IMPROVING SURVIVAL RATES WITH HIGH-TECH LUNG CANCER DETECTION AND TREATMENT

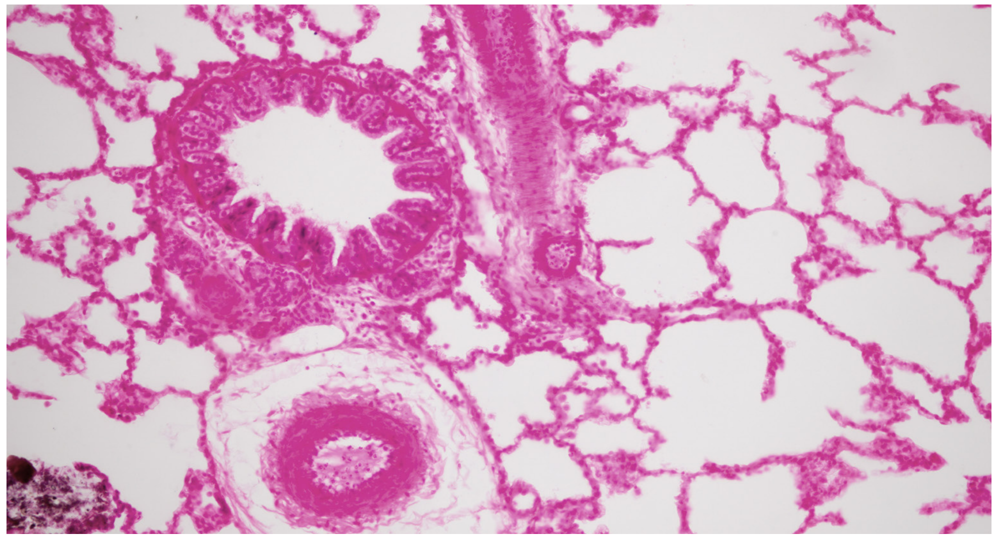
MINIMALLY INVASIVE DIAGNOSTIC AND SURGICAL TECHNOLOGIES could improve the care of people with early-stage lung cancers.

The five-year survival rate for lung cancer is around 56% when it is detected while the cancer is still localized. But few cancers are caught at this early stage.

To improve survival rates and patient experience, screening and treatment of early-stage lung cancer is shifting toward less invasive techniques.

Chang Chen leads Tongji University-affiliated Shanghai Pulmonary Hospital in China, the world's largest minimally invasive thoracic surgery centre by patient volume.

In this Q&A, Chen discusses some of the challenges of treating and detecting early-stage lung cancers, and how he and his colleagues have developed advanced approaches to overcome them.



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▲ Human lung tissue under the microscope. Researchers are developing liquid biopsies which detect lung cancer markers in blood.

What are the challenges with early detection?

Conventional diagnostic tools for identifying early-stage lung cancer include low-dose CT (computed tomography) scans and tissue biopsies. CT scans, while sensitive, can trigger false alarms, leading to unnecessary procedures. Interpreting biopsy results is less error-prone, but obtaining tissue samples is invasive and may cause pain, bleeding and infection.

To minimize the side effects, liquid biopsies that use blood have been developed. For example, lung cancer can be diagnosed by measuring DNA from the tumour in blood samples. But getting a reliable diagnosis has proved tricky because the amount of tumour DNA released into the blood is highly variable.

CHANG CHEN
Vice-president of Shanghai Pulmonary Hospital in China, which is affiliated with Tongji University.

How can we improve early detection?

We worked with researchers at the Chinese Academy of Sciences in Shanghai to develop a high-throughput liquid biopsy. This technology identifies long non-coding RNA from extracellular vesicles (EV-lncRNA). The vesicles are secreted by tumour cells and find their way into the blood. To increase sensitivity, we combined PCR with a microfluidic chip to detect low levels of different EV-lncRNA biomarkers. We called the technology miDER for multi-colour fluorescence digital PCR EV-lncRNA analysis chip. We published it in 2019[1].

Although miDER is currently less sensitive than standard tissue biopsy, it requires a smaller amount of blood than many other liquid biopsy methods. When miDER is used to target two lncRNA biomarkers, it is almost as accurate as tissue biopsy, and potentially more suitable for screening large numbers of people for early-stage lung cancer because it is less invasive. The miDER test is currently being developed for clinical use.

The test could also be used beyond diagnosis. Doctors could adjust treatment based on EV-lncRNA. Monitoring of EV-lncRNA could help spot small residue disease or early relapses.

How do you treat early-stage lung cancer?

We mainly use video-assisted thoracoscopic surgery or VATS — in which a thoracoscope, a thin flexible tube with a light and camera, is introduced into the chest through an incision.

The world's first VATS lobectomy — surgery to remove one of the lobes of the lungs — using a single incision was reported in 2011. At the Shanghai Pulmonary Hospital, we performed the first single-port VATS in 2012.

Compared with multi-port VATS, a single-port procedure further reduces trauma and post-surgery pain for patients, and the surgeon still gets a traditional open view via video.

By April 2023, our facility had completed more than 75,000 single-port VATS, the most in the world for a single hospital. Today, nearly 90% of our early lung cancer surgeries are done using this technique.

To help doctors better perform this procedure, we developed proprietary single-port VATS tool kits, containing specialised surgical equipment. They have been adopted globally.

How else has VATS improved lung cancer care?

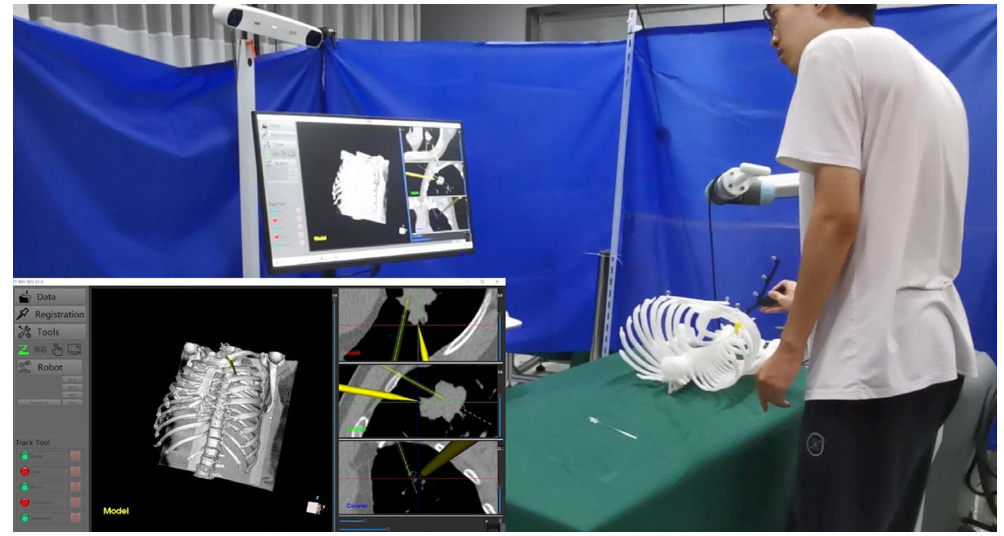
Our team has solved the key challenge of rebuilding, under single-port VATS, the pulmonary artery and trachea, which can be damaged by invasive lung cancer. This has established single-port VATS as a safe approach for complex thoracic surgeries. As we continue to perfect the method at Shanghai Pulmonary Hospital, our cure rate for locally advanced lung cancer under minimally invasive procedures has increased from 5% to 42%.

Our team also published 21 papers on single-port VATS in three of the world's leading thoracic surgery journals, making up 31% of the papers in this field.

How could more surgeons learn single-port VATS?

Our mission is not limited to improving care for our own patients. We also want to introduce these advanced techniques to our peers. So we have been hosting training courses since 2014, and have so far welcomed 842 doctors. We have a training centre with about 200 people enrolling annually.

We also established a minimally invasive thoracic surgery knowledge-sharing platform, online, aimed at a global audience.



▲ Computed topography (CT) scans, artificial intelligence software, and 3D printing are used to create a model of the chest to guide lung surgery at Shanghai Pulmonary Hospital in China.

PINPOINTING LUNG NODULES IS LIKE TRYING TO FIND A SUBMARINE FROM THE OCEAN SURFACE

Single-port VATS is still mostly performed at large healthcare facilities. Our analysis found that on average it takes a doctor 90 surgeries to become proficient using VATS for a complex procedure for lung cancer called a 'sleeve lobectomy'[2].

We hope with our new training centre and high patient throughput, we'll be able to standardize minimally invasive surgery education, shorten the learning curve and bring the technique to community hospitals in China.

What other technologies have you developed to assist in lung surgery?

Trying to pinpoint lung nodules to take a biopsy, or to operate on them, is like trying to locate a submarine in the ocean depths from above the water. So, we designed a 3D printing-based navigation system to help doctors locate the nodules.

With the standard protocol, surgeons use multiple 2D CT scans to guide them. We use CT images, computer software and 3D printing to create a 3D reconstruction of a patient's chest structures, which we use as a navigational template. The template is fixed to the patient's chest cavity to guide the surgeon. One key challenge is matching the 3D model with the patient's breathing pattern because breathing changes the shape of the lungs.

The 3D printing-based navigation system is currently as accurate as traditional CT-assisted nodule localization[3]. Our model can now help the surgeon limit deviation from the actual nodule site to around 6 mm. With the help of AI, we aim to bring this level down to below 1 mm, which is a lot better than traditional CT methods.

What is the future focus of your research?

We have built a database of two million patients, including information on radiology, pathology, genomics, metabolomics and clinical phenotypes. We plan to use AI to extract information from these data to assist in accurate diagnosis and to guide surgery or other precision treatment.

There is also room to refine miDER in multiple ways. For example, the expression of EV-lncRNA is affected by several factors that we are working to better understand. There is also no gold standard for purifying EVs, and we plan to develop one. Lowering costs for mass adoption is also a focus for developing next-generation miDER. ■

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