NewYork-Presbyterian
The University Hospital of Columbia and Cornell

ADVANCES IN ONCOLOGY

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SPECIAL EDITION

Minimally Invasive Strategies To Evaluate and Treat Lung Lesions May Improve Cancer Outcomes

At NewYork-Presbyterian Hospital, minimally invasive methods to confirm and stage lung cancer are complementing broad efforts to improve outcomes in the most common cause of cancer death. Many suspicious pulmonary nodules discovered inadvertently or as part of ongoing computed tomography (CT) screening programs once required open surgery for evaluation. Increasingly, minimally invasive strategies being pursued at the Hospital allow sufficient tissue to be acquired to confirm the diagnosis, provide information about the cancer stage, and identify molecular characteristics that may be relevant to choice of treatment.

Minimally invasive strategies are complementary to CT screening programs that have been initiated to identify lung cancers at an early stage in high-risk patients. Although studies suggest lung cancer deaths can be reduced by at least 20% with screening, "the majority of nodules found on CT scans are benign," explained Nasser Altorki, MB, BCh, Chief of Thoracic Surgery, NewYork-Presbyterian/Weill Cornell Medical Center. Dr. Altorki added, "The trick is to avoid invasive procedures or surgery in patients who do not have cancers. New minimally invasive techniques to obtain tissue samples significantly enhance our ability to improve early diagnosis."

EBUS-TBNA

The advances in minimally invasive strategies for sampling potentially cancerous lung tissue are largely derived from progress with imaging to guide needle biopsy. These strategies depend highly on technique to reduce the risk for false-negative results, and investigators at NewYork-Presbyterian Hospital have been leaders in identifying how to optimize diagnostic yield. William Bulman, MD, Director of Bronchoscopy at NewYork-Presbyterian/Columbia University Medical Center, has been at the forefront of an important effort to define optimal technique with endobronchial ultrasound real-time guided transbronchial needle aspiration (EBUS-TBNA).

NewYork-Presbyterian Hospital is implementing new minimally invasive techniques to reduce the need for invasive procedures and surgery on patients without cancer.

"EBUS-TBNA is now being used widely for diagnosing and staging malignancy in pulmonary nodules and thoracic lymph nodes, but the diagnostic yields vary," Dr. Bulman said. "Developing strategies to reduce the risk of false-negative results is an area in which we have developed expertise. We have addressed this in a very regimented way and recently summarized our strategies in a review article," noted Dr. Bulman, referring to an article in the *American Journal of Respiratory and Critical Care Medicine*.[1]

The goal is to obtain tissue samples that provide all of the information needed for management of a patient's cancer. While confirming diagnosis of lung cancer is the critical first step, adequate tissue samples are important for characterizing the cancer to provide prognostic information and guide therapy.

"We have characterized strategies that increase the likelihood of obtaining evidence of malignancy to permit more consistent and reliable findings," Dr. Bulman explained.

The importance of adequate tissue sampling has further intensified now that it is clear that the molecular profile of lung cancer is relevant to the individualization of pharmacologic therapies. Most importantly, novel small-molecule inhibitors

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Collaborations Across Specialties and Robust Research Heighten Gynecologic Oncology Care

Collaborative care, with support from multiple specialties, together with a determination to improve the quality of life (QoL) experienced by its patients are defining features of the gynecologic oncology care practiced at NewYork-Presbyterian Hospital. The Hospital is comprised of 2 cancer centers—the Herbert Irving Comprehensive Cancer Center, part of NewYork-Presbyterian/Columbia University Medical Center, which is a National Cancer Institute (NCI)-designated comprehensive cancer center, and the Weill Cornell Cancer Center, part of NewYork-Presbyterian/Weill Cornell Medical Center. In addition, a distinctive hallmark of the Hospital is its extensive involvement in clinical drug trials in pursuit of improved care.

"We provide care throughout the entire course of the patient's disease, from screening and diagnosis to surgical management and adjuvant therapy," said Jason D. Wright, MD, gynecologic oncologist at the Herbert Irving Comprehensive Cancer Center. "For patients with gynecologic cancer, it is very important that they be seen by a specialist in gynecologic oncology—that has been shown to improve survival.

"A major focus of our group has been to improve the quality of care for women with gynecologic cancers and develop programs to help them through the difficult time of being diagnosed with cancer," said Dr. Wright, who is also Levine Family Assistant Professor of Women's Health and Florence Irving Assistant Professor of Obstetrics and Gynecology at Columbia University College of Physicians and Surgeons.

The gynecologic oncology team at the Herbert Irving Comprehensive Cancer Center.

"In the past 2 to 3 years, we have dramatically increased the number of support services that are available for our patients from nutrition services, psychosocial support, and peer-support groups, to access to new drugs through clinical trials and palliative care. For example, my partner, Sharyn N. Lewin, MD, has developed a 'Woman-to-Woman' program to pair up patients who have been recently diagnosed with cancer with survivors of gynecologic cancer to help them navigate through the process of diagnosis and treatment, and to help them deal with the side effects of treatment. Those are resources that patients treated at smaller centers often don't have access to," he said.

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>
> —Jason D. Wright, MD

Evidence-based medical and surgical interventions can provide patients with better outcomes in the short term, reduced recurrences over the long term, and improved QoL. "One of the benefits of a place like the Herbert Irving Comprehensive Cancer Center is that our patients have access to a range of chemotherapeutic drugs and a number of different clinical trial options," said Dr. Wright.

Access to a network of surgeons and other experts in gynecologic oncology ensures that patients receive superior clinical care as they progress through treatment and management of their conditions. "At the Center, patients have access to many other medical specialists and collaborators, including medical, radiation, and surgical oncologists who can assist with their care," said Dr. Wright. "For instance, in the OR we sometimes perform collaborative procedures with hepatobiliary and colorectal surgeons and urologists if the cancer is encroaching on another organ. Certainly, the availability of those specialists is important."

Active Involvement in Clinical Trials

Patients at the Center, as well as those at the Weill Cornell Cancer Center, regularly participate in studies encompassing all areas of cancer diagnosis and treatment. A recent study into the novel serum biomarker human epididymis protein 4 (HE4) performed at NewYork-Presbyterian/Weill Cornell demonstrated that it had a superior ability to differentiate between benign and malignant adnexal masses in premenopausal women compared with the commonly used carbohydrate antigen 125 (CA-125) biomarker. Assisted by Robert C. Knapp, MD, Visiting Scholar at Weill Cornell Medical College and developer of CA-125, researchers now are evaluating the utility of HE4 in detection of recurrent ovarian cancer.

Other treatment-related clinical trials have included investigations into the safety and feasibility of surgical debulking with heated intraperitoneal chemotherapy combined with intraperitoneal chemotherapy for ovarian cancer and the use of aurora kinase inhibitors in conjunction with paclitaxel for recurrent ovarian cancer, both of which are ongoing. "We're members of the NCI's Gynecologic Oncology Group and participate in open chemotherapy trials and radiation trials, such as examining the effectiveness of positron emission tomography scanning to detect lymph nodes metastasis," said Kevin Holcomb, MD, Associate Attending in Obstetrics and Gynecology at the Weill Cornell Cancer Center, where he is

a member of the Gynecologic Oncology Clinical Program, and Associate Professor of Clinical Obstetrics and Gynecology at Weill Cornell Medical College.

In addition to conducting trials centered on medical treatment options, researchers at both the Herbert Irving Comprehensive Cancer Center and the Weill Cornell Cancer Center have focused on determining the benefits of minimally invasive, and particularly robotic-assisted laparoscopic surgery for gynecologic cancers. Dr. Holcomb, who also is Director of Minimally Invasive Surgery for the Department of Obstetrics and Gynecology, noted that the benefit of offering advanced robotics technology is to improve patient QoL while providing similar survival outcomes.

"A major focus for us at Weill Cornell Cancer Center is working to improve the quality of our patients' lives, leaving them with less morbidity from our treatments so they go on to live fruitful lives without any long-standing detriment. I think in that regard, robotics plays a major role," Dr. Holcomb said. He added that his team is studying robotic-assisted surgery, which involves the use of the da Vinci Surgical System, in gynecologic cancers other than those for which it has already demonstrated benefit, such as in endometrial cancer. "We've been performing many robotic surgeries for recurrent ovarian cancer, and really pioneering this," said Dr. Holcomb, who instructs other surgeons on the technology. "Recently I was able to debulk a patient's ovarian cancer robotically. She was rendered in complete clinical remission with a surgery that lasted about 2 hours and she didn't have to stay in the hospital overnight. I think that is a huge benefit and it isn't being offered in many places."

Additionally, patients contraindicated for a minimally invasive surgical approach, such as the morbidly obese and patients with severe comorbidities, also have shown positive outcomes when robotics were employed for surgery. "We're routinely approaching these patients and doing complete staging with robotic assistance," Dr. Holcomb said. "Obviously, performing primary abdominal surgery in the instance of big, bulky abdominal disease is problematic,

Kevin Holcomb, MD, gynecologic oncologist, NewYork-Presbyterian Hospital/Weill Cornell Medical Center.

but we are finding that there is a role for robotic-assisted surgery. There is the patient who has an isolated recurrence after 3 years of being disease-free, for example, or the patient who has undergone chemotherapy and whose tumor shrank appreciably—very often, I elect to go back and handle these types of cases robotically. They're not necessarily getting a survival benefit from it, but there is a huge benefit for QoL." ■

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can now be selected to address activated molecular pathways of proliferation.

"There is an evolving paradigm for lung cancer treatment. Therapy is becoming increasingly personalized on the basis of the molecular profile, and the beauty of EBUS-TBNA is that it is a relatively safe and minimally invasive approach for obtaining sufficient tissue that may subsequently guide therapeutic strategies as well as diagnose the disease," Dr. Bulman explained.

New Technologies Guide Biopsy

Dr. Altorki has led the effort at NewYork-Presbyterian/Weill Cornell to minimize false-negative results using CT-guided fine needle aspiration. The key strategies that he and his colleagues identified to improve the accuracy of this technique were recently published.[2] The work in CT-guided fine needle aspiration is part of a larger effort to derive tissue from all pulmonary nodules with minimally invasive strategies.

"Fine needle biopsy is one of several options for minimally invasive procedures to access suspicious lesions. Appropriate technique affects the accuracy of all of them," said Dr. Altorki, who described protocols to improve the diagnostic yield of fine needle biopsy and ongoing efforts to employ fiberoptic bronchoscopy more effectively. While this tool has long been used to biopsy lung lesions that are visible and accessible, the technology is being stretched. One approach is navigational bronchoscopy, which involves computer processing of CT imaging data to guide the bronchoscope to the target lesion.

"The computer processes images of the lung to identify the shortest possible route when navigating the bronchoscope—it is something like plotting a flight plan. This is a very useful technique that not only improves efficiency during the procedure but increases the diagnostic yield, especially when

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—William Bulman, MD

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attempting to access distant nodules," Dr. Altorki said.

In some cases, the site of the lesion is readily reached with a bronchoscope, but the lesion cannot be visualized because it is on the outside of the bronchial tube. In this case, EBUS has been employed to position the scope to facilitate placement of the needle into the target. The real-time sonar images allow precision adjustments of the needle and increase the likelihood of obtaining evaluable cells for pathologic evaluation.

Bottom Line: Several Strategies Exist

Due to the strengths and weaknesses of available options for reaching suspicious lesions in specific locations of the lung, the choice of strategy for minimally invasive access to pulmonary nodules is made on a case-by-case basis, according to Dr. Altorki.

"If all else fails, we can still consider a surgical biopsy, but this can almost always be performed with minimally invasive techniques. While the goal is to obtain a tissue sample with minimal risk to the patient, it is also critical to select the technique with the lowest likelihood of a false-negative result," Dr. Altorki said.

In some cases, a combination of approaches is employed. For an example, Dr. Altorki described very small lesions that can be difficult to locate by a minimally invasive technique. In this case, image-guided bronchoscopy can be performed to inject dye at the site of the lesion to ensure that the surgeon can see and access the affected tissue. These types of approaches have a large potential to improve outcomes in lung cancer. Because of the fact that screening CT scans have a high sensitivity but a low specificity for lung cancer, minimally invasive strategies are critical from a benefit-to-risk perspective.

The value of effective but minimally invasive methods of sampling lung tissue has only intensified now that several organizations, including the American Association for Thoracic Surgery (AATS), have advocated lung cancer screening in high-risk patients, generally defined as men or women older than age 55 years with a 30 pack-year history of smoking. While the screening is a strategy for catching cancers at a stage when they can still be cured, the efficacy of the screening is highly influenced by the diagnostic technique.

"There is a broad array of variables that affect the diagnostic yield, including the expertise of the pathologist reading the tissue samples. Progress in this area may be less immediately dependent on developing new tools for obtaining adequate tissue samples than in correctly using the tools that are currently available," Dr. Bulman observed.

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