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Fabrikant Award Lecture

Summary of the lecture given on June 1, 2017 on the occasion of the Jacob I. Fabrikant Award ceremony

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I thank the International Society for Radiosurgery (ISRS) and especially its Board of Directors for this prestigious award. An award, which carries the name of one of the pioneers within the field of stereotactic radiosurgery, Dr. Jacob I. Fabrikant. Jack Fabrikant was born in 1928 in New York. He received his MD from McGill University (1956) and his PhD in biophysics from the University of London (1964). He joined the Radiology faculty at Johns Hopkins University in 1964. In 1970, he was appointed as professor and chair of Radiology at the University of Connecticut and in 1975 of McGill University. Three years later, he accepted a position as professor of radiology at the University of California in San Francisco and at Berkeley.

Jack was a pioneer in the field of radiosurgery. In 1984, he already published on the use of helium-ion radiosurgery for inoperable AVMs [1], and he became a leader of one of the first radiosurgery programs in the USA. He is renowned for the use of CT-based planning, use of MRI for target localization and dose-volume-effects in SRS for AVM's. Jack Fabrikant passed away in 1993 and the ISRS installed this price to honor a member who has made longstanding and significant contributions to the field of radiosurgery. It is a great honor to receive this bi-annual price in his name, especially when looking at the names of the "radiosurgeons" who preceded me (Table 1).

My first steps in the field of radiosurgery were made in the department of Radiation Oncology at VU University medical center in Amsterdam in 1991. I was a resident at that time when the radiosurgery program was started. Three patients were scheduled in the Summer of 1991, one patient with an AVM, one with an acoustic neuroma and one with a brain metastases. There were three residents and each was assigned one patient. I treated the patient with a solitary brain metastases of a malignant melanoma. In the preparation of this lecture, I asked for a print of the microfilmed file of this patient. Looking back at this file, it becomes evident how little and at the same time how much has changed over 25 years. One of the most striking memories was the fact that we had to

Table 1. Jack I. Fabrikant awardees

1995	Erik-Olof Backlund, Borje Larsson
1997	L. Dade Lunsford, Juan Barcia-Salorio
1999	Christer Lindquist
2001	Jay S. Loeffler, Frank Bova, William Friedman
2003	Tatsuya Kobayashi, John Flickinger
2005	Federico Colombo, David Larson
2007	Douglas Kondziolka
2009	Jean Régis
2011	Masaaki Yamamoto
2013	Bruce Pollock
2015	Roberto Martinez, German Rey
2017	Ben J. Slotman

use a separate handheld computer to manually obtain the stereotactic coordinates from the CT scanner. The little computer than provided the coordinates, which had to be used in the treatment planning and setup, but with reversal of the x- and y-coordinates; an important cause of potential errors and impossible under current quality standards.

The ISRS was founded in 1991 and had its first meeting in Stockholm in 1993. In 1992, my center organized (one of) the first international conferences in radiosurgery/fractionated stereotactic radiotherapy. In 1992, pioneers and early adopters from all over the world gathered in Amsterdam to discuss the latest developments, exchange results and experiences and discussed future directions. Most of them used adapted linear accelerators for the treatment delivery. Since these early years, there have been great changes with a rapid growth and further improvements of the technique. Single fraction radiosurgery or fractionated stereotactic radiotherapy became alternative treatment options for the initial indications, including AVM's, acoustic neurinomas, meningioma and brain metastases, and an accepted treatment option for various new indications.

In 2003, VU University medical center was the first Dutch center who started a stereotactic body radiotherapy (SBRT) program. The largest group consisted of patients with early stage lung cancer [2]. The clinical team was in the forefront of introducing new technologies in the following years, including improvements in 4D-imaging and the use of RapidArc. In an update of the results in 676 patients, the local control rate was 90%, the regional control rate 87% and the distant control rate 80%, all at 5 years [3]. Population-based studies at the regional and national level, showed that the introduction of SBRT led to an increased use of radiotherapy [4] and significant improvements in overall survival [5].

Initially, SBRT was mainly used in lung cancer patients with severe comorbidities, who were unfit to undergo surgery and occasionally in patient who were medically operable, but refused surgery. With the excellent results of SBRT in medically inoperable patients, the percentage of potentially operable undergoing SBRT increased. In 2011, we had treated 177 operable patients and demonstrated that these patients had significantly longer survival than the medically inoperable group [6]. Various attempts have been made to complete randomized controlled trials comparing SBRT with surgery, but so far, all have failed due to poor patient accrual. The combined analysis of two prematurely closed randomized trials (ROSEL and STARS), including in total 58 patients, showed a significant benefit in overall survival of SBRT over surgery [7]. New attempts for randomized trials are currently underway. How can we explain the excellent results of SBRT in early stage lung cancer? It is conceivable that the avoidance of surgery, a procedure which may lead to suppression of the immune system, plays a role. Moreover, there is increasing evidence that SBRT may stimulate the immune system in various ways. Radiotherapy can trigger the immune system and cause an inflammatory effect in the tumor which further stimulates the immune response. For a recent overview, the reader is referred to Herrera et al. [8].

Since I completed my training in radiation oncology in 1993 there have been enormous changes in the way we select, image, plan and treat our patients. However, until recently, we still had a poor soft tissue resolution of the imaging used with the patient in treatment position, we had no continuous imaging during treatment when the beam is on, and we often had to rely on external markers or internal fiducials for positioning, and used only one treatment plan which was based on the anatomy at the time of simulation. Since May 2016, we use an MRI-guided treatment system (ViewRay MRIdian) which overcomes all these problems. Several prospective studies are underway to evaluate this technique in patient with pancreatic, liver, prostate, renal, rectal, lung, adrenal and breast tumors. I expect that this will lead to further improvements in the treatment outcomes and in the use of stereotactic techniques for new indications.

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Author's disclosure of potential conflicts of interest

Dr. Slotman reports grants and personal fees from Varian medical systems, personal fees from ViewRay, outside the submitted work.

Author contribution

Manuscript writing: Ben J. Slotman

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