Michael Goitein (1939–2016): inventor of three-dimensional planning systems with image-guided beam delivery for radiation therapy

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Radiation therapy for cancer involves high-precision modalities such as intensity-modulated radiation therapy, stereotactic body radiation therapy (SBRT), and particle therapy, with rapidly expanding indications and benefits for cancer patients. Three- and four-dimensional (3D/4D) treatment planning and image-guided beam delivery are essential for the safe and reliable administration of these high-precision treatments. These two closely related technologies were first developed by Michael Goitein (Fig. 1) of the Massachusetts General Hospital (MGH) in Boston to enable precise proton therapy. Although his career comprised other outstanding achievements in radiation therapy physics, such as quantifying uncertainty in planning and delivery, we will focus on the system he created.

1 Early life and education

Michael Goitein was born on November 14, 1939, in Broadway, a picturesque rural village in central England [1, 2]. His father was a law professor at Birmingham University, and his mother was a part-time artist and architect. Goitein enjoyed several early academic successes and won a scholarship to Balliol College in Oxford at the age of 16 years, deferring admission to study mathematics at the University of Sorbonne. Goitein earned a bachelor's degree in nuclear physics and mathematics from Oxford in 1961, and he pursued a fellowship at Harvard. He enjoyed his experience at Harvard to such a degree that he decided to continue as a

graduate student, earning a master's degree in 1963 and a Ph.D. in 1968.

2 LBL and MGH

After completing his graduate studies, Goitein stayed at Harvard as a post-doctoral fellow and accepted an appointment as a research associate at the University of California Lawrence Berkeley Laboratory (LBL). In 1971, Goitein shifted his career from basic to medical physics, inspired by his wife at that time, a physician as well as the inspirational leader of Cornelius Tobias within the LBL's biophysics department. His first project was to develop computed tomography (CT) technology with a special interest in image reconstruction. Goitein proposed an image reconstruction method using iterative approximation [3]. These methods, popularized in the 2000s for the reduction of CT exposure dose, were ahead of their time. Goitein also worked with Douglas Boyd at Stanford, who later invented Cardio-Vascular CT (CVCT), to develop one of the first methods for reconstructing CT images from fan-beam projection measurements. Following these projects, Goitein was hired to the newly founded Department of Radiation Oncology at MGH by Herman Suit in 1972.

Soon after joining MGH, he began working on the clinical physics of photon therapy with two physicists and several clinicians. He fully understood his limitations within medicine, particularly in radiation oncology, but he demonstrated commitment to becoming an expert in his new discipline; this drive was noticed, and soon, Suit asked Goitein to lead the proton therapy development.

In the early fall of 1971, shortly before Goitein joined MGH, there was an agreement between MGH, Harvard Cyclotron Laboratory (HCL), and Harvard Medical School that the MGH radiation oncology department would launch a conventional fractionated proton therapy program for cancer patients. An empty well-shielded room was converted

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Fig. 1 Michael Goitein in 2007 delivering an invited lecture in the Massachusetts General Hospital Ether Dome. Reprinted from [1] with permission from Elsevier

for this effort. In this study, Goitein worked in 1972 with Andreas Koehler and other physicists, using a 160 MeV cyclotron with fixed horizontal beams and evaluating the potential of multi-portal fractionated proton therapy. Together with the Koehler team, Goitein transformed the treatment room of HCL and prepared the first cancer patient to be treated with proton therapy at MGH in December 1973.

At that time, radiation therapy planning was performed using a simulator, and the field size and shape had to be adjusted until target coverage of the beam and avoidance of normal tissue were considered sufficient on radiographs and/or fluoroscopy. The simulator used diagnostic X-rays as the photon source and had the same source–isocenter distance as the treatment machine. To identify the specifics of patient anatomy, the skin surface was traced with solder wire, while internal anatomy, including the target, was outlined with an artful combination of information from radiographs and an atlas of human anatomy based on sectioned frozen cadavers. Dose distributions were calculated by batch processing using a mainframe computer or manually in limited transverse sections. This type of treatment planning method was useful to some extent for conventional radiation therapy at the time, such as two opposed photon beam irradiation, but it was truly inadequate for proton therapy capable of three-dimensionally shaping a beam with a collimator and compensator. The second patient undergoing proton therapy at HCL in 1974 was a woman with chondrosarcoma of the skull base requiring the use of a posterior oblique beam. Goitein spent 3 days and nights developing her plan using smearing tomograms

Fig. 2 A team of three senior physicists evaluating a complex treatment plan: Michael Goitein at the center with his colleagues. On the right side of the figure are an operation terminal (lower side) of the VAX computer and a computer-driven image display device (upper side) (probably in the early 1980s). Reprinted from [1] with permission from Elsevier

and more time implementing it. Leveraging these experiences, he decided to develop a computer system to carry out the treatment planning and implementation required for proton therapy.

3 System for 3D planning with image-guided beam delivery in proton therapy

Goitein developed a treatment planning system for more than a decade, a period during which key revolutions occurred in technology: the development of powerful minicomputers (especially Digital Equipment VAX computers with virtual memory) (Fig. 2), the development of interactive computer graphics (the result of the space program with military base), and the development and distribution of CT scanners with previously unknown anatomical details.

Goitein's system included [2]:

- (1) Fully three-dimensional geometry (patient and delivery equipment) enabling the planning of image-based non-coplanar treatments.
- (2) Use of CT images, based on which the three-dimensional shape, size, location of the tumor, and the normal anatomy could be defined.
- (3) Interactive tools for delineating the anatomy from the CT data.
- (4) Beam's-eye view of the anatomy (Fig. 3).
- (5) Interactive and automatic design of ancillary devices (e.g., collimators, compensators).

Fig. 3 Beam's-eye view of patient anatomy. A beam aperture is being drawn with the aid of a cursor whose radius equals the desired margin. Reprinted from [4] with permission from Elsevier

Fig. 4 Display of three orthogonal sections through the 3D data set, with dose displayed in color wash. In each image, the red lines indicate where other sections intersect that image. By dragging the red lines with a mouse, the display quickly updates to show the new set of orthogonal sections. Reprinted from [5] with permission from Springer

- (6) Modeling of the treatment equipment, allowing user interaction in the design (capabilities of 4–6 were later termed ‘virtual simulation’).
- (7) 3D dose calculation.
- (8) The dose was displayed as isodose contours or, preferably, as color-wash on transverse, sagittal, and coronal images (Fig. 4).
- (9) What came to be called digitally reconstructed radiographs (DRRs) (Fig. 5). At the time of proton irradiation

to a patient, the radiographs were obtained using orthogonal X-rays, and the radiographs and DRRs were compared side by side, measuring differences in patient position (Fig. 6) with corrections accordingly.

- (10) Dose–volume histograms (DVHs).
- (11) Plan comparison techniques; for example, the side-by-side display of two or more plans (in color-wash or with isodose lines), overlay of DVHs for two or more plans for a particular volume of interest, and side-by-side comparison of biophysical quantities such as tumor control probabilities and normal tissue complication probabilities.
- (12) Implementation of the capability to interact on treatment plans during departmental conferences and from a remote site, specifically HCL.

Goitein created essentially all of these features, and perhaps more surprisingly, MGH began using his system in routine clinical practice around 1980.

4 Distribution of the system for 3D treatment planning with image-guided beam delivery

Goitein's concept was adopted not only at the MGH, but also at other facilities that had started particle therapy. George Chen, a post-doctoral student in Goitein's laboratory, moved to the LBL radiotherapy section when LBL started heavy-ion (mainly neon-beam) therapy; he started developing his system based on Goitein's concept. LBL provided their treatment planning system to the University of Tsukuba, Japan, when the university started proton therapy in collaboration with the High Energy Accelerator Research Organization (KEK). In addition, the National Institute of Radiological Sciences developed a carbon-ion radiotherapy treatment planning system based on Goitein's design, incorporating the modern 1990s technology (graphical workstation instead of mini-computer, digital X-ray image instead of X-ray film) [6].

Of special note is the treatment planning system for eye melanoma. Eye melanoma is comparatively common in Europe and the USA, and it has been considered difficult to treat by external beam irradiation because of its proximity to structures critical for visual acuity, such as the lens and the optic nerve. MGH intended to treat eye melanoma by leveraging the low scattering nature of protons. Goitein developed a treatment planning system using a 3D eye model of a patient that was constructed using fundus photographs, ultrasound images, and sketches during surgery in which metal clips were sewn around the tumor. This

Fig. 5 **a** A lateral DRR generated by the treatment planning program, and **b** a lateral radiograph obtained with the patient in the treatment position. The patient's position was adjusted to ensure the same relationship between the anatomy and the crosshairs in both images. Reprinted from [5] with permission from Springer

Fig. 6 Therapist measuring the deviation from the reference on the X-ray films hung on the light box with a ruler and calculating the amount of movement of the patient couch (late 1980s at MGH)

system was successful, and the software was distributed to more than ten Western particle therapy centers, including LBL.

Goitein intended to apply his concept to photon treatment planning, and he attempted to develop a photon 3D treatment planning system with the medical equipment company, Siemens, in the 1980s. Although prototypes were tested at several radiotherapy facilities and he contributed more than 5 years of effort, this attempt failed, and he could not launch a commercial product. Goitein was ahead of his time; in the 1980s, CT was still expensive, and there was no dedicated CT for treatment planning. At best, only a few CT images were obtained using diagnostic CT for treatment planning. Moreover, the model-based 3D dose distribution calculation methods such as convolution/superposition had not yet been established. Most critically, linear accelerators were not at this time equipped with a multi-leaf collimator, and only a rectangular field or a field with selective blocking could be used. Goitein's 3D treatment planning system likely had too

much functionality for that era, and thus it was not suitable for the contemporary cost of installation.

Goitein participated in the NCI-sponsored Collaborative Working Groups (CWGs), which defined the elements of 3D treatment planning for photon therapy, in the late 1980s. The CWG was organized by researchers from four leading institutions (University of Pennsylvania, Memorial Sloan-Kettering Cancer Center, Washington University, and MGH). Although there were several disagreements, such as the method of dose distribution calculation, the elements necessary for 3D treatment planning (most of them derived from Goitein's original work as described in Sect. 3) were summarized and reported in the *International Journal of Radiation Oncology, Biology, Physics* (volume 21 issue 1, 1991). For the first time, general radiation oncologists had access to 3D treatment planning. In response to the commercialization of the multi-leaf collimator-equipped linear accelerators in the early 1990s and the subsequent widespread implementation of 3D conformal radiotherapy, the 3D treatment planning system came to fruition. Furthermore, with the commercialization of the linear accelerators equipped with X-ray imaging devices in the early 2000s, image-guided beam delivery using X-ray images and cone-beam CT images was also realized. Thus, 3D treatment planning system with image-guided beam delivery finally became widely used in clinical practice after more than two decades since Goitein had created it around 1980.

5 Relocation to Switzerland and death

In 1990, NIH design funds were made available for a completely new proton therapy facility, which included an accelerator, beam lines, and treatment rooms. Goitein was the principal investigator for the grant, and he was responsible for the design. Construction funds were made available in 1994. He was also the principal investigator of the

construction grant, and the Northeast Proton Therapy Center (NPTC) at MGH was completed in 2001. The first patient was treated in November 2001, and the entire proton therapy program began the switch to NPTC; full patient accrual was achieved by April 2002.

Just before completion of the NPTC construction project, Goitein retired from MGH and relocated to Switzerland to live with his wife, Gudrun, whom he had married 4 years earlier. She was the Chair of Radiation Oncology for the Paul Scherrer Institute in Switzerland, one of the world's leading centers for proton therapy. He continued his work as a consultant in proton therapy, focusing specifically on helping develop new proton centers. He assisted with the development of the proton facility in Trento, Italy, for instance, and he gave lectures on his research work during his spare time, including an annual presentation at MGH. He also wrote and published a textbook, entitled "Radiation Oncology-A Physicist's eye-view", in 2008 [5]. He retired completely in 2011 and died of pancreatic cancer on August 3, 2016, in Windisch, near Zurich, Switzerland.

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