



The road to innovation:
*Emerging technologies
in surgery*

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Throughout the centuries, the advancement of surgery has been synonymous with innovation or, as journalist Harold Evans says, “inventiveness put to use.”¹ Surgical innovators have dared to challenge the “standards of care” and explore alternative ways to treat surgical disease. A mere look into the second half of the 20th century is all it takes to appreciate how much surgery has advanced, thanks to a few of these visionaries. Examples include John Gibbon, MD, FACS (creator of the first cardiopulmonary bypass machine); Thomas Fogarty, MD, FACS (developer of the vascular thrombectomy catheter and pioneer of the field of vascular interventions); Joseph Murray, MD, FACS (performer of the first successful human organ transplant); and Mark Ravitch, MD, FACS (creator of multiple pediatric surgery procedures and developer of the modern surgical stapler). The last two decades have also seen the development of laparoscopy, now commonplace throughout the world, and the progressive development of minimally invasive surgery.

Technology is advancing at an outstanding pace. At the same time, the surgeon’s view is narrowing because of increased specialization and higher clinical workload. The complexity of technology, combined with this narrowing view, is leading to an expanding gap between surgeons and surgical technologies. Surgeons are becoming less involved in the early development of technology and leaving innovation to industry or nonsurgical clinicians. Lack of surgical involvement in medical innovation may lead to the development of ineffectual answers to the clinical problems that afflict our patients.

Surgeons, being at the forefront of patient care, have a vantage point that allows them to identify unmet clinical needs, characterize them, and conceptualize techniques and technologies to address those needs. No one is better poised than the surgeon to recognize the clinical problems that afflict surgical patients and to do something about them. It is therefore imperative for surgeons to be at the core of innovation, oversee the ethical integration, and direct the implementation of effective new techniques and technologies into current practice in our field.

The purpose of this article is to briefly analyze the process of innovation, explore ways for

surgeons to become involved in surgical innovation, and showcase some of the technical and technological advances currently taking place in our field at large.

Redefining surgery

As technology is allowing us to perform the same procedures through smaller and smaller incisions, there is a growing concern among some that the field of surgery will shrink or even disappear. This obviously depends on how we define surgery.

In his editorial “What is surgery?”, Tom Krummel, MD, FACS, analyzes how the definition of “surgery” can have an impact on the scope of our field. Based on his conversations with Dr. Ravitch, he concludes that rather than a place, an event, or a particular procedure, surgery is “fundamentally an intellectual discipline, frequently involving a surgical procedure, but most importantly characterized by an attitude of responsibility toward the care of the sick.”² According to this definition, shock lithotripsy is part of urological surgery just as endovascular stent graft placement for aneurysms is within the scope of vascular and cardiothoracic surgery. The definition of surgery goes beyond performing a particular operation on a patient. Instead, it implies the delivery of integral care to a patient with the use of the most appropriate methods.

Krummel then goes on to define a surgical operation as an act that entails two components: an image and a manipulation. In conventional surgical procedures, the image is provided by direct visualization of the operative field by the surgeon and the manipulation is performed by the hands and conventional instruments of the surgeon. However, both image and manipulation can take different forms without altering the principles and goals of the procedure. For example, the image could be the one magnified by the loupes of the surgeon, digitally transmitted from a laparoscopic or endoscopic camera to a monitor, or captured by a computed tomography (CT) or an ultrasound and sent to a digital display. Similarly, a manipulation may be performed by way of conventional surgical instruments, laparoscopic or endoscopic devices, instruments connected to a robotic arm, or energy sources capable of

crossing the skin without any incisions.

It is not uncommon for surgeons to stay away from new technology as it is adapted into areas that perform procedures that are very different from the procedures that they currently perform. As technology advances, imaging and manipulation techniques will certainly change; however, regardless of the type of image or manipulation used, the principle will still be the same. All of the technologies being showcased in this article—robotic surgery, natural orifice transluminal endoscopic surgery, implantable one-way bronchial valves, stereotactic radiosurgery, and radiofrequency ablation of lung tumors—abide by this same principle of an image and a manipulation. As such, these technologies should be considered part of the armamentarium of surgical procedures that the surgeon has in order to care for patients.

The process of innovation

by Carlos M. Mery, MD, MPH

Innovation is the process by which creative ideas are successfully implemented. Innovation is not only about creating a new widget, developing a new process, or coming up with a new procedure, and it is more than mere creativity or idea generation. Innovation entails the identification of a problem, the generation and development of an idea, and the translation of that idea back to the bedside to have an impact on patient care. Innovation is about creating value—value for patients, health care providers, and society.

There is a common misconception that the most difficult part of the process of innovation is the creative “eureka” moment when the idea first occurs to the innovator. On the contrary, it is just the beginning. A drawing on a napkin may represent the foundation for a great innovation. However, unless that idea is fully developed and physicians and patients can use it and benefit from it, it will remain just that: an idea on a napkin. It is the responsibility of the innovator to translate that idea into a tangible product or procedure that can really have an impact on patients and health care providers.

Transforming an idea into a useful innovation requires time, perseverance, commitment,

and, particularly for medical devices, money. Who provides each of these components will vary in every single case. Surgeons, because of their direct role in the care of patients, should undoubtedly play a pivotal role in different parts of the development. Engineers, designers, and other people with technical skills will likely participate in the actual development of the concept. The government may help by way of grants. Private investors and industry (such as large corporations, small startups, and so forth) will assist in translating that technology back to the bedside. The details of the interaction between physician-innovators and industry have been the subject of recent debate and are beyond the scope of this article. Suffice it to say that physicians and industry are both essential pieces of the innovation process.

Innovation is a discipline and, as such, it can be learned, stimulated, and enhanced. The following sections of this article describe a process of innovation that has been followed by several serial innovators in the surgical field, albeit with some differences between them.³ This process is described in order to provide an overall framework to help surgeons engage more actively in the innovation of our field. Independent of the surgeon’s entry point in the development cycle or the duration of his or her involvement, as an inventor, he or she must have a good understanding of the entire innovation process. This understanding leads to optimal development.

An important characteristic of this particular process is that it starts with the identification of a clinical need rather than with a particular technology looking for an application. A good a priori characterization of the need to be solved will increase the possibilities of working on something with a significant impact.

Step 1: Needs identification

Identification of a legitimate, yet unmet clinical need is the single most important step in developing a successful innovation. A good solution for a suboptimal need will yield an imperfect innovation, independent of how good the solution may be. Unmet clinical needs are ubiquitous in our environment, but it takes an open and perceptive state of mind to be able to identify those needs. Stop and think throughout the day

about those clinical conundrums that bother you the most and impede the optimal care of your patients. These are usually latent problems in need of someone to solve them.

The natural tendency after identifying a problem is to immediately think of potential solutions. This approach, although successful sometimes, may hinder innovation. At this stage of the process, you haven't studied the problem well enough and you may overlook better ways of solving it.

After identifying a need, try to specify it in a single sentence that concisely summarizes what you are trying to accomplish. A needs statement—such as, “A less invasive method to reduce the pain in patients with compression fractures of the spine”—is a powerful tool that delineates the characteristics of the problem at hand and helps you generate possible solutions.

Step 2: Need validation and specification

Once a need has been identified and a need statement created, perform extensive research in order to fully understand the problem. Talk to people who may face the same issue but might have different perspectives (for example, patients, nurses, and so on). Read the literature. Talk to other colleagues. Become an expert. You will find that this process will give you a different insight and allow you to rephrase the need statement in a more specific way.

Create a list of “requirements” that your solution must have in order to fully solve the problem identified. Which of those requirements does your solution have to have (musts) and which of those items on the list would be advantageous for your solution to have (desirables)?

Step 3: Idea generation

Once the clinical need is well characterized, try to generate possible solutions. Most innovators in the field have formal or informal “brainstorming” sessions.⁴ In general, three to five creative and open-minded people get together for one or two hours to find as many solutions as possible to the problem being studied. A mix of people with some clinical depth and people with some technical expertise (in any area) is adequate for a brainstorming session.⁵ Try to get people with different experience than you,

Suggested resource guide

The references listed in the series of resource guides are presented as additional sources for the reader interested in learning more about each topic.

Innovation

Books

- Evans H. *They Made America*. New York: Little, Brown and Company; 2004.
- Grossman JS. *Innovative Doctoring: Solutions Lie Within Us*. Atlanta: Innovative Doctoring; 2006.
- Kelley T. *The Art of Innovation*. New York: Currency Doubleday; 2000.

Article

Gertner, M. You have an idea, now what? *Semin Pediatr Surg*. 2006;15:302-8.

Web sites

- BME Source. www.bmesource.org. (Organized and edited Web portal with links to medical, engineering, and business resources related to biomedical engineering).
- FreePatentsOnline. <http://www.freepatentsonline.com>. (Free site for searching U.S. and European patents and patent applications).
- USPTO. www.uspto.gov. (Official site of the U.S. Patent and Trademarks Office).

as some of the most innovative ideas in medicine have come from the application of concepts that previously had been used to solve nonmedical problems.

Idea generation is an iterative process that may require several brainstorming sessions, going back to experts in different areas (for example, clinical, technical, and product development), or answering questions that arise from the previous sessions. The need statement and the solutions being generated may change as the process evolves. Once a series of concepts have been generated, these concepts are assessed in terms of feasibility, novelty, possible efficacy, regulatory burden, and how well these

concepts fulfill those items previously specified as requirements.

Step 4: Prototyping

Prototyping, or creating a visual demonstration of a concept, is a useful tool to help the inventors better conceptualize their ideas and, most importantly, to answer some simple questions about that idea. For example, will magnets be strong enough to pull apart the tissue? Will an endoscope allow for adequate visualization when placed inside a balloon? A prototype does not need to be an elaborate device that performs the function that the final device will accomplish. On the contrary, the simpler the prototype, the better. Simple prototypes will enhance creativity and may prompt the inventors to change their concept in unexpected ways. As the idea evolves, more complicated prototypes can be created in order to provide some “proof of principle” that the concept is likely to indeed solve the particular need.

Step 5: Intellectual property

A patent gives the inventors the right to “exclude others from making, using, offering for sale, or selling” the claimed invention.⁶ A good patent gives significant value to a concept, making it more likely for a company to try to translate that particular technology in the future. Submitting a patent can be an expensive and complicated feat and the details of this process are beyond the scope of this discussion. Suffice it to say that the U.S. Patent and Trademarks Office (USPTO) offers a fast and efficient way to obtain initial protection for your idea. For \$100, an inventor can send a “provisional patent” that can be as simple as a drawing on a napkin or as complicated as a formal document specifying all the details of the invention. This provisional patent serves as a 12-month “placeholder” for a formal patent application and sets a priority date, that is, the date when the rights of a patent would begin if a patent is eventually filed and approved. If a formal patent application is not sent to the USPTO within 12 months, the priority date of the provisional patent is lost. These 12 months provide a window of time to allow the inventors to talk to people about their idea, define if an idea is feasible to pursue, or

find people interested in continuing with its development.

Step 6: Development plan

The development pathway of an idea after initial prototyping varies depending on the particulars of the project. Usually the next step after initial development is to find the right people to help with development—that is, to create a multidisciplinary team. It is impossible for a single inventor to transform an invention into a product ready for patient care. Different team profiles are required at different stages of the development. The initial team may require a set of people with deep clinical and technical expertise, whereas a later team may need experts in regulatory affairs, clinical trials, manufacturing, and administration.

Once the team is assembled, a development plan is designed based on different milestones. The particular milestones will depend on the project itself but may likely include project financing, acute and chronic animal testing, human testing, regulatory process, and commercialization.

Funding is one of the most important aspects of the project because without funding, an innovation will never be realized.⁵ The most common forms of funding are government-sponsored (in the form of research grants, development grants, or small business grants), angel or venture capital investments, or corporate sponsorship from major corporations. The type of funding sought out will obviously depend on the scope of the project and on the ultimate intention of the innovators.

An important decision that the physician-inventor will face is how far he or she wants to go with the idea. Some inventors accompany the product throughout the process, up to the first use in patients or even commercialization. Other inventors start the project and take it to varying points before transferring the project to others willing to take it forward. The extent of involvement is essentially a matter of personal preference. Regardless of the ultimate decision and direction of the project, surgeon involvement will undoubtedly help with the development of the concept and, ultimately, with the ethical and responsible incorporation of effective technology into patient care.

In the following sections, five emerging technologies that are the products of the careful application of the process of innovation will be presented.

Emerging technologies

I. Robotic surgery

by Venita Chandra, MD

Decades ago, computer-enhanced robotic surgical systems were originally conceived as a military tool for remote surgical care of the injured soldier on the battlefield. By the late 1990s, rapid advances in computer science and robotics technology have helped bring a number of surgical robotic systems into the modern operating room. These systems come in a wide variety, ranging from simple adjustable arms supporting instruments or cameras to automated fixed-path robots with programmed motion planning based on preoperative imaging studies. The most frequently used surgical robot today is a tele-operating system called the da Vinci Surgical System® (Intuitive Surgical, Sunnyvale, CA), a sophisticated, multi-armed machine that enables complex endoscopic procedures. What makes this type of robotic system attractive stems from its ability to overcome many of the limitations of conventional endoscopic techniques such as difficulties with dexterity and challenges of two-dimensional optics.⁷

The da Vinci Surgical System is composed of two major components. The first component is the surgeon's console, which can be placed up to 10 m away from the operating table and contains the following: (1) the surgeon's control handles that direct movements of the robotic arms inside the patient's body, (2) the visual display, and (3) the user interface panels. The second component is the patient's side cart, which consists of two or three arms that contain the operative instruments and another arm that controls the video endoscope.⁸ Highly magnified three-dimensional stereoscopic images, in combination with improved hand-eye coordination, tremor filtration, and motion scaling are features of the da Vinci Surgical System, which allow delicate motions in small areas, thus enabling surgeons to perform minimally invasive procedures that

Suggested resource guide

Robotic surgery

Book

Gomez G. Emerging technology in surgery: Informatics, electronics, robotics. In: Townsend CM, Beauchamp RD, Evers BM, Mattox K, eds. *Sabiston Textbook of Surgery*. 17th ed. Philadelphia: Elsevier Saunders; 2004.

Articles

- Camarillo DB, Krummel TM, Salisbury JK Jr. Robotic technology in surgery: Past, present, and future. *Am J Surg*. 2004;188:2S-15S.
- Satava RM. The future of surgical simulation and surgical robotics. *Bull Am Coll Surg*. 2007;92(3):13-19.

Product information

Intuitive Surgical da Vinci Surgical System official Web site. http://www.intuitivesurgical.com/products/davinci_surgicalsystem/index.aspx.

NOTES

Article

Baron TH. Natural orifice transluminal endoscopic surgery. *Br J Surg*. 2007;94:1-2. (Overview of the history, current status, and challenges of NOTES).

Web site

Official Web site of the Natural Orifice Surgery Consortium for Assessment and Research. www.noscar.org.

would otherwise be nearly impossible using standard techniques. In addition, one of the innovative features of this device is that the instruments are "wristed," thus providing up to seven degrees of freedom. This enhances dexterity compared with standard minimally invasive surgical instruments, which allow for only five degrees of freedom.⁹

There are a number of limitations with robotic surgical systems, which restrict their widespread adoption. Current teleoperating systems such

as the da Vinci lack the ability to provide force feedback or “haptic” input. Instead, the operating surgeon must rely on visual cues such as tissue compression and blanching, and suture stretch (such as knot deformation) to determine the tensile strength of tissue and sutures. In addition, robotic surgical systems generally are substantially more expensive and more complex than conventional techniques, often resulting in longer operating room times as well as increased total costs.^{9,10}

To date, the majority of published clinical experience using robotic technology has consisted primarily of retrospective case reports and case series. Robotic surgical systems have been used in many different surgical disciplines including general surgery, urology, cardiac surgery, gynecology, and pediatric surgery. Initially, robotic technology was used primarily in procedures that were already performed laparoscopically, such as cholecystectomy, splenectomy, and Nissen fundoplication. With these procedures, robotic and standard approaches yield similar clinical results; however, given the longer preparation and operating room times, using a robot for routine cases does not appear to offer a significant advantage. Nonetheless, there is literature that supports the adoption of robotic technology to enable surgeons to perform more complex reconstructive procedures, such as the Kasai procedure, coronary revascularization, and especially transpubic radical prostatectomy. Robot-assisted prostatectomies have been shown to be associated with significantly reduced blood loss and similar if not decreased risks of incontinence and impotence. These benefits have resulted in a substantial increase in patient and urologist demand for robotic technology.⁹⁻¹²

The future of robotic surgery lies in its ability to extend the boundaries of a surgeon’s skill. Already, procedures once thought to be impossible to perform with minimal access are now done routinely. Exciting prospects for robotic technology in the future include development of high-fidelity force sensors to improve tactile sensation, device miniaturization to allow surgeons to access increasingly remote anatomy, and increasingly sophisticated graphic interfaces involved in image-guided procedures.

II. Natural orifice transluminal endoscopic surgery (NOTES)

by *Ali Tavakkolizadeh, MD*

The definition of minimal access surgery is continuously expanding. In the field of gastrointestinal surgery, minimal access surgery has become synonymous with laparoscopic surgery, where an increasing body of data has documented the safety and superiority of laparoscopic approaches over open surgery. The key question is not how successful laparoscopy is today, but rather how the field of minimal access surgery will develop in the future with key interest in developing new concepts that will lead to even less invasive procedures.

A developing field is endoluminal therapy, which allows endoscopists to perform procedures previously in the domain of open or laparoscopic surgeons. More recently, endoluminal therapy has been taken a step further with investigators breaching the luminal barrier to access the peritoneal space and performing procedures transluminally. This approach avoids the need for any abdominal incisions and has been referred to as “scarless surgery,” or natural orifice transluminal endoscopic surgery (NOTES).

Anthony Kalloo, MD, from Johns Hopkins Hospital, published the first paper on a NOTES procedure using a porcine survival model.¹³ After lavaging the stomach with antibiotic solution, gastrotomies were made with a needle-knife puncture. The peritoneal cavity was insufflated with air using the endoscopic air channel and exploratory peritoneoscopy and liver biopsies were performed.

An expanding body of the literature has confirmed the feasibility of a variety of transluminal procedures, including tubal ligation, gastrojejunostomy, nephrectomy, pancreatectomy, and splenectomy. Transluminal access for gallbladder surgery has been evaluated by a number of studies, using both transgastric and transcolonic approaches. Although transgastric and transcolonic have been the most reported routes, other natural orifices, namely the vagina and urethra (transvesical), have also been used.¹⁴ These animal studies, all performed in pigs, have proved the feasibility and short-term safety of NOTES.

The reported, but as yet unpublished, case of a transgastric appendectomy performed by

N. Nageshwar Reddy, MD, FRCP, DSC, and G. Venkat Rao, MS, MAMS, from Hyderabad, India, is regarded as the first case of a NOTES procedure in humans.¹⁵ There are currently multiple approved or pending institutional review board protocols for NOTES procedures in humans in the U.S. Although a true, completely transluminal endoscopic NOTES procedure has not yet been performed in this country, some have reported on laparoscopic-assisted transvaginal cholecystectomy. Such hybrid procedures are likely to be the next step in the human application of this concept.

Recognizing the potential impact of this new technology, a meeting of the expert representatives from the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) and the American Society of Gastrointestinal Endoscopy (ASGE) was organized in 2005 to identify the potential applications and the challenges facing this novel field. During their meeting, the panel identified eight fundamental barriers to clinical application of NOTES and proposed guidelines and a road map to the development of this field and its eventual human application. Their recommendations have been published in a white paper.¹⁵ A joint subcommittee between the two societies, NOSCART (Natural Orifice Surgery Consortium for Assessment and Research), was also set up. NOSCART has a dedicated Web site (www.noscar.org), a useful resource for those interested in this field. NOSCART is gaining increasing momentum with recent funding opportunities through the society in the area of transluminal surgery. NOSCART will likely take on an increasingly important role in coordinating NOTES research and developing a NOTES patient registry as human studies begin.

NOTES is an exciting new concept and holds promise to become a useful technique in some clinical settings. To fulfill this potential, however, there is a need for extensive research into the physiological changes and potential complications of this technology. There is also a critical need for new devices that will allow reliable closure of enterotomies, as well as endoscopic suturing and visualization. As demonstrated through the advent of laparoscopy, surgeons are slow in adopting new technology, and therefore, even after overcoming the technological hurdles,

it will likely take some time for NOTES to gain professional acceptance. However, hopefully we, as a profession, are prepared to evaluate this concept without bias and get involved in its evolution.

Many have asked who will be performing NOTES procedures: surgeons or gastroenterologists? The answer is unclear at this time and may require “hybrid training” for those interested. Going beyond the “natural” boundaries of medical specialties may enrich all sides. An interdisciplinary and collaborative effort will be the most beneficial approach in this field. Surgeons are well positioned to be actively involved in this field, and ultimately perform new and innovative procedures with potential benefits to patients.

III. Minimally invasive treatment of emphysema with implantable bronchial valves

by David T. Cooke, MD

Chronic obstructive pulmonary disease (COPD) is a devastating disease that significantly affects the U.S. health care system. COPD is the fourth leading cause of death in this country, with 123,884 deaths in 2004.¹⁶ Among patients with COPD, emphysema affects 2 million patients and is characterized by alveolar wall destruction and coalescence of alveolar units. Loss of elastic recoil results in hyperinflation of emphysematous lung and impairs the function of spared lung.

The surgical approaches for emphysema include lung transplantation and lung volume reduction surgery (LVRS). LVRS, by resection of hyperinflated nonfunctional lung tissue, improves the mechanics of the remaining lung, respiratory muscles, and diaphragm. LVRS was first described in the 1950s with limited success, and because of high mortality, the procedure was abandoned until the 1990s when Cooper et al described LVRS via a median sternotomy and use of reinforced stapling techniques.¹⁷ LVRS can also be performed by video-assisted thoracic surgery.

The National Emphysema Treatment Trial identified specific subgroups of emphysema patients who benefit from LVRS; patients with primarily upper lobe disease and poor exercise tolerance demonstrate improved quality of life and survival, and patients with primarily upper

Suggested resource guide

Bronchial valves

Articles

- Fishman A, Martinez F, Naunheim K, et al. A randomized trial comparing lung-volume reduction surgery with medical therapy for severe emphysema. *N Engl J Med.* 2003;348:2059-2073. (Classic multi-institutional randomized study identifying patient subpopulations that would benefit from LVRS)
- Wan IY, Toma TP, Geddes DM, et al. Bronchoscopic lung volume reduction for end-stage emphysema: Report on the first 98 patients. *Chest.* 2006;129:518-526. (The largest multi-institutional trial evaluating the use of implantable valves)
- Wood DE, McKenna RJ Jr, Yussen RD, et al. A multicenter trial of an intrabronchial valve for treatment of severe emphysema. *J Thorac Cardiovasc Surg.* 2007;133:65-73. (First multi-institutional trial evaluating the Spiration implantable bronchial valve)

lobe disease and high exercise tolerance demonstrate improved quality of life but no significant increase in survival.¹⁸ Despite the benefits of LVRS, it is an invasive procedure with a number of potential complications. Morbidity includes, but is not limited to, persistent air leak (~40%) and pneumonia (~11%), and mortality is between 5 percent and 16 percent.¹⁸⁻²⁰

Because of these drawbacks of LVRS, minimally invasive approaches to the treatment of emphysema are being developed. One of these innovations is the bronchoscopic treatment of emphysema with implantable one-way bronchial valves. These valves are implanted in the segmental bronchi of hyperinflated lung and allow air and secretions to egress but do not allow air to enter the target airway. The objective is to allow passive atelectasis of emphysematous segments and redistribute ventilation to normal lung segments.

Three current bronchial valves have been extensively studied. The Spiration Implantable

Intrabronchial Valve (Spiration IBV[®], Spiration Inc., Redmond, WA) is a nitinol umbrella-shaped implant covered with a synthetic polymer. The device can be delivered through the working channel of a flexible fiber-optic bronchoscope, and the umbrella opens to conform to the targeted airway. The device can be removed via the bronchoscope by grasping the central bar. The second-generation Emphasys Endobronchial Valve (Emphasys[™] EBV, Emphasys Medical, Redwood City, CA) is composed of a nitinol framework with a silicone seal, and a silicone internal one-way valve. Unlike the Spiration IBV, the device does not expand when deployed. Fine placement is achieved with the use of the bronchoscope and a guidewire-based delivery system. The third-generation Emphasis Zephyr EBV is a self-expanding nitinol valve similar to the Spiration IBV. The umbrella-like device is passed down the working channel of the bronchoscope and self-expands in the appropriate bronchus, facilitating its placement into the airway. The device can be removed if needed.

Wood and colleagues have published a phase I multicenter clinical trial evaluating the Spiration IBV.²¹ In this study, 30 patients with primary upper lobe emphysema were treated on average with six implantable devices. Minimum follow-up was six months. There were no adverse events that the authors definitively associated with the valves, and there was no evidence of valve migration, erosion or valve-induced hemoptysis, or death. Patients demonstrated significant improvement in quality of life as measured by the St. George's Respiratory Questionnaire, but there were no significant quantitative improvements in functional benchmarks such as forced expiratory volume in one second (FEV₁), lung volume, diffusing capacity for carbon monoxide (D_{LCO}), and six-minute walk distance (6MWD). A broader, randomized, blinded clinical trial, the planned IBV Valve Trial, will compare the treatment group receiving Spiration IBV valves with a control group not receiving valves.²² The treatment cohort will be monitored up to five years.

There are numerous studies evaluating the Emphasys EBV. Wan et al recently reported the first multicenter study using the Emphasys EBV.²³ In this study, 98 patients were treated

with an average of four valves per patient and follow-up was 90 days. There was one death (a patient who developed pneumonia in a treated lobe). Despite variations in target lobes (upper and lower lobe emphysema), and patient selection between institutions, the study demonstrated significant improvements in forced vital capacity (FVC), residual volume, FEV₁, and 6MWD. The Endobronchial Valve for Emphysema Palliation Trial will evaluate the Emphasys Zephyr EBV.²⁴ This trial will randomize patients with heterogeneous emphysema to either treatment with the Emphasys Zephyr EBV, or medical management.

Treatment of emphysema with implantable one-way bronchial valves shows promise. Studies including the reports mentioned in this section and others demonstrate both qualitative and functional improvements in patients with emphysema. It is interesting to note that all studies have achieved their results without demonstrating consistent atelectasis of hyperinflated segments targeted by implanted bronchial valves. This suggests that bronchial valves may improve lung function in a different manner than classic LVRS without definitively eliminating hyperinflated tissue. In addition to emphysema, one can imagine other indications for bronchial valves, such as bronchopleural fistulas or hyperinflation syndromes.

IV. Stereotactic radiosurgery by *Bilal M. Shafi, MD, MSE*

Stereotactic radiosurgery (SRS) has emerged as a novel technique to eliminate pathological tissue with minimal effects to the surrounding normal tissue. This technology employs two main concepts to achieve this goal. First, it localizes the diseased tissue with a combination of imaging techniques and both artificial and anatomical landmarks. Then, it delivers a high dose of ionizing radiation to ablate the pathological tissue. To ensure that surrounding tissue is not damaged, multiple low energy beams of ionizing radiation are fired from multiple directions. At their point of intersection, which happens to be the location of the diseased tissue, the level of ionizing radiation increases to ablative levels.

Radiation, first discovered by Roentgen in 1895

as X rays,²⁵ is now known to be part of the electromagnetic spectrum that includes light and consists of photons or packets of energy. The ionizing radiation is either produced in the form of X rays, generated by the destabilization and restabilization of a stable atom, or gamma rays, produced by the radioactive decay of radioactive substances such as Cobalt-60. Initially, the amount of energy that could be produced by radiation sources was small, subsequently limiting the use of radiation to diagnostic applications or treatment of superficial pathological lesions such as skin cancer. As technology advanced, radiation sources produced higher doses of ionizing radiation, allowing for deeper tissue penetration. Most recently, modern linear accelerators, or LINACs, have allowed the production of very high amounts of energy that can be manipulated through various filters and beam-conforming collimators to accurately target deep-seated diseased tissue.

Radiation affects biological tissue in a complex manner.²⁶ Photons—whose energy is characterized by the rad (radiation-absorbed dose) or, more recently, the Gray (energy deposited per kilogram of tissue)—destabilize the atoms of biological tissue at a specified depth depending on the initial energy. This destabilization leads to an energy release that can affect the cells either directly by damaging the deoxyribonucleic acid (DNA) or indirectly through the creation of oxygen free radicals that can then damage the DNA. The resulting DNA damage can lead to permanent injury, apoptosis, genetic mutation, or repair depending on the sensitivity of the cells to radiation and the stage of the cell cycle. Ultimately, the lethality of ionizing radiation depends on the extent of DNA damage and the cell's capacity for repair.

Radiation therapy was used as early as 1899 to treat basal cell cancer but its use was limited because of the collateral damage to normal skin.²⁷ In 1932, Claude Regaud and Henri Coutard found that delivering a number of smaller doses of radiation in multiple sessions over a longer period of time eliminated the pathological tissue while sparing the surrounding normal tissue. Later, it was determined that these advantages were based on the four principles of radiobiology: repair, redistribution, repopulation, and reoxygenation. Smaller

multiple doses (that is, fractionation) limit the damage to normal tissue and allow the cells to repair themselves before the next dose. At the same time, fractionation allows pathological cells to redistribute themselves into more radiosensitive cell cycle phases and previously less-perfused tumor cells to reoxygenate so that more oxygen free radicals can be generated. Overall, this promotes the eradication of some rapidly proliferating cancer cells while relatively sparing normal and slowly proliferating tissue.

Unfortunately, fractionated radiotherapy is ineffective against some slowly proliferating cancer tissues. In 1951, Lars Leksell, MD, PhD, a Swedish neurosurgeon, developed the concept of SRS. Using a rigid frame attached to the patient's skull, he was able to deliver multiple low-energy beams fired from different directions to converge on a specified target in the cranium with minimal damage to surrounding tissue. This ultimately resulted in the Gamma Knife™ (Elekta, Stockholm, Sweden), which is still in use today. This device was limited to intracranial targets because it required a rigid frame to be attached to the patient. With the development of the LINAC, a number of systems, including Cyberknife™ (Accuray, Sunnyvale, CA) and ExacTrac X-ray 6D™ (BrainLAB AG, Munich, Germany), have allowed the delivery of targeted radiation without the use of rigid frames. Instead, these systems use radiological imaging and a combination of anatomical landmarks and markers placed in the body to target the lesion. The Cyberknife uses a LINAC attached to a robotic arm to deliver the radiation from multiple directions while the ExacTrac rotates the patient around a fixed beam. Both systems open up the possibility of fractionated radiosurgery and radiation therapy to extracranial targets. These systems also allow more accurate delivery of radiation to nonuniform lesions and lesions located next to critical structures.

The development of SRS has allowed the expansion of delivering radiation to previously overlooked targets. With the help of various tracking devices to account for respiratory motion, lesions in the lung, liver, and kidney can now be treated. Ultimately, SRS provides patients with unresectable disease another option that could potentially help palliate their

disease without exacting collateral damage. Because this therapy should be seen as within the scope of “surgical treatment” of disease, it is imperative for all general surgeons to understand and consider incorporating this new technique into their tool arsenal for treating surgical disease.

V. Radiofrequency and radiosurgical ablation of thoracic tumors

by Thomas K. Varghese, Jr., MD

Lung cancer is the leading cause of cancer-related mortality in U.S. men and women. It was estimated that 174,470 new cases of lung cancer (92,700 in men, and 81,770 in women) would be diagnosed in 2006 and that the disease would lead to 162,460 deaths (90,330 in men, 72,130 in women).²⁸ Only 15 percent of all lung cancer patients are alive five years or more after their diagnosis. Surgical resection offers the best chance for cure in early stages, with five-year survival rates of 67 percent for stage I and 57 percent for stage II. Unfortunately, only 10 percent of patients will have stage I disease and 20 percent will have stage II disease.

Early-stage patients with multiple comorbidities who are not surgical candidates are typically offered conventional external beam radiotherapy as treatment, with reported five-year survival rates of 10 percent to 20 percent.²⁹ Chemotherapy in this patient population is palliative in nature. The lung is also the second most frequent site of metastatic disease, and several studies have reported surgical resection of pulmonary metastasis as a viable option for treatment. However, often the number and location of the lesions would require a sacrifice of too much functional lung tissue. Surgical resection in patients with widespread metastatic disease often compromises quality of life. As a result of these dismal outcomes, newer treatment modalities have been used in thoracic surgery, such as CT-guided radiofrequency ablation (RFA) and SRS.

RFA

RFA is a thermal energy delivery system, where a probe is introduced percutaneously under ultrasound or CT-guidance into the tumor,

with deployment of multiple tines. The tines allow for maximal distribution of energy. Radiofrequency energy is then applied in order to achieve a temperature greater than 60°C (in most cases 90°C). Thus, coagulative necrosis of the tumor is induced in a controlled manner. This method has been successfully used for the treatment of hepatocellular carcinoma, hepatic metastases, osteoid osteoma, and other solid tumors. The first percutaneous RFA of a lung tumor was reported by Dupuy et al in 2000.³⁰ They treated three patients for whom the main purpose of RFA was palliation, with results that were technically successful and uneventful. Others have applied the technique to pulmonary tumors with promising preliminary results.³¹ These studies have reported a good local response, tolerability, and a very low rate of complications. However, they have a short follow-up period and little is yet understood about the efficacy of RFA in the mid- to long-term. Initial experience suggests that RFA is most effective for lesions smaller than 3 cm and for metastases. When compared with surgery, as expected, there is a higher recurrence rate locally and in the mediastinum. Caution for use of RFA is needed in those patients with high pulmonary arterial pressures and central lesions, as there have been reports of increased risk of hemoptysis.

SRS for lung cancer

Failure to attain local control has been one of the biggest obstacles blocking the success of radiotherapy for many common epithelial cancers, including lung cancer and a variety of metastases in solid organs. Higher radiation doses will enhance local control. However, increased doses of radiation will also result in increased toxicity and damage to surrounding lung parenchyma. SRS was developed in response to a clearly identified need in oncology to improve local control of deep-seated tumors.

SRS provides selective delivery of an intense dose of high-energy radiation to destroy a tumor with precision targeting (see the “Stereotactic radiosurgery” section of this article). The improved accuracy is achieved by very precise spatial localization of the tumor and the delivery of multiple cross-fired beams of radiation to converge upon the tumor. This technology

Suggested resource guide

Stereotactic radiosurgery/ Radiofrequency and radiosurgical ablation of thoracic tumors

Book

Smith RP, McKenna WG. The basics of radiation therapy. In: Abeloff MD, et al. *Clinical Oncology*. Philadelphia: Elsevier Churchill Livingstone; 2004. (Overview of the physics and biology of radiation therapy)

Articles

- Dupuy DE, Zagoria RJ, Akerley W, et al. Percutaneous radiofrequency ablation of malignancies in the lung. *AJR*. 2000;174:57-59. (First description of radiofrequency ablation of lung tumors)
- Kavanagh BD, McGarry RC, Timmerman RD. Extracranial radiosurgery (stereotactic body radiation therapy) for oligometastases. *Semin Rad Oncol*. 2006;16:77-84.
- Pennathur A, Luketich JD, Burton S, et al. Stereotactic radiosurgery for the treatment of lung neoplasm: Initial experience. *Ann Thorac Surg*. 2007;83:1820-1824. (Study that reports some early results with stereotactic radiosurgery for lung tumors and provides a background of the technology)

has become standard treatment for intracranial tumors in many centers. However, unlike the brain, respiratory motion creates difficulties in the delivery of precise radiation to lung tumors. These respiratory displacements are greatest near the diaphragm and least near the lung apex and adjacent to the carina. One option is the use of breath-holding techniques, sometimes in combination with an abdominal compression device, to limit the ability of the diaphragm to move caudally.

Another option is the use of a frameless system such as the Cyberknife Stereotactic Radiosurgery System. The Cyberknife system consists of a 6-MV linear accelerator mounted on a computer-controlled robotic arm. Before

initiating treatment, fiducials (small tumor markers that are seated percutaneously with CT-guidance for precise localization) are placed adjacent to the tumor. The addition of the Synchrony™ option enables dynamic radio-surgery during respiration. The Synchrony option records the breathing movements of a patient's chest and combines that information with sequential X-ray pictures of the fiducials to facilitate delivery of radiation during any point in the respiratory cycle. This allows further precision with radiation delivery (reducing normal tissue exposure) and is also more comfortable for patients because of the shorter treatment times compared with breath-holding techniques.

Whyte and colleagues provided the first report from the U.S. using a similar system for frameless SRS in 23 patients treated with a single fraction of 15Gy.³² The mean follow-up was seven months and the reported response rates were complete in two patients, partial in 15, stable in four, and progressive in two. Pennathur and colleagues at the University of Pittsburgh recently reported their results in 32 high-risk patients treated with SRS for lung neoplasms.³³ A median dose of 20 Gy was administered in a single fraction. This is equivalent to a biologically effective dose (BED) of 60 Gy to 70 Gy. A total of 32 patients, 27 with nonsmall cell lung cancer and five with pulmonary metastases, underwent SRS over a two-year period. The median overall survival for the entire group was 26 months. Onishi evaluated the clinical outcomes in 245 patients with stage I non-small cell lung cancer from 13 Japanese institutions.³⁴ The overall response rate was 13.5 percent. A lower recurrence rate was seen when BED greater than 100 Gy was used. Overall three-year survival was 56 percent. Caution is needed when using high-dose radiation, as there have been reports of peribronchial abscesses and hemoptysis.³³

Surgery clearly remains the best treatment for resectable lung cancer. However, newer modalities such as RFA and SRS may play a role in medically inoperable patients. Well-designed clinical trials with a long-term follow-up are required to confirm the initial promising results.

Conclusion

The involvement of surgeons in the development, testing, and adoption of new techniques and technology is of paramount importance for the future growth of our field. Surgeons, with their unique perspective in terms of patient care, should actively engage in identifying unmet clinical needs and in developing adequate solutions for these needs.

Emerging technologies such as bronchoscopic valves for emphysema, robotic surgery, SRS, transluminal endoscopic surgery, and RFA of tumors are examples of new tools that the surgeon now has to enhance the treatment of his or her patients. It is only with an open and a flexible mind that we, as surgeons, will rise above the usual definition of surgery as a particular procedure and embrace the variety of tools that are now (and will be in the future) at our disposal. Ω

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