Profile of a pioneer in Nuclear Medicine

Abass Alavi (Persian: علوی ع باس): A giant in Nuclear Medicine turns 80 and is still going strong!

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Little was written in the stars above the city of Tabriz in Iran on March 15, 1938 indicating that a newborn citizen would immigrate to America and become a master of modern molecular imaging with a sharp focus on ^{18}F-FDG PET to the benefit of millions of people around the world. Nonetheless, that's what happened. A gifted boy who lost his farther early and grew up with his uneducated mother and two siblings in humble circumstances to become a premium student, nationally no. 1 in mathematics while in school, and later a medical doctor before he decided in 1966 to seek his fortune in the US.

Here he started education in internal medicine, hematology and oncology, albeit found this unsatisfactory due to tradition and rote learning. He turned to radiology and nuclear medicine in a search for new knowledge and better methods to benefit patients and society, an attitude he had been taught from early childhood. The very same attitude has been the beacon for Alavi's activities throughout his professional life, instead of money, power, and social status. He married into a highly academic environment. His wife, Jane Bradley Alavi, was a specialist in hematology and oncology and is still his life partner. They never had children, so their many students and the numerous medical doctors, physicists and other academics they coached became their family. While Jane Alavi retired some years ago, Abass Alavi (Figure 1) continued his professional career and has no plans of retirement when he turns 80 on March 15, 2018 after 46 years in nuclear medicine at the University of Pennsylvania and with an admirable network of pupils and colleagues across all five continents.

On the contrary, Alavi has probably never been busier, his scientific work goes on, his multinational scientific "family" steadily increases all over the world as does the application of PET in the shape of PET/CT or PET/MRI. Alavi's contributions to the scientific literature has more than doubled within the last decade making him one of the most cited researchers at the University of Pennsylvania with a production of more than 1,200 articles, a similar number of published abstracts and close to 58,000 citations according to Google Scholar, of which about 20,000 since 2012 when he was 74.

This is just part of an amazing story. Having turned to nuclear medicine in 1971, Alavi entered into one of the World's most ingenious and productive medical research environments comprising collaboration of experts in nuclear medicine (David Kuhl) and neurology (Martin Reivich) at Penn, and in physiology and pharmacology (Louis Sokoloff) at the NIH, all of whom contributed significantly to the development of PET. Focus was on cerebral research with beta-emitting ^{14}C-labeled deoxyglucose for mapping regional cerebral glucose metabolism by means of autoradiography. Alavi became a junior member of this collaboration in which the idea of labeling deoxyglucose with a gamma-emitting isotope arose to allow in vivo examination of the normal and diseased human brain. They contacted Alfred Wolf at Brookhaven National Laboratory who had an interest in synthesizing positron-emitting compounds. He suggested labeling instead with ^{18}F-FDG and in 1975 Wolf's group in-cluding Tatsuo Ido and Joanna Fowler succeeded in synthesizing ^{18}F-FDG. In the meantime, investigators at Penn had developed high energy collimators for the Mark IV scanner to allow imaging with ^{18}F-FDG, so in August 1976, two normal volunteers were the first to receive a dose of ^{18}F-FDG for tomographic brain imaging showing concentration of ^{18}F-FDG in the gray matter while in one volunteer a "whole-body" scan from the top of the scull to mid-thigh was also obtained (Figure 1). A year before, investigators at Washington University, i.e., Michel Ter-Pogossian in collaboration with Michael Phelps, Edward Hoffmann, and Nizar Mullani had developed what they termed a positron-emission transaxial tomograph for nuclear imaging, i.e. a machine which was the starting point of today's PET scanners. Alavi understood from the beginning the potential of PET and in particular ^{18}F-FDG PET even if PET images at that time were blurry and difficult to interpret, a circumstance which for a quarter of a century brought the method in poor standing in the minds of many. Alavi started as a brain researcher, but training in internal medicine, hematology, radiology and nuclear medicine broadened his scope and over the years there are few diseases and clinical specialties in which Alavi has not provided results obtained with molecular imaging. He was a pioneer in using iodine-123 in thyroid cancer, MIBG in pheochromocytoma, radiolabeled white blood cells in infection, and ^{99m}Tc for the detection of gastrointestinal bleeds, and together with his wife ^{18}F-FDG PET for the demonstration of recurrent brain tumors. Thus, Alavi has contributed often very successfully by promoting new ideas and their implementation to achieve improved ways of examining a variety of medical disorders.

Alavi has been accused of seeing ^{18}F-FDG as the only useful PET tracer. In a way this is true. FDG became the dominant tracer

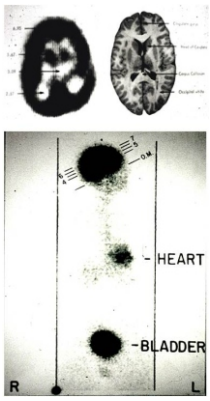

Figure 1. Top left: The first tomographic ^{18}F-FDG image of the brain acquired on August 7, 1976 at the University of Pennsylvania using a Mark IV scanner equipped with modified high-energy collimators for detection of positron emission photons. Top right: comparable brain structures. Bottom: The first whole-body ^{18}F-FDG image acquired on the same day using a dual-head Ohio Nuclear rectilinear scanner equipped with high-energy collimators for Sr-85 bone scans. Both images are reproduced with permission from Semin Nucl Med 2002; 32: 2-5.

and has remained so for over 40 years now. In his 2008 SNM Highlight Lecture, Henry N. Wagner, Jr. called FDG the "tracer molecule of the 20th century". According to a recent forecast of the Global Nuclear Medicine Radioisotopes Market, the global ^{18}F-FDG market is expected to grow from an estimated $1.233 billion in 2014 to $2.148 billion in 2019 and the vast majority of this growth is due to a continued increase in the use of ^{18}F-FDG, indicating that this tracer may remain the tracer molecule of at least the first half of the 21st century.

The world calls for more specific tracers than ^{18}F-FDG, and like others Dr. Alavi has constantly been looking for these, but with time, it became apparent that our body holds few organ or disease specific targets, so that the concept of very specific disease-characterizing tracers is not as rosy as previously assumed. Thus, in cancer, genetic profiling has demonstrated that tumors are genetically often a mixture of cellular clones and that these are not necessarily also present in local, regional or remote metastases, meaning that ultra-specific PET tracers for cancer diagnosis and staging may be more a utopian vision than a realistic future possibility. This, together with inborn limitations of the PET technique has made Abass Alavi more prudent and hesitant toward reports of highly promising new PET tracers and an advocate of timely carefulness when using our limited financial resources.

Teaching and education of talented young individuals is one of Alavi's main academic missions. Thus, with Gerald Mandell, MD, he established the Alavi-Mandell Award, presented for the first time at the SNM meeting in 1999 to a candidate selected from among all those in a given year who were trainees at the time their names appeared as first authors of papers in JNM. Together with his wife Jane, Alavi established the Bradley-Alavi Student Fellowship which was presented for the first time in 2001 and is given to the top students selected by the SNMMI Education and Research Foundation.

Alavi himself is a recipient of multiple awards, including the Georg Charles de Hevesy Nuclear Pioneer Award (2004), the Benedict Cassen Prize for Research in Nuclear Medicine (2012), the Honorary Citizen-ship of his native town Tabriz (2015) (Figure 2) and the Gold Medal of the National Institute for Medical Research Development, Tehran (2015). In addition, he has received the Honorary PhD Degree in Molecular Biology of the University of Shiraz (2007), and the Honorary Doctoral Degrees of the University of Bologna (2007), the University of the Sciences in Philadelphia (2008), the Medical University of Gdańsk (2016), and the University of Southern Denmark (2016) (Figure 3).

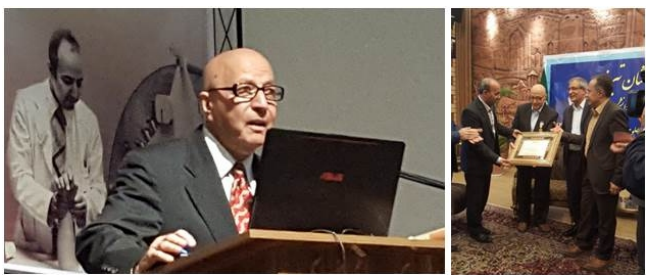

Figure 2. Left: Dr. Alavi 2015 giving a presentation in front of a photo of himself as a young doctor in nuclear medicine. Right: Abass Alavi became Honorary Citizen of his native town Tabriz on October 8, 2015.

Figure 3. Abass Alavi being appointed Honorary Doctor of Medical Sciences, University of Southern Denmark, on October 28, 2016 in the presence of Her Majesty Queen Margrethe II of Denmark (with her back to the camera).

Since January 2011, Alavi has been a frequent guest in the city of Odense, Denmark. Its University Hospital holds one of the biggest departments of nuclear medicine and PET in Northern Europe. From being behind, Denmark has become the country in the world with the highest relative number of PET/ CT scanners and PET scans, i.e., an estimated 0.7 and 1000, respectively, per 100 000 inhabitants in 2017. At 17 consecutive interdisciplinary Abass Alavi Meetings in Odense, he has been inspirer and initiator of multidisciplinary scientific projects that have resulted in more than 100 publications and as many scientific presentations.

Abass Alavi personifies the polymath, a species rarely found today. He discusses and produces science in as diverse areas as brain, cardiovascular, and musculoskeletal diseases, inflammation, cancer and many more disorders that plague humanity, and he has a clear eye to make results clinically useful. Had the Noble Prize been awarded not only for single inventions but also for the cumulated contribution of an outstanding researcher to patients who suffer and mankind as a whole, Dr. Abass Alavi would be on top of the candidate list.

What may such an experienced birthday-person foretell about the future? He would probably say that the gamma camera and SPET will be entirely substituted by PET, that skeletal metastases are bone marrow and not bone metastases and that all indirect methodologies for imaging of skeletal metastases, including bone scintigraphy and CT, will be replaced by PET imaging with ^{18}F-FDG or more cancer specific tracers. Also that motion and partial volume correction will be satisfactorily dealt with to allow calculation of a global disease score representing the total burden of disease in the body, whether caused by cancer, atherosclerosis or other severe disorders, and that, thus, PET will take its lead position as the diagnostic imaging modality of the 21st century.

It is hard to say how many of these predictions will come true while Dr. Alavi is still going strong. What is certain is that very few persons, if any, has contributed so significantly to the development and clinical implementation of PET imaging worldwide as have this 80 year old giant in modern nuclear and molecular medicine! Abass Alavi currently holds appointments as Professor and Director of Research Education in the Department of Radiology, Perelman School of Medicine, of the University of Pennsylvania and as Honorary Fellow of the International Society of Medical Olympicus Association in Greece.

A letter from the Editors of the Hell J Nucl Med

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