"Lax and Gale weigh up the risks and benefits of industrial, medical and natural radiation clearly, logically and with ample science."
—*Nature*

RADIATION

WHAT IT IS, WHAT YOU NEED TO KNOW

ROBERT PETER GALE, M.D.
AND ERIC LAX

tains small amounts of benzene) or when you stand on a busy street corner in New York or Cairo during a traffic jam.

To keep perspective, it is important to recall that all food treatment causes chemical changes. Freezing food causes what could be called "cryolytic products." Cooking causes more changes than irradiation—the taste and smell of cooked food are produced from chemical changes brought about by heat. Barbecuing a steak produces many known carcinogens on the steak surface from the interaction with charcoal, a hydrocarbon. That increases global warming.

The American Medical Association's policy toward food irradiation is that it is "a safe and effective process that increases the safety of food when applied according to governing regulations." The U.S. Food and Drug Administration (FDA), the World Health Organization, the International Atomic Energy Agency, and scientific organizations in many countries confirm the safety of food irradiation. Irradiated food is permissible in more than 50 countries, with a variety of clearances: the European Union, for instance, allows only irradiated spices, whereas Brazil permits all foods to be irradiated. The FDA has approved irradiation to, among many other uses, control sprouting of food grown in the ground (such as onions, carrots, potatoes, and garlic); delay the ripening of bananas, mangos, papayas, and other noncitrus fruits; and kill insects in wheat, potatoes, flour, spices, tea, fruits, and vegetables. The FDA also approves irradiation of pork to control trichinosis and to eradicate *Salmonella* and other harmful bacteria in chicken, turkey, and other fresh and frozen uncooked poultry.

Food irradiation has the potential to save millions more lives than it harms, especially since it very probably does *no* harm. It is especially important in developing countries where most cases of food poisoning occur.

CHAPTER 6

RADIATION AND MEDICINE

MAMMOGRAMS

Breast cancer is the most common cancer in women worldwide. The World Health Organization reports that it caused about 458,000 deaths in 2008, about 14 percent of all cancer deaths in women. There are around 180,000 new cases of breast cancer in the United States annually and about 40,000 deaths. Breast cancer is the second leading cause of cancer death in American women, after lung cancer. (Breast cancer was the leading cause in women until 2000, when the effects of women smoking cigarettes, which became popular in the 1920s and increased in the following decades, made their fatalities similar to men's.) The American Cancer Society estimates that an average woman's chances of developing breast cancer in a normal life span is 10 to 15 percent, depending on nationality, family history, age of first pregnancy, breast-feeding, alcohol use, and other factors. Some women—about 5 percent—with a heritable genetic risk for breast cancer, such those who have BRCA1 and BRCA2, have a more than 80 percent likelihood of developing it.

(Men can develop breast cancer, but the disease is about 100 times less common.)

Survival of women with breast cancer correlates with the extent to which the cancer has spread and other factors, such as whether the cancer cells respond to estrogen and progesterone, and whether they have certain specific genetic abnormalities. Women whose breast cancer is small and remains within the breast (and possibly the local lymph nodes) are much more likely to be cured than women who have large cancers in their breast or whose cancer has spread beyond the breast or to many lymph nodes. The main reason for this correlation is mostly simple: breast cancers that remain in the breast can be cured by surgery (with or without other therapies like radiation), whereas metastatic cancer is mostly incurable. But another reason for this correlation is biological. Some breast cancers spread outside the breast soon after they develop, often before they can be detected, whereas other cancers remain in the breast for a very long time despite growing larger. The latter have a much better prognosis than the former. There are more than 2.5 million breast cancer survivors in the United States.

Regardless of these complex considerations, the correlation between early detection of breast cancer and increased likelihood of cure with less intensive therapy has resulted in considerable efforts in early breast cancer detection or screening. And because breast cancer is so common, this involves screening millions of women.

Mammography is the only screening test for breast cancer that has been shown to reduce deaths from breast cancer. (The effectiveness of breast self-examination is controversial.) Each year about 40 million American women have a mammogram in the hope of early detection of breast cancer. Their greater hope, of course, is that no abnormality will be found.

Mammograms use low-energy X-rays to detect abnormalities in breast tissue. The whole body dose from the average mammogram is about 0.2–0.4 mSv, which is about one-tenth of a woman's average annual dose from background radiation. The radiation dose from a mammogram is considered to be too low to pose substantial individual risk; however, as with any use of ionizing radiation, repeated exposures can, at least in theory, cause or contribute to the development of cancer, including breast cancer. And some women with genetic abnormalities that predispose to breast cancer and who are already at high risk of breast cancer (such as those with the BRCA-2 mutation) seem at special risk to develop more breast cancers if they receive chest X-rays or mammograms.

The decision to recommend any medical screening procedure, including mammograms, is based on a delicate balance of estimating potential benefit and risk. So there is heated controversy regarding the age women should begin having annual or biannual mammograms for early detection of breast cancer, and at what age they should stop.

As we discussed, exposure to high doses of ionizing radiations causes breast cancer, leukemia, and other cancers. In the A-bomb survivors, breast cancer was one of the cancers most likely to be caused by ionizing radiation. The likelihood that radiation will cause or contribute to breast cancer development is greatest in women who are young at time of exposure, and this risk decreases with increasing age. Whether a very low dose of radiation, like that associated with a mammogram, can cause breast cancer and leukemia is controversial. Most scientific and regulatory agencies and scientists agree that to protect the public, we should assume that even the smallest radiation dose can potentially cause cancer. Others disagree, some strongly.

So we are left with a complex decision as to what recommendation to make. The earlier the age women begin having mammograms, the greater the possibility that some may develop breast cancer or another cancer or leukemia from radiation exposure. But paradoxically, women who are at the highest risk of developing breast cancer—perhaps because of an inherited genetic susceptibility or strong family history—and are therefore most likely to benefit from screening mammograms, are those most likely to be at risk of developing breast cancer from low-dose radiation.

The bottom line of this complex calculus is that breast cancer screening using mammograms saves lives and reduces the amount of therapy that some women need because their cancers are detected early when they remain in the breast; they may receive only surgery and local radiation therapy rather than anticancer chemotherapy or hormone therapy. Between 15 and 20 percent of breast cancer deaths, perhaps more, are prevented by screening mammograms. So this issue is not yes or no; it is when, and how often.

Here controversy prevails. The U.S. Preventive Services Task Force (USPSTF) and the CDC recommend that women with no risk factors for breast cancer have a screening mammogram every two years between the ages of 50 and 74. In contrast, the National Cancer Institute, American Cancer Society, and several other professional organizations recommend annual mammograms beginning at age 40 and continuing as long as the woman is in good health. In a USPSTF analysis, beginning screening at age 40 saved about 5 percent more lives than beginning screening at age 50, but it was associated with many more inaccurate and ultimately incorrect diagnoses. (Abnormalities on mammograms thought to be cancers were shown to have a cause other than cancer. This result is referred to as a false positive.) Although a correct diagnosis was finally made, these false-positive mammograms incurred considerable physical, psychological, and economic costs. Some women required one or more breast

biopsies; others developed a perhaps irrational, sometimes disabling, fear of developing breast cancer. Also, screening annually or every two years had similar reductions in breast cancer deaths but fewer false-positive breast cancer diagnoses. Recently, several states enacted laws requiring physicians to advise women with dense breasts that mammography may not be sufficient to detect breast cancer and that additional tests, like ultrasound and MRI, may be needed. The problem is we lack good data on the added benefit of these procedures in most women with dense breasts. We regard this as an unfortunate intrusion (confusion) of politics and science.

Ionizing radiations play a complex role in breast cancer. They can cause it, they can be used to diagnose it early and save lives, and they can be used to treat it and save lives. From a radiobiology perspective, screening mammograms are a good example of the benefits (early diagnosis of breast cancer) exceeding the potential risks (exposure to ionizing radiations).

LUNG CANCER SCREENING

Lung cancer is the most common cause of cancer death in men and women worldwide: an estimated quarter-million cases will occur in the United States in 2012, resulting in about 165,000 deaths. Most lung cancers are diagnosed at an advanced stage, when they are no longer curable or even effectively treatable. Because of the high death rate (the average survival is less than one year from diagnosis), there is considerable interest in early diagnosis. The situation here is rather different from that of breast cancer. Although lung cancer is common, not everyone is at risk; the lifetime risk of lung cancer in American males who are nonsmokers is less than 1 percent, and it is even lower in females. But males who are heavy smokers have a more than 25 percent lifetime risk, so lung cancer screening is best directed at high-risk smokers (or former smokers) rather than at all people of one sex, as is the case in breast cancer.

Prior methods of lung cancer screening used conventional chest X-rays and analysis of sputum samples for abnormal cells. Results were disappointing, and there are no convincing data that these interventions save lives. Recently, a special radiological study—a low-dose helical CT scan of the chest—was tested as a lung cancer–screening technique in people at high risk: smokers (or former smokers) with a history of smoking for more than 30 pack-years, such as two packs a day for 15 years or one pack per day for 30 years. A study of more than 50,000 persons showed that the group screened with low-dose helical CT scans had a 20 percent decrease in lung cancer deaths over those who were screened with conventional chest X-rays.

But what does this really mean? One would have to do helical CT scans biannually over six years in about 30,000 high-risk people for three years to prevent about 60 lung cancer deaths. Nevertheless, based on these data, the American Society for Clinical Oncology, the American Lung Association, and the American College of Chest Physicians now recommend screening for persons at high risk of lung cancer. Other health organizations such as the USPSTF have yet to endorse this recommendation. We should recall about half or more of lung cancers occur in nonsmokers or persons smoking less than 30 pack-years. These people were not included in the above study because, although they contribute a large proportion of lung cancer cases, the risk in any one person is so small that the potential benefit-to-risk ratio of screening is unfavorable. Even with the smoker population, risks of developing lung cancer vary greatly. Consequently, the likelihood screening will prevent a lung cancer death in a person varies more than tenfold. Therefore, recommendations regarding lung cancer screening should be individualized.

The impact of a successful lung cancer screening program is anticipated to be small—less than 5 percent of lung cancer deaths could be prevented. In contrast, the benefit-risk of the radiation involved is favorable, as only persons at high risk of developing lung cancer are to be screened. People selected for screening have a much higher risk of lung cancer than the average woman has of developing breast cancer. The conclusion that people at high risk for lung cancer should have screening radiological studies remains controversial but presently favors screening.

COMPUTED TOMOGRAPHY (CT) SCANS

Allan Cormack (1924–1998), a South African–born physicist, was so entranced by the stars as a boy that he studied physics in order to become an astronomer. In time, however, the appeal of the vastness of space was replaced by a fascination with the subatomic universe of particle physics and a parallel interest in X-ray technology. These interests, combined with the serendipity that is so much a part of science, led him to figure out how to make a three-dimensional image of something inside a body. He was amazed that no one had thought to do it sooner.

In 1955, fresh from two years of postgraduate study at Cambridge University, Cormack was asked by a Cape Town hospital to fill in part time in the radiology department, a post for which there was no competition, as he was the only person in the city with training both in physics and in handling radioisotopes. His task was to figure out how to deliver