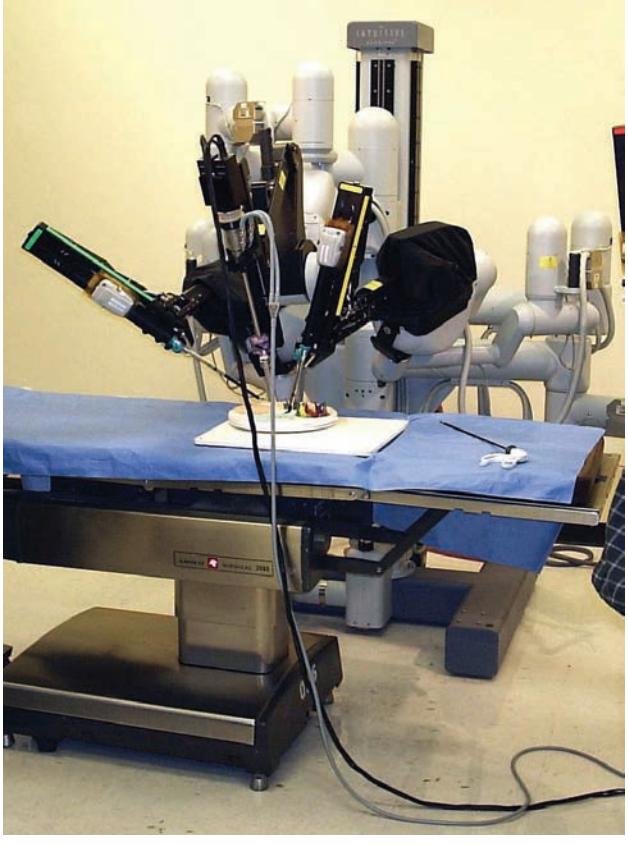

Fig 3. — Surgeons can operate the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA) by controlling the robotic arms from a separate computer console connected via cables. © 2006–2015 Nader Moussa, Sunnyvale, CA.

Mechanical Factors

Mechanical factors are constraints placed by the manufacture on any part of the robotic system. The design of these parts dictates the function and application of the system. In general, relevant factors are in the tool and arm portions of the machine because they represent the closest interaction points of the surgeon.

Rigid Tools

Straight, long, and rigid manipulators with a clamp on the end are among the most common tools. Surgeons use them in endoscopic surgeries, but they also use the DoF of their hands to move them in space. By contrast, robots require additional DoF in the tool itself so that the robot can move the tool around in space. The general requisite is 6 DoF to move in a 3-D environment, yet the approach of rigid tools is limited to a straight line. Typically, rigid tools with multiple DoF effectors are the standard set of equipment for robotic systems, but engineers can still make advancements in tool design.

Curved Tools

Concentric tube tools are commonly used in autonomous robotic-assisted surgery. A concentric tube tool has several tubes nested inside one another and can be elongated in a telescoping fashion. This technology is useful when navigating confined areas (eg, performing transnasal sphenoidotomy for pituitary resection).[23]

A straight line is the closest distance between 2 set points, but a vital obstacle may be between those points. One of the challenges of brain tumor resection is the location of the tumor, where it can be semi-surrounded by sensitive tissue and the anatomy forces the approach through it. Thus, maneuvering in relative safe areas with these tools is optimal and possible.[24] Neurosurgeons can benefit from using these tools and techniques for transnasal approaches, biopsies, and endoscopic craniotomies to minimize invasiveness and reduce recovery time, particularly for cases requiring tumor removal. For example, imagine a small mass superior and lateral to the hippocampus that requires the surgeon to create a path through the temporal portion of the brain. With a curved-guided system, the surgeon could approach the lesion without extensively disrupting the brain tissue.

Concentric tube–curved tools have several benefits but also present technical challenges.[25] The calculation of where the tip is located is relatively simple with kinematic or Jacobian calculations, but only if the tool is rigid (unbendable). However, minimal tool diameters reduce the invasiveness of the procedure, creating non-

rigid (bendable) pieces; thus, the tip location depends on the Jacobian calculations and on the deformation from the applied stresses. This, in turn, complicates how to determine the position of the device. Gilbert et al[25] showed that several ways exist for getting around this issue, ie, imaging guidance, magnetic/fiber-optic shape sensing, and force sensing.

Limited DoF with the manipulator are another limitation that hinder what can be done with these types of tools after the concentric tube is in position. Some manipulators, such as clamps, require a tension wire, but this tension can cause the curved tool to deform; this in turn limits the applications of such curved tools. However, curved tool applications have benefits in some removal techniques, such as suction, and, in particular, brain tumor removal and biopsies.

Compromises

The challenges of tool design for endoscopic, minimally invasive, and robotic-assisted surgery are similar. The surgeon must be able to operate the tools in confined spaces. If the tool is too large, then it will crowd the space; by contrast, if it is too small, then the tool will be difficult to control. Thus, its design requires a balance between strength and size. The type of stress the tool is under is also another parameter that determines where the strength needs to be. Stress is closely related to the end effector because it determines how the surgeon must move the tool (eg, grasping, probing, pulling).

Another important factor is the geometrical constraints of the tool. Tool diameter and length determine how flexible the tool can be. If the tool is long and has a small diameter, then it is relatively easy to deflect. Thus, the greatest difficulty in designing tools for use in microenvironments is overcoming the tradeoff between rigidity and size. Stiffness is inversely proportional to the length, making the port design popular in some neurosurgical robots because it can reduce the length.[26]

Neurosurgery involves a microscopic field with minimal room to work, which creates challenges relating to instrument crowding, triangulation, and movement. The designs of robotic arms have assuaged the issue of triangulation and movement,[26] but crowding and workspace still add to the technical challenge of tight spots during surgery. Although surgeons have successfully performed dissections of superficial brain tumors,[27] robotic-assisted endoscopic surgery requires more research and technical improvements to comfortably access deep portions of the brain for everyday neurosurgical applications.

Motion

Manufacturers often describe surgical robots by the DoF in each articulating arm. DoF depend on the number of links in the system and the allowable directions in each motion. Six DoF allow a robot arm to move anywhere in the work envelope, but only 1 possible solution (joint angles) exists for each position in space. Thus, many robotic designs add redundancy — extra DoF — to allow multiple joint solutions/angles to reach the same position. Extra DoF are ideal in teleoperated surgeries because the surgeon has real-time control of each position; however, extra DoF in autonomous systems leave each desired position with multiple solutions, thus requiring extensive programming to optimize and coordinate motions.

One important factor of DoF is the amount of force delivered. The strength of the motor and mechanical advantage determine the applied force or force the motor can apply to maintain position; this is important when a surgeon wants to manipulate an object. Brakes are a way of increasing the force at which a motor can hold, but the applied force is still needed for manipulation. Including larger and more powerful motors in the system may sound like the solution, but the tool now creates a bottleneck in which the deflection and stiffness determine the applied force. Strength in DoF is another important factor, but its magnitude depends on the application. For example, manipulating portions of the brain does not require extensive applied forces, but manipulating bone or cartilage does.

Human–Robot Interactions

Haptic Feedback

A common natural mechanism that surgeons rely on is haptic feedback, or sense of touch, which can help determine how much force is being applied or provide information on the medium being manipulated. Proprioception, which is the sense of where one's connected extremities are in space, is another natural mechanism used during surgery. During minimally invasive and endoscopic surgery, long tools attenuate and distort the tactile sensation and proprioception of the surgeon.

Force Sensing

Telesurgery separates the direct connection between surgeon and patient, thus removing all haptic and proprioception feedback. Haptic feedback is a common concern in robotics because oftentimes the surgeon must know what forces are being applied to the workspace. This is particularly important in neurosurgery because delicate tissues can be permanently damaged by excessive force. Wagner et al[28] have shown that surgeons damage less tissue and apply minimal force to tissues when force feedback is received during robotic-assisted surgery. Thus, the topic of haptic feedback for robotics is an important area of research.

Force sensing for robotic applications is complicated in biomedical applications. Sterilization, MRI, size,

electronics, and cost are factors that add to this complexity. Nevertheless, the minimally invasive field of neurosurgical robotics is a promising area of current research.

Some promising types of force feedback are in strain gauges and optical force measurements. For example, Yoneyama et al[29] developed a micromanipulator capable of providing clamp and tension feedback for deep-seated tumors through the use of strategically placed strain gauges. Doing so gives surgeons the ability to gather information on a tumor prior to resection. However, strain gauges are difficult to sterilize and have wires connecting them to other devices, causing researchers to pursue alternative ideas. Watanabe et al[30] developed a force-sensing device with a smaller probe diameter than the previous sensor capable of providing compression feedback by measuring the optical displacement of high elastic fiber. Optical displacement force is a promising application, and we expect this to become the future of force-sensing technology because endoscopic cameras are evolving and its potential for use in minimally invasive surgery is high.

Regardless of how force is measured, the main goal of such technology is to create a convincing virtual environment for surgeons. However, neurosurgery is potentially a few steps behind in haptic breakthroughs because of the microscopic requirements of the surgical environment.

Proprioception Feedback

Natural haptic feedback is the body's ability to determine the spatial location of our arms and hands without visual confirmation, and the loss of this sense contributes to the learning curve of telesurgery. Transferring our proprioception to a robotic arm is easier to imagine than it is to accomplish, which explains the limited research on this topic. However, it is an entertaining notion to consider because properly applying proprioceptive haptic feedback may provide the same "feel" as open surgery with minimally invasive procedures.

Calculating complex motions and training to operate robotic systems are highly dependent on the application of proprioception. Given enough time and training, a surgeon can gain a degree of proprioception when operating a robotic system. The time it takes to gain the skills to fluidly operate a robotic system is often referred to as the learning curve, which relates to the similarities of natural motions with robotic controls.

Kinematics

Robotic-assisted telesurgery can provide the surgeon with several advantages, such as comfort, accuracy, stamina, and dexterity. In addition, motion amplification and filtering can be included in robotic-assisted minimally invasive surgery. Because neurosurgery involves a microscopic field in which the surgeon must make accurate small incisions and resections, the use of motion filtering removes hand tremors from the surgeon by clever programming, thus allowing the surgeon to make smaller resections with larger applied motions. This, in turn, provides a factor of safety to the surgery.

Visualization

Visualization is the key component of successful haptic feedback and successful surgery. Several methods of visualization are available to surgeons, including CT, MRI, fluoroscopy, and endoscopic optics. Autonomous robotic assistance (eg, stereotactic applications) benefits from the use of CT and MRI because autonomous robots require a 3-D model of the workspace and presurgical programming. Master/slave or telesurgery applications benefit from endoscopic optics for real-time and perspective visualization during surgery and MRI and CT visualization for presurgical strategies.

Technological advancements have made endoscopy an attractive option for neurosurgeons, particularly robotic-assisted minimally invasive teleneurosurgery. Endoscopic optic cameras are useful in telesurgery because they can be flexible and have high resolution. However, telesurgery shares similar visualization challenges as endoscopic surgery, such as lens obstruction and blood clouding, and the approach to the workspace places limits on visualization and ease of manipulation.

Visualization is important for surgeon–workspace interaction. Because haptic feedback is limited, surgeons rely on visual feedback alone for telesurgery. Visual feedback is more useful than other feedback mechanisms and, thus, has received the most attention in surgery. Surgeons lose a degree of depth perception during operations by trying to process a 3-D environment from a 2-D image; this loss of perception can lengthen the duration of operating time. Therefore, current endoscopic designs include stereoscopic cameras. Some researchers have advocated stereoscopic over monoscopic surgeries,[31,32] but others question their efficacy.[33] Nevertheless, the topic is debatable as stereoscopic visualization does have potential advantages.

Microscopic visualization is important in neurosurgery and has potential in robotic surgery. Currently, NeuroArm is capable of microneurosurgery and has micro–end effectors for its tools.[34] However, not all systems are adaptable to microscopic visualization. Rather, integrating microsurgery into endoscopic robotic systems is more likely with the development of micro-endoscopy, but doing so may be difficult for minimally invasive systems because they may interfere with the view in the surgical field.

Augmented reality (AR) can provide advantages for visualizing surgical procedures. The concept of AR is to overlay artificial images from intraoperative CT scans or radiographs onto the current visual field. For example, AR can accentuate important but hidden anatomical structures and show the surgeon the position of lesions beneath tissue so that the lesions can be removed. Thus, adding AR technology to robotic systems is needed to help surgeons regain insight during surgery.

Training

A challenging issue with robotic-assisted surgery is the training of surgeons. Such training involves learning the basic kinematics of the robotic system. Training is an important factor and can occur in 2 different types of environments — virtual reality (VR) and deceased donor — and each has advantages and disadvantages.

In general, there are 2 types of VR: programmed VR and preoperative-preparation VR. Programmed VR is the first step in training and provides specific obstacles for the surgeon to practice so he or she gains anatomical experience prior to the actual surgery. One benefit of programmed VR training is its ability to provide tuned haptic feedback that a surgeon might encounter during surgery. Preoperative-preparation VR uses data from the patient (preferably from a high-resolution scan) to create a 3-D virtual representation of the surgical field that the surgeon then uses to rehearse the surgery and learn the anatomical features specific to the patient. The inclusion of haptic feedback in this type of VR may produce better emulation, but, to our knowledge, preoperative-preparation VR does not currently provide haptic feedback.

Surgeons can use robotic systems on deceased donors to rehearse potential surgeries prior to operating on patients. This type of training can also include a stereoscopic element to allow surgeons to learn and experience how the pseudo–3-D environment of robotic systems works, thus allowing extended proprioceptive feedback of the tools. Although the cost of deceased-donor training cost is higher than VR, deceased-donor training is still the best representation of the surgical field.

Future Directions

Several directions are possible for robotic-assisted minimally invasive surgery. In the future, robots may be completely autonomous, completely dependent, or even a hybrid of these 2 types of machines.

The notion of a completely autonomous robot is entertaining, but several complexities still exist. Treatment is not universal. Anatomy and medical history both differ from patient to patient. Currently, adjusting movement on demand is not yet possible, and the inability of robotic systems to make such on-demand adjustments makes troubleshooting or unexpected maneuvers an issue. Autonomous technology may be in the future, but strenuous work is needed to get there; thus, for the time being, autonomous robots are used for stereotactic assistance or equipment positioning alone. However, room for improvement still exits, including the addition of subroutines to current autonomous robotic systems, such as wound closing, clamping, and basic manipulation.

Completely dependent robotic-assisted surgery has become popular, and the future of dependent systems will rely on the miniaturization of robotic tools and the incorporation of curved endoscopic ports. The shortcomings of small, long parts relate to their flexibility, which limits how small each arm can be. However, future directions might include using several small robotic arms to assist 2 controlled hands to accommodate the limited forces that they can apply. For example, a system might include several robotic arms: the surgeon would control 2 of these small arms, and the other arms would be programmed to assist the surgeon. Nevertheless, once the technology is available, robotic-assisted endoscopic surgery is likely to become a major trend in neurosurgery.

Conclusions

The use of robotic systems in neurosurgery may help increase surgical accuracy and allow surgeons to perform more complicated operations. However, our current robotic technology is limited due in part to anatomical challenges, so other specialty areas have grown much faster than neurosurgery. Several technical challenges, including design issues and limited haptic feedback, have slowed down robotics in the field of neurosurgery, but researchers continue to work on creating a believable virtual environment that can replicate actual surgeries.

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Association of Lymphomagenesis and the Reactivation of Hepatitis B Virus in Non-Hodgkin Lymphoma

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Background: *Hepatitis B virus (HBV) has been associated with the development of non-Hodgkin lymphoma (NHL) and can be reactivated in patients being treated for NHL.*

Methods: *Articles published between 2000 and 2015 that discussed an association between NHL and HBV, mechanisms of HBV induction of NHL, and HBV reactivation in patients with NHL were reviewed and the results compiled to help health care professionals better understand the risk of developing NHL in HBV-seropositive individuals, describe potential etiologies by which HBV infection may lead to lymphomagenesis, and highlight the recent medical literature with respect to the reactivation of HBV in the setting of NHL.*

Results: *An association exists between HBV infection and NHL development. Immunosuppression due to HBV, chronic viral stimulation, and dysregulation of the immune system are possible ways in which lymphoma can develop in patients with HBV infection. All patients being treated with anti-CD20 antibodies or those from or living in HBV-endemic regions should be tested for hepatitis B surface antigen, core antibody, and surface antibody prior to initiating therapy. HBV DNA polymerase chain reaction (PCR) may also be useful in certain cases. Among HBV-seropositive patients or those with detectable HBV DNA, prophylaxis with an antiviral agent should be initiated for 1 year after NHL therapy. HBV DNA PCR monitoring should be undertaken each month during the course of treatment and every 3 months after treatment for a 1-year duration.*

Conclusions: *Health care professionals should become more comfortable treating these high-risk patients with NHL as they become more informed about potential lymphomagenesis and the reactivation of HBV.*

Introduction

Non-Hodgkin lymphomas (NHLs) are a heterogeneous group of malignancies arising from lymphoid tissue that have varied clinical and biological features. NHL is the most prevalent hematological malignancy, the seventh most common cancer in the United States, and the sixth leading site of new cancer cases; in addition, it is estimated to have accounted for 4.3% of all malignancies and 3.8% of cancer deaths in 2015.[1,2] Approximately 72,000 people will be diagnosed with NHL this year, and almost 20,000 patients will die from the disease.[1,2] Both infectious and environmental etiologies have been implicated as possible causes of NHL, and approximately 15% to 20% of NHL cases are associated with certain viral and bacterial causes, including HIV, Epstein–Barr virus, human herpesvirus 8, human T-lymphotrophic virus type 1, *Helicobacter pylori*, hepatitis C virus (HCV), and hepatitis B virus (HBV).[3-10]

Worldwide, HBV infection is a leading cause of acute and chronic cases of hepatitis.[11] It is a small DNA virus that is a member of the *Hepadnaviridae* family. HBV has a human-only reservoir and is transmitted via parenteral or mucosal exposure to infected blood, bodily fluids, or both. The virus is endemic in Africa, Asia, the Middle East, and parts of eastern Europe and South America.[12] In the United States, 12 million people are estimated to have been infected (approximately 1 in 20 persons) and an estimated 1 million people or more may have chronic hepatitis B.[13] The global incidence of HBV is larger: 2 billion people are estimated to be infected and 400 million people have chronic hepatitis B.[9,13] The World Health Organization reports that up to 30 million people are infected with HBV every year.[13]

The results from 2 meta-analyses suggest that HBV-seropositive patients may be at risk for developing NHL; in addition, patients treated with certain medications for NHL — in particular, anti-CD20 antibodies — are at increased risk for the reactivation of HBV with a high rate of morbidity.[9,14] Thus, health care professionals who treat patients with NHL must understand how HBV may be implicated as a causative agent and how the virus has the potential to further complicate NHL treatment.

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Methods

Articles published between January 2000 and January 2015 were included in our review if they discussed either an association between the development of NHL and HBV infection, mechanisms of HBV induction of NHL, and the reactivation of HBV in patients with NHL. Using these articles, we summarized the current literature with regard to HBV and its association with NHL, possible mechanisms for how HBV may induce NHL, the clinical characteristics of HBV reactivation, and the use of prophylaxis for the prevention of HBV reactivation in at-risk patients with NHL.

Causal Associations

Many epidemiological studies during the last decade have shown mixed results as to whether a causal relationship exists between HBV infection and NHL.[12,15-44] Two meta-analyses summarized these epidemiological studies, and their conclusions suggest that an association might exist between HBV infection and the development of NHL.[9,14] In a comprehensive meta-analysis of 17 case-control studies and 5 cohort studies, which made up more than 40,000 cases of NHL, HBV-seropositive individuals had an odds ratio of 2.24 (95% confidence interval [CI]: 1.80–2.78) for developing NHL.[9] Similarly, Nath et al[14] reported an odds ratio of 2.67 (95% CI: 2.04–3.49) for detecting HBV infection in individuals with NHL when compared with controls, suggesting a high prevalence of HBV-carrier states in patients with NHL.

Furthermore, in the meta-analysis by Dalia et al,[9] risk was stratified by common NHL subtypes (eg, diffuse large B cell, follicular) and by World Health Organization (WHO) high, intermediate, and low-prevalent HBV countries. In this subanalysis, an increased risk for diffuse large B-cell lymphoma was seen, as well as an overall trend toward increased risk for developing follicular and T-cell lymphomas; this trend was driven by WHO high-prevalent HBV countries.[9] These findings suggest that the risk for developing NHL in patients with HBV infection may be more driven by the high prevalence of HBV in HBV-endemic countries. Thus, HBV-endemic countries may be a target population for future research to better understand whether HBV seropositivity leads to an increased risk for developing NHL.

Based on the findings from those 2 meta-analyses,[9,14] health care professionals must keep in mind that patients with HBV seropositivity may be at risk for developing NHL, and this is particularly true for patients from or living in high HBV-endemic regions. If patients with HBV infection are symptomatic (eg, B symptoms, lymphadenopathy), then further work-up should be undertaken to rule out NHL; however, NHL screening has no role in patients with HBV seropositivity, and further research is needed to confirm such an epidemiological association.

Mechanisms

The biological mechanisms responsible for the development of NHL are ambiguous and unclear; however, genetics may predispose certain families to NHL.[45] Genetic alterations, such as translocations and growth-factor damage, may lead to immunosuppression, cell-growth dysregulation, cell-signaling pathway dysfunction, lack of programmed cell death, and the dysregulation of immune processes. Multiple hypotheses have been suggested to explain the underlying etiology of these changes and alterations, particularly in relation to viral infections that may lead to lymphomagenesis.[45-47] Chronic viral infections stimulate the proliferation of B cells, leading to a higher probability of random genetic mistakes and errors — particularly those related to immunoglobulin genes. Irrespective of whether immunosuppressive states are directly related to the viral infection itself or indirectly related by down-regulating the responses of T cells, these immunosuppressive states may lead to the body's inability to eliminate malignant cells as a consequence of impaired immune surveillance. Such cases have been observed in the context of inherited or acquired immunodeficiency syndromes as well as among patients receiving immunosuppressive therapy.[46,47] All of these mechanisms — genetic predisposition, impaired immune surveillance, and chronic viral infection — likely cooperate to influence the development of lymphoma.

Mechanisms that may be specific to HBV-associated NHL have been largely extrapolated from studies evaluating HBV-associated hepatocellular carcinomas and HCV-associated NHL.[21,25,29,31,48-55] In particular, HBV-specific nucleic acid sequences in peripheral blood mononuclear cells and hematopoietic tumor cells among patients positive for hepatitis B surface antigen (HBsAg) suggest that HBV may have a direct cellular effect that impacts lymphomagenesis.[21,25,29,48] The chronic stimulation of B cells encountered by this mechanism may predispose these patients to increased DNA damage, thus leading to the transformation of B cells into malignant B cells. The immunological response to chronic, local antigenic stimulation has been proposed as a mechanism of HCV-mediated lymphomagenesis and may also be a way in which HBV mediates lymphomagenesis because the 2 viruses are similar in structure.[49-51] HBV-encoded X protein has been shown in liver cells to inhibit p53 and lead to the abnormal division of liver cells, thus leading to hepatocellular carcinoma.[30,52-55] A similar B-cell mechanism is possible and may contribute to the malignant transformation and development of B-cell NHL.[29,30,48,54] Similar to hepatocellular carcinoma, an indirect role of lymphomagenesis may exist via HBV-specific, immune-mediated cell injury and im-

munodeficiency.[25,31] HBV infection of endothelial cells may also serve as a trigger for the increased production or release of hematopoietic tumor growth factors, stimulating cell proliferation and leading to NHL.[33] It may also be possible that an unknown virus with a mode of transmission similar to HBV might be cotransmitted with HBV and is responsible for lymphomagenesis, but no such virus has been found to date.[21,29,56] Thus, additional research is needed to better understand the mechanisms by which HBV seropositivity may lead to the development of NHL.

Reactivation

The role of the oncologist in recognizing and communicating the risks of chemotherapy to his or her patients has become complex with the addition of biological agents. These agents have various adverse events that can impact immune function for extended periods of time. Therefore, health care professionals must be aware of the reactivation of HBV among HBV-seropositive patients receiving chemotherapy and anti-C20 antibodies (eg, rituximab, ofatumumab).[57-69]

Rituximab-associated HBV reactivation was investigated in a systematic literature review and meta-analysis first published in 2010.[66] In this study, the authors concluded that 55% of the 183 cases reported in the medical literature experienced liver failure and had an associated mortality rate of 48%.[66] A fivefold increase in HBV reactivation was also seen in the participants positive for hepatitis B core antibody (HBcAb) who received rituximab-containing treatments compared with those who received chemotherapy alone.[66] The association between anti-CD20 antibodies and HBV reactivation with subsequent hepatic failure resulted in a black box warning for both rituximab and ofatumumab regarding the risks of HBV reactivation.[60]

HBV reactivation defines a specific syndrome marked by the rise of HBV DNA in a patient with previously resolved or inactive HBV infection. A common definition of reactivation involves demonstrating 2 distinct components: (1) a threefold increase in serum transaminase level (alanine transaminase > 3 times the upper limit of normal), and (2) a tenfold increase in the HBV DNA above baseline or at a level of more than 20,000 IU/mL and clinical evidence of hepatitis.[70] The clinical spectrum of acute reactivation of chronic hepatitis B can range from subtle elevations in transaminase to frank hepatic failure. Patients who develop HBV reactivation are treated with antiviral therapies, such as lamivudine, and with supportive care; rates of morbidity and mortality continue to be high.

Vega et al[71] demonstrated that 43% of study patients with positive serology developed liver-related adverse events, defined as an elevated transaminase level more than twice the upper limit of normal, new or progressive cirrhosis, hepatic necrosis, and mortality related to liver failure. In this study, study patients with underlying liver disease appeared to have worse outcomes than those with no baseline liver dysfunction.[71] The rate of short-term mortality depended on the degree of hepatic necrosis and was not directly dependent on HBV load.[71]

The exact frequency of spontaneous reactivation remains unclear; however, the results of one study suggest that the annual incidence may be 7.3%.[72] Typically, reactivation occurs in the setting of immunosuppression or immunodeficiency (eg, patients with NHL).[70] Reactivation rates in patients treated with cytotoxic chemotherapy or anti-CD20 antibodies who are positive for either HBsAg or HBcAb range from 24% to 88% and 3% to 22%, respectively.[69,73,74] In the setting of chemotherapy, the mortality rate from HBV reactivation ranges from 23% to 71%.[75,76] False-negative results for HBsAg can occur in patients with chronic liver disease and, thus, patients with a history of hepatitis in need of chemotherapy or immunotherapy should be assessed by HBV load.[77]

Because of the morbidity and mortality associated with HBV reactivation, particularly among patients with NHL receiving anti-CD20 antibody therapy, guidelines suggest that testing for both HBsAg and HBcAb should be performed in all patients receiving anti-CD20 antibody therapy.[58,78] In addition, testing should be performed for all patients receiving any treatment for NHL who are from or live in a highly prevalent HBV region because research indicates that HBV can be reactivated in patients who have received cytotoxic chemotherapy without any prior immunotherapy.[58,78] Hepatitis B surface antibody (HBsAb) should also be tested in all patients receiving anti–B-cell therapy; among those positive for HBcAb or HBsAb but negative for HBsAg, HBV DNA levels should also be measured.[79] Of note, patients receiving intravenous immunoglobulin may be positive for HBcAb as a result of that treatment, so HBV DNA levels should also be measured in these patients (Table).[80] Study results have also suggested that screening for patients with NHL receiving anti-CD20 antibodies was a cost-effective measure, thus providing additional evidence for the screening of all patients for HBV seropositivity receiving treatment for NHL.[61,81,82]

Because patients with NHL treated with lymphoma-directed therapy are at high risk for HBV reactivation, the National Comprehensive Cancer Center (NCCN) recommends either prophylaxis or active surveillance of patients with NHL undergoing immunosuppressive therapy (chemotherapy or anti-CD20 antibody therapy).[83] Prophylaxis with antiviral therapy should be provided for patients positive for HBsAg. Among those positive for HBcAb or HBsAb but negative for HBsAg, the HBV DNA load should determine

Table. — HBV Testing and Prophylaxis in NHL

Whom to Test	All patients treated with anti-CD20 antibodies Patients treated with any therapy for NHL from HBV-endemic countries Patients treated with IVIG
Assays to Test	HBcAb HBsAb HBsAg HBV DNA PCR[a]
Agents for Prophylaxis	Active surveillance with HBV DNA PCR (select cases) Adefovir Entecavir[b] Lamivudine Tenofovir
Duration of Prophylaxis	During therapy and 12 mo post-therapy
Monitoring of Seropositive Individuals	HBV DNA PCR every 3 mo post-treatment for 12 mo Monthly HBV DNA PCR while on treatment

[a]To be used in patients with chronic liver disease or history of hepatitis and negative HBcAb, those taking IVIG, or those negative for HBsAg and positive for either HBcAb or HBsAb.

[b]Preferred agent.

HBcAb = hepatitis B core antibody, HBsAb = hepatitis B surface antibody, HBsAg = hepatitis B surface antigen, HBV = hepatitis B virus, IVIG = intravenous immunoglobulin, NHL = non-Hodgkin lymphoma, PCR = polymerase chain reaction.

whether prophylaxis is required rather than active surveillance.[79] For example, if the HBV DNA load is detectable, then prophylaxis is recommended.[79] In patients for whom prophylaxis cannot be provided, then close surveillance with quantitative HBV DNA levels can be performed and antiviral therapy can be initiated early in patients with a rising HBV DNA load.[74]

Studies supporting the use of antiviral prophylaxis include a small, randomized trial of 30 participants with lymphoma and positive for HBsAg who were randomized to either prophylaxis with lamivudine or deferred, preemptive therapy (antiviral therapy was started at the time of serological evidence of HBV).[84] Those assigned to preemptive therapy had a reactivation rate of 53%, whereas those assigned to lamivudine had a reactivation rate of 0% during lymphoma-directed therapy.[84] Other studies with lamivudine showed similar rates of efficacy.[76,85-90] In a meta-analysis, patients positive for HBsAg on lamivudine prophylaxis had a reduced rate of HBV reactivation (risk ratio 0.21; 95% CI: 0.13–0.35) and there was a trend toward reduced HBV-related deaths compared with those who had no prophylaxis.[90] It is worth noting that most of these studies of lamivudine followed study patients for serological relapse, not detectable HBV DNA loads, and this may be why salvage antiviral therapy was ineffective in most study participants.

Other antiviral agents, such as entecavir, have been shown to be more effective at preventing HBV reactivation in patients who are HBV seropositive.[74,91,92] In a prospective study of 229 study patients with diffuse large B-cell lymphoma treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, those positive for HBsAg were randomized to receive either entecavir or lamivudine.[92] Entecavir was associated with lower rates of HBV-related hepatitis (0% vs 13.3%; $P = .003$) and HBV reactivation (6.6% vs 30%; $P = .001$).[92] This finding suggests that entecavir may be a more appropriate antiviral agent for prophylaxis than lamivudine,[92] although more studies are needed to confirm this result. Other potentially effective antiviral agents include tenofovir or adefovir, although data relating to oncology patients are lacking. The NCCN recommends using entecavir for prophylaxis in HBV-seropositive patients receiving therapy for NHL and monthly surveillance with HBV viral load via polymerase chain reaction during treatment and then every 3 months after treatment for a duration of 1 year (see Table).[84]

Conclusions

Health care professionals should be suspicious of hepatitis B virus (HBV) infection in patients who develop non-Hodgkin lymphoma (NHL) and live in or are from HBV-endemic areas. Patients receiving chemotherapy — in particular, anti-CD20 antibodies — should be tested for hepatitis B surface antigen, core antibody, and surface antibody as well as HBV DNA load in certain cases prior to the initiation of therapy. Patients who have HBV seropositivity or a detectable HBV DNA load should be prophylactically treated with antiviral therapy (eg, entecavir) while receiving treatment for NHL; this prophylaxis should continue for 1 year after the therapy for NHL has ended. By clinicians becoming more aware of the possible reactivation of HBV and by understanding the use of antiviral prophylaxis and surveillance, the high rates of morbidity and mortality from HBV reactivation might be avoided. Further research is needed to better understand the lymphomagenesis of HBV to NHL and to find better agents for prophylaxis and treatment options for patients with NHL who develop HBV reactivation.

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Cancer Control
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Stromal Overgrowth in a Brenner Tumor or Ovarian Fibroma With Minor Sex Cord Elements?

Julia A. Ross, MD, PhD, and Ozlen Saglam, MD

Summary: Computed tomography obtained as part of a urinary tract assessment in a 68-year-old woman incidentally detected a solid adnexal mass. Bilateral salpingo-oophorectomy revealed a unilateral, 4-cm, white to tan-yellow colored, focally calcified, left ovarian mass. Microscopically, the tumor was composed of bland fibroblasts, abundant collagen, and areas of calcification with a minor component composed of nests of epithelial cells with nuclear clefts focally evident, some of which contained central lumens with eosinophilic secretions. The major considerations were fibromatous overgrowth in a Brenner tumor or ovarian fibroma with minor sex cord elements. Immunostains for cytokeratin 7 showed diffuse positivity in the epithelial nests, whereas cytokeratin 20 and inhibin were negative, further supporting the diagnosis of a Brenner tumor.

Background

Most ovarian neoplasms are surface epithelial tumors, 2% to 3% of which represent Brenner tumors.[1] Incidental Brenner tumors are not uncommon in oophorectomy specimens, and the true incidence of these lesions may be higher than estimated. The clinical significance, if any, of incidental Brenner tumor is unknown. Because of the common presence of mucinous epithelium lining the central space in Brenner nests, a variety of mucinous tumors may arise within a Brenner tumor. Brenner tumors also commonly occur in association with other ovarian tumors, including serous adenofibroma and mature cystic teratomas.[2] Sex cord–stromal tumors represent approximately 6% to 8% of ovarian neoplasms, with fibromas accounting for the majority.[3] A small portion of fibromas have minor sex cord elements.

Case Report

A 68-year-old white, gravida 4, para 4, postmenopausal woman was referred for computed tomography as part of a urinary tract assessment. The imaging study incidentally revealed an adnexal mass with calcifications. Ultrasonography was obtained and showed a 3.3 × 2.4 cm left adnexal mass with no blood flow, which was suspicious for a possible dermoid cyst. Subsequently, magnetic resonance imaging demonstrated a 3 × 2.6 × 2.2 cm mass in the left ovary with a homogeneous, low T2 signal and very minimal enhancement following the administration of gadolinium, a finding suspicious for ovarian fibroma (Fig 1A). Her level of cancer antigen 125 was normal (3.1; normal < 35 U/mL). Given the suspected benign nature of the ovarian mass, surgery limited to bilateral salpingo-oophorectomy was performed.

Grossly, the left ovary was firm with a smooth and glistening external surface. The ovary was sectioned to reveal a 4-cm solid mass with a tan-yellow to white-colored, focally calcified, cut surface (Fig 1B). The lesion replaced nearly the entire left ovary measuring 4.5 × 2.8 × 2.2 cm. Microscopically, the lesion had well-circumscribed borders. It was predominantly composed of fibrous stroma with bland spindle cells and collagen with large areas of calcification distributed in the abundant stromal collagen (Fig 2A and B). Admixed with the fibrous stroma and calcifications were multiple small epithelial nests comprising 10% to 15% of the entire lesion, some of which had central lumens filled with eosinophilic secretions (Fig 2C). Although the epithelial nests made up a minor component of the lesion, they were scattered throughout multiple sections and were found in close proximity of the calcifications under high-power examination. The epithelial cells were relatively uniform in size with scant cytoplasm and nuclei with occasional longitudinal grooves. No related mucinous epithelium was identified.

The epithelial nests showed strong and diffuse immunoreactivity with cytokeratin (CK) 7 (Fig 2D) but were negative for CK20 and inhibin. The contralateral ovary measuring 2.8 × 2.4 × 1.8 cm revealed cortical inclusion cysts. The fallopian tubes demonstrated paratubal cysts with no additional pathological findings.

Discussion

The pathological findings in this case supported the

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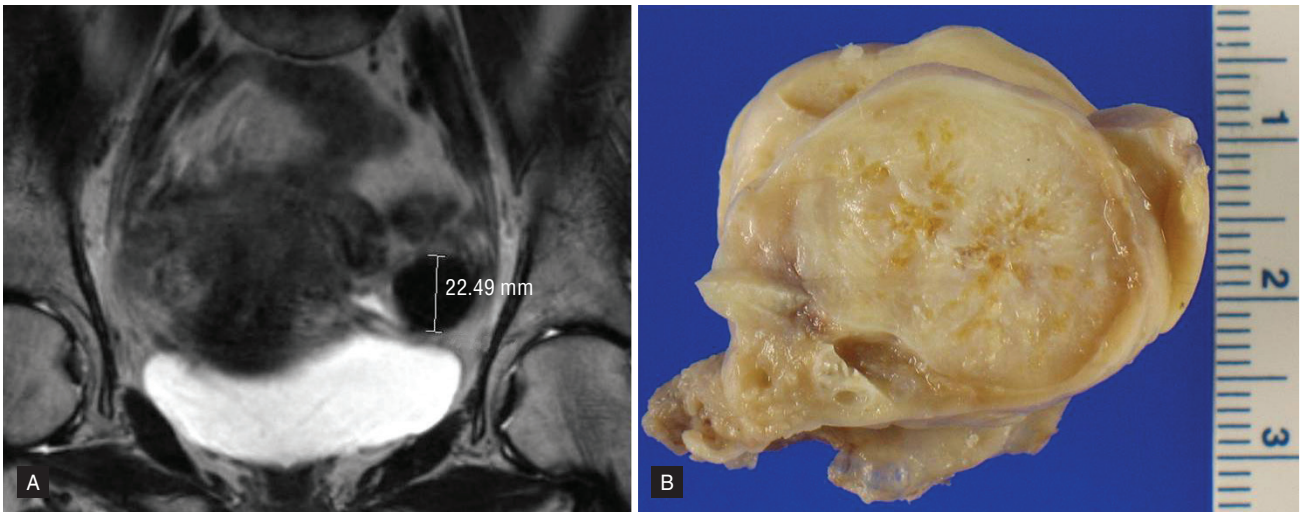

Fig 1A–B. — (A) Magnetic resonance imaging of the left ovarian mass that showed homogeneous, low T2 signal and minimal enhancement after the administration of gadolinium. (B) Gross pathology showing the cut surface of the 4-cm ovarian mass.

clinical and radiological findings of a benign ovarian neoplasm. The gross examination was characteristic of an ovarian fibroma with a solid, firm, cut surface. The presence of focal microscopic epithelial nests within the fibrous stroma suggested the differential diagnosis of ovarian fibroma with minor sex cord elements, a rare entity described by Young and Scully in 1983.[4] By definition, the sex cord elements represent less than 10% of the lesion and are composed of granulosa cells, Sertoli cells, or indifferent cells of a sex cord–like type. Our case was predominantly a fibrous tumor with a small component of transitional-type epithelial islands (10%–15%) distributed within fibrous stroma. By contrast to typical sex cord elements, the epithelial nests in this case had cystic lumina with eosinophilic secretions. In addition, the presence of nuclear grooves was an indication of a transitional-type epithelium. These entities can be further distinguished with immunohistochemistry, because sex cord–stromal elements stain positively with inhibin and Brenner tumors stain with CK7. In our case, the epithelial groups showed CK7 positivity and inhibin negativity, supporting the findings on hematoxylin and eosin staining.

Given the patient's presentation, which included urinary tract complaints, the possibility of metastatic urothelial carcinoma was considered, but the nests of transitional cells lacked significant proliferation, atypia, or mitotic activity. In general, metastatic tumors of the ovary present as multiple bilateral lesions, which is in contrast to the unilateral presentation of this lesion. Furthermore, urothelial carcinomas coexpress CK7 and CK20. The latter marker was negative in the epithelial nests.

The distinction can be more challenging in a case of borderline or malignant Brenner tumor, or a transitional variant of high-grade serous carcinoma, as any and all of these may and, not infrequently, present as cystic lesions.[5] The cytological features of borderline or low-malignant potential Brenner tumors can be similar to that of benign Brenner tumors; however, their architectural features are more complex, forming papillae or polypoid structures.[6]

Approximately 50% of Brenner tumors are associated with calcifications and fibromas may show dense calcifications as well.[3,7,8] The distinction between a Brenner tumor with fibrous stroma and ovarian fibroma may seem to be an academic exercise, particularly because both entities are benign; however, despite the benignity of both lesions, the characterization can be important because multiple reports of tumors metastasizing to ovarian lesions such as Brenner tumor — and, to a lesser extent, fibroma — have been described.[9-12] These examples include renal cell carcinoma metastasizing to mixed Brenner tumor with mucinous cystadenoma,[9] squamous cell carcinoma of the cervix metastasizing to Brenner tumor,[10] breast cystosarcoma phyllodes to Brenner tumor,[11] and breast adenocarcinoma metastasizing to benign ovarian fibroma.[12]

Conclusions

Imaging, microscopic, and immunohistochemical features of a Brenner tumor with abundant fibrous stromal overgrowth were presented. The rare entity of fibroma with minor sex cord elements was excluded by morphological and immunophenotypical features. Ovarian fibroma with an incidental Brenner tumor component may also be considered in the differential diagnosis. By contrast to the localized nature of the epithelial component in a Brenner tumor with fibrous stroma, the presence of relatively scattered epithelial elements is an atypical finding in this case. Brenner tumors can occur with other ovarian neoplasms; however, a description of Brenner tumor coexisting with ovarian fibroma has, to our knowledge, never been de-

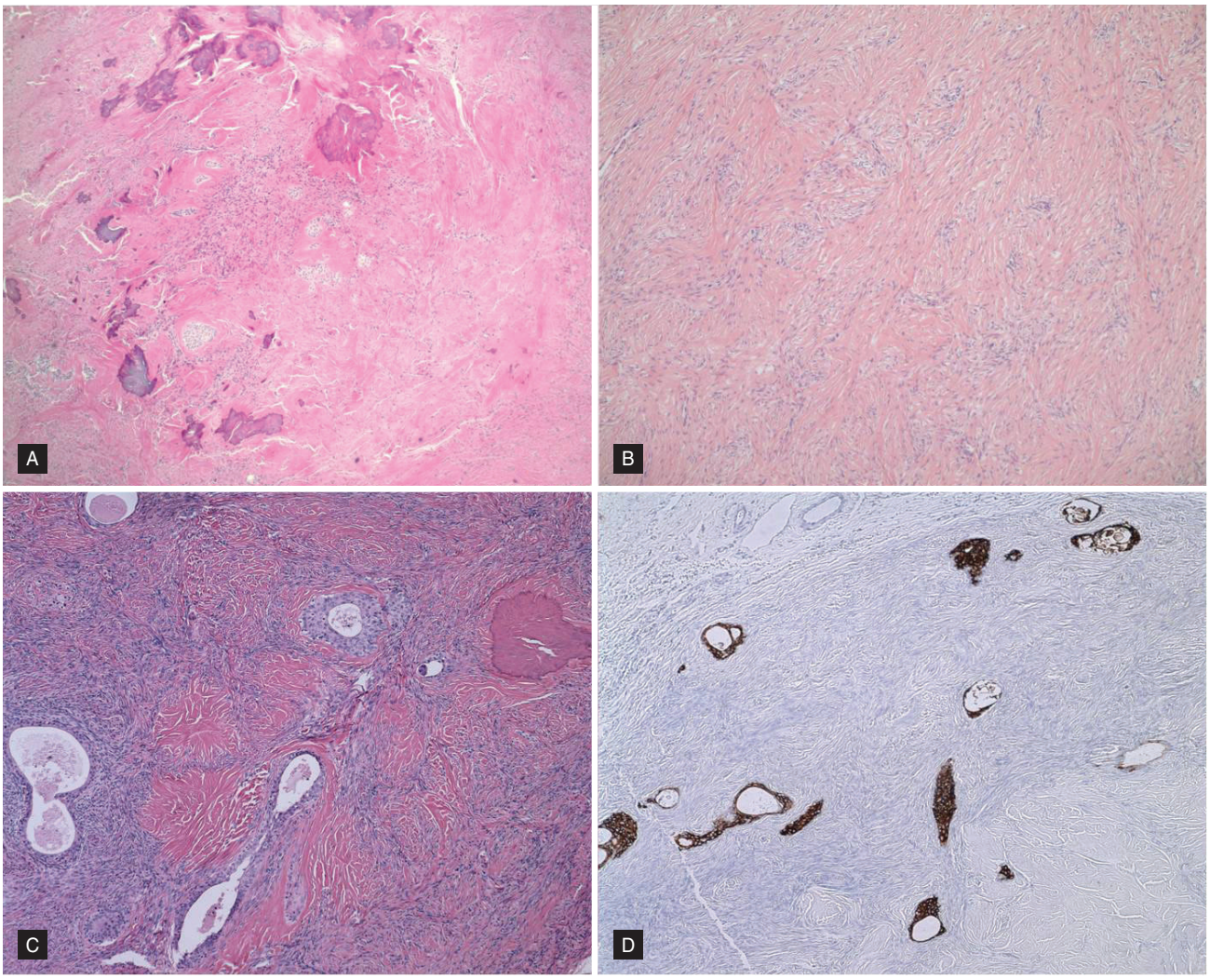

Fig 2A–D. — (A) Ovarian mass with calcifications, abundant fibrous stroma, bland spindle cells, and collagen. Focal areas contain small epithelial nests with central lumens filled with eosinophilic secretions (H & E, × 40). (B) Higher power microscopy of fibromatous area (H & E, × 100). (C) Higher power view of epithelial nests with central lumens filled with eosinophilic secretions (H & E, × 100). (D) Cytokeratin 7 immunoreactivity of epithelial nests (× 100). H & E = hematoxylin and eosin.

tailed. Although this may be the scenario in the case presented, the diagnosis of Brenner tumor is favored in the presence of a single gross nodular lesion. Despite the benign nature of both lesions, an awareness of the potential for tumors to metastasize to these lesions should be noted.

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Recurrent Systemic Anaplastic Lymphoma Kinase–Negative Anaplastic Large Cell Lymphoma Presenting as a Breast Implant–Associated Lesion

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Summary: A woman aged 48 years presented with fevers, chills, weight loss, and night sweats. She had significant lymphadenopathy of the left neck as well as the left axilla. Her history was significant for bilateral breast augmentation with textured silicone implants more than 25 years ago. Excisional biopsy of a cervical lymph node revealed large, atypical cells positive for CD4 and CD30 and negative for Epstein–Barr virus–encoded ribonucleic acid, CD2, CD3, CD5, CD7, CD8, CD15, CD20, pan-keratin, S100, anaplastic lymphoma kinase (ALK), and paired box 5. These findings were consistent with Ann Arbor stage IIIB ALK– anaplastic large cell lymphoma (ALCL). The patient was started on 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone. She initially had no signs or symptoms of breast involvement; however, after developing seroma during the clinical course, the patient underwent capsulectomy and removal of the intact, textured silicone implants. Pathological evaluation demonstrated ALK– ALCL in the left breast capsule with cells displaying a significant degree of pleomorphism with binucleated forms and numerous mitoses. Fluorescence in situ hybridization confirmed the tumor was negative for t(2;5). She presented 8 weeks later showing evidence of recurrent systemic disease.

Background

Breast implant–associated anaplastic large cell lymphoma (ALCL) is a rare T-cell neoplasm typically presenting in women as a mass or late seroma in the breast implant capsule.[1,2] Textured silicone implants have been associated with an increased risk for the development of ALCL, which may occur as a reactive process involving the fibrous capsule.[3-6] Breast implant–ALCL is histologically and molecularly indistinguishable from anaplastic lymphoma kinase (ALK)–negative ALCL.[7,8]

In 2011, the US Food and Drug Administration reported a possible association between breast implants and ALCL.[3] To date, approximately 173 cases have been published in the English literature.[9] The estimated yearly incidence of primary ALCL of the breast is 1 per 100,000,000, and the estimated 5-year overall survival rate is 92%.[10] By contrast, systemic ALK– ALCL accounts for 2% to 3% of all non-Hodgkin lymphomas and has a poorer prognosis (5-year overall survival rate of 20%–50%).[11,12] More than 80% of patients with breast implant–ALCL present with stage 1 disease.[10] Most patients with breast implant–ALCL have small clusters of neoplastic cells lining the fibrous capsule within serous effusions, whereas some patients present with a tumor mass within or beyond the capsule.

Although it may disseminate, the disease typically remains indolent such that the distinction between de novo systemic ALK– ALCL and breast implant–ALCL has prognostic implications. Current treatment for breast implant–ALCL restricted to the breast implant capsule consists of bilateral implant removal and capsulectomy with subsequent close follow-up.[9,10] In cases of disseminated disease, chemotherapy, radiation, bone marrow transplant, or all 3 options can be considered. It is important for health care professionals to be aware of the association between breast implants and ALK– ALCL, the ways in which the disease may present, and, as illustrated in this case report, the importance of differentiating between ALCL types.

Case Report

Clinical History

A woman 48 years of age presented with fevers, night sweats, and weight loss accompanied by masses in

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the left neck and left axilla. Excisional biopsy of a cervical lymph node was consistent with ALK– ALCL. Bone marrow biopsy was performed and no involvement was noted. Positron emission tomography showed hypermetabolic left cervical lymphadenopathy, left axillary lymphadenopathy, and splenic hilar lymphadenopathy without contralateral involvement, consistent with Ann Arbor stage 3B ALK– ALCL. The patient was without signs, symptoms, or radiographic evidence of breast involvement.

Her history was significant for bilateral breast augmentation with textured silicone breast implants at the age of 21 years via a transaxillary approach. Thirteen years after implantation, she had left capsular contracture and underwent left capsulectomy and exchange of the left breast implant via an inframammary fold approach.

The systemic ALK– ALCL was treated with 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone, and resolution was seen at all sites of disease by positron emission tomography 1 month after her last cycle. Two months after completion of the chemotherapy, the patient reported swelling of the left breast (Fig 1). In addition to swelling and firmness, a new 10 × 4 cm erythematous area overlying the site of the prior implant incision was discovered. Ultrasonography demonstrated periimplant seroma, which was subsequently aspirated. Cytological evaluation was consistent with recurrent ALK– ALCL.[13,14]

The patient underwent bilateral total capsulectomy and removal of the intact, textured silicone implants (see Fig 1). A large fluid collection was encountered in the left breast, and approximately 200 cc of fluid was collected for cytology. No palpable masses were appreciated. Scarring extending toward the axilla on the left breast was noted and was believed to have been a result of the transaxillary approach used when placing the implants. The postoperative course was without complications.

Positron emission tomography performed 8 weeks later showed evidence of recurrent bilateral systemic disease, and multiple new hypermetabolic lesions were seen above and below the diaphragm. Biopsy of the right axillary lymph node confirmed recurrent ALK– ALCL. The patient underwent salvage chemotherapy with 2 cycles of etoposide, methylprednisolone, cytarabine, and cisplatin but did not achieve remission. The patient achieved complete remission following 3 cycles of anti-CD30 therapy with brentuximab vedotin and was scheduled to receive an allogeneic hematopoietic stem cell transplant.

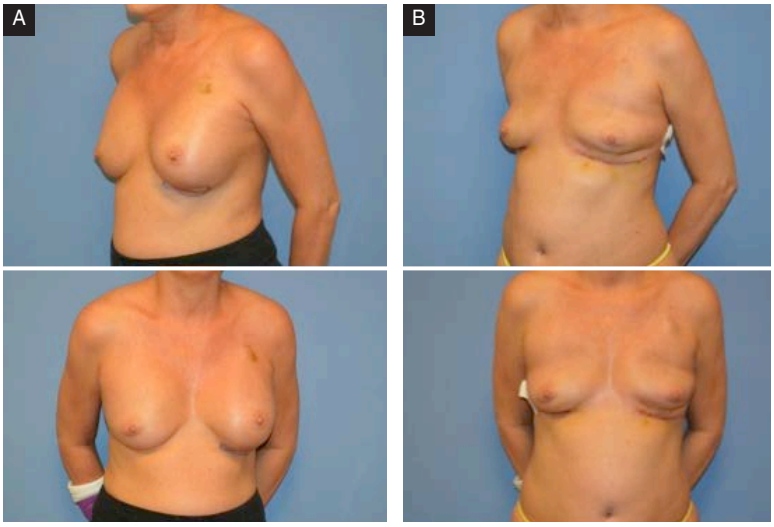

Fig 1A–B. — Preoperative and postoperative imaging. (A) These images show the preoperative presentation with notable left breast swelling. (B) These images demonstrate the appearance of the left breast following implant removal and capsulectomy.

Pathological Findings

Initial excisional biopsy of a cervical lymph node revealed cells positive for CD4 and CD30 and negative for Epstein–Barr virus–encoded ribonucleic acid, CD2, CD3, CD5, CD7, CD8, CD15, CD20, pankeratin, S100, ALK, and paired box 5, consistent with ALK– ALCL. The capsulectomy specimen had tumor involvement that consisted of large, single, scant CD30-positive tumor cells along the inner surface of the fibrous capsule. Cytologically, the malignant cells were large and had abundant cytoplasm, mostly eccentric nuclei, and multiple prominent nucleoli. The cells displayed a significant degree of pleomorphism with binucleated forms and numerous mitoses (Fig 2A–C). Fluorescence in situ hybridization confirmed the tumor was negative for t(2;5) (Fig 2D).

Discussion

This report represents a notable case of systemic ALK– ALCL in a patient with breast implants. It underscores the importance of a thorough clinical examination and, if warranted, pathological evaluation of the breasts in women with a history of breast implants and ALK– ALCL. The patient initially presented with systemic disease localized to the left axilla, left neck, and splenic hilum, but she did not have breast signs or symptoms. At the time of progression, the disease mimicked breast implant–ALCL of the left breast with isolated unilateral, effusion-only disease without a breast mass. It is prognostically important to establish whether breast involvement is secondary to systemic ALK– ALCL or a truly implant-associated process; however, doing so is not possible on morphological or immunohistochemical grounds alone. Tissue collected at diagnosis from an outside institution was inadequate to perform T-cell receptor rearrange-

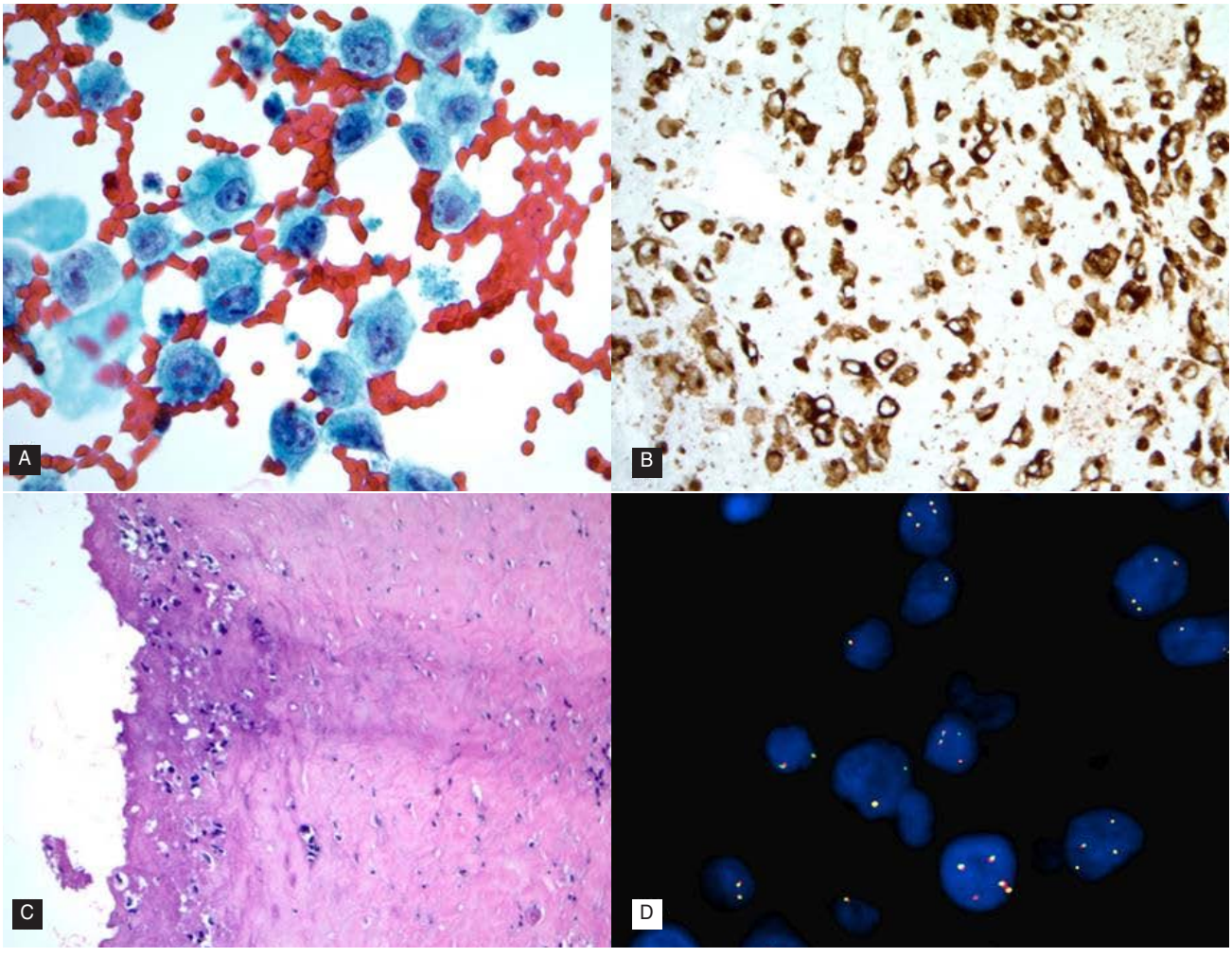

Fig 2A–D. — (A) Fluid cytology reveals large, highly pleomorphic cells with abundant foamy cytoplasm and eccentric nuclei with several prominent nucleoli (Papanicolaou stain, × 40). (B) Histological section of the capsule showing involvement in the inner surface by malignant cells (hematoxylin and eosin, × 10). (C) Anaplastic malignant cells are strongly positive for CD30 immunohistochemistry (× 20). (D) Fluorescence in situ hybridization is negative for t(2;5). Panel D photographed by Dr Kenian Liu.

ment analysis, but tissue obtained via both the left capsulectomy and subsequent axillary node biopsy was confirmed to be of the same clonal origin. This finding proved that the systemic disease at relapse was of the same origin of breast implant–ALCL and strongly suggested that the initial systemic ALCL was not a separate clonal entity from the breast implant–ALCL in this case.

The possible explanations for the origin of the patient's disease are either that the tumor systematically arose de novo and secondarily tracked to the breast where it progressed, or that the disease originated in the breast but remained undetectable at that site until shortly after initial chemotherapy, which is when breast involvement was noted. It is possible that the breast implant capsule favored the spread of disease to that site; however, based on the unilateral localization of nodal disease in the axilla and neck at presentation, we believe the likely origin of the tumor was the left breast implant capsule.

Conclusions

This case has implications for health care professionals given the statistical link between anaplastic large cell lymphoma (ALCL) and breast implants. Our case illustrates the importance of a thorough breast examination and low threshold for mammography or ultrasonography in women with breast implants presenting with systemic anaplastic lymphoma kinase (ALK)–negative ALCL. In our opinion, bilateral capsulectomies should be considered as treatment for all patients with breast implant–ALCL. In addition, ALK– ALCL associated with breast implants can aggressively behave and become resistant to chemotherapy. Health care professionals should also consider brentuximab as a treatment option for patients with CD30-positive, breast implant–ALCL.

The authors would like to thank Dr Kenian Liu for performing the molecular test.

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Shazly SA, Murad MH, Dowdy SC, et al. Robotic radical hysterectomy in early stage cervical cancer: A systematic review and meta-analysis. *Gynecol Oncol*. 2015. [Epub ahead of print].

Robotic-assisted radical hysterectomy (RARH) may be superior to abdominal radical hysterectomy due to decreased rates of estimated blood loss, length of hospital stays, wound-related complications, and febrile morbidity. Laparoscopic radical hysterectomy and RARH may also be equivalent in intraoperative and short-term postoperative outcomes.

Park HK, Helenowski IB, Berry E, et al. A comparison of survival and recurrence outcomes in patients with endometrial cancer undergoing robotic versus open surgery. *J Minim Invasive Gynecol*. 2015. [Epub ahead of print].

A retrospective chart review compared survival and recurrence outcomes in patients undergoing open or robotic-assisted surgical procedures for endometrial cancer. Compared with laparotomy, robotic staging was associated with decreased rates of postoperative morbidity without affecting survival outcomes or short-term recurrence rates.

Cirocchi R, Partelli S, Trastulli S, et al. A systematic review on robotic pancreaticoduodenectomy. *Surg Oncol*. 2013;22(4):238-246.

The use of robotic-assisted pancreaticoduodenectomy (RAPD) appears to be ncreasing. When compared with open or laparoscopic approaches, similar rates of morbidity and mortality are achieved with RAPD. Although more data and cost analyses are needed to determine the cost-effectiveness of RAPD vs other laparoscopic techniques, RAPD may be useful in planning clinical trials.

Zureikat AH, Moser AJ, Boone BA, et al. 250 robotic pancreatic resections: safety and feasibility. *Ann Surg*. 2013;258(4):554-562.

In a large series of robotic-assisted pancreatic resections, the authors found that, compared with open surgery, computer-aided, robotic-assisted surgery aids surgeons in complex resections and anastomotic reconstructions with nearly identical standards. The safety and feasibility metrics studied supported the robustness of this platform.

Kent M, Wang T, Whyte R, et al. Open, video-assisted thoracic surgery, and robotic lobectomy: review of a national database. *Ann Thorac Surg*. 2014;97(1):236-244.

Outcomes related to open, robotic-assisted, and videothoracoscopic surgical methods using the State Inpatient Databases were reviewed. Robotic resection was associated with improved outcomes compared with open thoracotomy and could be an alternative to videothoracoscopic surgery.

Park BJ, Melfi F, Mussi A, et al. Robotic lobectomy for non-small cell lung cancer (NSCLC): long-term oncologic results. *J Thorac Cardiovasc Surg*. 2012;143(2):383-389.

A large series of patients with early-stage, non–small-cell lung cancer undergoing robotic-assisted lobectomy (RAL) was reviewed to assess long-term oncological efficacy. The authors determined that RAL is associated with low rates of morbidity and mortality as well as acceptable long-term, stage-specific survival rates.

Cerfolio RJ, Bryant AS, Minnich DJ. Operative techniques in robotic thoracic surgery for inferior or posterior mediastinal pathology. *J Thorac Cardiovasc Surg*. 2012;143(5):1138-1143.

This study evaluated the efficacy of robotic assistance for the resection of mediastinal tumors located in the posterior and inferior chest. The authors determined that robotic assistance provides safe access when a complete portal approach is used for tumors located in either the inferior, posterior, or anterior chest.

Schwartz GS, Yang SC. Robotic thymectomy for thymic neoplasms. *Thorac Surg Clin*. 2014;24(2):197-201.

Short- and long-term safety and efficacy have been reported for robotic-assisted thymectomy for the management of myasthenia gravis and thymic masses. Although the surgical approaches may vary, the technique for thymic excision/dissection is universal.

Hernandez JM, Dimou F, Weber J, et al. Defining the learning curve for robotic-assisted esophagogastrectomy. *J Gastrointest Surg*. 2013;17(8):1346-1351.

Robotic assistance during surgery has been increasing, but pinpointing the "learning curve" for its use during complex esophageal procedures remains elusive. The study authors found that, among surgeons proficient in performing minimally invasive esophagogastrectomies, the learning curve for a robotic-assisted procedure was about 20 cases. Infrequently, operative complications and conversions occurred, but they remained unchanged among 10 patient cohorts.

Abdollah F, Sood A, Sammon JD, et al. Long-term cancer control outcomes in patients with clinically high-risk prostate cancer treated with robot-assisted radical prostatectomy: results from a multi-institutional study of 1100 patients. *Eur Urol*. 2015 [Epub ahead of print].

Researchers evaluated the long-term cancer control outcomes in 1,100 study patients with clinically high-risk prostate cancer treated with robotic-assisted radical prostatectomy (RARP) at 3 tertiary care centers. They stratified the study patients according to novel risk groups based on their biochemical recurrence-free survival rate and preoperative characteristics. Most patients with clinically high-risk prostate cancer treated with RARP were free of clinical recurrence in the long term. Thus, grouping patients according to their level of risk may be useful for setting expectations and counseling them regarding postoperative outcomes.

FACULTY POSITION: HOSPITALIST

Moffitt Cancer Center is seeking a candidate at the level of assistant/associate member to join the Program of Internal and Hospital Medicine within the Department of Internal Medicine. The position includes inpatient attending and consultation, admitting team duties, and participation in resident education.

Successful candidates must have an MD or DO and be board certified/eligible in internal medicine. Experience in a multidisciplinary academic inpatient setting is preferred. Licensure or eligibility for licensure in the state of Florida is required.

Moffitt Cancer Center serves an appreciative and diverse patient population with a wide range of malignant and nonmalignant diseases. Moffitt, an NCI-designated Comprehensive Cancer Center, is composed of a large ambulatory care facility, a 206-bed hospital, with a 36-bed blood and marrow transplant program, 15 state-of-the-art operating suites, a 30-bed intensive care unit, a high-volume screening program, and a basic science research facility.

For inquiries about the position, contact Bjorn Holmstrom, MD, interim chair, Department of Internal Medicine, at 813-745-4119 or Bjorn.Holmstrom@MOFFITT.org.

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FACULTY POSITION: PATHOLOGISTS

Moffitt Cancer Center is seeking to fill surgical and clinical pathologist positions in its Departments of Anatomic Pathology and Hematopathology and Laboratory Medicine. The candidates will be members of a multidisciplinary team of physicians and scientists, and they will have opportunities to join established basic research programs, with excellent opportunities for translational research in areas of related interest. Candidates will confer and interact with physicians, medical students, residents, and fellows, as well as participate in multidisciplinary case conferences.

Successful candidates should be board certified/eligible and fellowship trained in pathology. Experience in an academic multidisciplinary university clinical setting is preferred. Licensure or eligibility for licensure in the state of Florida is required. Excellent opportunities for basic and clinical research collaboration exist.

Moffitt Cancer Center is a rapidly growing center affiliated with the University of South Florida committed to education through a wide range of residency and fellowship programs. Moffitt, an NCI-designated Comprehensive Cancer Center, is composed of a large ambulatory care facility, a 206-bed hospital, with a 36-bed blood and marrow transplant program, 15 state-of-the-art operating suites, a 30-bed intensive care unit, a high-volume screening program, and a basic science research facility. The Moffitt Research Institute is composed of approximately 150 principal investigators, 58 laboratories, and 306,000 square feet of research space.

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FACULTY POSITION: ACADEMIC NOCTURNIST

Moffitt Cancer Center is seeking a candidate at the level of assistant/associate member to join the Internal and Hospital Medicine Program within our Department of Internal Medicine for the Direct Referral Center's Urgent Care outpatient on-site facility. This full-time position would involve 3 to 4 separate 12-hour shifts each week and include didactic resident teaching responsibilities. No on-call duties are required.

Successful candidates must have an MD or DO and be board certified/newly board eligible in internal medicine. Experience in a multidisciplinary academic inpatient setting is preferred. Licensure or eligibility for licensure in the state of Florida is required.

Moffitt Cancer Center is affiliated with the University of South Florida. Primary and secondary university appointments are available as applicable. Academic rank is commensurate with qualifications and experience. An outstanding compensation package with competitive benefits and a relocation allowance is provided.

Moffitt Cancer Center serves an appreciative and diverse patient population with a wide range of malignant and nonmalignant disease. Moffitt, an NCI-designated Comprehensive Cancer Center, is located adjacent to the Health Sciences Center of the University of South Florida and is committed to education through a wide range of residency and fellowship programs. Moffitt is composed of a large ambulatory care facility, a 206-bed hospital, with a 36-bed blood and marrow transplant program, 15 state-of-the-art operating suites, a 30-bed intensive care unit, a high-volume screening program, and a basic science research facility.

For inquiries about the position, contact Bryan Bognar, MD, chair, Department of Internal Medicine, at 813-745-3134 or Bryan.Bognar@MOFFITT.org.

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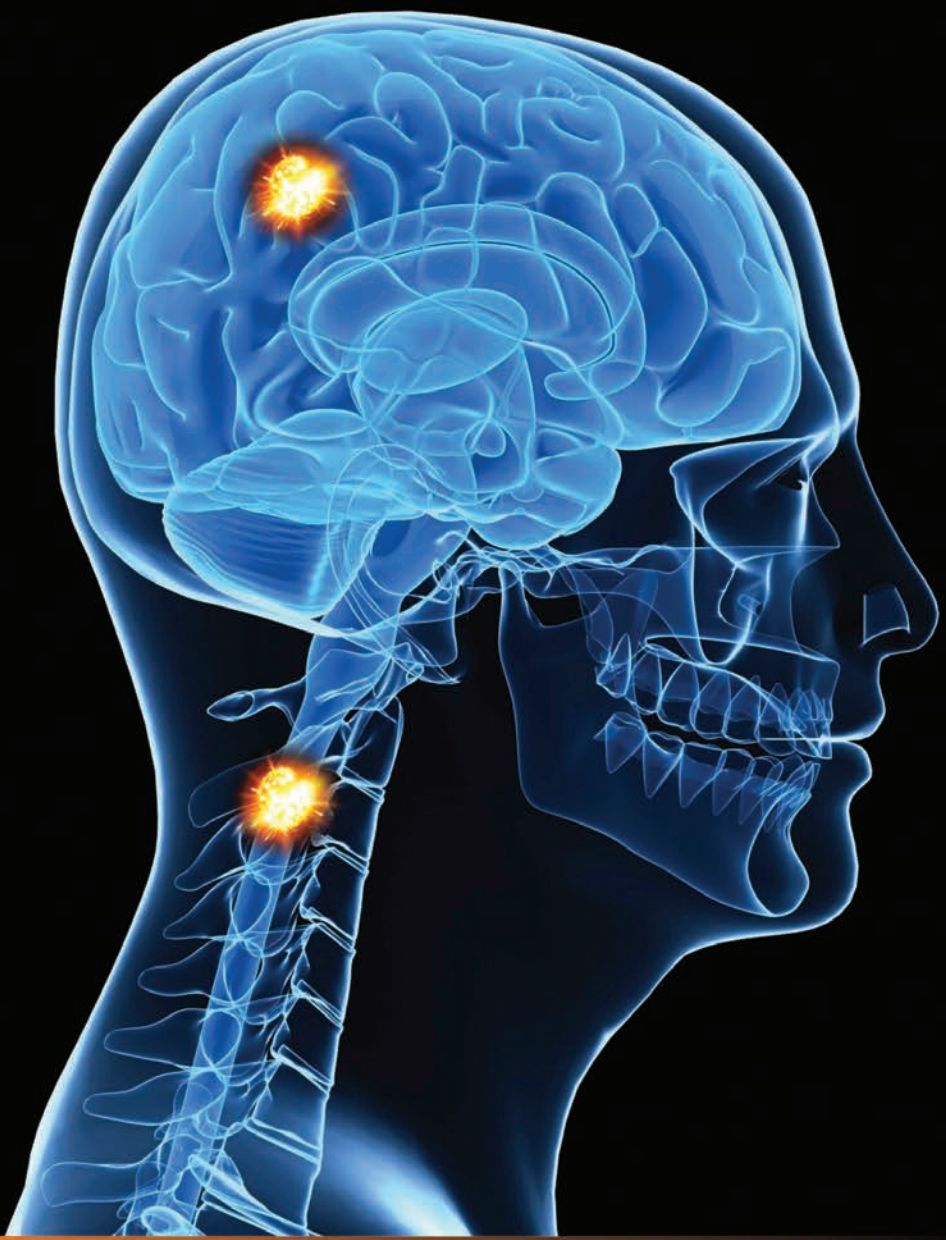

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