The key to bringing high-throughput sequencing to the clinic will be reducing turnaround time, identifying enough mutations that can affect clinical decision making, and providing reports in a format that fits into what oncologists are used to seeing, she said, adding that rapid progress is being made on all three fronts.

“We’re at the point where we can handle significant throughput, and the price point is already competitive with what they do now,” Robins said about the MRD test. Over time, he added, as physicians become comfortable with the technology and realize they get more information than from flow cytometry, he predicted it will become hard not to adopt it. However, how the test would be administered remains unclear, because the technology supporting it is so new to CLIA (Clinical Laboratory Improvement Amendments)-certified reference labs.

“A bit needs to get figured out,” said Robins. “Who would actually be running the test? Is our best path to use local reference labs to use the technology, or is it better off being centralized and having people send us samples? Those are questions that we are wrestling with a little bit now. Part of the issue is that the sequencing technology can be a bit finicky, and being experts in it makes a big difference.”

Working Models of Genomics in the Clinic
Few working models exist to describe how genomics would fit into the clinic, and one of the largest is being organized by John McPherson, Ph.D., genome technologies director, and his colleagues at the Ontario Institute for Cancer Research in Toronto.

The Toronto research team is using whole-genome sequencing to guide treatment for late-stage patients with 10 types of solid tumors at four hospitals, along the lines of the proposed WINTHER trial. McPherson reports that in about one-third of cases, they find mutations that suggest treatment with a therapy targeted to a particular metabolic pathway. Results are presented at a regular tumor board meeting, one that included the genomics researchers.

“I think we are ready now to make a clinical difference,” said McPherson. “Looking for recurrence and residual disease, I think, is a really important application.”

McPherson said his research team is publishing results from the research team’s first 2 years of experience.

“What [the Ontario group has] done is actually really impressive,” said Michael Berger, Ph.D., a genomics researcher at Memorial Sloan–Kettering Cancer Center in New York. “I think we are all headed in that direction, but what they’ve done in setting up a system is admirable. They are leading the way to some degree.”

Berger said current efforts in his lab, which involve complete sequencing of a large bank of tumor samples housed at Memorial Sloan–Kettering, aim to offer a retrospective database of mutations against which to compare future samples. However, he added that for the foreseeable future, an expert level of analysis will be necessary to interpret findings, because mutations, even in the same gene, may not have the same effect; conversely, mutations in different genes along the same metabolic pathway can lead to a similar deleterious result.

Mardis concurs, “Just getting the central facts that you need is important,” she said. “Medical interpretation is a much harder, human-centric activity that’s going to require the ability to coalesce that information into a tangible set of clues for the patient’s oncologist in an evidence-based approach to medicine. That’s the hard part.”

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A Tale of Two Countries: Lung Cancer Care in Brazil and China
By Merrill Goozner

Lung cancer persists throughout the world, but wide disparities in care exist, particularly between developing countries and advanced industrial nations. Even developing countries with high-growth economics face obstacles not often encountered in developed nations. Screening is not as widely available, so diagnoses often come late, decreasing survival rates.

Brazil and China are two examples of high-growth developing countries facing challenges in delivering lung cancer care, as revealed at the 2012 annual meeting of the American Society of Clinical Oncology in Chicago.

Antismoking Campaigns
Brazil has been a global leader in smoking reduction. Beginning in the early 1990s, the nation of 190 million banned smoking in public places, restricted tobacco advertising, hiked cigarette taxes, and initiated smoking-cessation counseling through its public health system. In 2003, Brazil became one of the first countries to sign the World Health Organization’s (WHO) Framework Convention on Tobacco Control.

Smoking rates dropped dramatically, going from nearly a third of the adult population in the late 1980s to 17% in the 2000s. The ongoing campaign has aims to reduce...
the adult smoking rate to 11% by 2020—half the projected rate in the U.S.

“Vigorous antismoking campaigns worked, ranging from graphic warnings on cigarette packages to bans on advertising,” Gilberto Schwartsmann, M.D., Ph.D., professor of medical oncology at the Federal University of Rio Grande do Sul in Porto Alegre, Brazil, told the conference attendees. “Brazil has half the incidence of lung cancer of the U.S.”

China, however, is a picture of indifference. Its failure to curb tobacco addiction among its estimated 356 million smokers—more than every person in the U.S.—has put that 1.3 billion-person nation on track to become the center of the cancer pandemic in the 21st century. According to Tony Mok, M.D., professor of clinical oncology at the Chinese University of Hong Kong, smoking prevalence in China is 35.8%, including 66% of adult men. By middle school, 11% of Chinese teenagers smoke, according to a national survey of 30 provinces.

Though the Chinese government signed the WHO Framework, it spends less than $1 million per year on tobacco-control efforts. Laws that prohibit smoking in public places and selling cigarettes to minors are on the books but are not enforced. Observers say China’s failure to act stems from a desire to protect its tobacco farmers. The government also raises substantial revenue from a relatively low tobacco tax. Some provinces, such as Yunnan in its agricultural southwest, depend on tobacco taxes for most of their revenue.

**Epidemic Cancer in China**

WHO projects the number of new lung cancer cases in China will soar from an estimated 240,000 in 2005 to more than 1 million in 2025, most of which will be fatal. “China is already 20% of the global cancer burden,” Mok said. “We have a very serious problem with both incidence and mortality from lung cancer in China.”

Failure to tackle its tobacco-abuse problem will force China to confront inadequacies in its cancer care delivery system, Mok said. Facilities in rural areas, which still house two-thirds of the population, are rudimentary. Only a small share of those stricken with the disease in the hinterlands can afford to travel to nearby cities for treatment.

Although large cities have up-to-date facilities that offer a full range of services—Chinese health authorities have translated and adapted the National Comprehensive Cancer Network’s guidelines for use by oncologists, many of whom have been trained in the West—day-to-day practice often does not meet those standards. For instance, though just 11% of Western patients with non–small-cell lung cancer (NSCLC) have mutations of the epidermal growth factor receptor (EGFR), estimates for Asian patients range as high as 40%. Yet only 6% of Chinese patients in one study were tested for EGFR. “Only 26 hospitals in China routinely provide the EGFR testing service,” Mok said.

Shortcomings in its cancer-care delivery system haven’t prevented China from pushing hard to become a major center for testing new oncology drugs. About a third of the 1,217 patients in the IPASS trial that compared gefitinib (Iressa) with a chemotherapy regimen of carboplatin and paclitaxel came from China. The results, announced in 2010, showed that the EGFR inhibitor extended progression-free survival for about 3 months, with the best results seen in EGFR-positive individuals. The drug did not prolong life.

Chinese clinicians are participating in more than a dozen trials for EGFR inhibitors, Mok said, and AstraZeneca and Roche have already opened major research and development centers there. Though China represents only 1.5% of the global drug market today, that’s bound to grow because of the looming lung cancer epidemic due to uncontrolled smoking rates, Mok suggested.

**Lagging Cancer Care in Brazil**

Although Brazil has done admirably well on the prevention front, it has yet to extend advanced care to its general population, most of whom remain poor and rely on the national health care system. “Government reimbursement is insufficient to pay for diagnostic tests,” Schwartsmann said. “It leads to substantial delays in access to treatment.”

Whereas two-thirds of U.S. lung cancer patients live at least 1 year behind their initial diagnosis, about 90% of Brazilian patients do not. About 85% of Brazilians with lung cancer present with the non–small-cell variety—typical of lung cancer patients around the world. But 80% present with locally advanced or advanced disease, less susceptible to interventions. Even then, patients wait on average 2 months before beginning chemotherapy and 3 months for radiation treatment, Schwartsmann said.

Oncologists at Brazil’s leading research universities and institutes are avid participants in the global clinical trial system, and national guidelines for treatment parallel National Comprehensive Cancer Network guidelines. But clinical practice falls well short of those standards. The latest technologies, such as positron-emission tomography scans or mediastinoscopy to test for lymph node involvement, are rarely deployed. A 2010 study of 291 patients treated at an academic hospital in São Paulo found that the staging of the disease based on pathology reports...
differed from the clinical diagnosis in 33% of cases, with 15% upstaged and 18 percent downstaged.

A major issue facing U.S. oncologists is the relative value of the newer targeted chemotherapy agents, which can cost $50,000–$100,000 per year with only a limited ability to extend life. Brazilian guidelines call for using erlotinib as first-line therapy for patients with EGFR-positive mutation NSCLC and for using cetuximab in combination with standard chemotherapy drugs in patients with stage IV disease. However, “at present [those] biological agents are not provided routinely as part of the standard treatment of patients with NSCLC through the Brazilian National Health System,” Schwartsmann said.

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PDQ (Physician Data Query) is the National Cancer Institute’s source of comprehensive cancer information. It contains peer-reviewed, evidence-based cancer information summaries on treatment, supportive care, screening, prevention, genetics, and complementary and alternative medicine. The summaries are regularly updated by six editorial boards. The following PDQ summaries were recently updated:


The PDQ Prostate Cancer Treatment summary was recently updated to include results from the Prostate Intervention Versus Observation Trial (PIVOT-1), the only published randomized trial conducted in the PSA screening era that directly compared radical prostatectomy with watchful waiting. Men aged 75 years or younger with localized prostate cancer and a life expectancy of at least 10 years were randomly assigned to radical prostatectomy versus watchful waiting. After a median follow-up of 10 years, all-cause mortality was 47.0% in the prostatectomy arm versus 49.9% in the watchful-waiting arm, and prostate cancer-specific mortality was 5.8% versus 8.4%. These differences were not statistically significant. To review the summary, please use the following link:

http://www.cancer.gov/cancertopics/pdq/treatment/prostate/HealthProfessional/Page4#Section_785


The PDQ Prostate Cancer Treatment summary was also updated to include the results of a study that showed that enzalutamide, an androgen receptor signaling inhibitor, increased survival in patients with progressive prostate cancer who had received prior androgen deprivation therapy as well as docetaxel. To review the summary, please use the following link:

http://www.cancer.gov/cancertopics/pdq/treatment/prostate/HealthProfessional/Page9#Section_784

The PDQ Pediatric Treatment Editorial Board recently completed a major update of the Childhood Hodgkin Lymphoma Treatment summary. The Board conducted a review of the published literature and revised the text of the summary and updated the citations. To review the summary, please use the following link:

http://www.cancer.gov/cancertopics/pdq/treatment/childhoodhodgkins/HealthProfessional

The PDQ Pediatric Treatment Editorial Board recently completed a major update of the Ewing Sarcoma Treatment summary. The Board conducted a review of the published literature and revised the text of the summary and updated the citations. To review the summary, please use the following link:

http://www.cancer.gov/cancertopics/pdq/treatment/ewings/HealthProfessional

The PDQ Adult Treatment Board recently completed a major update of the Vaginal Cancer Treatment summary. The Board conducted a review of the published literature and revised the text of the summary and updated the citations. To review the summary, please use the following link:

http://www.cancer.gov/cancertopics/pdq/treatment/vaginal/HealthProfessional

The PDQ Adult Treatment Board recently completed a major update of the Vulvar Cancer Treatment summary. The Board conducted a review of the published literature and revised the text of the summary and updated the citations. To review the summary, please use the following link:

http://www.cancer.gov/cancertopics/pdq/treatment/vulvar/HealthProfessional

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