in whom a completion ALND was systematically omitted. This analysis of unselected patients provides evidence that a completion level I and II ALND may be safely omitted in early stage breast cancer patients with SLN micrometastases." However, they acknowledge the relatively small sample size and the limited follow-up time of their study.

Other Recent Studies

Three recent research articles illustrate the complexity of this question. A retrospective analysis of data from the National Cancer Database (*Journal of Clinical Oncology* 2009;27:2946–2953) found that completion ALND did not influence axillary recurrence or survival for patients with microscopic SLN metastases.

In a prospective study from the John Wayne Cancer Institute (*Journal of Clinical Oncology* 2009;27:4679–4684), neither micrometastases nor isolated tumor cells seemed to influence 8-year disease-free or overall survival. The vast majority of patients with micrometastases and isolated tumor cells received adjuvant systemic therapy (96.3% and 92.8%, respectively), and the authors expressed concern about overtreatment.

On the other hand, a retrospective study from Maastricht University Medical Center in the Netherlands (*New England Journal of Medicine* 2009;361:653–663) found that in the absence of adjuvant systemic therapy, isolated tumor cells or micrometastases adversely influenced disease-free survival.

Another Perspective

"When I read [the Langer] paper, I get worried about drawing larger conclusions from a small study," says Kimberly Van Zee, MD, MS, an attending surgeon in the breast service at Memorial Sloan-Kettering Cancer Center and professor of surgery at Weill Medical College of Cornell University, both in New York City. "There are other data that very clearly show that micrometastases are associated with a much worse prognosis." This is especially true in patients who do not receive adjuvant systemic therapy, she explains.

Dr. Van Zee expressed concern that the article by Langer and colleagues represented another step in the movement toward the systematic omission of ALND in SLN-positive low-risk patients without adequate evidence that this will not negatively affect long-term outcomes.

"You know that in the absence of axillary dissection, there is a higher chance of residual disease and, therefore, probably a higher local recurrence rate," she explains. "The Langer paper didn't show this, but the groups are small [n=27] and biased toward chemotherapy in the group with micromets. Other groups have shown a higher risk of local recurrence in a selected low-risk group of women with micromets who do not undergo axillary dissection. And we know that local recurrence in the breast does impact on survival, though it takes some time to show it, in a non-one to one ratio. Prevention of 4 local recurrences at 5 years saves 1 life at 15 years. It's not true that every local recurrence leads to death."

"I think it is going to be the case that it's going to have a small, long-term impact on survival. It's going to take us roughly 15 years to figure this out. I don't want people to adopt this now and figure out 15 years later that ALND confers, for example, a 5% survival benefit."

Still Another Perspective

In an editorial referring to the study by Langer and colleagues in the same issue of the *Journal of Clinical Oncology*, Thomas B. Julian, MD, associate director of the Breast Care Center at Allegheny General Hospital in Pittsburgh, Pennsylvania, and associate professor of human oncology at Drexel University College of Medicine, in Philadelphia, Pennsylvania, suggests that the prognostic significance of isolated tumor cells and micrometastases is influenced by other factors, such as systemic therapy. Dr. Julian notes that 2 randomized trials (the National Surgical Adjuvant Breast and Bowel Project's B-32 trial and the American College of Surgeons Oncology Group's Z0010 study) will provide additional data on the prognostic significance of axillary micrometastases, and that both have completed accrual, and "data are expected to mature in the next 6 to 18 months." ■

doi:10.3322/caac.20053

Simulation Model Predicts Cost Savings from Colorectal Cancer Screening

There is already clear evidence that colorectal cancer screening is cost effective in saving lives. A modeling study by Lansdorp-Vogelaar and colleagues from the Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands recently published in the *Journal of the National Cancer Institute* (2009;

101:1412–1422) now predicts that some colorectal screening tests may provide a net savings by reducing a later need for expensive treatment.

The microsimulation study modeled the costs of 6 screening and 3 treatment scenarios in a theoretical population that is representative of the US population. The screening scenarios included 5 options recommended by both the American Cancer Society/US Multisociety Taskforce/American College of Radiology 2008 guidelines and by the US Preventive Services Taskforce. Options include fecal occult-blood testing (FOBT) with Hemoccult II (Beckman Coulter, Fullerton, California), immunochemical FOBT, flexible sigmoidoscopy, flexible sigmoidoscopy plus FOBT, and colonoscopy, as well as no screening. (Three other options from the American Cancer Society/US Multisociety Taskforce/American College of Radiology guidelines, computed tomography [CT] colonography [also known as virtual colonoscopy], double contrast barium enema, and stool DNA testing, were not considered).

The analysis also included cost estimates for past, present, and near-future treatment regimens at stages I-IV and for terminal disease. Resulting from the addition of new drugs such as irinotecan, oxaliplatin, and bevacizumab, the clear trend was one of substantially increasing costs over time for treating late stage and terminal disease.

CRC Screening Saves Money

The result of this analysis was that screening with all options except colonoscopy provided a net savings when treatment included newer and more expensive drugs. In the present treatment scenario, colonoscopy was already highly cost effective in terms of the usual standards of dollars per year of life saved. Colonoscopy's cost effectiveness was even better for models based on near-future treatment assumptions, although it still had a small net cost. The researchers pointed out that colonoscopy is more costly than other screening methods and that its main advantage over other tests is additional prevention of early stage disease, for which treatment is less expensive.

"Our study shows that the treatment savings from screening will be larger than screening costs in the near future when the new chemotherapy regimens become general practice. This reflects the higher costs per life-year saved of these new treatments compared with screening," says first author Iris Lansdorp-Vogelaar, PhD, in an e-mail interview with *CA: A Cancer Journal for Clinicians*.

"If screening becomes cost saving, it can play an important role in containing the increasing costs for the treatment of colorectal cancer," says Lansdorp-Vogelaar.

Using the microsimulation model, Lansdorp-Vogelaar and colleagues found that "compared with no screening, the treatment savings from preventing advanced colorectal cancer and colorectal cancer deaths by screening more than doubled with the widespread use of new chemotherapies."

"The advantage to this study is that it was not just a cost-effectiveness model alone: this is an entire disease model. The accuracy and validity of these results are probably better than other, similar studies," says Richard Wender, MD, alumni professor and chair of the Department of Family and Community Medicine at Thomas Jefferson University, Philadelphia, Pennsylvania. "We have known for some time that screening for colon cancer constitutes good public health. Proving that it is a sound economic investment can help us overcome one barrier to universal screening," he adds.

Cost Saving Takes Time

Lansdorp-Vogelaar and colleagues also point out the chronology of cost savings in their article. "It takes 25 to 40 years after the start of a screening strategy before the treatment savings of that strategy outweigh its costs," they write. "If insurers anticipate that beneficiaries will not stay in their program for more than 5 years, they may be less inclined to cover a colorectal cancer screening program despite long-term savings of such a program." They also note that in the United States, most of the screening costs would be paid by private insurance

A fecal occult-blood test card is shown.
Credit: Beckman Coulter, Inc.

and that Medicare would reap most of the benefit from less treatment.

"I think that the people who conducted the study believe, as I do, that it is in the public health interest to undergo screening, and that they are frustrated, as I am, by the shortsightedness of payers," says Leonard Saltz, MD, professor of medicine at Weill Cornell Medical College and attending physician at the Memorial Sloan-Kettering Cancer Center, both in New York City. "But I don't think their findings are going to change the opinions of payers. The idea to a third-party payer of 'I will save money. . . 20 years down the road' is not going to fit into the [current US insurance] business model," he says.

Dr. Wender says most payers have already figured out that the public expects to be supported in their personal efforts to prevent cancer. "But ultimately, the public will have to stand up and clearly state, through their votes and advocacy efforts, what value they expect to receive for their healthcare dollar," he says. ■

doi:10.3322/caac.20054

Mixed Results on Link Between Cellular Telephones and Cancer

A recent meta-analysis and a conference have renewed attention to the question of whether cellular telephone use increases brain-tumor incidence.

"Cell phones are now used worldwide by more than 3 billion people, and there is increasing heavy use by children," says Michael J. Thun, MD, MS, American Cancer Society vice president emeritus of epidemiology and surveillance research.

According to Thun, approximately 30 epidemiological studies have looked at the possible relation between cellular telephones and benign and malignant brain tumors as well as acoustic neuroma and salivary-gland tumors. Although most studies found no significant associations, some did. Nearly all available evidence is from case-control studies with less than 20 years of follow-up since the introduction of cellular telephones, and these studies have some methodological limitations. "The 2 greatest limitations are that the information about cell-phone use is obtained retrospectively from people who have already been diagnosed with cancer and that participation in the studies has been considerably lower among controls than cases. Uncertainties about the evidence can only be resolved by longer-term epidemiologic follow-up and by critical evaluation of experimental studies that report biological effects from cell phones," said Thun.

While epidemiologists continue to collect new data and reanalyze available data, individuals and policymakers struggle with the need to base today's decisions on what is known today.

Meta-analysis is a valuable statistical tool for combining results from multiple studies, but the conclusions are subject to the same methodologic limitations as the studies themselves and can be influenced by assumptions and choices in the way data are collected and analyzed. Among the 4 meta-analyses in the published literature as of October, 2009, 3 found no significant association.

The most recent meta-analysis was conducted by researchers from several South Korean institutions, including the National Cancer Center in Goyang, the Ewha Womans University in Seoul, and the National University Hospital in Seoul, and from the University of California, Berkeley. The results were published in the *Journal of Clinical Oncology* (epub ahead of print on October 13, 2009; DOI: 10.1200/JCO.2008.21.6366). Lead author, Seung-Kwon Myung, MD, MS, and colleagues reported no overall association for the combined results of 23 relevant studies, but they found a statistically significant 9% increased risk when the meta-analysis was limited to the 10 studies the authors classified as low bias, and a significant 15% lower risk for data from the remaining studies labeled as high bias.