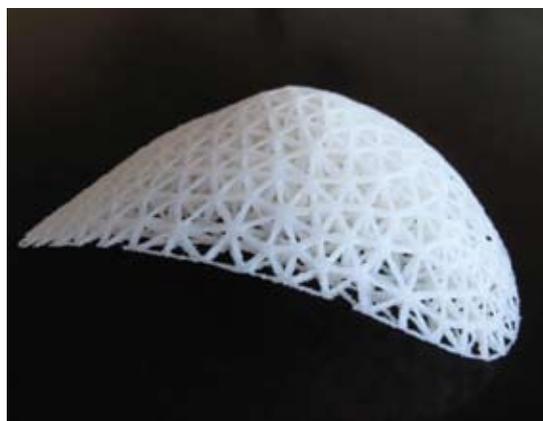


CAD/CAM aids breast reconstruction

COMPUTER-AIDED design and computer-aided manufacturing (CAD/CAM) are extending their reach from industrial and engineering pursuits into the patient care arena, with the technology now being used to aid in breast reconstruction for people with cancer, as a recent project has demonstrated.

Normally employed in such undertakings as the design of buildings, bridges, and aircraft, CAD/CAM techniques allow for the fabrication of tailor-made, complex parts with high precision. As Professor Dietmar Werner Hutmacher of Georgia Institute of Technology in Atlanta and Queensland University of Technology in Kelvin Grove, Queensland, Australia, and study coauthors explain in the journal *Biofabrication* (http://iopscience.iop.org/1758-5090/3/3/034114/pdf/1758-5090_3_3_034114.pdf), the ability to build patient-specific models based on medical imaging data offers major potential. A relatively new clinical area of application for these techniques is breast reconstruction.

More than 300,000 breast reconstructions are performed annually in the United States alone, using nondegradable silicone implants or by means of transplantation of autologous tissue consisting of



Prototype of a porous model for a personalized tissue engineering scaffold.

skin, fat, muscle, and connected vasculature. A new approach based on tissue-engineering principles is under development. Multiple studies have demonstrated the creation of vascularized adipose constructs; current efforts are directed toward making the concept clinically relevant.

Hutmacher's group received informed consent to obtain images from a 46-year-old female patient with invasive ductal carcinoma. They performed laser scanning from three angles as the patient remained in an upright position with each arm at a 90° angle. The images were then imported into a software package that produced a single image representing the patient's breast and surrounding thorax region. That image was then used to form a three-dimensional (3D) model

that the surgical team used as an operative aid during autologous tissue reconstruction.

The result was a more perfect breast shape with a higher degree of symmetry between the breasts. However, the procedure does have drawbacks: It requires a long duration of anesthesia (5 to 10 hours), causes considerable blood loss, and raises problems at the donor site including wide and unsightly scars, abdominal weakness, abdominal bulge, and hernia. Researchers have begun exploring ways to bypass these problems, possibly by following a tissue-engineering approach to breast reconstruction. The investigators were able to derive from the imaged data a solid breast model that they digitally processed for the fabrication of customized scaffolds for breast tissue engineering. In theory, a patient's own cells could be harnessed and grown onto the highly specific scaffold and then transferred to the affected area, thus eliminating the need to transfer tissue from other parts of the body. This, in turn, would reduce anesthesia duration, blood loss, and scarring.

Hutmacher and team have a long-term goal of providing a CAD/CAM-based solution to the breast solution field following a tissue-engineering approach. But as they demonstrated in the current study, laser imaging and rapid prototyping can already be employed for better outcomes in surgery using the current gold standard of autologous breast reconstruction. ■

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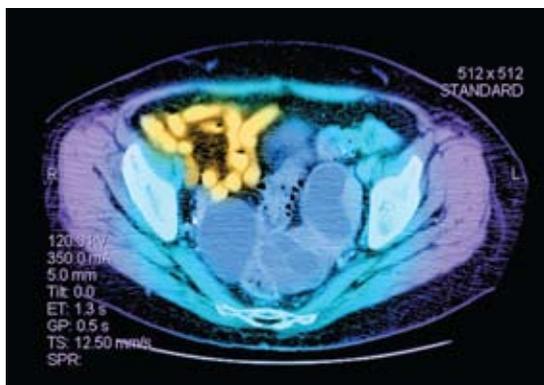
FDA Update

A new drug for certain patients with locally advanced or metastatic non-small cell lung cancer (NSCLC), **crizotinib (Xalkori)**, is approved along with a companion diagnostic test to determine whether a person has the abnormal anaplastic lymphoma kinase (*ALK*) gene. Crizotinib works by blocking kinases, including the protein produced by the abnormal *ALK* gene.

The FDA approved a treatment for Hodgkin lymphoma, **brentuximab vedotin (Adcetris)**, and has also made it the first to be specifically indicated for the treatment of a rare malignant tumor known as systemic anaplastic large cell lymphoma (ALCL). Brentuximab uses an antibody to direct the drug to a target on lymphoma cells known as CD30. It is to be used after Hodgkin lymphoma has progressed following autologous stem cell transplant, or—in those who cannot undergo a transplant—after two prior chemotherapy treatments.

The boxed warning for the entire class of **tumor necrosis factor (TNF) alpha blockers** has been updated to reflect the risk of infection from two bacterial pathogens, *Legionella* and *Listeria*. In addition, the boxed warning and Warnings and Precautions sections of the labels for all

PARP inhibitor found effective in women without *BRCA* mutation



A POLY(ADP-RIBOSE) polymerase (PARP) inhibitor that has shown promising anticancer activity in the presence of *BRCA1* or *BRCA2* gene mutations also appears to be effective in the treatment of more common, non-hereditary ovarian tumors.

Olaparib (also known as AZD2281) is an oral drug that blocks the activity of the protein poly(ADP-ribose) polymerase. Because both PARP and *BRCA* proteins are involved in DNA repair, inhibiting PARP in a tumor that already lacks a *BRCA* gene prevents cancer cells from repairing their DNA, thus enhancing the effectiveness of DNA-damaging chemotherapy. Approximately 5% to 10% of cases of breast cancer and ovarian cancer exhibit a mutation of the *BRCA1* or *BRCA2* gene.

Recently, a Canadian research team undertook a phase 2, multicenter, open-label, nonrandomized study to assess whether olaparib could be safely used in women with advanced triple-negative breast cancer or high-

Large, multilobulated cystic mass (yellow) seen on axial cross-sectional CT scan.

grade serous and/or undifferentiated ovarian cancer who had not inherited the *BRCA* mutations. The 65 women with ovarian cancer and 26 with breast cancer received olaparib 400 mg twice per day for 4 weeks.

Of the 63 evaluable women with ovarian cancer, 11 of the 46 women (24%) without *BRCA1* or *BRCA2* mutations experienced a substantial reduction in tumor size, as did 7 of the 17 (41%) with mutations. None of the women with breast cancer had a confirmed objective response as per Response Evaluation Criteria in Solid Tumors (RECIST) rules (www.recist.com), which define when a person with cancer improves, or responds, as opposed to staying the same (stable) or worsening (progression).

Olaparib was generally well tolerated and most adverse effects were mild. The most common were:

- fatigue in 70% of patients with ovarian cancer and 50% of patients with breast cancer
- nausea in 66% of ovarian patients and 62% of breast patients
- vomiting in 39% of ovarian patients and 35% of breast patients
- decreased appetite in 36% of ovarian patients and 27% of breast patients.

The researchers conclude that olaparib may be a promising treatment for women with ovarian cancer, and that therapies targeting DNA repair mechanisms seem to provide new hope for the treatment of ovarian cancer (*Lancet Oncol.* 2011;12[9]:852-861). ■

Spicy foods boost broccoli's benefits

COMBINING broccoli with a spicy food that contains the enzyme myrosinase significantly enhances the anticancer properties of each, indicates a recent study.

Sulforaphane is the component of broccoli considered to be responsible for the reduction in cancer risk associated with broccoli consumption. Its inactive precursor, glucoraphanin, becomes hydrolyzed when fresh broccoli is crushed or chewed, and needs the plant thiohydrolase myrosinase to form sulforaphane. New findings suggest that spicing up broccoli with broccoli sprouts, mustard, horseradish, or wasabi raises the cancer-protective effects of broccoli, as do radishes, cabbage, arugula, watercress, and Brussels sprouts.

In the 4-week study, four healthy men, aged 18 to 30 years, each ate four meals (one meal per week) consisting of:

- dry cereal and yogurt with broccoli sprouts equivalent to 70 μ mol of sulforaphane
- glucoraphanin powder equivalent to 120 μ mol of sulforaphane (this powder did not contain myrosinase)
- both components
- neither component.

As investigators Jenna M. Cramer and colleagues from the



Broccoli should be steamed lightly for 2 to 4 minutes to protect its healthful properties.

University of Illinois at Urbana-Champaign reported in the *British Journal of Nutrition*, when fresh broccoli sprouts were eaten with glucoraphanin powder, these spicy sprouts were able to lend their myrosinase to the myrosinase-free powder. Bioactive compounds found in the blood were much higher when the sprouts and powder were eaten together than when either product was consumed by itself. Urine samples corroborated the blood results.

Broccoli should be steamed lightly for 2 to 4 minutes to protect its healthful properties. If the vegetable is overcooked, however, it can still provide benefit as long as it is paired with another food that contains myrosinase. Another benefit of myrosinase is that when this enzyme is present, sulforaphane is released into the ileum, where absorption occurs better and more quickly than in the colon. ■

FDA Update

TNF-alpha blockers have been revised to include consistent information about the risk for serious infections and the associated disease-causing pathogens.

Fujirebio Diagnostics, Inc. received 510(k) clearance from the FDA to market a biomarker test for ovarian cancer. The company will market its HE4 blood test in an algorithm called **ROMA (HE4 EIA + ARCHITECT CA 125 II)** to identify patients with adnexal mass who are likely to have malignancy, and thus should have their surgery performed by a gynecologic oncologist. HE4 has been shown to be elevated in epithelial ovarian cancers but is not elevated in many benign gynecologic diseases.

The FDA has notified health care professionals and patients of an ongoing safety review and labeling changes for the anti-nausea drug **ondansetron (Zofran ODT, generics; ondansetron hydrochloride [Zofran, generics])**. This 5-HT₃ receptor antagonist, which is used to prevent nausea and vomiting caused by cancer chemotherapy, radiation therapy, and surgery, may increase the risk for prolongation of the QT interval of the electrocardiogram. This, in turn, can lead to an abnormal and potentially fatal heart rhythm. ■

ESTIMATED NEW CASES OF CANCER

240,890

prostate cancer

230,480

female breast cancer

231,130

Lung cancer (including bronchus)

Source: American Cancer Society. Cancer Facts & Figures 2011.

Oxygen generators help kill tumors from within

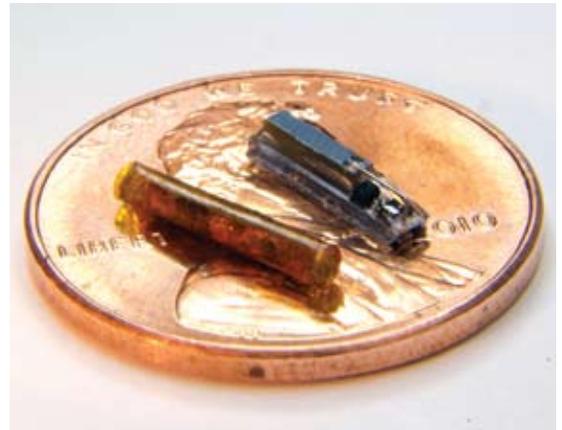
AN ELECTRONIC device that can be implanted in a tumor uses the energy from ultrasound signals to generate oxygen, boosting the effectiveness of radiation and chemotherapy.

The ultrasonically powered implantable micro oxygen generator (IMOG) is designed to treat solid tumors that are hypoxic at the core, achieving in situ tumor oxygenation through water electrolysis: The IMOG receives ultrasound signals and uses the energy to generate a small voltage to separate oxygen and hydrogen from water. This active mode of oxygen generation is not affected by increased interstitial pressure or

abnormal blood vessels, conditions that typically limit the systemic delivery of oxygen to hypoxic regions of solid tumors.

The scientists from Purdue University in West Lafayette, Indiana, and Indiana University School of Medicine in Indianapolis who created the IMOG tested the devices in pancreatic tumors implanted in mice. Adequate in situ tumor oxygenation occurred in less than 10 minutes.

“Pancreatic and cervical cancers are notoriously hypoxic,” commented Babak Ziaie, professor of electrical and computer engineering and biomedical engineering at Purdue, in a statement



BIRCK NANOTECHNOLOGY CENTER, PURDUE UNIVERSITY

The miniature device (right) fits into a tube (left) that is inserted into a tumor with a biopsy needle.

announcing his group’s work, which is further described in an online report for *IEEE Transactions on Biomedical Engineering*. “If you generate oxygen you can increase the effectiveness of radiation therapy and also chemotherapy.”

The IMOG is small enough to be implanted using a hypodermic needle or a trocar. ■