Radiation is widely used as an adjuvant treatment after surgery for breast cancer. It is primarily administered to prevent recurrences and is quite effective at doing so. But a study published in the March 7, 2007 Journal of the National Cancer Institute (JNCI) has shown that radiation also increases the risk of heart disease in women who receive it following surgery for breast cancer. Using modern radiation delivery techniques shifts the pattern of harm, but does not remove it.

It has long been acknowledged that the type of radiation used in the 1960s and 1970s elevated women's risk of subsequent cardiovascular disease. However, techniques have changed since then, and radiation oncologists have often stated that newer radiation delivery procedures have been deliberately designed to minimize this sort of heart damage. The dangers of radiation to the heart have therefore frequently been dismissed as a thing of the past, and countless women have been told that the procedures performed on them were safe.

For example, in Clinical Oncology, a textbook published in 2001 by the American Cancer Society, the problem is downplayed. In the course of two paragraphs, its seriousness is minimized half-a-dozen times:

Cardiac toxicity due to irradiation is rare...Effects on the endocardium are rare...Below a total dose of 4500 cGy, radiation-induced damage is uncommon...Tamponade [a life-threatening compression of the heart resulting from a collection of fluid in the pericardium (the sac surrounding the heart), ed.] occurs infrequently. In general, pericarditis is self-limited... Chronic pericarditis is uncommon. Acute myocardial infarction [is] rare... (Lenhard 2001: 243-244).

Many websites similarly claim that modern radiation therapy is entirely safe. Here is an example of such a statement from breastcancer.org:

Radiation therapy techniques have changed dramatically since then [the 1970s, ed.]. New technology allows doctors to use the lowest dose of radiation possible. They can also more precisely target the radiation to the breast and away from the heart - so the heart receives a minimal amount or none at all.

This is what the orthodox medical profession believed - and wanted us to believe. However, the facts now speak otherwise. The JNCI study is unquestionably a major blow to the orthodox medical profession's insistent claims that radiation has evolved into a safe modality for the post-operative treatment of breast cancer.

In the JNCI study, researchers at the Netherlands Cancer Institute in Amsterdam evaluated 4,414 breast cancer patients who survived for at least ten years after receiving radiotherapy between the years 1970 and 1986. The patients were followed for a median of 18 years. These patients' rates of cardiovascular disease were then compared with those seen in the general population (Hooning 2007). In other words, this was a very large and prolonged study.

There were a total of 942 "cardiovascular events" during the follow-up period. The good news was that radiation therapy limited to the breast itself did not increase the risk of cardiovascular disease. However, when either the left or right internal mammary chain of lymph nodes was included in the radiation field, as is common in post-operative radiotherapy, it did significantly increase that risk.

Internal mammary chain irradiation performed during the 1970s increased the risk of a heart attack (myocardial infarction) by 2.55 times compared to no radiation. It also raised the risk of congestive heart failure 1.72-fold. Radiotherapy given in the 1980s was also associated with an increased risk of heart disease: a 2.66-fold greater risk of heart failure and a 3.17-fold greater risk of dysfunctional heart valves. (This was one...
of the first studies to investigate radiation-related heart valve failure.)

In the 1980s, it became common to add adjuvant chemotherapy to radiotherapy. The standard chemotherapy regimen used during the 1980s was CMF (which stands for the three drug combination of cyclophosphamide, methotrexate, and 5-fluorouracil). However, this study found that the addition of CMF chemotherapy to radiation conferred a 1.85-fold increased risk of congestive heart failure. This finding has caused a great deal of surprise since this combination was never thought to be particularly cardiotoxic.

It is chilling to realize that nowadays CMF chemotherapy has been replaced by regimens based around so-called anthracycline drugs, the most prominent of which is Adriamycin (doxorubicin). This class of drugs is already well-known to carry serious risks of cardiotoxicity, including life-threatening congestive heart failure. This risk increases exponentially the greater the lifetime dose.

A recent review in Seminars of Oncology concluded that "10 percent to 26 percent of patients administered cumulative anthracycline doses above those recommended... develop congestive heart failure, and that more than 50 percent of patients administered these doses will experience measurable functional impairment months to years after the end of therapy." Also, the susceptibility of patients to anthracycline-induced cardiotoxicity varies widely, with a dramatic increase with advancing age (Jensen 2006).

The risk is further augmented by the addition of Herceptin (trastuzumab), another cardiotoxic drug that is increasingly used in the treatment of breast cancer. Herceptin can cause heart damage ranging from mild and transient to life-threatening congestive heart failure. To quote the package insert warning, mandated by the Food and Drug Administration, Herceptin "has been associated with disabling cardiac failure, death, and mural thrombosis leading to stroke" (FDA 2003). (Mural thrombosis is the formation of a fibrinous clot on the endocardial lining of the heart or on the wall of a large blood vessel). In view of these ominous warnings, studies focusing on the cumulative cardiac risk of radiation therapy in patients who have also been given Adriamycin and/or Herceptin-containing chemotherapy regimens are urgently needed.

The JNCI study also found a disturbing threefold increase in the risk of heart attacks among radiotherapy-treated patients who also smoked tobacco. The authors properly caution that "irradiated breast cancer patients should be advised to refrain from smoking to reduce their risk for cardiovascular disease." Easier said than done! The more logical solution would surely be to refrain from giving adjuvant radiation to patients who insist on smoking.

Medical Detective Work

The fact that breast irradiation increases the risk of heart disease is not a new finding. Starting in the late 1960s, it became known that, after receiving adjuvant radiation to prevent breast cancer recurrence, more women than expected were dying of heart disease, sometimes decades after their initial surgery. It took brilliant medical detective work to prove that this apparently successful use of radiation therapy was also the cause of many cardiac deaths (Fajardo 2001). So many women were dying of the long-term adverse effects, in fact, that it more or less counterbalanced any survival benefit from the treatment itself.

There was great resistance to this discovery. Reports of heart damage from radiation began emerging as early as 1927, but even so, for the first 60 years of the twentieth century, the heart was routinely described a "radioresistant" organ (i.e., resistant to the negative effects of radiation), and cardiac complications of radiation therapy were often described as rare and insignificant (Desjardins 1932 and Leach 1943).

It took systematic studies, over several decades, by Prof. Luis Fajardo of Stanford University to dispel this tenacious misperception (Cohn 1967 and Fajardo 1968). The sensitivity of the heart to radiation therapy was only really acknowledged in the early 1970s (Bouyer-Dalloz 2003). Even then, a long time elapsed before the complete picture of radiation-induced heart disease finally became accepted in medical thinking (Hancock 1993).

Further evidence began to emerge in the 1970s. A Swedish team conducted a randomized, controlled clinical trial (RCT) involving 960 breast cancer patients over the period 1971 to 1976. These patients received either surgery alone or surgery preceded or followed by radiation. A total of 58 patients had heart attacks during the follow-up period, which averaged 20 years. Patients who received high doses of radiation had twice the risk of those who did not. There was also a 2.5-fold increased risk of ischemic heart disease (i.e., the kind caused by a decrease in the blood supply to the heart). The difference between the two groups began to appear after four to five years, and the heart attack incidence rates continued to increase in the irradiated group for ten to 12 years. There was some evidence that most of the deaths were due to radiation-induced damage to the small blood vessels of the heart (Gyenes 1998).

In another study, the strength of the heart was measured 15 to 20 years after treatment for breast cancer. It was found that 25% of patients treated with radiation to the left breast had heart-related problems on standard stress tests, compared to none in the control group. The authors' main conclusion was that left-sided chest irradiation (which more frequently affects the heart) might represent a risk factor for ischemic heart disease (Gyenes 1994).

Because of these studies, modifications were made in the 1980s to the way that radiation was delivered after surgery for breast cancer. Radiation oncologists have
often claimed that with more precise equipment and techniques, heart damage was no longer a clinically relevant problem. This seemed plausible. However, the latest study shows that such complacency was ill-founded. The range of cardiovascular problems that can follow intense irradiation of the heart is in fact very broad. It includes six major categories and various subcategories:

1. Pericardial disease
   - Acute pericarditis during irradiation
   - Delayed acute pericarditis
   - Pericardial effusion (delayed)
   - Constrictive pericarditis
2. Myocardial dysfunction
3. Diffuse myocardial fibrosis
   (with or without pericardial disease)
4. Coronary artery disease (CAD)
5. Electrical conduction abnormalities
6. Valvular heart disease

What complicates the issue is that radiation affects the heart and cardiovascular system unevenly: different parts of the system are affected in different ways, and individuals differ in their responses. For the sake of simplicity, I will not discuss the complicated mechanisms by which radiation damages the heart and circulatory system. What is most relevant is the experimental and clinical evidence of such damage.

**Considerable Laboratory Data**

There is a considerable body of laboratory data demonstrating the harmful effects of radiation on the heart. Most of these experiments have been carried out on the New Zealand white rabbit, because it has reactions to heart irradiation that are similar to those of humans. In one such study, after a single 20 Gy dose of radiation, fully 94% of the rabbits developed some form of heart disease (Fajardo 1970). First, there was an acute reaction, which disappeared within 48 hours. But starting at the 50th day, a delayed reaction set in, and this reached its full development by 90 days. By 150 days, half the experimental animals had died. What is particularly striking about these experiments is the degree to which radiation was shown to cause myocardial fibrosis (a thickening of the heart muscle).

Similarly, in the human clinical situation, the heart’s response to radiation is also divided into an acute and a long-term response. As in the test animals, the initial response vanishes rather quickly. But then, some months or even years later, the patient may experience heart pain (angina), difficulty breathing, or even a full-scale myocardial infarction (heart attack). The problem is that since they occur a considerable time after treatment, these radiation-induced effects are indistinguishable from “ordinary” (i.e., randomly occurring) heart problems. There is nothing about such events that screams out “radiation-induced heart disease.” The cardiologist therefore may not make a connection to the patient’s prior exposure to radiation.

The latest findings should caution us against hubris in the medical field. It took tremendous investigative work by Professor Fajardo and others to prove that radiation damages the heart. As a result of their work, some changes were indeed made – and radiation oncologists hailed these changes as proof that radiation treatment was now safe. Although the accuracy of radiation delivery and targeting has improved considerably, other problems, such as the cumulative cardiotoxic effect of chemotherapy and radiation, remain largely unaddressed. This is especially relevant now that Adriamycin-based chemotherapy has become the standard of care for breast cancer.

Radiation is a classic two-edged sword. It does substantially reduce the risk of recurrences of breast cancer in the irradiated field. But this comes at the price of an increased risk of damage to the heart, especially when the internal mammary lymph node chains are irradiated or when the patient is a smoker. Patients and their physicians need to carefully weigh benefits and risks before agreeing to this or any other potentially toxic treatment.

**References**


