Donald L. Morton, MD.... A Legendary Surgical Oncologist and Consummate Investigator

Charles M. Balch[a] & Dave S.B. Hoon[b,*]

[a]Division of Surgical Oncology, University of Texas Southwestern Medical Center, Dallas, Texas; [b]Department of Molecular Oncology, John Wayne Cancer Institute at Providence Saint John's Health Center, Santa Monica, California

*Address all correspondence to: Dave S.B. Hoon, Department of Molecular Oncology, John Wayne Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA 90404; hoond@jwci.org

Donald L. Morton was a true legend in the field of surgical oncology, as well as a translational investigator and pioneer in the field of immunotherapy. Indeed, he was just as passionate and engaged in laboratory research as he was in the clinical care of his patients and the conduct of clinical trials. Very few surgeons have achieved such distinction for their scholarly contributions in both spheres of translational and clinical research.

When Dr. Morton's scientific journey is examined from the perspective of a surgical investigator, he has few peers. He defined his approach as follows: "Our goal as cancer researchers is to make things better. We identify problems with the status quo, then try to discover better ways to do things." His research has credibility and reproducibility because he tested his hypotheses rigorously using the structure of prospective clinical trials, sophisticated database analyses, and multidisciplinary collaborations. At the same time, his strategies and design of clinical studies were rooted in previous or concomitant studies in the laboratory. He was a strong advocate of using biostatistics in clinical research.

His accomplishments are prodigious and have been described in more detail elsewhere,[1] but here are just a few in summary:

- Dr. Morton authored more than 850 publications and received competitive research funding from the National Cancer Institute for more than 38 years;
- He trained more than 150 fellows, of which 80% are now in leadership roles in academic institutions or major cancer centers;
- He had an uncanny skill in shaping his ideas and visions into successful federal grants (the journal Science placed him at the top of a list of clinical investigators who received the most grant funding from the National Institutes of Health during 2000; Science, June 15, 2001); and
- He was able to compete nationally with his ideas and hypotheses and garnered RO1 grants, T32 training grants, and PO1 grants—astonishingly, having two program project grants at one time that lasted more than 35 years.

Dr. Morton was a prodigious writer whose publications covered many different fields. The ISI Web of Science (Thomson Reuters) lists 924 of Dr. Morton's publications (as of January, 2014) that have been cited more than 35,000 times in the biomedical literature (an average of 38 times per article). More than half of these publications involve the field of melanoma and these have been cited more than 19,000 times. Any of us would be pleased that a publication was cited 50 or 100 times, but Dr. Morton had more than 60 articles that have been cited more than 100 times. Indeed, over the past few years, his collective publications have been cited more than 1600 times per year! One also must note the diversity of his top 10 "high-impact" publications as a lead author or co-author, for which seven of the 10 articles advanced the field of melanoma.

Over a half-century career, Dr. Morton changed our melanoma surgical practice and our oncology management on a global basis. He also conducted numerous clinical research projects that have

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shaped our perspective and clinical management of our cancer patients, particularly in the field of melanoma. His pioneering work with intratumoral Bacillus Calmette-Guerin (BCG) for melanoma represented the first successful clinical application of immunotherapy against a metastatic human cancer. His work with BCG in melanoma metastatic to the bladder also laid a foundation for the use of intravesical BCG in superficial bladder cancer, which became the first US Food and Drug Administration-approved cancer immunotherapy.[2] He was also one of the pioneers in performing limb salvage surgery and pulmonary metastasectomy for soft tissue sarcomas.[3] Whereas all of these made significant advances using the instrument of clinical trials, Dr. Morton was also a translational researcher who made fundamental discoveries in the field of tumor immunology and immunotherapy that has stimulated an entire field of inquiry.

His pioneering clinical research efforts in the development and clinical application of sentinel lymph node biopsy (SNB) transformed the surgical management of many solid tumors, particularly melanoma and breast cancer.[2,3] In these latter two cancers, SNB has replaced complete lymphadenectomy for staging the regional nodes, thereby reducing healthcare costs in the United States by about $3.5 billion each year. First through observational clinical studies and then systematically in an animal model,[4] Dr. Morton developed and tested the clinical application of the SNB technique to improve the staging of melanoma. His first results were presented at the Society of Surgical Oncology meeting in 1990. The manuscript describing this methodology was rejected by several "high-impact journals." Undaunted, he persisted until the paper was published in the Archives of Surgery in 19925; his tenacity, which many remember him by, had prevailed. It became a classic article with more than 2400 citations to date! To his credit, he went on to validate this technique through a series of brilliantly designed clinical trials, first at his own institution and then with two landmark international studies, the Multicenter Selective Lymphadenectomy Trial (MSLT) I and the MSLT II surgical trials on the role of the SNB and therapeutic lymphadenectomy for melanoma trials.[6] His final major contribution was published several months after his death in the New England Journal of Medicine and involved the final results of the MSLT 1 SNB trial.[7] The MSLT-1 trial is a landmark prospective, randomized clinical trial that caps a 35-year effort to resolve the controversy surrounding the survival benefit of surgical excision of regional lymph nodes as a component of the initial management of patients with primary melanoma.[8] The integration of SNB into the management of intermediate- and high-risk primary melanomas has changed the melanoma landscape significantly by clarifying the prognostic heterogeneity of stage I and II melanoma and unraveling the prognostic heterogeneity of stage III melanoma. This practice-changing trial demonstrates the important role of early identification and surgical removal of regional metastases, both for staging value and for improved survival in defined cohorts of melanoma patients.[7,8]

Dr. Morton's other passion was adjuvant active specific immunotherapy, such as the melanoma vaccine. He was a strong advocate of implementation of adjuvant immunotherapy after surgical resection of metastatic melanoma to prevent recurrence. He was also the primary investigator of two international phase III clinical trials.

Donald L. Morton was an inspiration to us all. His prowess as a clinical surgeon has saved the lives of many patients, his research has contributed to our fund of knowledge that we use every day around the world in our own clinical practices, he has trained a cadre of surgeons and investigators who in turn have become leaders in their field, and he has influenced us all in the field of surgical oncology with his professional standards, strategies, and approaches that we all emulate in our own professional lives.

Indeed, in the annals of surgical research, there are very few who have contributed such a wealth of biological and clinical knowledge through the decades. His legacy will continue for years to come through his impact on international randomized surgical trials, translational research programs, and his trainees.

Donald Morton was truly a legend in surgical oncology, an icon as a surgical investigator, a pioneer in melanoma, a valued mentor, an authentic role model, and a cherished friend to many of us around the world. Though he led a busy professional life, he was also a devoted husband to his wife Lorraine and his family. His presence will be missed, but his impact on a myriad of colleagues, friends, and patients will live on.

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