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MEETING PROCEEDINGS

Summary of Seventh Annual Diabetes Technology Meeting October 25–27, 2007 San Francisco, California

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The seventh annual Diabetes Technology Meeting was held in San Francisco from October 25 to 27, 2007. In attendance were over 625 scientists, engineers, and doctors from government, industry, academia, and clinical practice. The attendees hailed from 25 countries. The meeting was presented by the Diabetes Technology Society in cooperation with Centers for Disease Control and Prevention (CDC), the U.S. Army Technologies for Metabolic Monitoring Research Program, National Space Biomedical Research Institute, University of California at Berkeley Bioengineering Department, Georgia Tech/ Emory Center for the Engineering of Living Tissues, and Mills-Peninsula Health Services. During the 4 half-day workshops and 2 days of general sessions, speakers shared information on topics related to applications of bioengineered technologies to diabetes, such as continuous glucose monitoring, noninvasive glucose monitoring, glycemic variability, closed loop control of blood glucose, alternate needle-free routes of insulin delivery, and software for describing and managing multiple blood glucose measurements.

Workshop A, entitled "Investment Opportunities in Diabetes Technologies," was composed of four panels where (1) diabetes from an investor's perspective, (2) devices for measuring glucose and delivering insulin, (3) drugs for diabetes and obesity, and (4) current opportunities for investing in diabetes technology were discussed. The speakers concluded that new advanced technologies for patient monitoring must go through a scientific, regulatory, and political process in order to be eligible for reimbursement from Centers for Medicare & Medicaid Services and from private insurance companies. There was also a consensus among the speakers that creation of a repository of outcomes evidence from randomized controlled trials published in peer-reviewed journals will accelerate the approval process for new technologies.

Workshop B, entitled "Noninvasive Glucose Monitoring," was composed of both an academic panel and an industry panel. Methods for measuring glucose by way of infrared spectroscopy, Raman spectroscopy, optical coherence tomography, and a combination of occlusion spectroscopy and light scattering were presented. In addition, two products that are being commercially developed, but are not currently approved in the United States, for measuring skin autofluorescence from infrared light interacting with tissue advanced glycation end products were also presented. One product is from the United States and the other is from Holland. These last two devices could be used either to diagnose diabetes or to determine the risk of microvascular disease occurring. The consensus of the speakers and attendees was that a commercial noninvasive glucose monitor is possible, but it is still at least 5 years from approval

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Abbreviations: (CDC) Centers for Disease Control and Prevention, (DEXA) dual energy X-ray absorptiometry, (FDA) Food and Drug Administration, (HbA1c) hemoglobin A1c, (MEMS) microelectrical mechanical systems

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by U.S. government regulatory agencies, whereas the measurement of tissue advanced glycation end products will become commercially viable much sooner.

Workshop C, entitled "Glycemic Variability," discussed a new concept that has been proposed to be an independent risk factor for microvascular complications. Short-term prospective data have linked glycemic variability with the production of oxidative stress metabolites, whereas a prospective study for another purpose that was not powered to identify these analytes and not intended to look for these analytes when it was conceived has failed to demonstrate a relationship between glycemic variability and elevated levels of oxidative stress substances. Glycemic variability can be expressed with multiple equations with or without a time component. The speakers and attendees all agreed with the conclusion that continuous glucose monitoring is the optimal tool for measuring glycemic variability and that it remains to be seen whether glycemic variability will prove to be as important of a risk factor as mean glycemia.

Workshop D covered hospital management of diabetes. The workshop began with an overview of technologies that can be utilized in the intensive care unit, such as algorithms for determining insulin. The workshop included a discussion of how to set and achieve goals for intensive insulin therapy in hospitalized patients (both children and adults) with diabetes and how to interpret point of care test results in the hospital setting. The risks of excessively aggressive therapy in surgical patients, which can lead to hypoglycemia, were discussed in a context of establishing goals for intensive therapy. Strategies were presented for initiating insulin in patients on hospital wards and for discharging these patients on an effective insulin regimen. Transplantation as a possible cure for type 1 diabetes and bariatric surgery as a possible cure for type 2 were also discussed. The consensus of the speakers was that new technologies and goals for the appropriate management of diabetes in hospitalized patients will significantly decrease morbidity and mortality outcomes in this population.

The first general session of the meeting, entitled "Technologies for Metabolic Monitoring," was moderated by Colonel Carl Castro, Ph.D. (U.S. Army, Fort Detrick, MD). Welcoming remarks were made by Dorian Liepmann, Ph.D., Professor and Chair, Department of Bioengineering at University of California, Berkeley. He reviewed the 7-year history of the meeting and described the links between the bioengineering community and the medical community. The keynote address on the first day of the meeting was delivered by Richard Kahn, Ph.D., Chief Scientific and Medical Officer of the American Diabetes Association. He discussed how new technology is needed for diabetes, but that the best technologies must be economically attractive. He pointed out that merely being cost-effective compared to other interventions for other diseases may not be enough reason to convince payers to provide coverage because so many cost-effective technologies are being developed lately for many diseases. He suggested that new technology has the best chance for adoption if it can be made particularly inexpensive. Stuart Weinzimer, M.D. (Yale University) presented original data about the performance of the Freestyle Navigator continuous glucose monitor. He discussed safety and tolerability data in children. Guido Freckmann, M.D. (Institute for Diabetes Technology, Ulm, Germany) discussed the performance of two microdialysis methods for measuring glucose levels continuously. These non-Food and Drug Administration (FDA)-approved methods were relatively accurate but had a longer lag time than the current FDA-approved needle sensors. Volker Lodwig, Ph.D. (Institute for Medical Informatics and Biostatistics, Basel, Switzerland) presented an economic analysis of self-blood glucose monitoring. His multicentric group in Europe found this practice to provide additional life free of complications and to be cost-effective compared to other generally accepted health interventions. George Cembrowski, M.D., Ph.D. (University of Alberta, Edmonton, Canada) presented surprising data about how the "normal" levels for hemoglobin A1c (HbA1c) rise with increasing age. He cautioned that normative data are needed to interpret outcome studies using HbA1C given this age-related rise in the normal range. The speakers agreed that new technologies for metabolic monitoring will provide additional perspectives on the control of diabetes and that many additional routine measurements besides blood glucose will be introduced over the next decade.

The second session, entitled "Obesity Technology: Measurement of Body Composition," was moderated by Colonel Karl Friedl, Ph.D. (U.S. Army, Frederick, MD). Topics relating to the measurement of body mass index, body fat percentage, and body fat composition according to whether the fat stores are subcutaneous or visceral were presented. Frank Greenway, M.D. (Louisiana State University), William Cameron Chumlea, Ph.D. (Wright State University), and Thomas Kelly, M.B.A. (Hologic, Inc., New Bedford, MA) discussed the performance of various technologies for assessing body composition. The consensus of the speakers was that the best tool for body composition measurement is determined by the purpose

of the measurement and the available financial resources. Whereas dual energy X-ray absorptiometry (DEXA) scanning is the most accurate, this method is used mostly as a research tool, and other screening technologies for estimating body fat percentage are easier to use, more portable, and less costly, which makes them preferable to DEXA scanning for population screening.

The third session, entitled the "Artificial Pancreas," discussed potential multicomponent systems to create a closed loop device for measuring glucose, calculating the dose of insulin necessary for controlling the glucose level, and delivering insulin automatically from an attached reservoir. Thomas Pieber, M.D. (filling in for Martin Ellmerer, Ph.D.) presented data from the European CLINICIP project on closed loop control. Dr. Pieber presented data on how subcutaneous insulin delivery adjacent to a subcutaneous sensor does not interfere with the performance of the sensor. This type of study offers hope that a combined sensor and insulin delivery system will eventually be fashioned into a single device with the glucose sensor at one end and the insulin delivery catheter at the other end. Data on the performance of continuous glucose sensors collected by the Freestyle Navigator® and the Guardian® REAL-Time systems were presented, respectively, by Marc Taub, Ph.D. (Abbott Diabetes Care) and John Mastrototaro, Ph.D. (Medtronic MiniMed). Geoffrey Chase (University of Canterbury, Christchurch, New Zealand) presented data on an algorithm for closed loop control of hospitalized patients using a system that takes feeding into account. Arleen Pinkos (FDA, Rockville, MD) discussed the FDA multidiscipline Artificial Pancreas Working Group's perspective on closed loop control. She presented issues for scientists to consider regarding the optimal type of sensor and software. She invited scientists working on this technology to discuss their planned experiments with the FDA before initiation to ensure that the experiments will be in line with providing the type of information that the FDA is seeking. The consensus of the speakers was that closed loop control of glucose is advancing increasingly closer to becoming a reality.

The fourth session, entitled "Should an Artificial Pancreas Be Controlled by Multiple Glucose Sensors?," addressed the control-theory issue of whether improved accuracy from the use of multiple sensors would outweigh the risk of a greater number of outlier sensors. Ken Ward, M.D. (iSense, Portland, Oregon) presented data from his continuous glucose sensor demonstrating the benefits of using as many as four glucose sensors simultaneously. He stated that he intends to continue using multiple glucose sensors in his implanted sensor system. Brian Hipszer, M.S. (Thomas Jefferson University) presented data from a study that he and Jeffrey Joseph, D.O. have been performing on the use of multiple continuous glucose sensors simultaneously in hospitalized patients. Differences among the sensors were significant, which calls into question the accuracy of selected individual sensors. Andreas Caduff, Ph.D. (Solianis Monitoring, Zurich, Switzerland) presented data from a noninvasive glucose monitoring model that demonstrated the potential benefit of monitoring multiple glucose sensors simultaneously. His radiofrequency impedance technology is still far from being ready to be incorporated into a commercially viable product, however. Finally, Robert Mah, Ph.D. (NASA Ames, Mountain View, CA) presented data from the U.S. space program demonstrating how from a control theory standpoint, multiple sensors with overlapping types of information collected from multiple types of sources provide input to achieve the best control. He urged developers of continuous glucose sensors to develop multiple types of glucose sensors in order to achieve similar stable control as rocket ships. The consensus of the panel was that multiple glucose sensors used for glycemic control can provide additional useful information; however, some outlier information necessarily must be eliminated. The result of this data collection process can be improved for closed loop control.

The fifth session, entitled "Insulin and Metabolic Peptide Delivery," addressed the challenges and opportunities in delivering insulin and other metabolic peptides without needles. The keynote address on the second day of the meeting was delivered by Ann Albright, Ph.D., R.D., Director of Division of Diabetes Translation at the CDC in Atlanta, Georgia. She discussed how the CDC is studying new technologies and is receptive to promoting the use of new technologies for diabetes. Lutz Heinemann, Ph.D. (Profil Institute for Metabolic Research, Neuss, Germany) presented data on a new form of inhaled insulin called PROMAXX. This insulin is a dry powder form of insulin whose particle diameters are in the 1- to 5-μm range. Anthony Cheung, Ph.D. (enGene, Inc., Vancouver, Canada) presented data on a new type of gene therapy to create insulin-producing cells from K cells of the gut. These gut cells would be transformed to produce and release insulin in response to meals. Andreas Pfützner, M.D., Ph.D. (IKFE, Mainz, Germany) presented data on a rapidly acting insulin that is currently under development called VIAject. This insulin reaches peak levels sooner than standard regular insulin and even sooner than analog insulins currently available

on the market. Klaus Jensen, M.D. (Novo Nordisk A/S, Virium, Denmark) presented data on the use of insulin therapy by way of an insulin pump during pregnancy. The consensus of the speakers was that in the future, insulin therapy and other metabolic peptide therapy will be administered by way of routes other than a syringe and needle injection because of new insulin formulations with unique properties. They also agreed that gene therapy would offer a method of therapy that could avoid the administration of any external peptides.

The sixth session, entitled "Nanotechnology and Microelectrical Mechanical Systems (MEMS)," addressed the use of microneedles for interstitial fluid sampling and drug delivery. Amy Herr, Ph.D. (University of California at Berkeley) presented data on how laboratory-on-a-chip technology could be used for measuring analytes for diabetes. This technology utilizes MEMS to transfer blood across multiple microchannels where analytes can be measured simultaneously. She filled in for Matthew Glucksberg, Ph.D. (Northwestern University, Evanston, Illinois). Leah Tolosa, Ph.D. (University of Maryland at Baltimore) presented new data on a nanotechnology-based glucose sensor. This technology utilizes lifetime-assisted ratiometric sensing by a novel fluorescent glucose-binding protein labeled with two fluorophores. The assays can be conducted at low excitation frequencies to keep the costs down. Göran Stemme, Ph.D. (Royal Institute of Technology, Stockholm, Sweden) presented data on a MEMS system for insulin delivery by way of a patch of microneedles. A heat-sensitive polymer will expand in the presence of heat to push a reservoir of insulin out of the microneedles into the patient wearing the microneedle array or patch. A battery will provide the necessary heat. This method was effective in a rodent model, and Dr. Stemme explained that in the future, his team's insulin reservoir volume must be expanded and that a very concentrated insulin must be used to facilitate practical use of this approach in humans. He felt that the heated polymer would not cause denaturation of the adjacent insulin, but he did not have data on this topic. The annual Diabetes Technology Leadership Award was awarded to the person who has done the most to further the development of diabetes technology over the previous year. The recipient this year was Lutz Heinemann, Ph.D. from Profil Institute for Metabolic Research in Neuss, Germany. This session also included the presentation of the Peterson Student Research Awards to the three students conducting research in diabetes technology who first authored the highest rated abstracts submitted to the meeting. The meeting's planning committee members scored every abstract. The winners were students from University of Connecticut at Storrs (Gold), Stanford University (Silver), and Georgia Institute of Technology (Bronze). The Peterson Student Prize Gold awardee, Upkar Bhardwaj, M.Pharm. from University of Connecticut at Storrs, then gave an oral presentation. He discussed how a glucose sensor could be implanted subcutaneously for prolonged periods of time without a local inflammatory response if various composites containing anti-inflammatory properties were utilized. He suggested that very small amounts of dexamethasone would have excellent local anti-inflammatory properties without systemic absorption or an effect locally on the interstitial fluid glucose concentration. The speakers agreed that the use of MEMS and nanotechnology will (1) facilitate the development of new products for measuring glucose and delivering insulin and (2) provide alternatives to finger-stick puncture for blood glucose monitoring and the use of large needles for insulin injection.

The seventh session, entitled "Telemedicine and Diabetes," addressed the use of remote case management of diabetes through the use of telemedicine technology for data transmission from patients to health care providers and back to patients. Sven Bursell (Harvard University, Joslin Clinic) presented data about the performance of a teleopthalmology program. He will be establishing a new telemedicine program later this year at the University of Hawaii. Kun-Ho Yoon, M.D. (The Catholic University of Korea, Seoul, Korea) presented data about how an Internet-based program can tie in with a case management care program. He presented cost-effectiveness data to show that Internet-based care can be economically attractive. Robert Vigersky, M.D. (Walter Reed Army Medical Center, Washington, DC) presented a description of a novel comprehensive care protocol that he is developing entitled Computer-Assisted Decision Support for diabetes. This complicated algorithm determines optimal treatment through a branching system that incorporates the clinical condition, the laboratory test results, and the responses to previously prescribed treatments and then recommends the next treatments. Madeleine Fackler, M.S. (LifeScan, Inc., Milpitas, CA) discussed the potential benefits of using information technology to create care algorithms for determining medication dosages based on blood glucose levels. She advocated that industry create a common interface between glucose monitors and computers. This interface might pertain to both cable wires and wirelessly transmitted data. The speakers agreed that telemedicine will be used increasingly for the case management of groups of diabetes patients because of the need for this type of inexpensive, appropriate, and

standardized care that can be delivered to patients on demand.

The eighth session, entitled "Survey and Demonstration," utilized an audience response system with instant tabulation of responses to ask the audience multiple-choice questions whose response could be displayed in real time and discussed during this session. A panel of technology experts from the United States and a moderator from Europe led the discussion. This session concluded with a pair of live demonstrations of new technologies for the prevention of obesity and type 2 diabetes. The first live demonstration was by Tiffany Stewart, Ph.D. from the Pennington Biomedical Research Center at Louisiana State University in Baton Rouge, Louisiana. She surveyed the audience for the mean height and weight of the attendees. She then applied this information to an interactive Web site that her team is developing to promote weight management. This Web site is currently intended for members of the U.S. military and their families. Eventually it will be expanded to other groups. The second live demonstration was by David Andre, Ph.D. and Donna Wolf, Ph.D., both from BodyMedia, Inc. in Pittsburgh, Pennsylvania. They demonstrated a portable device that can be worn that measures energy expenditure and other parameters to assist with lifestyle modification to lose weight. The device can be used for weight management to prevent obesity and type 2 diabetes. The consensus of participants and presenters at this session was that (1) both the Internet and physiological monitoring with remote transmission will be increasingly utilized for both medical and military purposes and (2) the two systems that were presented live represent some of the first examples of how these approaches to telemedicine can provide assistance with weight management.

After the live demonstrations, the 3-day meeting was adjourned. During the course of the meeting, 72 presentations were made and 128 posters were presented. The meeting proceedings are featured in this issue of *Journal of Diabetes Science and Technology*, a peer-reviewed scientific e-journal published by the Diabetes Technology Society.