Applications of Physics, Mathematics, and Computer Science to Challenges in Proton & Ion Therapy

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From the visionary suggestion to use protons to treat human cancer in 1946 by Robert Wilson, Ph.D., who later became the first director of Fermi National Accelerator and the first applications of protons and heavier ions on humans at the Lawrence Berkeley National Laboratory in 1954 to the opening of the first proton treatment center in Loma Linda, California in 1990 it took more than 40 years. Many factors have contributed to this relatively slow development, among which were lack of appropriate 3D imaging techniques and adequate computer technology, and the high initial capital costs of particle accelerators. Despite of this, proton and ion therapy appear to be poised for changing the landscape in radiation therapy and may lead to the cure of many cancers currently considered challenging to treat. Yet, much has to be developed to make this happen, and this requires expertise and talent of scientists from many disciplines, just as it did in the early years. Many hints of can be accomplished with improved understanding and more advanced technology came from the pioneers themselves. For example, Alan Cormack, a physicist who shared the 1979 Nobel Prize in Medicine for the development of x-ray computed tomography suggested that protons may in fact be more advantageous not only for treating but also for imaging human disease. We are still awaiting the advent of a clinical proton CT scanner, but with the help from high-energy physics, mathematics, and computer science we are now getting close. In this presentation, I will give an overview of the many aspects of proton and ion therapy, including physics, dosimetry, and radiobiology, and will present our work on proton computed tomography. In the second half of the talk, I will give practical examples of how protons and ions are currently applied in clinical practice and where we can further improve.

Biography Dr. Reinhard W. Schulte is professor in the School of Medicine at Loma Linda University and Translational Research Specialist in Department of Radiation Medicine and James M. Slater M.D. Proton Treatment and Research Center at Loma Linda University Medical Center. Dr. Schulte received his Diploma in Physics (M.S. equivalent) with the highest grade from the University of Dortmund in Germany and a Doctorate in Medicine (Dr. med.) with summa cum laude from the Medical School at the University of Cologne, Germany. Besides being a certified medical doctor and board-certified radiologist with specialization in radiation oncology in Germany, he is also a licensed physician in the State of California and board-certified in radiation oncology by the American Board of Radiology. Dr. Schulte has more than 20 years of experience in proton radiation in particular in the

treatment of arteriovenous malformations with protons, a program started at Loma Linda University Medical Center in 1993 with his colleagues from Lawrence Berkeley Laboratory. Dr. Schulte has a long track record in multidisciplinary translational research related to proton therapy. He is currently PI of an NIH R01 grant for the development of a clinical proton CT scanner, which will be the first of its kind. During his career Dr. Schulte has authored or coauthored more than 60 publications in peer-reviewed journals and 25 conference papers. Dr. Schulte has given many invited talks at national and international meetings and workshops covering a diverse range of medical and scientific fields including radiation oncology, radiology, physics and engineering, and applied mathematics. In addition, he is listed as inventor on more than 30 patents and patent applications.

Superiorization via Feasibility-Seeking Projection Methods and Applications

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The Superiorization Methodology is a novel approach to constrained optimization. Many iterative algorithms for finding a constraints-compatible solution are perturbation resilient in the sense that, even if certain changes are made at the end of each iterative step, the algorithm still produces a constraints-compatible solution. This is exploited by using permitted changes to steer the algorithm to a solution that is not only constraints-compatible, but is also desirable according to a specified optimization criterion although it not necessarily minimizes that criterion. The approach is applicable to many iterative procedures and optimization criteria used in Medical Physics and other applications. Juxtaposing the Superiorization Methodology with the well-known Subgradient Projection Method for constrained minimization reveals the motivation of the approach.

Biography Yair Censor received his D.Sc. degree in mathematics from the Technion – Israel Institute of Technology in Haifa, Israel, in 1975, and joined the faculty of the University of Haifa in 1979, where he is a full professor since 1989. He published over 130 research articles in refereed scientific journals, conference proceedings, and as book chapters. He co-authored with S.A. Zenios the book: *Parallel Optimization: Theory, Algorithms, and Applications*, Oxford University Press, New York, NY, USA, 1997. For this book he received, together with Professor Zenios, from the Institute for Operations Research and the Management Sciences

(INFORMS) "The 1999 ICS (INFORMS Computing Society) Prize for Research Excellence In The Interface Between Operations Research and Computer Science". His fields of interest include optimization theory, convex analysis, and numerical analysis, and their application to inverse problems in image reconstruction from projections, in intensity-modulated radiation therapy (IMRT), in proton computed tomography (pCT), and in intensity-modulated proton radiation therapy (IMPRT).

PROton FUTURUS: What Baylor Can Bring to Proton and Ion Therapy

Keith Evan Schubert
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From mathematical algorithms and high performance computing through circuit design and high energy physics to radiation biology and radiation potentiated chemotherapy; proton an ion therapy offers a wealth of research topics that are available to students and faculty at Baylor University. Building on almost a decade of work with Dr. Reinhard Schulte of Loma Linda University Medical Center, Dr. Schubert will cover what work is being done at Baylor University and how we can expand this to include additional collaborators.

Biography Dr. Schubert has a BS in General Engineering from the University of Redlands, and a MS in Electrical Engineering from UC Los Angeles. He did his Ph.D. in Electrical and Computer Engineering at UC Sanata Barbara under Shivkumar Chandrasekaran in robust estimation. He was a visiting professor at the University of Redlands for two years before going to California State University, San Bernardino, where he designed and started the engineering and bioinformatics programs and achieved the rank of full professor. Dr. Schubert is now an Associate Professor in ECE at Baylor and an adjunct full professor of basic sciences at Loma Linda University Medical Center, where he does research on medical imaging and the use of protons in medicine. Dr. Schubert has supervised over 40 graduate students, including the California State University, 2006 state-wide outstanding thesis student, Tom Lee, whose thesis was on medical imaging. He has over 50 peer-reviewed papers and has been on over $ 3 million in grants, and a patent. He has 20 years of experience in controls, estimation, imaging, numerical computation and hardware design and extensive industry experience ranging from aerospace to medical equipment and robotics to fire tracking. He also works with NASA

Ames on extremophiles in astrobiology and with JPL on mission autonomy.