Entering the Era of "Precision Cancer Surgery"

Recent studies and trends suggest we are at the beginning of a sea change in the management of lung cancer. These trends, which encompass a shift in early diagnoses and the growing use of Video-Assisted Thoracoscopic Surgery (VATS), a minimally invasive surgical technique, underlie the increasing opportunity for the NaviSci™ Intelligent Surgical System that Navigation Sciences is developing.

According to a recent study in Clinical Lung Cancer, the number of lung cancer cases diagnosed at Stage 1 or 2 has been increasing to the point where surgical treatment can produce long-term, positive outcomes.

In 2017, 40 percent of cases diagnosed were Stage 1 and 2. Based on industry and Navigation Sciences data, from 2022 to 2028, Stage 1 and Stage 2 diagnoses are expected to grow from 37% to 67% of diagnosed nodules, driven by a 6.5% CAGR of Stage 1 diagnoses.

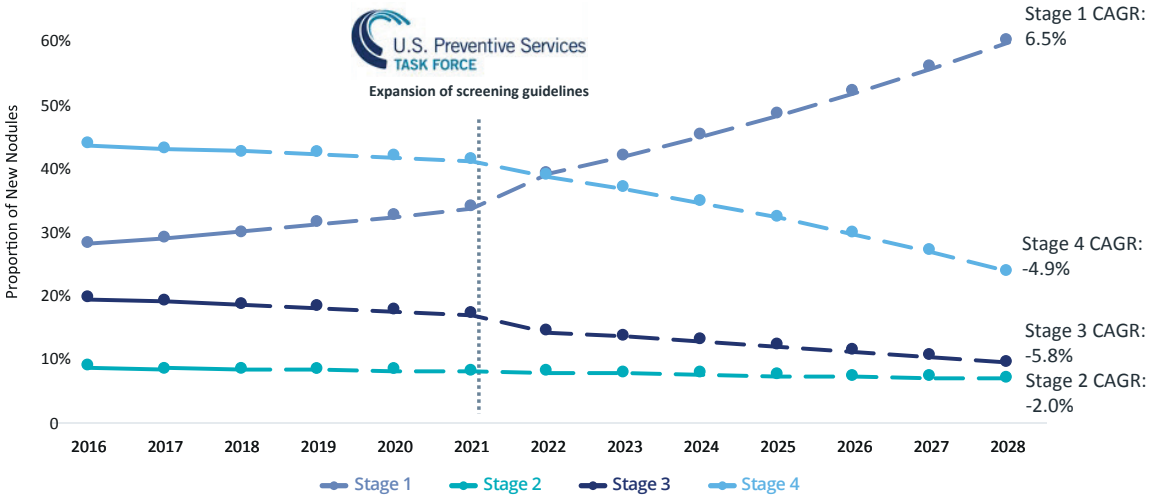
Expanded use of CT X-ray screening and favorable CMS reimbursement will partly drive the increase. Until recently, most of these diagnoses occurred in the absence of screening. According to a NORC at the University of Chicago study, in 2021, only three percent of lung cancers were detected by screening, and an American Lung Association study found that screening was performed in only 5.8 percent of eligible patients. The screening numbers contrast with the proportion of diagnoses for common cancers, e.g., prostate, breast, and colorectal, that have been used for many years.

The impact of annual screening on patient outcomes is dramatic. A major international study published November 7, 2023 in *Radiology* estimated a 20-year survival rate of 81% among participants undergoing annual CT scanning. For patients diagnosed with Stage 1 disease the survival rate was even higher, at 95%. This contrasts with an average five–year survival rate of 25 %, according to the American Lung Association.

There are signs that awareness of CT scanning is growing among clinicians and patients, with the potential to increase the addressable market for the NaviSci System. On November 1, 2023, the American Cancer Society (ACS) published updated **guidelines** for lung cancer screening that recommended a significant increase in the population of asymptomatic individuals who should be screened annually with low dose CT scanning. The new guidelines, published in ***CA: A Cancer Journal for Clinicians***, newly cover an estimated five million people and 19 million people overall. The principal changes from previous guidance issued in 2013 are:

- An expansion of the age range for screening to 50-80 years from 55-74 years of age,
- Inclusion of persons who currently smoke or who quit, regardless of how long ago they stopped, vs. previous smokers who quit within the past 15 years,
- People with a 20 or more packs/year history vs. 30 or more packs/year.

US Lung Cancer Surgical Procedure Breakdown with Addressable Uses for NaviSci System



The updated guidelines received extensive media coverage in publications such as the *Washington Post*, CNN, and the online healthcare journal, STAT.

The Wall Street Journal presaged the ACS study in a consumer health-focused article in the June 1, 2023 edition highlighting the potential patient impact of CT screening.

Carrying a headline, "**More People Should Get this Test to Detect a Deadly Cancer**," the article begins, "There is a test that could diminish the toll of the nation's top cancer killer – if people would use it. Doctors are pushing harder to make that happen."

The ACS guidelines generally align with previous recommendations by the US Preventative Task Force and a **National Coverage Determination** by CMS that in February 2022, effectively expanded the number of individuals eligible to be reimbursed for CT lung cancer screening by 6.4 million, bringing the total number of eligible screenings to 14.2 million per year. The coverage determination followed a report by the **US Preventative Task Force** that lowered the recommended age for screening from 55 to 50 years old and reduced the smoking history from 30 to 20 years.

As more early-stage cancers are diagnosed, a growing proportion of surgical procedures are projected to employ the VATS minimally invasive, tissue-sparing approach. These procedures can reduce procedure time and length of stay and improve patient outcomes. By 2028, VATS procedures are expected to reach 82 percent (~113,000) of lung cancer surgical resections in the US. According to Navigation Sciences and industry data, approximately 85 percent (92,000) will be addressable by the Navigation Sciences' NaviSci System.

The growth will be driven in part by recent large prospective clinical trials that, for many Stage 1 lung cancers, outcomes with tissue-sparing resection are comparable to lobectomy, which has been the standard of care for early-stage tumors. For example, a study published in the Feb. 9, 2023 issue of the ***New England Journal of Medicine (NEJM)*** found long-term survival in patients undergoing tissue-sparing wedge resections or segmentectomies was comparable to patients who received full lobectomies. Similar results were reported recently in a large clinical trial in Japan, which compared lobectomy to segmentectomy. Declaring "the era of 'precision' surgery for NSCLC has arrived," an editorial accompanying the *NEJM* study said, "these two landmark trials are practice changing as they establish sublobar resection as the standard of care for a select group of patients with NSCLC."

In the *NEJM* trial, which involved 697 patients with lung tumors 2 cm in size or less that had not spread to lymph nodes, after a median follow up of seven years, disease free survival in the sublobar group was similar (non-inferior) to lobectomy. Five-year overall survival was 80.3% (95% after sublobar resection and 78.9% after lobar resection). In addition, six months post-surgery, there was a between group difference favoring the sublobar resection group of 2 percentage points in the predicted forced expiratory volume in one second, a standard measure of lung function. The study, "*Lobar or Sublobar Resection for Peripheral Stage IA Non-Small-Cell Lung Cancer*," was conducted at 18 centers in the U.S. and Canada.

Outside of the U.S., there are significant opportunities for the NaviSci System in lung and other soft tissue cancers. The global total addressable market for lung cancer resections is estimated to exceed $250 million by 2028.

In the U.S. alone, there are approximately 450,000 soft tissue cancer cases per year, where Navigation's technology may provide benefits. In addition to lung cancer, these include liver, head and neck, thyroid, brain, and breast cancer. The addressable U.S. market for Navigation's technology, including systems and consumables, is estimated at approximately $1.26 billion.