More data flaws mar breast cancer trials

New data irregularities have emerged in a continuing federal probe of a breast cancer research group. National Cancer Institute (NCI) audits of two Louisiana medical centers failed to find some required information on many patients enrolled in several key breast cancer studies.

These new reports add to the growing concern about the quality of data collected by the National Surgical Adjuvant Breast and Bowel Project (NSABP), a group that includes 484 medical centers in the United States and Canada.

NSABP first came under fire after reports that a Montreal physician had falsified data underlying a study reported in 1985 that compared lumpectomy to mastectomy for the treatment of breast cancer (see p.282). Now, Tulane University and Louisiana State University (LSU) medical centers, both in New Orleans, have been drawn into the fray.

At Tulane, NCI auditors reviewed 75 charts for patients enrolled in a number of NSABP clinical trials between 1976 and 1994. In about 70 percent of the cases, they found insufficient documentation to determine the patient's eligibility for inclusion in the trials. Auditors could not find the required results of certain lab tests in some cases. In others, they found no documentation that patients had consented to participate in a trial.

LSU fared little better. The NCI squad reviewed 80 charts for patients enrolled in NSABP studies between 1971 and 1994 and failed to find sufficient documentation to confirm eligibility in about half the cases.

The missing data make it impossible to ensure that the patients enrolled by the Louisiana centers met the standards required by the various NSABP trials, says NCI's Michael A. Friedman. Both Tulane and LSU had trouble producing the original documentation to support data they submitted to NSABP's central office, located at the University of Pittsburgh.

The auditors unearthed no sign of fraud at the Louisiana medical centers. However, Tulane and LSU certainly demonstrated sloppy data management, NCI charged. "The standards of record keeping and reporting at these institutions were unacceptable," said NCI.

At a meeting this week of an NCI scientific advisory board, institute officials outlined their actions to improve the quality of the data collected by NSABP, including the monumental task of auditing the primary records of patients enrolled in NSABP studies. NCI must go back and audit those records because lax procedures by NSABP's central office allowed such data problems to continue for years.

So far, NCI has audited roughly half of the patient charts that contributed to the study, known as B-06, comparing lumpectomy to mastectomy. Many of the patient records for that trial have been warehoused or stored on microfilm, making it difficult to check the originals against the data turned in to NSABP. So far, NCI has found no evidence of systematic manipulation of data or fraud in the B-06 trial other than a center in Montreal.

In a conference room on the National Institutes of Health's campus in Bethesda, Md., NCI's Bruce A. Chabner emphasized to the advisory board the importance of verifying the B-06 trial. Preliminary analysis of that trial suggests that many clinical investigators did not obtain proper informed consent from their patients. If those patients qualified for B-06 in every other way, the consent problem probably wouldn't undermine the study's scientific findings, Friedman says.

At the meeting, NCI officials outlined a number of measures to help maintain the accuracy of NSABP data in the future. For example, NCI wants audit schedules provided on a regular basis and immediate notification of any suspect data. In the end, the NCI advisory board approved a 1-year increase in funding so that NCI could step up its auditing of NSABP centers.

"The record simply must be set straight," Friedman says.

— K.A. Fackelmann

ASCA probes the X-ray universe near and far

From studies of celestial powerhouses far beyond the Milky Way to the nature of exploded stars within it, the X-ray eyes of the orbiting Japanese telescope ASCA have uncovered several surprises.

Astronomers described these and other intriguing discoveries last week at a meeting of the American Physical Society in Crystal City, Va.

ASCA's observations of the diffuse glow of X rays, known as the cosmic X-ray background, suggest that the output of quasars and the brightest active galaxies can't by themselves account for most of the background at X-ray energies below 10,000 electronvolts. According to ASCA astronomer Hajime Inoue of the Institute of Space and Astronautical Science in Tokyo, the emissions from active galaxies at these low energies don't match the relatively flat X-ray spectrum recorded by the telescope.

Instead, he suggests, the combined X-ray emissions from the vast number of seemingly mundane galaxies in the universe produce the low-energy part of the X-ray background. The smoothness of the observed background suggests that the X-ray glow is formed by many relatively dim galaxies rather than a few very bright ones.

Inoue proposes that most galaxies have at their center a small black hole and that these central powerhouses provide the galaxy's X-ray background. Thus, most galaxies may be active. ASCA researcher Stephen S. Holt of NASA's Goddard Space Flight Center in Greenbelt, Md., says that less exotic sources of radiation, such as a cluster of rotating neutron stars, could produce the galactic X-ray emissions.

Closer to home, ASCA observations of the Milky Way have prompted researchers to refine their view of what happens when a star explodes as a supernova, hurling its remains through space.

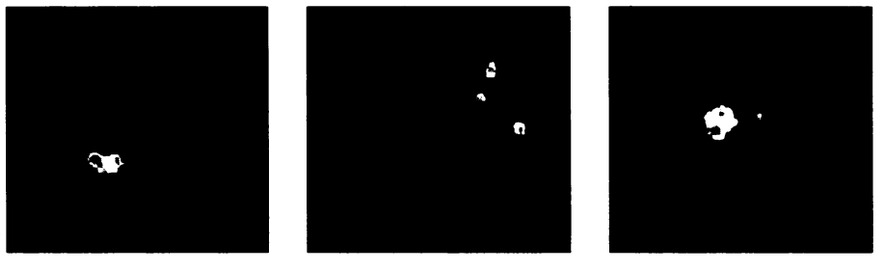
Spectra taken with ASCA reveal that the remnants of some supernovas, though born in a powerful explosion, manage to preserve the layered structure of their parent star. This finding might provide a new tool for analyzing supernovas, says Robert Petre, an ASCA investigator at the Goddard Space Flight Center.

Stars shine by squeezing together the nuclei of lighter elements, such as hydrogen or helium, to make heavier elements. As a star ages, its center — the hottest, densest area — becomes the birthplace of the heaviest elements. Indeed, the classic model of a massive, older star depicts a layered structure akin to an onion — an iron core surrounded by concentric shells of lighter elements.

In examining the elderly supernova remnant W49B, ASCA found that this exploded star retains the onionlike layering of light and heavy elements. ASCA images show iron concentrated close to the core, with silicon and sulfur lying nearer the outskirts of the remnant, report Ryuichi Fujimoto of the Institute of Space and Astronautical Science and his colleagues.

"It is astonishing that supernova rem-

False-color X-ray images from ASCA trace the distribution of (left to right) silicon, sulfur, and iron in supernova remnant W49B. Yellow and red denote the brightest emissions.



Fujimoto, E. Gotthelf