1000 Genomes Project Doubles Variation Data

The world's largest, most detailed catalog of human genetic variation has more than doubled in size with the 1000 Genomes Project's latest publication in the Oct. 31 issue of *Nature*. The National Human Genome Research Institute, part of the National Institutes of Health, helps to fund and direct this public–private consortium of researchers in the United States, Britain, China, Germany, and Canada. The goal of the 1000 Genomes Project is to identify and compile variants in the human genome that occur at a frequency of at least 1 in 50 people. The expanded catalog allows medical researchers to locate genetic differences contributing to rare and common diseases more precisely. Planning for the $120 million project began in 2007. In 2010, researchers published data on 3 pilot studies. The 2012 data set will be followed by the last addition to the catalog in 2013.

"I view this project as a Lewis and Clark expedition to the interior of the human genome," said Stephen Sherry, PhD, chief of the Reference Collections Section, Information Engineering Branch, at the National Center for Biotechnology Information, part of the National Library of Medicine. "We knew the outlines and contours [of the genome]. Now, we're trying to document all the fine details such as the rivers and tributaries." To date, project researchers have sequenced the genomes of 1,092 individuals from 14 populations in Europe, East Asia, sub-Saharan Africa, and the Americas. They plan to study more than 2,500 individuals from 26 populations.

All participants consented to inclusion in an open online database of sequence data derived from their anonymous DNA samples. Each part of these genomes was read (or sequenced) an average of 6 times, which provides accurate information about common genetic variants but misses many rare variants. To identify rare variants in the exome, the researchers sequenced the exons of 15,000 genes in each genome an average of 80 times. The study discovered 99.8% of exome variants with a frequency of at least 1% and 99.3% of variants elsewhere in the genome with a frequency of at least 1%.

Phase one of the 1000 Genomes Project, the subject of the *Nature* paper, has produced massive amounts of genomic data. Simply recording the raw information takes ~180 terabytes of hard-drive space. All of the information is freely available on the Internet through public databases. Data from the project have been available to researchers since 2008. The massive dataset became available in the cloud this year via Amazon Web Services. Cloud access enables users to analyze large amounts of data much more quickly, because it eliminates the time-consuming download of data and because users can run their analyses over many servers at once. Researchers pay only for additional resources as needed.

"Project researchers discovered that each person carries a handful of rare variants that would currently be recognized as disease causing and a few hundred more rare variants that are likely to have a detrimental effect on how genes work," said Gilean McVean, PhD, professor of statistical genetics at the University of Oxford (UK) and coleader of the 1000 Genomes Project Analysis Group. "It's fortunate that most of us usually carry only one copy of these variants, since 2 copies might lead to disease."

The 1000 Genomes Project data are available at: www.1000genomes.org or http://s3.amazonaws.com/1000genomes.

National Human Genome Research Institute

Image Wisely Groups Target Lower Radiopharmaceutical Doses

Image Wisely, in collaboration with the SNMMI, SNMMI Technologist Section, and American Society of Nuclear Cardiology (ASNC), announced on November 20 the creation of easily accessible online educational materials to help providers use the lowest radiopharmaceutical dose necessary to perform nuclear medicine exams. The participating groups urged physicians, medical physicists, and imaging technologists to visit a centralized Web site to review materials and use the information in routine clinical practice.

The new initiative urges nuclear medicine providers to: perform nuclear medicine procedures only when clinically indicated; individualize administered doses based on the specific clinical task; employ maneuvers to minimize radiation dose; and familiarize themselves with recommended administered activities. "Radiation dose for all nuclear medicine and molecular imaging procedures should be optimized so that the patient receives the smallest possible amount of radiopharmaceutical that will provide the appropriate diagnostic information. I ask that nuclear medicine providers take advantage of the important materials offered and that they demonstrate their commitment to patient care by taking the pledge to 'image wisely,'" said Frederic H. Fahey, DSc, SNMMI president and representative to Image Wisely.

Image Wisely encouraged imaging providers to demonstrate their commitment to patients by earning accreditation from appropriate professional organizations and by taking the Image Wisely pledge. Online pledges can be made by individuals, facilities, and associations. Information on the nuclear medicine initiative is available at: www.imagewisely.org/Imaging-Professionals/Nuclear-Medicine. The Image Wisely pledge is available at: www.imagewisely.org/Pledge.

Image Wisely

Strong Nuclear Medicine Market Predicted

A report released on November 1 by Global Industry Analysts, Inc. (San Jose, CA), a marketing research publisher, contained detailed data forecasting that the international market for nuclear medicine would reach US$2.46 billion by the year 2018, primarily driven by the rising incidence of neurologic and cardiac diseases, continued technologic enhancements in nuclear medicine imaging equipment, growing popularity of hybrid technologies such as SPECT/CT and PET/CT, and widening applications of nuclear medicine in a range of clinical procedures.

The report, titled "Nuclear Medicine: A Global Strategic Business Report," offered a comprehensive industry overview and outlook, including major trends and issues, product innovations, recent industry activity, and profiles of select market players worldwide. Analysis and overview was presented for major geographic markets including the United States, Canada, Japan, Europe, Asia–Pacific, and other world areas for the period 2010–2018. The report provided global and regional market estimates and projections (in US$) for gamma cameras and PET systems.

The report noted that after years of strong growth, the global nuclear medicine market entered into a "tumultuous" phase in 2008. The global economic downturn and changes in reimbursement and insurance requirements in developed markets resulted in market declines that lasted until 2010. Other factors such as saturated Western markets, restrictions imposed by governments in certain high-potential countries (such as China), and low rates of reimbursement have slowed market growth and resulted in a decline in sales of imaging equipment.

Decreased demand in the U.S. market, the leading and mature nuclear medicine market worldwide, was one of the major reasons for revenue decline. Although the developed markets underwent significant pressures, India and other countries in the Asia–Pacific region were somewhat less affected. The report detailed the effects of worldwide radioisotope shortages during this period. The market bounced back to positive growth in 2011, as molybdenum supply issues and procedural growth recovered. Going forward, advances in technologies that are expanding in clinical scope and an increasing target patient base are expected to help regain lost momentum in the market.

Projected new growth in markets can be attributed in part to a continued rise in the incidences of neurologic and cardiac diseases worldwide. Increasing cardiac disease rates emerged as a significant growth factor for advanced diagnostic and medical imaging devices. Rising incidences of cardiac arrests and brain disorders, increasing propensities to acquire cancerous growths, and aging populations are resulting in heightened health concerns and are popularizing preventive medicine in specific consumer groups, with a greater number of periodic diagnostic tests performed. Alzheimer disease, Parkinson disease, dementia, and heart failure are also fueling the demand for preventive diagnostics. More details about the report are available at: www.strategyr.com/Nuclear_Medicine_Market_Report.asp.

Global Industry Analysts, Inc.

CT/Nuclear Imaging and Breast Cancer Risk

Researchers reviewing the records of approximately 250,000 women enrolled in an integrated health care delivery system concluded that increased CT utilization between 2000 and 2010 could result in an increase in the risk of breast cancer for certain women, including younger patients and those who received repeat exams. According to the study, which was presented on November 27 at the annual meeting of the Radiological Society of North America, nuclear medicine examinations may also contribute to increased breast cancer risk.

The study, led by Ginger Merry, MD, MPH, breast imaging fellow at Prentice Women's Hospital—Northwestern Memorial Hospital (Chicago, IL), found that among the system's female enrollees, CT utilization increased from 99.8 CT scans per 1,000 women in 2000 to 192.4 CT scans per 1,000 women in 2010 (an annual increase of 6.8%). In 2010, 46% of those CT examinations exposed the breast to radiation. Nuclear medicine imaging decreased from 39.3 scans per 1,000 women in 2000 to 27.5 scans per 1,000 women in 2010 (a 3.5% annual decline); however, in 2010, 84% of nuclear medicine studies exposed the breast to radiation.

"Until now, the impact of this increased use of imaging on radiation exposure to breast tissue and the subsequent risk of breast cancer has not been known," said Rebecca Smith-Bindman, MD, professor of radiology and biomedical imaging at the University of California, San Francisco. "Our goal was to quantify imaging utilization and radiation exposure to the breast among women enrolled in an integrated health care delivery system and to use these data to determine the imaging-related risk of breast cancer from those studies."

The research team collected CT dose information from 1,656 patients who underwent CT examinations that exposed the breast to radiation and, using an automated computational method, estimated the patients' effective radiation dose and the amount of radiation absorbed by the breast. The team also analyzed radiopharmaceutical volume and associated radiation exposure in 5,507 nuclear medicine exams that exposed the breast to radiation. "We found that the estimated breast radiation doses from CT were highly variable across patients, with the highest doses coming from multiple-phase cardiac and chest CT examinations, where successive images of the organ being studied are captured," Smith-Bindman said.

The researchers then estimated each women's imaging-related risk of breast cancer and compared it with their underlying risk of developing breast cancer. Each woman's 10-y imaging-related risk of developing breast cancer, beginning 10 y after her exposure to imaging and based on age at exposure, was es-

timated using the breast-specific radiation data and a statistical risk model. A woman's underlying risk of developing breast cancer was estimated based on data collected by the National Cancer Institute–funded Breast Cancer Surveillance Consortium.

To lower imaging-related risk of developing breast cancer, Smith–Bindman said imaging providers should analyze radiation doses associated with each exam, reduce the use of multiphase protocols, and employ dose-reduction software wherever possible to minimize exposures. "If imaging is truly indicated, then the risk of developing cancer is small and should not dissuade women from getting the test they need," she said. "On the other hand, a lot of patients are undergoing repeat chest and cardiac CT, many of which aren't necessary. Women, and particularly young women, should understand there is a small but real potential risk of breast cancer associated with cardiac and chest CT, and the risk increases with the number of scans."

Radiological Society of North America

2013 HOPPS and MPFS Final Rules

In the first 2 days of November, the Centers for Medicare & Medicaid Services finalized the 2013 Hospital Outpatient Prospective Payment System (HOPPS) and Ambulatory Surgical Center (ASC) rule and the 2013 Medicare Physician Fee Schedule (MPFS) rule. The final HOPPS rule updates Medicare payment policies and rates for hospital outpatient and ASC services beginning January 1, 2013. This rule affects hospital outpatient departments in more than 4,000 hospitals in the United States, including general acute care hospitals, inpatient rehabilitation facilities, inpatient psychiatric facilities, long-term acute care hospitals, children's hospitals, and cancer hospitals, as well as ~5,000 Medicare-participating ASCs. This final rule increases payment rates for hospital outpatient departments by 1.8%, with total payments to hospitals at $48.1 billion. The rule provides for an increase of 0.6% in payment rates to ASCs with total payments at $4.01 billion.

The MPFS final rule included a statutorily required 26.5% across-the-board reduction to Medicare payment rates for more than 1 million physicians and nonphysician practitioners under the Balanced Budget Act of 1997 Sustainable Growth Rate (SGR) methodology. At Newsline press time, it was not clear whether Congress would once again enact a short-term "fix" postponing these cuts. More than 100 medical groups have lobbied against the SGR cuts and against the uncertainties imposed by short-term countermeasures.

Both final rules were issued with a comment period that closed on December 31. The HOPPS/ASC final rule is available at: www.gpo.gov/fdsys/pkg/FR-2012-11-15/pdf/2012-26902.pdf. The Physician Fee Schedule final rule is available at: www.federalregister.gov/articles/2012/11/16/2012-26900/medicare-program-revisions-to-payment-policies-under-the-physician-fee-schedule-dme-face-to-face.

Centers for Medicare & Medicaid Services

CPT Changes for Endocrine System Services

The 2013 *Current Procedural Terminology* (CPT) electronic file was released by the American Medical Association (AMA) on August 31, 2012. New, deleted and revised codes became effective this month on January 1, and SNMMI has compiled and highlighted important changes made to the endocrinology section of nuclear medicine services, along with minor changes to the nuclear medicine introductory language.

The new uptake and/or thyroid imaging codes are the result of action taken by the AMA Relativity Assessment Workgroup and the Centers for Medicare & Medicaid Services, which work to identify potentially misvalued codes and services. They identified CPT 78007 (Thyroid imaging, with uptake; multiple determinations) as requiring a review by the societies because these services are performed >30,000 times each year and had not been AMA Resource-Based Value Scale Update Committee reviewed. In response to this requested review, 2 code change proposals (CCP) were submitted jointly to the CPT editorial panel by the SNMMI, American College of Nuclear Medicine (ACNM), American College of Radiology (ACR), American Association of Clinical Endocrinologists, and The Endocrine Society. The multispecialty society team collaborated over the course of 1 year and developed 1 application with 3 new simplified codes that describe the entirety of these thyroid uptake and imaging procedures. Providers will continue to bill separately for any drug and radiopharmaceutical supply codes administered with these procedures.

New CPT 78012 will be used for performing thyroid uptakes only; specifically for performance of a single uptake or multiple uptakes (such as at 4–6-h and 24- or 48-h time intervals). CPT 78013 will be used for performing thyroid imaging only. It would also include vascular flow if that technique is performed, although vascular flow is not a required element of the new code. New CPT 78014 is used for the performance of a thyroid imaging study plus a single- or multiple-uptake procedure on the same date of service.

As the endocrine section was under review, several participating societies also noted confusion about billing for parathyroid studies. After reviewing current coding opinions, the SNMMI, ACNM, and ACR jointly submitted a CCP to modify the current parathyroid code and create 2 new bundled/packaged codes. The revised CPT code 78070 makes clear that this code represents the service utilizing the planar technique and may include subtraction; however, subtraction is not a required element of the CPT code. New CPT code 78071 is used to report the planar plus a SPECT study of the parathyroid gland. Finally, new CPT 78072 is used to report the planar plus a SPECT/CT study of the parathyroid gland. Much like PET/CT codes, the SPECT/CT code pertains when CT is used for attenuation correction only and not for a fully diagnostic CT procedure. If a fully diagnostic CT is separately ordered and medically neces-

sary those services would be reported with the appropriate CT procedure code from the CPT radiology section.

The final change made to the nuclear medicine section of the AMA CPT book is in the introductory paragraphs. These changes are minor and consistent with many other changes in the CPT book this year to eliminate the word "physician" to make clear that other qualified individuals who are licensed will be able to report the services with these codes. SNMMI has created a detailed table outlining changes in codes and highlighting wording with significant implications for performance. The table is available at: www.snmmi.org/index.cfm?PageID=12159.

SNMMI

GAO Imaging Self-Referral Report

The Government Accountability Office (GAO) on October 31 released a report titled "Higher Use of Advanced Imaging Services by Providers Who Self-Refer Costing Medicare Millions," which found that physician self-referral of medical imaging exams is driving up imaging utilization and exposing patients to unnecessary health risks while increasing Medicare costs. GAO specifically investigated the role of self-referral in MR imaging and CT services from 2004 to 2010. The agency found that the number of self-referred MR services increased by more than 80%, compared with a 12% increase for non-self-referred MR services. For CT services, the growth of self-referred services more than doubled, whereas non-self-referred CT services increased by about 30%. The report also documented the serious financial impact of self-referral–driven overutilization on America's health care system. GAO estimated that Medicare spent approximately $109 million more in 2010 than it would have without self-referral incentives.

GAO's analysis showed that providers' referrals of MR and CT services substantially increased the year after they began to self-refer; that is, the year in which they purchased or leased imaging equipment or joined a group practice that already self-referred. Providers that began self-referring in 2009 (referred to as switchers) increased MR and CT referrals on average by about 67% in 2010 compared to 2008. In the case of MR imaging, the average number of referrals each switcher made increased from 25.1 in 2008 to 42.0 in 2010. In contrast, the average number of referrals made by providers who remained self-referrers or non-self-referrers declined during this period. This comparison suggests that the increase in the average number of referrals for switchers was not the result of any general increase in the use of imaging services among all providers. GAO's examination of all providers that referred an MR or CT service in 2010 showed that self-referring providers referred about twice as many of these services as providers who did not self-refer. Differences persisted after accounting for practice size, specialty, geography, or patient characteristics. These 2 analyses suggest that financial incentives for self-referring providers were likely a major factor driving the increase in referrals.

Overall, medical imaging use and associated costs are down significantly since 2006. Medicare spends the same amount on imaging scans now as in 2003. Only self-referred imaging grew significantly since the middle of the last decade. The complete report is available at www.gao.gov/products/GAO-12-966.

Government Accountability Office

Microwave Ablation and Thyroid Nodules

MedWaves, Inc. announced on November 26 that physicians at the Department of Nuclear Medicine at the Frankfurt (Germany) University Hospital had become the first group in a European hospital to use microwaves to ablate thyroid nodules. The technique has been reported in numerous preclinical studies and in clinical studies from South Korea and China, among others.

The success of the new treatment is especially relevant in Germany, where 20% of the population have 1 or more thyroid nodules and nearly 1 in 2 individuals older than 65 y is affected by a thyroid disorder. Microwave ablation offers a number of advantages over surgery, radiotherapy, or other forms of ablation, according to MedWaves and the Frankfurt medical team. The procedure is fast, lasting between 10 and 15 min, depending on the number of nodules. "The microwave ablation also causes significantly fewer side effects because no anesthesia is required. This makes it a very promising alternative to the established procedures," said Hudayi Korkusuz, MD, who performed the microwave treatment.

MedWaves, Inc.

FROM THE LITERATURE

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.