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## A Tribute to Dr. Bernard Fisher

by Carl G. Kardinal, M.D.

**O**n March 31, 1994, Bernard Fisher, M.D., issued a letter to the membership of the National Surgical Adjuvant Breast and Bowel Project (NSABP). The letter began: "It is with regret that I have been mandated by the NCI to resign as chairman of the NSABP. After 38 years, I am sad to relinquish this position as chairman of the group that has made most of the major outstanding contributions to the management of breast cancer and the health of women in this world."

It is not the purpose of this editorial to discuss the circumstances that precipitated this event, but rather to review the enormous contributions of Bernard Fisher, a giant in the history of oncology.

Prior to the contributions of Fisher, breast cancer was believed to be a localized disease that originated in the breast, then spread to regional lymph nodes, and later to other systemic organs, such as bone, lung, liver, or brain. This concept of breast cancer biology, initially proposed by a French surgeon, Henri Francois Le Dran, was carried to its logical conclusion by William Stewart Halsted, who in 1890 described and subsequently popularized the radical mastectomy for the treatment of breast cancer. The basic premise of the radical mastectomy was to remove *en bloc* the breast, pectoral muscles, and axillary contents (i.e., to remove all regional tissue to which breast cancer would logically spread if it progressed in an orderly manner). The radical mastectomy became the standard of practice and was not to be challenged until an individual of Fisher's intellect and courage came on the scene.

The standard radical mastectomy was followed by the superradical mastectomy; but the astute observer, Bernard Fisher, noted that bigger

operations were not better and did not cure more women with breast cancer. Fisher then deduced that the fundamental concept of breast cancer biology must not be correct. Working with his brother Edwin in the laboratory, Bernard Fisher noted that tumor cells traverse lymph nodes with ease and that lymph nodes are not efficient filters. He also noted that tumor cells traversed the venous system as readily as the lymphatics. He concluded that if these laboratory observations are valid, breast cancer is a systemic disease early in its clinical course and that smaller operations should be equally as effective as larger ones.

Clinically, the concept that lymph nodes were ineffective filters and were primarily prognostic indicators in breast cancer was verified by Fisher and the NSABP in 1968. In a milestone publication based upon control group data from the preceding 10 years of NSABP trials, Fisher confirmed that patients with negative axillary nodes had the best prognosis and that the prognosis became sequentially poorer with each increase in the number of positive nodes.

To test the validity of this new concept of breast cancer biology, Fisher and the NSABP initiated two landmark protocols in the early 1970s. These were B-04 (simple vs. radical mastectomy) and B-05 (L-PAM vs. placebo in node-positive breast cancer). B-04 confirmed that smaller operations were as effective as the mutilating Halsted radical mastectomy. This was a major milestone in breast cancer research, and the results of this trial have been thoroughly incorporated into surgical practice. The standard radical mastectomy, the gold standard for 80 years, is now so passé that it is all but forgotten (thanks to Bernard Fisher and the NSABP).

Although no one currently uses

single agent chemotherapy, B-05 is the basis for all subsequent adjuvant chemotherapy trials. Thus, with two landmark studies, Fisher and the NSABP established the theoretical and clinical basis for our current concepts of breast cancer biology. He humbly referred to this as the "alternative" hypothesis. Clearly this should be known as the "Fisher" hypothesis.

Since simple mastectomy was as effective as radical mastectomy in the treatment of breast cancer, and since the alternative (Fisher) hypothesis of breast cancer biology appeared to be valid, the next logical step was to test even smaller operations. In 1976, Fisher and the NSABP initiated the B-06 trial (lumpectomy ± radiation therapy vs. modified radical mastectomy). Despite the current controversy, the data still stand that lumpectomy in a majority of women is as effective as mastectomy. Breast preservation is now possible for thousands of women with breast cancer. The B-06 protocol is the final proof of the validity of the alternative (Fisher) hypothesis of breast cancer biology.

I have participated in NSABP clinical trials since 1975 and was elected to the NSABP Executive Committee in 1987. It is with a great deal of pride that I have been privileged to serve in that capacity. True giants walk on the earth only rarely. How fortunate I have been to have known Bernie and to have worked closely with him. How fortunate the world has been that Bernard Fisher and the NSABP have been a reality. No other single individual has ever made as big an impact on breast cancer treatment.

On March 31, 1994, Bernard Fisher relinquished the chairmanship of NSABP. A giant has been forced aside. The world is not likely to find one of this caliber, even in the next century. ■