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

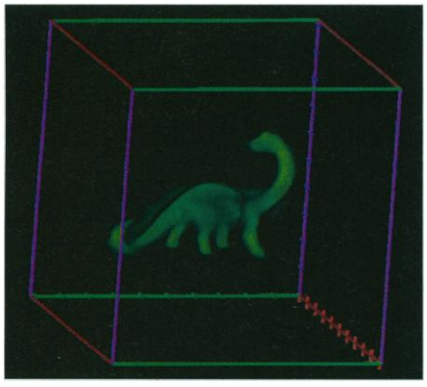
3D Camera Has No Lens, Great Depth of Field

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

Other researchers are impressed, saying the technique could capture cells and tissues in three dimensions and give depth to machine vision. Kelvin Wagner, an electrical engineer at the University of Colorado, Boulder, who is familiar with the work, calls the group's method "an amazingly elegant way of turning the problem from something very messy into something far simpler."



3D dino. A (2D) rendering of the 7-centimeter dinosaur used to test the imaging system.

The technique grew out of a mathematical insight that joined two traditionally separate imaging tools. One, widely practiced in radio astronomy, is interferometry, in which radio waves collected by separate dishes from the same point in the sky are allowed to interfere. The waves' interference can be translated into the position and intensity of their source, and combining interference data from many different points yields precise 2D maps of quasars, supernovae, or galaxies. The other mathematical tool is tomography—the T in x-ray CT scans, which pinpoint the body's internal structures by analyzing x-rays sent through the body along many different paths.

The mathematical match was made when Daniel Marks, an Illinois graduate student, noticed that applying a mathematical tool called a Fourier transform to interference measurements would yield a data set ready-made for a particular type of tomographic analysis. By dovetailing the tomographic and interferometric algorithms and applying both of them to visible light, the group came up with its 3D lensless camera.

The imaging begins as the object—in this case a small plastic dinosaur—is rotated in front of an interferometer. For each viewing angle, the interferometer collects light that follows many different paths from each point on the object, filters it, and allows it all to interfere. The result is a pattern of light and dark spots, captured by an array of detectors. Then the algorithms kick in. First comes the analysis of the interference data, which transforms it into a two-dimensional projection—something like a shadow of the object. Next is the tomographic algorithm. It analyzes the two-dimensional projections, each one analogous to the x-rays collected along a single viewing direction in CT scanning, to build up a set of image slices representing the three-dimensional object.

The tomographic algorithm was designed for x-rays, which pass virtually unhindered through most tissues, but the Urbana-Champaign team has found that it also works surprisingly well for light reflected from opaque objects, allowing them to map the surface of their dinosaur with a resolution better than 1 millimeter. And the result is far richer than a hologram, which is made by recording the interference patterns of laser light, says David Brady, an electrical engineer with the Illinois group. Holography, which generally does not scan all viewing angles, "is not really a 3D imaging technique; it's a 3D perspective preserver," explains Brady.

Thomas Cathey, an electrical engineer and colleague of Wagner's at Boulder, cautions that the technique may be too slow for use in real-time applications such as robotic vision or automated quality control in manufacturing. But George Barbastathis, an electrical engineer at the Massachusetts Institute of Technology, thinks that for imaging biological samples, the new system could ultimately surpass techniques such as confocal microscopy, which builds up 3D images by illuminating and imaging samples point by point.

"Confocal systems acquire intensity data one point at a time," notes Barbastathis. "With Brady's method you scan in parallel. If they can manage to make the resolution comparable to confocal microscopy—and I believe that with their method it's actually possible to make the resolution better—then in that case it wins hands down." **–DANIEL RADOV**

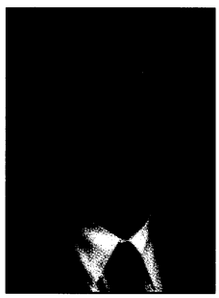
Daniel Radov is a free-lance writer in Brookline, Massachusetts.

CREDIT: (TOP TO BOTTOM) MARKS *ET AL.*; CATHALEEN CURTISS; CARL COX

BIOPATENTS

Legal Fight Over Patents on Life

Biologist Stuart Newman of the New York Medical College in Valhalla is trying to get a patent on a "humanzee"—a chimeric animal made from human and chimpanzee embryos. Not because he really wants to create one, but because he wants to prevent other people from making one, and to challenge the rules for patenting life. Together with Jeremy Rifkin, president of the Founda-



Provoking a debate. Jeremy Rifkin.

ScienceScope

Change of Heart When it comes to evaluating the effectiveness of federal R&D programs, you can't have too much input. At least that's what Neal Lane (below), the president's science adviser, has decided in lifting his objections to a congressional suggestion that the National Academy of Sciences (NAS) examine how well federal science agencies are complying with a 1993 law that calls for annual reviews of their research portfolios.

Last fall Lane complained to legislators that an NAS study, recommended in a bill funding the National Science Foundation, would be redundant and out of step with the Government Performance and Results Act. But now he has given NAS president Bruce Alberts the green light for such an "independent assessment," suggesting in a letter that the academy write up case studies of a half-dozen federal programs. The House and Senate science panels have chimed in too, stating in separate letters that they "look forward to seeing the results."

Academy staffers hope that the support from Lane and Congress will persuade agencies to pony up the needed $300,000 for the study. If funded, they say, the project would take about a year.

Sounding Out The U.S. Office of Naval Research (ONR) wants to continue the once-controversial Acoustic Thermometry of Ocean Climate (ATOC) project, which measures sea temperatures by clocking underwater sound pulses.

In 1994, activists stalled the installation of ATOC emitters off California and Hawaii, worrying that the pulses would deafen whales; that fear proved unfounded (*Science*, 27 February 1998, p. 1302). But ATOC's $40 million seed grant ran out last year and the California station is being dismantled. Last week, however, ONR signaled its desire to keep the Hawaii source running for at least a few more years, saying it will sponsor an environmental study necessary for obtaining new operating permits. ATOC researchers are thrilled by the move, which could take a year to complete, because it will allow them to collect valuable long-term data.

Contributors: Robert Koenig, Elizabeth Pennisi, Jeffrey Mervis, David Malakoff