Lung cancer is the leading cause of cancer death among both men and women in the United States. In fact, more patients die of lung cancer each year than the other most common cancers (breast, colon and prostate) combined. Whereas the five year survival seen in many cancers has improved significantly over the last two decades, there has been importantly less improvement seen in the outcomes for the patient having lung cancer.

The major survival advantages seen with the other cancers mentioned are primarily related to earlier diagnosis of disease at a limited, curable stage and improvements in the systemic treatment of more advanced stages of lung cancer. In this issue of the Esophageal and Lung Institute (ELI) quarterly report series Gullet and Chest, we discuss the exciting activities and the developments within Allegheny Health Network (AHN) and ELI focusing on state-of-the-art diagnosis and treatment of the lung cancer patient.

Cancer early detection and screening efforts for breast, colon, prostate, cervical and cutaneous malignancies have been successful in reducing the mortality rates from these malignancies. Recently, periodic Low Dose Computed Tomographic (LDCT) screening of patients at the highest risk for developing lung cancer (older, long term, past or present tobacco smokers) has been determined to reduce lung cancer related mortality. The details and successes of the AHN Low Dose CT screening program for lung cancer are described here.

The advances in radiation therapy approaches to lung cancer have led to improved local control of lung cancer in medically inoperable, early stage lung cancer patients. The results with these radiation therapy approaches by the nationally recognized Department of Radiation Oncology of AHN are described in this issue of Gullet and Chest. Additionally, the important new opportunities in the control of advanced lung cancer through systemic “immune system enhancement” therapy are being explored by the lung cancer medical oncology team of ELI are described.

Finally, the “natural approaches” to reducing/avoiding lung cancer risk and improving the patient’s own ability to fight lung cancer are discussed in this issue. An emphasis on a healthy immune system, enhancing nutritional decisions and cancer risk reduction measures through smoking cessation are emphasized.

We hope that you find this summary of the activities being led by ELI’s clinical team of physicians, nurses, and therapists valuable to you.
Lung cancer is the leading cause of cancer-related mortality with 160,000 deaths per year in the United States. The five year survival rate for lung cancer is only 17.4% since most patients have advanced disease at initial diagnosis. For those patients diagnosed with stage I disease, the five year survival is much better at 54.8%. A test that could detect lung cancer at an earlier stage would have a dramatic survival benefit. That test may be Low Dose Computed Tomographic (LDCT).

Many studies including the National Lung Cancer Screening Trial (NLST) have examined screening patients with a smoking history using annual LDCT. In 2010, the NLST demonstrated a 20% decrease in lung cancer mortality and a 7% decrease in all-cause mortality. As a result, the US Preventative Task Force Services formally recommended lung cancer screening with LDCT last year.

Allegheny Health Network (AHN) began offering free LDCT screening at several sites in 2014. The pilot program was initially funded by a grant from Highmark. Exam interpretations are provided by Allegheny Radiology Associates at no cost. The program employs a nurse navigator, utilizes a database to monitor patient results, ensures appropriate follow-up, and offers a smoking cessation program.

To date, 515 patients have had LDCT through the program. Of those patients, five lung cancers (most stage I) and one kidney cancer have been diagnosed. Several other patients have had suspicious nodules identified that are being further evaluated and monitored. Two-hundred sixty-two (262) patients have received smoking cessation assistance as a result of the program.

The Center for Medicare & Medicaid Services (CMS) recently announced it will cover lung cancer screening with LDCT nationwide. Many private insurance plans have approved coverage including Highmark Inc.

Patients eligible for screening include asymptomatic individuals between 55 and 74 years of age with 30 pack year history (one pack a day for 30 years or two packs a day for 15 years) including those patients who quit smoking within the last 15 years. Patients not eligible for screening include those with a lung cancer history in the last five years and people who quit smoking more than 15 years ago.

Current AHN lung cancer screening sites include West Penn Hospital, McCandless, Allegheny Valley Hospital, Peters Township Health + Wellness Pavilion, Canonsburg Hospital, Jefferson Hospital, and Saint Vincent Hospital. Allegheny Health Network hopes to expand screening at additional sites including Allegheny General Hospital, Forbes Hospital, Wexford Health + Wellness Pavilion, and a community site in Robinson Township.

For more information, please call 1.844.AHN.LUNG (1.844.246.5864)
Successful surgery begins in the clinic setting during the preoperative visit. A key factor of that success is adequate nutrition. At the Esophageal and Lung Institute (ELI), adequate nutrition during the preoperative, perioperative and postoperative phases contributes to successful surgery and positive outcomes.

Patients who come to ELI clinics receive individualized nutrition care. The registered dietitian assesses the patient’s nutritional status and provides nutrition education and counseling tailored to the patient’s specific condition or needs. If a patient is to have surgery, nutrition education and counseling are provided at the time of the preoperative evaluation. The nutrition education provided is based upon the planned procedure and its impact on the patient’s ability to consume adequate nutrition postoperatively. Patients are followed during the postoperative period and receive further nutritional assessment, education and counseling as needed.

Adequate nutrition is especially imperative in the esophageal or lung cancer patient undergoing surgery. ELI has adopted the nutrition component of the Strong for Surgery initiative created by the Surgical Care and Outcomes Assessment Program (SCOAP) in the state of Washington and introduced to Allegheny Health Network in the summer of 2014. The goal of Strong for Surgery is for patients to be at optimal health during the perioperative period which, with early intervention, will decrease nutritional risk before hospitalization, leading to better outcomes.

A key aspect of the Strong for Surgery initiative is the use of Nestlé Nutrition’s immune modulating formula, Impact Advanced Recovery®, which contains arginine (a conditionally essential amino acid), dietary nucleotides, and omega-3 fish oils. Clinical studies have shown improved outcomes in surgical patients who consume Impact Advanced Recovery® prior to surgery. Specifically, the outcomes include less incidence of pneumonia, wound infection, urinary tract infection, anastomotic leak, and abdominal abscess as well as decreased hospital length of stay.1,2 One study of esophageal cancer patients undergoing esophagectomy who drank Impact® prior to surgery showed similar results of reduced infectious complications, mostly pneumonia, and shorter length of hospitalization postoperatively.3

All ELI patients with esophageal or lung cancer who will have surgery receive nutrition education on Strong for Surgery and the use of Impact Advanced Recovery®. The clinical dietitians track and monitor these patients to help determine ELI surgical outcomes and to further highlight the importance of nutrition in the thoracic surgical patient.

References
Stereotactic Body Radiotherapy in Non-Small Cell Lung Cancer

By Vijay Kudithipudi, MD and Athanasios Colonias, MD - Department of Radiation Oncology

Stereotactic body radiotherapy (SBRT) or stereotactic ablative radiotherapy (SABR) is a form of external beam radiotherapy characterized by multiple fields or arcs of radiation delivered in five or fewer high dose ablative fractions to the tumor with sharp dose fall off to surrounding normal tissues. It is commonly utilized for the treatment of high-risk early stage non-small cell lung cancer (NSCLC) patients. Treatment is performed on an outpatient basis usually with 4-dimensional (4-D) CT simulation to characterize tumor motion followed by either 3-D or IMRT treatment planning and treatment delivery with daily image guidance. Figure 1 depicts a right lung nodule contoured in multiple phases of the 4-D CT characterizing significant nodule motion during breathing (GTV_0In: gross tumor volume 0% inspiration phase; GTV_50In: gross tumor volume 50% inspiration phase; GTV_100In: gross tumor volume 100% inspiration phase).

Timmerman et al. published results on a phase II study of early stage high-risk stage I NSCLC patients treated with SABR and found a 95.7% local control rate at median follow up of 17.5 months. Grade 3 or greater toxicity including six treatment related deaths was correlated with “central” tumor location (vs. no mortality and significantly less toxicity with peripherally located tumors). Onishi et al. reported their multi-institutional experience on 245 NSCLC patients treated with various SBRT dosing regimens and established a dose-response relationship with local failure of 8.1% above a threshold dose. A phase II multicenter trial from the RTOG for peripheral tumors demonstrated local control (within the involved lobe) of 90.6% and three year locoregional control of 87.2% with acceptable toxicity.

In conclusion, SBRT/SABR is a viable treatment option for peripheral high-risk stage I NSCLC patients and associated with high local control and acceptable rates of toxicity. Further study is warranted to define the optimal safe dose for central tumors. Prospective comparison of SBRT/SABR vs. surgery in these high-risk patients is also warranted and will be studied in the Joint Lung Cancer Trialist’s Coalition (JoLT-Ca) STABLE-MATES trial which is set to open for enrollment at the Esophageal and Lung Institute soon.

We stand at the crux of a new era in oncology in which an understanding of the molecular pathogenesis of cancer and new understanding of the immune system has led to a revolution in cancer treatment. While a definitive cure remains elusive for most patients with advanced lung cancer, doctors are optimistic that these new treatment paradigms will improve treatment and patient outcomes.

In 2015, the CDC estimates there will be 220,000 new cases of lung cancer in the US and more than 150,000 deaths making lung cancer more lethal than breast, colon and prostate cancer combined\(^\text{(1)}\). While this is a daunting statistic, a new era of better and more advanced treatment has begun and the pace of discovery is accelerating. Since the first papers were presented at the American Society of Clinical Oncology in 2012 and simultaneously published in the New England Journal of Medicine\(^\text{(2)}\), doctors have been able to use the immune system to effectively attack a patient’s cancer. This has led to notable and durable responses, even in patients whose cancer has become resistant to chemotherapy and radiation.

Immune function is tightly regulated such that while we are protected against the onslaught of infectious bacteria and viruses, our immune cells can still recognize other cells of the body as “self” and spare them from attack. To accomplish this, the body has adopted a series of checks and balances to prevent unwarranted immune attack. Activation of the immune system requires the activation of two related stimulatory pathways, while negative regulatory signals are suppressed to allow for immune destruction of foreign invading microorganisms (Figure 1). In theory, this system can also recognize and kill cancers at their earliest stages.

Unfortunately, cancer cells are clever and have adopted strategies to harness the negative regulatory signals of immune cells and switch them off when they would have otherwise destroyed the tumor.

Decades of research by several laboratories has culminated in the discovery of blocking antibodies which can switch off the negative regulatory pathways protecting the cancer cell, allowing the immune system to recognize and eliminate the tumor (Figure 2)\(^\text{(3)}\). Medical oncologists at AHN are working with these new immune reagents in new ways by combining them with traditional chemotherapy and targeted therapies.

The second important change in lung cancer care is the discovery that in certain types of lung cancer (especially in people who never smoked) mutations occur in critical genes that are essential to cancer growth\(^\text{(4)}\). Inhibition of these activated genes using drugs known as targeted agents can improve survival and quality of life relative to chemotherapy treatment. As many as 30% of lung cancers harbor such “driver mutations” and are amenable to effective treatment with oral drugs, reducing or eliminating the need for more toxic IV chemotherapy. The furious pace of research in this area promises to expand our drug armamentarium and reduce the need for chemotherapy; a welcome advance in the treatment of lung cancer patients.

It is an exciting time in oncology, with a host of new treatments and research initiatives that promise to revolutionize the way to combat cancer and improve the outlook for patients.

**References**

1. SEER database 2015 statistics


Truly Minimal Incisional Thoracic Surgery: The Bi-Port VATS Approach

Minimally invasive, video-assisted thoracic surgery (VATS) has particular advantages over standard “open” thoracotomy approaches to lung cancer removal which primarily relate to decreasing surgical incisional pain-related morbidity. These less invasive surgeries allow for decreased postoperative pain, shorter hospital stays, quicker return to normal activities, and work without compromise of surgical lung cancer care effectiveness.

This less invasive surgery is achieved by performing the lung surgery through band-aid sized incisions for videoscope entry into the chest and imaging of the lung and thoracic space. These small incisions are also used for introduction of surgical instrument between the rib spaces without spreading of the ribs or significantly traumatizing the chest wall tissues.

Nevertheless, traditional VATS techniques, including robotic assisted VATS procedures, require the use of a number of small incisional sites (typically 3 to 5 in number) to accomplish the lung surgery. Each of these incisions is associated with discomfort to some degree. Chronic pain at each incision site has been noted to occur in up to 2% of patients; equivalent to the risk of chronic chest wall pain associated with larger, “open thoracotomy” incisional surgeries. (Figures 1&2)

The most posteriorly located incision site can be particularly problematic and is used in traditional VATS approaches for lung resection. (Figure 3) Trauma to the intercostal nerves and the ribs and soft tissues at this site are more frequent due to the narrow nature of the rib space. (Figure 4) Torqueing of instrumentation and frequent “re-entry” of surgical tools through this posterior site also increases the potential for local, long lasting trauma. This may be an even more problematic issue with robotic assisted VATS techniques where the inability to “feel pressure” – i.e. Haptic human sensory feedback of the robotic instrumentation is an inherently negative circumstance of the approach.

Surgeons of ELI were the first in the world to utilize the minimally invasive VATS approach to remove lung cancer. (Figure 5) They have been leaders in the investigation of the outcomes of VATS for lung cancer surgery and minimizing surgical trauma and lung functional loss following lung surgery.

ELI surgeons’ backgrounds and research interests have led them to the development of an even more “minimally invasive” VATS approach to lung cancer resection – the “bi-port” VATS access approach. (Figure 6) The procedure is performed using only one functional incision (3 centimeter in length) to accomplish the surgical dissection and removal of the malignant lung tissue by anatomic segmentectomy or pulmonary lobectomy. A second 3-5 mm incision, placed at a lower intercostal site where the necessary chest drainage

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Continued from Page 6.
catheter is positioned after surgery, allows for videoscope introduction. (Figure 7) Precise thoracic mediastinal and hilar lymph node dissection is also performed. Most of the lung cancer resections are accomplished in less than an hour of surgical time. The first key to the successful performance of this minimalist VATS surgical approach is mature experience with VATS approaches to lung cancer resection. Additionally, the use of differential length, minimally invasive surgical hand instruments avoid crowding of the surgeon’s hands during the lung dissection. New designs in electrocautery and tissue fusion / ligation instrumentation have also facilitated this new minimal bi-port VATS lung resection approach. (Figure 8)
(Figures 9 through 10c)
Since initiating this less invasive bi-port VATS approach earlier this year, ELI thoracic surgeons have had success in removing lung cancer from over 50 consecutive patients, without important morbidity or mortality. Postoperative recovery has been enhanced and overall narcotic pain medication needs have been reduced. Overall costs of the bi-port VATS approach compares favorably against other minimally invasive thoracic surgical techniques.

ELI’s surgical team, as national leaders in the development of optimal minimally invasive surgical strategies, continues to expand the use of this intriguing, minimally invasive surgical approach and other means of providing cutting edge care for the person with lung cancer.

References
Lung cancer is the leading cause of cancer death in the United States and the world. It is the third most common cancer diagnosed. This news can be daunting.

The Esophageal and Lung Institute clinical team is fighting this cancer battle daily through early diagnosis with lung cancer screening, prevention, multidisciplinary treatment plans, enrollment in national clinical trials and research.

When your physician gives you the diagnosis of lung cancer, it is important to have your support systems with you. There will be further testing ordered to establish your clinical stage of cancer. These tests may include a PET/CT, MRI or CAT scan of the brain and possibly biopsies collected for pathological staging. If the stage is determined to be early, stage I or II, surgery may be offered as first line treatment. Many of the surgeries for lung cancer are now done with a minimally invasive approach with video assistance and Band-Aid-size incisions. Studies have shown excellent surgical outcomes with less pain and quicker return to daily activities for patients. If the stage is more advanced, you will be referred to an oncologist for possible chemotherapy and possibly also to a radiation oncologist. Chemotherapy regimens are tailored to the patient and tolerated well by most patients. Currently, clinical trials for more personalized treatments are being offered with exciting promise.

**What can you do to improve your outcomes?**

It is very important to quit smoking if you are currently smoking. Understandably, this is a very stressful time but you are not alone. There are smoking cessation specialists at the Allegheny Health Network that can help you quit. Also, ask your loved ones to not smoke around you. Any treatment will require the lungs to be as healthy as possible and studies show that stopping smoking decrease rates of complications and pneumonia during and after treatment. Eat well and stay hydrated. Improved nutrition allows your body to fight the cancer and also tolerate the treatments better. Stay active if possible to keep your body fit and try to keep a positive attitude.

Remember, you are not alone. There are many support groups with patients in your same situation. Your physician and medical team are your biggest advocates. Discuss any issues or concerns with them. They are available to you daily.

The Esophageal and Lung Institute is starting a new Nurse Navigator Program for people with lung cancer. This nurse will be guiding you through every step of the process including testing, procedures, and helping you understand your diagnosis.

**Helpful Online Support Groups:**
- [www.Lungcancer.org](http://www.Lungcancer.org)
- [www.Lungcanceronline.org](http://www.Lungcanceronline.org)
- [www.cancer.org](http://www.cancer.org)

**Survivorship:**
- [http://www.lcfamerica.org/get-involved/survivors.html#sthash.Q014JDre.dpbs](http://www.lcfamerica.org/get-involved/survivors.html#sthash.Q014JDre.dpbs)
- [http://www.mylungcancersupport.org/support-from-day-one/survivorship.html](http://www.mylungcancersupport.org/support-from-day-one/survivorship.html)
We are pleased to announce several exciting clinical trials for lung cancer.

**GO29436 and GO29437 (Genentech/Roche)**

**GO29436** is a randomized, Phase III, multicenter, open-label study designed to evaluate the safety and efficacy of MPDL3280A (PDL-1 inhibitor) in combination with carboplatin + paclitaxel with or without bevacizumab compared with treatment with carboplatin + paclitaxel + bevacizumab in chemotherapy-naïve patients with Stage IV non-squamous NSCLC.

**GO29437** is a randomized, Phase III, multicenter, open-label study designed to evaluate the safety and efficacy of MPDL3280A (PDL-1 inhibitor) in combination with carboplatin + paclitaxel or with carboplatin + nab-paclitaxel compared with treatment with carboplatin + nab-paclitaxel in chemotherapy-naïve patients with Stage IV squamous NSCLC.

Both of these industry-supported trials require tumor tissue to test PDL-1 status prospectively, which will be used for treatment response stratification. The objective of both trials is to test the efficacy of MPDL3280A in the intent-to-treat (ITT) population as measured by investigator-assessed progression-free survival (PFS). MPDL3280A targets human programmed death–ligand 1 (PD-L1) and inhibits its interaction with its receptors, constitutively improving immune response to tumor antigens. Dr. Gene Finley leads this initiative at the Esophageal and Lung Institute, and enrollment is expected to begin in July 2015.

**LUNG MAP Trial – SWOG 1400**

The National Cancer Institute (NCI), along with Foundation Medicine and several pharmaceutical companies, are currently sponsoring the LUNG MAP Trial. Lung MAP is a multi-drug, multi-arm, biomarker-driven clinical trial for patients with advanced squamous cell lung cancer. The trial uses genomic profiling to match patients to one of several different investigational treatments that are designed to target the genomic alterations found to be driving the growth of their cancer. This innovative approach to clinical testing should both improve access to promising drugs for patients and ease the significant recruitment and infrastructure burdens on researchers involved in traditional clinical trials. The trial will initially test five experimental drugs — four targeted therapies and an anti-PD-L1 immunotherapy. Lung-MAP uses a single “master protocol,” which can be amended as needed as drugs enter and exit the trial. Dr. Antonios Christou leads this effort at the Esophageal and Lung Institute, and he and his sub-investigators plan to enroll 15 patients to the trial.

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**Contact Us**

To schedule an appointment: Call **724.260.7300**
or visit [www.ahn.org](http://www.ahn.org).

To make a donation: Call **412.578.4427**
or visit [www.wphfoundation.org](http://www.wphfoundation.org).

For overnight lodging: Family House: for out-of-town patients and their families traveling to any AHN location who require overnight lodging, visit [www.familyhouse.org](http://www.familyhouse.org/).

For clinical trial enrollment: Call **412.578.1343**
Your Care Team

Rachel Harken, MS, RD, LDN – Clinical Dietitian: Rachel joined ELI at the beginning of January after working in acute care at West Penn Hospital. Rachel provides nutritional assessment, education and counseling for ELI patients at multiple sites.

Ann DeWitt, RD, LDN – Clinical Dietitian: Ann brings to the practice a diverse background as a Registered, Licensed Dietitian including acute/trauma care, bariatrics, enteral nutrition/DME, LTC, Skilled and Rehab. She is available for nutritional counselling for ELI patients at multiple sites.

Heather Rommes, MSOL, BA – Regional Practice Manager: Heather joined ELI in May and will be supporting clinical operations. She is returning to Allegheny Health Network after 7 years at Children’s Hospital as the manager of the patient representative department. Heather is looking forward to her role in ongoing process improvement and clinic growth initiatives.

Patricia Heilman - joined the team as director of operations in late April, bringing years of experience as a clinician and administrative leadership across the patient care continuum including outpatient and inpatient services and service line management.

Mara Yerk, BS - Clinical Research Manager: Mara joined ELI in March continuing her 11 year career in clinical research. Mara works within the Oncology Division of ELI supporting the enrollment and study treatment of patients on clinical trials.

Lauren Kratsas, BA – Research Coordinator: Lauren joins the team with several years of experience working as a Clinical Research Associate for the UPMC Hillman Cancer Center. Lauren will be enrolling patients in clinical trials for the treatment of cancer and coordinating new research trial implementation.

Reality Price, MS, GGCP – Research Coordinator: Reality has a strong background in Regulatory Affairs and research study coordination. Reality will focus on opening new clinical trials, maintaining regulatory documents, and coordinating patient care for research subjects at the Esophageal and Lung Institute.

Michelle Morris, MSPAS, PA-C - Physician Assistant: Michelle joined the team mid-April and will be working alongside Dr. Hoppo and Dr. VanDeusen. Her focus will be on treating esophageal disease and lung cancer patients.

Ashley Grenier - joined the team as a physician’s assistant in April after working in gastroenterology. She graduated from the Chatham University Physician Assistant program in July 2014. Her focus will be on treating lung cancer patients and esophageal disease. She will work alongside Dr. Van Deusen and Dr. Hoppo.

Sherri Shen, MS PA-C - Physician Assistant: Sherry joined the team in April after graduating from The University of Pittsburgh Physician Assistant Program. Sherry will be focusing on treating esophageal disease and work alongside Dr. Blair Jobe.

Support for those with Cancer

The Esophageal and Lung Institute strives to provide the most convenient and reliable cancer support for those immediately affected by the disease. Immediate clinic visits are offered to all patients with a new diagnosis of esophageal cancer where patients and families are supported through the process by trained nurse navigators.

For individuals who travel long distances to seek treatment, the Family House offers affordable accommodations and is located in close proximity to West Penn Hospital in Pittsburgh, Pa. Patients and families are provided with housing and shuttle transportation to and from the hospital, as well as many activities. For more information on pricing or to book a room, please call 412.647.7777.

Allegheny Health Network offers emotional support and has a variety of resources to help those with cancer and their loved ones through their cancer journey. Support group meetings occur the second Tuesday of every month, from 7 to 8:30 p.m. at Jefferson Hospital in Jefferson Hills, Pa. Other meetings will soon be available at West Penn Hospital and the Wexford Health + Wellness Pavillion, located in Wexford, Pa. Registration is easily accessible by calling 412.622.1212. For more information and a comprehensive schedule of other general support groups, please visit https://www.ahn.org/events/.

Whether it is finding an affordable and convenient place to stay or learning more about the disease and treatment options, the Esophageal and Lung Institute, as part of Allegheny Health Network, pledges to provide a supportive environment for those affected by cancer.
Esophageal and Lung Institute
Visiting Lectureship Series

Chevalier Jackson General Thoracic Lectureship

Honored Guest Speaker: Nasser K. Altorki, MD

Lectureship Overview:
The purpose of this lectureship series is to bring in outside thought leaders in the field of esophageal and lung surgery who are innovators in the field. The visit is designed for the exchange of ideas and to enrich and energize practitioners, faculty, trainees and staff.

Friday, September 18, 2015
Magovern Conference Center
Allegheny General Hospital, Pittsburgh, PA

Objective:
• Review the current medical and surgical approaches to resectable and advanced non-small cell lung cancer.
• Discuss recent innovations made in the diagnosis and treatment of lung cancer.
• Describe outcomes and adverse events noted following surgical, medical, and radiation therapy approaches to non-small cell lung cancer.

December 4, 2015
George Liebler Thoracic Oncology Lectureship
Honored Guest Speaker: Wayne Hofstetter, MD
MD Anderson Cancer Center, Houston, TX

To Register:
Online registration is preferred. To register online or download a brochure, please go to www.aghcmce.org. Select Conference Schedule on left, then scroll to find the ELI Lectureship Series.