degrees at the fault at the time of the earthquake, Mori says. "By a year later, we are looking at a few tenths of a degree. It's a simple conduction experiment. Rock holds heat pretty well." Patrick Fulton from UCSC explains, "We see an extra bump in the temperature that indicates extra heat at the fault. Since we know that the fault slipped 50 meters, based on the extra heat we can back out what the friction was during the earthquake. It was low." The small friction could have contributed to the large slip, he says. "And large slip and [the earthquake's] shallow depth probably contributed to the large tsunami."

The JFAST friction measurements are consistent with laboratory experiments. Kohtaro Ujiie, a structural geologist at the University of Tsukuba, says that by sandwiching fault-zone material between a pair of rock cylinders and holding one fixed while rotating the other, "we reproduce high-speed shearing, and measure the shear stress in the fault-zone material." Those experiments use about half a gram of fault-zone material.

The researchers also found the clay content in the fault-zone samples to be unusually high. Says Ujiie, "We think the low friction of the Tohoku material is due to the abundance of weak clay."

The huge slip observed in the Tohoku earthquake is rare. "We have fewer than 10 examples in the known history," says Shuichi Kodaira, a JAMSTEC scientist. Predicting earthquakes is still not possible, he says, "but at least we know the frictional properties of this earthquake, so we can understand why it occurred."

The JFAST researchers plan to install a pressure sensor at the opening of the observatory borehole—the one where temperature sensors were—to monitor fault movement. Another group is studying the much deeper Nankai Trough seismogenic zone south of Japan. "We have the same science goals," says Mori. The two projects are complementary, he adds. "Ours is unique in that we are drilling into the fault and making direct measurements after the earthquake. For the Nankai project, there are plans to drill to a fault several kilometers below the sea floor before the major earthquake occurs."

Toni Feder

Livermore program accelerates cancer diagnostics

Lasers could eventually replace accelerator mass spectrometry for many biomedical applications, but they haven't yet.

A former Lawrence Livermore National Laboratory (LLNL) chemist is attempting to commercialize an accelerator-based measurement technology, developed at the lab, that predicts whether some cancerous tumors will respond to a widely used chemotherapy agent. If the test is approved for use, patients who won't respond to the drug would be spared from having to endure the toxic side effects and could pursue other therapies.

The technology employs radiocarbon tracing using accelerator mass spectrometry (AMS) to determine if the chemotherapy agent carboplatin will be effective in treating individuals with bladder and lung cancer. Carboplatin is effective in nearly two-thirds of patients with those cancers, but there is no currently approved method for determining *a priori* who will and will not respond.

In current clinical trials, lung and bladder cancer patients are given a microdose of carboplatin tagged with carbon-14, says Paul Henderson, CEO of the LLNL spinoff Accelerated Medical Diagnostics. Biopsies of the tumors are taken 24 hours later, and the samples are analyzed at LLNL's accelerator mass spectrometer to determine the extent to which the drug with the ^{14}C has bound with cancer-cell DNA. Trial patients then undergo a course of treatment with carboplatin. So far, the patients who showed the highest level of drug–DNA binding from the microdose responded positively to the carboplatin, Henderson says.

To finance the trials, the company has pulled together grants from the National Institutes of Health, the Susan and Gerry Knapp Family Fund, NSF, the Department of Energy, and the University of California, Davis, Comprehensive Cancer Center. All told, about $3 million has been spent on developing the technology. Henderson expects that between $30 million and $50 million will be needed to gain Food and Drug Administration approval. In addition to completing a second, larger round of clinical trials, the company must build and obtain quality certification for a facility to manufacture the radiocarbon-labeled microdoses. That facility will include a purpose-built accelerator mass spectrometer.

Financing for the second set of trials and the manufacturing facility will be raised from venture capital and other private equity sources, says Henderson. With 300 000 cancer patients annually undergoing treatment with drugs similar to carboplatin, he says he doesn't expect trouble attracting investors. The company recently received FDA approval for trials to assess radiocarbon microdosing as a diagnostic for another chemotherapy drug, oxaliplatin, in the treatment of metastatic breast cancer. About 20% of patients with that disease will respond favorably to the drug, he says.

From brains to toxins

There are other biomedical applications for AMS. It has been used to conduct metabolite analysis at the picomole to attomole level and to identify macromolecular targets such as proteins for drugs. Using a different ^{14}C methodology, researchers at LLNL and Sweden's Karolinska Institute reported in June they had found evidence that new neuron formation occurs in the hippocampus region of the brain. Previously, using the same ^{14}C technique, scientists at the two institutions had determined that neurogenesis does not occur in either the cortex or cerebellum regions of the brain. Other applications of AMS in the biological sciences include the investigation of tissue turnover rates and the pharmacokinetic parameters of drugs, toxicants, and nutrients, including their absorption, distribution, metabolism, and excretion.

LLNL

Ted Ognibene analyzes data at the NEC 1 MV tandem accelerator at Lawrence Livermore National Laboratory's Center for Accelerator Mass Spectrometry.

The neurogenesis research relies on the spike in ^{14}C levels that resulted from atmospheric testing of nuclear weapons (see the Physics Update on page 18). Since aboveground tests were banned by treaty in 1963, ambient levels of ^{14}C have steadily declined. When a cell divides, the newly synthesized DNA incorporates a trace amount of ^{14}C that is proportional to the environmental level at the time of mitosis. The radioactive carbon in a cell nucleus can thus be used as a time stamp of when the cell was born.

Several NIH institutes provide a total of about $3.5 million annually to LLNL's AMS program, including a core grant of $2 million a year to support a user facility. But Graham Bench, the AMS program director, says that lasers may replace AMS for biomedical applications by the end of the decade. "It's a fundamentally different way to quantify ^{14}C," Bench says. The sample is combusted in excess oxygen to oxidize the carbon to carbon dioxide, he explains. The CO_2 can be separated from other gases cryogenically. "You shine a laser beam having a specific wavelength that gets preferentially absorbed by ^{14}C. The amount of that absorption can tell you the amount of ^{14}C content in the CO_2 sample."

A laser-based device could lower the cost of equipment needed for analyzing radiocarbon tracers by a factor of 10, to as little as a few hundred thousand dollars. And the instrument might be small enough to fit on a tabletop, Bench says. He adds that the expertise and infrastructure required to operate an accelerator and associated equipment would be eliminated. Researchers from LLNL are working with Picarro, a company that manufactures spectroscopic instruments for methane leak detection, to develop a tabletop version of the laser device. Data from a prototype instrument have been promising, he says. Other entities pursuing the technology include Sweden's Lund University, Rutgers University, Italy's National Institute of Optics, and the European Laboratory for Non-Linear Spectroscopy, also in Italy.

"The overarching vision would be one in every clinic, one in every research lab," says Bench. "Once you make the instrumentation cheaper and easier to operate, the number of people who want to use it will rapidly increase." There are hundreds, if not thousands, of scintillation counters in the US measuring radiocarbon decay, he notes. "Think about something that size and that easy to use, but with the sensitivity of AMS."

David Kramer

Sharing samples to advance knowledge

"Smooth single-layer graphene films want to meet new instruments for exotic experiments and unique measurements." Well, not quite, but matchmaking is the goal of Sample of Science, a website launched in June to help scientists who make samples connect with scientists who need them (see http://www.sampleofscience.net).

"Conferences have been the main place to get in touch with people," says