vides access to dozens of chemistry journals, while HighWire Press of Stanford University Press in California has created a site with some 130 crosslinked online journals, including *Science* Online. Commercial giant Elsevier Science also has backed several sites, including BioMedNet and ChemWeb, stocked with dozens of its titles.

But many aggregators continue to hunt for the right combination of pricing, advertising, and access policies. And some predict BioONE may have trouble satisfying everyone. Librarians, for instance, may be loath to sign up for the whole collection when they now have the freedom to select individual journals. "It should be a very interesting experiment—they will be wrestling with the same economic issues we do," says Don Muccino, executive vice president of the Online Computer Library Center in Dublin, Ohio, a library-backed nonprofit aggregator that puts more than 1600 journals online.

BioONE backers, however, are confident they can devise a workable solution that others may want to emulate. Says the University of Kansas's Beth Forrest Warner: "We're real excited about the possibility of breaking some new ground here." **–DAVID MALAKOFF**

SCIENCE IN SOCIETY

Panel Discounts Implant Disease Risk

A blue-ribbon panel has concluded that silicone breast implants do not increase the risk of diseases such as lupus or cancer, rejecting a theory invoked in countless claims against implant manufacturers. But the report, released earlier this week, is unlikely to be the last chapter in the lawsuit-weary saga: The Institute of Medicine (IOM) panel cites evidence that silicone implants can leak and cause infections or painful scarring around the implants.

Anecdotal reports blaming implants for serious health problems first arose in the late 1980s and led to billions of dollars worth of legal claims against manufacturers. Most of those claims are now being resolved, as Dow Corning, Bristol-Myers Squibb, and other manufacturers have agreed to create settlement funds totaling about $7.2 billion. In the meantime, studies on implants and chronic disease risk have been coming up empty-handed. The IOM panel "is simply saying over again what we already knew—that the case for autoimmune disease was extremely weak," says Yale University immunobiologist Charles Janeway. But he and others say the imprimatur of the nation's top medical advisory body gives that conclusion more weight, shifting the scientific focus and legal battleground from systemic disease to local problems caused by ruptured implants.

The IOM stepped into the thorny arena of implant science in late 1997, at the request of the Department of Health and Human Services. The 13 panelists, led by Stuart Bondurant, a professor of medicine at the University of North Carolina, Chapel Hill, examined some 2000 peer-reviewed studies and 1200 other data sets and reports, searching for links between implants and lupus, rheumatoid arthritis or other connective tissue diseases, cancer, or neurological diseases. The committee also heard testimony from sick women and was "moved by their suffering," it said.

But the touching personal stories failed to sway the panel's views on the data. It concluded that the 1.5 million to 1.8 million U.S. women with implants are no more susceptible to serious diseases than are women without implants, according to available evidence. This conclusion, the panelists noted, is consistent with reports in the past year from U.K. experts and a panel appointed by a U.S. judge overseeing breast cancer litigation (*Science*, 11 December 1998, p. 1963).

But the panel did not give implants a clean bill of health. Essentially plastic bags filled with silicone gel, implants can rupture in an unknown percentage of women—studies have cited rates as low as 0.3% or as high as 77%. The pain of breast tissue contracting around implants, as well as infections and other health risks from surgery to replace implants, are "the primary safety issue[s] with silicone breast implants," the report found. The panel recommends more research to track women with implants to get a better handle on problems such as rupturing and second surgeries, and improved tests to gauge silicone concentrations in body fluids and tissues.

> **The IOM panel "is simply saying over again what we already knew."**
>
> **—Charles Janeway**

Some observers who are not ready to dismiss the disease threat say they are waiting for the results of a major epidemiological study on women with implants by the National Cancer Institute (NCI), due out later this year. That study, however, may be predetermined to find problems, says IOM president Kenneth Shine: Materials for recruiting participants may have "encouraged women with symptoms and problems to enroll," he says, rather than gathering a sample that would include healthy women with implants

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ScienceScope

Enriching Debate An expert panel has presented the German government with some choices for a controversial new reactor near Munich that's designed to produce neutrons for materials science and other research. The $500 million FRM-II neutron source, due to be completed in 2001, would be fueled by highly enriched uranium, which can be used to make weapons. Nonproliferation advocates want the reactor to be reconfigured to use a low-enriched uranium fuel. The German government appointed a committee in January to review alternatives (*Science*, 5 February, p. 785).

This week, the seven-member panel concluded that it would be costly and time-consuming to alter FRM-II's design this late in the game. But the panel, led by science ministry official Wolf-Michael Catenhusen, said that the reactor might be able to make a less costly switch by 2008 to a low-enriched uranium fuel in development.

The German cabinet is expected to decide how to proceed within a few months. But any changes in the FRM-II must be coordinated with the state of Bavaria, which oversees the project.

Biology Boost An alumnus who made a fortune selling car insurance has pledged $35 million to a new genome research center at Princeton University. The gift from Peter Lewis, CEO of Progressive Corp. in Cleveland, Ohio, will cover almost half the planned $75 million budget of the Institute for Integrative Genomics.

The donation marks the latest gain for genome studies at major research universities. Harvard recently decided to spend $40 million on a center to apply genomics to the study of evolution, while the California Institute of Technology is more than halfway toward a goal of raising $100 million for interdisciplinary research on the brain and development. The Princeton center, launched last year, is probing how a cell's many molecular components fit together as a functional unit of life, says cell biologist Shirley Tilghman, the institute's director.

"This is a trend you are going to see more of," says Bruce Umminger, division director of integrative biology and neuroscience at the National Science Foundation.

who could serve as controls. NCI study leader Louise Brinton responds that "there has been some misrepresentation of our study," but she declined to address its design until the findings are published. The IOM report may carry weight, but it will not be the last word on the contentious issue of silicone implants and health. –JOCELYN KAISER

GENE THERAPY

RAC Nixes Plan to Treat Retinoblastoma

Since losing its approval authority over gene therapy protocols 2 years ago, the Recombinant DNA Advisory Committee (RAC) has been out of the news—and out of the minds of many people working in the field. 1997 appointee Jon Wolff says that some colleagues have been baffled by his RAC activities. "People's first reaction was, 'Is it still in existence?' " he says. But the RAC may be regaining its clout.

One sign of life came last week when the committee turned thumbs down on a gene therapy protocol for treating retinoblastoma,

Target. Baylor scientists hope gene therapy can shrink retinoblastomas such as this one.

a rare childhood cancer of the eye—and the lead investigator listened. Also last week, RAC got a strong endorsement from National Institutes of Health (NIH) director Harold Varmus, who 3 years ago proposed doing away with the committee but then, in response to much protest, agreed to keep it to advise on policy matters.

Speaking to gene therapists assembled in Washington, D.C., for their annual meeting, Varmus delivered a barely veiled threat. Gene therapy protocols now need only the approval of the U.S. Food and Drug Administration (FDA). But in an otherwise optimistic talk, he warned that the "double approval" process that ended 2 years ago might be restored if researchers don't submit their proposals simultaneously to RAC and the FDA. "Departure from standards of gene therapy must be publicly discussed," Varmus said, emphasizing that the RAC is the proper forum for hashing out the scientific, ethical, and societal issues surrounding new forms of gene therapy.

NIH isn't likely to restore protocol approval power to the RAC, but the director did capture his audience's attention. "Varmus's talk really put us back on the map, in terms of clarifying our role," says Wolff, a gene therapist at the University of Wisconsin, Madison. Such clarification may be needed. NIH records show that since 1997 about 10% of gene therapy protocols haven't gone to the RAC. Others, including the one for the retinoblastoma trial, came in late. The trial's lead investigator, Richard Hurwitz of Baylor College of Medicine in Houston submitted his protocol to the RAC only after the FDA had approved it, he says, because of a "completely inadvertent" oversight.

When the RAC finally reviewed the protocol, safety was the big sticking point. The strategy is not new. It involves injecting the eye tumors with an adenovirus vector that carries the herpes simplex virus thymidine kinase gene into cells, making them susceptible to killing by the antiviral drug ganciclovir. The goal, Hurwitz says, is to reduce the size of the tumors at least to the point where they can be removed by freezing or by laser surgery. Standard therapy, which almost always cures the disease, is to remove the eye. Gene therapy holds out the promise of saving the eye and some vision.

But the trial also raises a policy issue—or so RAC members believe. In the words of RAC consultant Pedro Lowenstein of the University of Manchester, U.K., this may be "the first gene therapy protocol focused on improving quality of life" as opposed to just curing disease or disability. Although removal of an eye seems draconian, retinoblastoma expert Thaddeus Dryja of Harvard Medical School in Boston describes its impact as "gratifyingly tolerable." Thus, the Baylor trial involves treating babies, whose average age is 18 months, for a condition that already can be cured.

RAC members cited several risks: The needle could lead to the cancer's spread through the blood vessels; the adenovirus vector might trigger inflammation that would damage the diseased eye and perhaps the normal eye as well; and ganciclovir could damage normal tissue. "I question whether we are introducing a very dangerous protocol ... or one with unknown risk, in something that usually, with standard care, can be 100% cured," said RAC member Louise Chow of the University of Alabama, Birmingham. Consequently, the RAC voted unanimously (with four of 13 members abstaining) to urge Hurwitz to treat only patients with tumors in both eyes, because these children face blindness anyway, making the therapy's risks easier to justify.

Hurwitz argued that retinoblastomas do not usually metastasize through blood vessels, and that Baylor's eye surgeons can largely avoid them, anyway. As for the risk of inflammation, he notes that the aim of this first trial is precisely to see whether the gene therapy produces such toxic effects. Hurwitz also pointed out that evaluating adverse effects would be harder in patients with bilateral retinoblastoma because they, unlike the patients he proposes to treat, have already had potentially toxic therapies.

FDA reviewers deemed the protocol safe enough to proceed, although they would have preferred that Hurwitz treat bilateral retinoblastoma. "A close call," remarks the FDA's Philip Noguchi. But Hurwitz will comply with the RAC's decision—"at least [with] our first few patients," he says. "We want to proceed very carefully." After that, he's keeping his options open.

With gene therapy trials expected to increase by up to 25% this year, the RAC may see more controversial protocols. "I think there are some real cowboys out there," says Wolff. But will Varmus have to make good on his threat to restore teeth to the RAC? "We don't want to go there," says NIH science policy director Lana Skirboll, speaking on behalf of Varmus, who was unavailable for comment. Much depends, she says, on how the gene therapy community responds.

–KEN GARBER

Ken Garber is a writer in Ann Arbor, Michigan.

IMAGING

3D Camera Has No Lens, Great Depth of Field

The traditional camera is a threatened species. Digital cameras, which replace photographic film with electronic light detectors, are on sale at your local photo shop. Lensless cameras, in which a computer does the job of the lens and digitally processes light to make an image, are taking shape in the lab. And in this issue of *Science*, the camera takes another step away from its roots. Since the days of Louis Daguerre, cameras have captured reality in two dimensions. But the lensless camera that a team of electrical engineers at the University of Illinois, Urbana-Champaign, describes on page 2164 makes the jump to three.

By bathing an object in ordinary light, rotating it on a stage, and recording the interference of thousands of pairs of light rays reflected from or transmitted through the object, the system builds up a 3D representation that captures far more information than a hologram or stereo images. The "lens" responsible for this feat is a pair of mathematical algorithms, one borrowed from radio astronomy and the other from x-ray imaging.

CREDIT: P. CHEVEZ-BARRIOS/BAYLOR COLLEGE OF MEDICINE