

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 lumpec-

tomy 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 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.

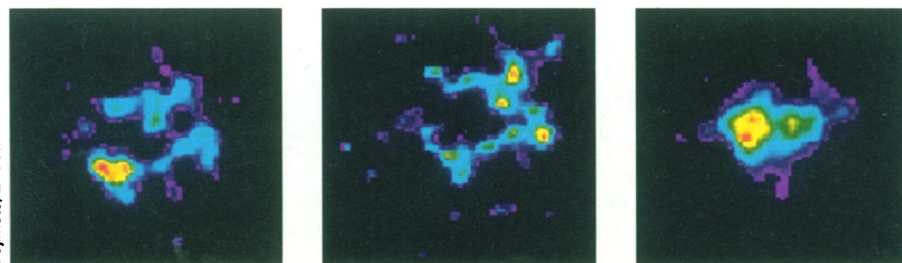
Spectra taken with ASCA reveal that the remnants of some supernovas, though born in a powerful explosion, manage to preserve the layered structure of their parent star. This finding might provide a new tool for analyzing supernovas, says Robert Petre, an ASCA investigator at the Goddard Space Flight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

nants can retain the memory of the explosion for several thousand years," comments Petre.

In contrast, Cassiopeia A, the youngest known supernova remnant in the Milky Way, appears messier. ASCA images indicate that sulfur and silicon concentrate in lumps rather than shells. In addition, material from the southern half of the remnant moves toward Earth, whereas the northern half recedes. This suggests that the supernova explosion flung a broken ring of material, rather than a spherical remnant, into space, says Petre.

Holt says that the ASCA images of Cassiopeia A reveal for the first time two distinct types of X-ray emission in a single remnant. The X-ray glow from specific elements, including sulfur and silicon, lies in the northern and eastern parts of the remnant. But at higher X-ray energies, which may indicate emissions from hot electrons and ions, the southwest section appears brightest.

According to Holt, the X-ray-emitting electrons and ions represent material from the interstellar medium that got heated and swept up by the expanding blast wave from the supernova explosion. In contrast, the X-ray glow from the elements stems from heating by a reverse shock wave — the secondary wave of energy created when the original, outgoing blast slams into interstellar space.

— R. Cowen

Seismologists track tremors in Tennessee

Despite the tornadoes, floods, blizzards, and hurricanes that ravage the eastern United States, residents there can console themselves with the thought that they need not worry about earthquakes. That is, until the next deadly jolt strikes the East. Seismologists have calculated that the region east of the Rocky Mountains stands a 40 to 60 percent chance of suffering a magnitude 6 or greater quake before the year 2020.

Although they occur rarely in eastern states, significant shocks have previously rattled many regions, including the Mississippi River valley, Charleston, S.C., Cape Ann, Mass., and even New York City. To this list of potential quake sites, researchers now add a seismically active zone in eastern Tennessee.

"There is a chance that eastern Tennessee can generate a damaging earthquake. We have no doubt it can do that," says Christine A. Powell of the University of North Carolina at Chapel Hill. She and her colleagues report their findings in the April 29 *SCIENCE*.

No large jolt has shaken this area in recorded history; the strongest was a magnitude 4.6 tremor in 1973. Nonetheless, Powell and her coworkers detected a pattern of seismic activity in the Appala-

Clinton emissions program under fire

Nasty weather, a surging economy, a fall in oil prices, and other factors have left the Clinton administration's plan to reduce atmospheric concentrations of greenhouse gases in need of repair, an environmental group asserts.

The scheme to trim output of gases such as carbon dioxide, which many researchers believe contributes to global climate change, will fail to meet its goals, according to an April 19 report by the Natural Resources Defense Council (NRDC). The plan seeks to lower the country's net emissions by 106 million metric tons by the year 2000—to a level equaling the amount spewed into the air in 1990. Announced in October, the initiative stems from a United Nations environmental treaty developed at the 1992 Earth Summit in Rio de Janeiro (SN: 10/23/93, p.263).

"Under the administration's current climate plan, U.S. greenhouse gas emissions in 2000 are likely to exceed 1990 levels by about 70 [million metric tons]," the report predicts. The effort underestimates the amount of emissions the country will produce and the ability of initiatives to reduce them, says Daniel A. Lashof, the report's author.

NRDC published its analysis after reviewing a supplement to the plan released last month by the Department of Energy. That document describes assumptions the Clinton team used to develop its emissions goals. Also in March, DOE's Energy Information Administration made public data showing that by the end of 1993, energy-related

carbon emissions had increased to levels predicted for 1996.

"The [NRDC] report is in the ballpark," asserts DOE's Arthur T. Andersen. "We took a look at [NRDC's figures] and didn't find any egregious errors."

But administration officials argue that it's too early to say the plan needs refurbishing, as Lashof urges. The administration is, however, considering whether to revise the document, says DOE's Abraham E. Haspel.

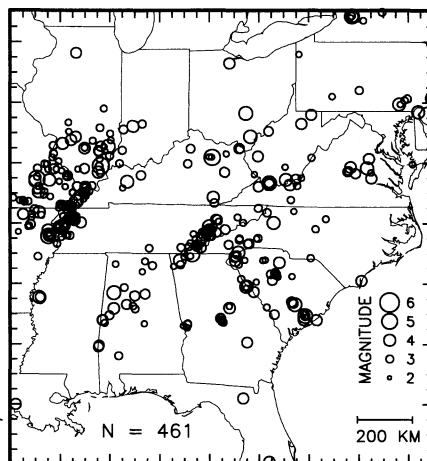
Increased industrial productivity and use of automobiles, triggered by lower oil prices and an improved economy, contributed to the U.S. emissions picture, Haspel says. Also, increased energy consumption due to extreme weather accounted for 16 million metric tons of the 1993 emissions increase.

Lashof also claims that the climate plan errs by painting an overly optimistic picture of how much money Congress will provide for the initiative. Moreover, he says, its architects assumed substantial improvements in car and truck fuel efficiency — but fuel efficiency has remained essentially constant since 1981.

Moreover, Lashof dismisses the initiative's assertion that trees will absorb significant quantities of greenhouse emissions. The plan recommends planting more trees to sop up carbon dioxide. But forests can't be considered safe storage areas, since a forest fire could release tons of gases, he points out.

If that were to happen, Haspel counters, "We could always plant new trees."

— Tina Adler



Map shows quakes greater than magnitude 2 in the central and southeastern United States between 1965 and 1985. A line of seismic activity in eastern Tennessee appears in center of figure.

chians near the border between Tennessee and North Carolina. Measurements of tiny earthquakes during the last decade reveal that they occur along a well-defined

line between Chattanooga and Knoxville.

The researchers also note that quake activity has grown more concentrated in the last 15 years. Prior to 1977, the jolts occurred over a broad area reaching into western North Carolina. Since that time, the quake zone has narrowed.

During the last decade, eastern Tennessee has released more seismic energy per square kilometer than any other part of the eastern United States, except for the region around New Madrid, Mo., site of four great quakes in the winter of 1811-1812.

The line of eastern Tennessee quakes coincides with the location of a major geological boundary between two crustal blocks. Powell and her colleagues suggest that this junction could represent a major fault capable of producing large earthquakes. They plan to recheck the location of past quakes to determine whether they actually line up along a fault.

Powell notes that the eastern Tennessee seismic zone runs near several hydroelectric dams and two nuclear power plants.

— R. Monastersky