

Doctor Honoris Causa

H. WILLIAM STRAUSS



Universitat Autònoma de Barcelona

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Discurs llegit a la
cerimònia d'investidura
celebrada a la sala d'actes
de l'Hospital de la Santa Creu
i de Sant Pau
el dia 4 de maig de
l'any 1995

Bellaterra, 1995



Universitat Autònoma de Barcelona

Editat i imprès pel
Servei de Publicacions
de la
Universitat Autònoma de Barcelona
08193 Bellaterra (Barcelona)

Imprès a Espanya

PRESENTACIÓ
DE H. WILLIAM STRAUSS
PER
IGNASI CARRIÓ GASSET

H. WILLIAM STRAUSS EL CIENTÍFIC I L'HOME

El científic

William Strauss va néixer ara fa cinquanta-quatre anys a Brooklyn. Educat a Nova York, es va graduar com a metge el 1965. Després de dos anys de postgrau a la State University de Nova York, es va incorporar al Departament de Medicina Nuclear del Johns Hopkins Hospital de Baltimore, dirigit pel professor Henry Wagner Jr. Allà va esdevenir en primer lloc professor auxiliar de Medicina (1972-1975) i després, professor adjunt de Radiologia i Salut Ambiental (1975-1976). Després es va traslladar a Boston, al Massachusetts General Hospital i a la Harvard Medical School, on va desenvolupar la que fins ara ha estat la part més llarga i productiva de la seva carrera, primer com a professor adjunt i després com a catedràtic de Radiologia i director del Departament de Medicina Nuclear del Massachusetts General Hospital (1979-1992). Darrerament s'ha traslladat a Stanford, on és catedràtic de Radiologia i director del Departament de Medicina Nuclear de la Stanford University School of Medicine.

Si hom repassa el seu currículum de publicacions, sorprèn no solament el nombre (quatre-cents articles originals, múltiples col·laboracions, capítols de llibres, llibres i patents), sinó també la gran qualitat. Tenint en compte només les publicacions de més impacte (*New England Journal of Medicine*, *Circulation*, *Science*, etc.) i aplicant el factor d'impacte del JCI de 1993, surt un total de mil quatre-cents punts! Realment, es poden veure ben pocs currículums científics d'aquesta magnitud arreu del món.

Si hem de mencionar les seves contribucions científiques més rellevants, citariem, al començament dels anys setanta, les primeres descripcions de l'estudi de la funció ventricular cardíaca amb isòtops (*American Journal of Cardiology* 1991, *New England Journal of Medicine* 1973), és a dir, l'ara universalment utilitzada ventriculografia isotòpica. També són seves les primeres descripcions de l'estudi de la perfusió miocàrdica amb isòtops (*Radiology* 1973, *Circulation* 1973 i 1974), que han donat lloc als universalment utilitzats estudis de perfusió miocàrdica amb tal·li. Aquestes dues contribucions van establir les bases científiques del que després ha estat la cardiologia nuclear, de la qual ell és un dels exponents més assenyalats. Posteriorment, podem remarcar, entre altres, la seva contribució al desenvolupament dels anticossos monoclonals antimiosina per detectar una lesió miocàrdica (*Science* 1980), la utilització dels àcids grassos marcats per a l'estudi del metabolisme miocàrdic (*Circulation* 1982), la recerca de marcadors de la placa d'ateroma metabòlicament activa (*Arteriosclerosis* 1988), la descripció de la immunoglobulina policlonal per detectar infeccions (*New England Journal of Medicine* 1989) i la descripció d'un sistema per mesurar la funció ventricular de forma ambulatoria (*American Heart Journal* 1990). William Strauss no és, doncs, un investigador amb una sola línia

específica. És, al contrari, un autor prolífic en diversos camps, on ha descobert, innovat i obert nous camins per a les aplicacions científiques i la recerca d'altres.

Cal destacar, també, la seva labor editorial, ja que és membre dels consells de redacció de diverses de les principals revistes de cardiologia i de medicina nuclear del món, i director del *Journal of Nuclear Medicine* (1989-1993), revista que sota la seva direcció ha esdevingut la revista de radiologia i diagnòstic per la imatge amb el factor d'impacte més alt del món, segons el SCI.

La seva tasca investigadora i docent continuarà ara a Stanford, on cal esperar que, amb el potencial científic de la institució californiana, l'activitat científica de William Strauss sigui tan productiva com fins ara, obri nous camins per a la recerca en medicina i contribueixi al progrés de la ciència i la salut.

L'home

Les principals qualitats humanes de William Strauss són la intel·ligència combinada amb una profunda sensibilitat, la curiositat intacta, la tenacitat i la capacitat d'escoltar. Em comentava, no obstant això, un company d'aquells anys a Boston, ara director d'un departament de Cardiologia a Itàlia, que el que impressionava més de la personalitat de William Strauss era la seva generositat intel·lectual. Aquesta és una qualitat essencial per a un vertader líder científic. Aquesta característica permet que els seus col·laboradors desenvolupin idees que moltes vegades són originalment d'ell, però els cedeix tot el protagonisme científic i intel·lectual. Això ha fet que al seu entorn hagi sorgit l'escola de medicina nuclear al meu entendre més important del món, quant a nombre i quant a qualitat. Els seus *ex-fellows* estan escampats arreu del món desenvolupant moltes vegades tasques de direcció de departaments de medicina nuclear, radiologia i cardiologia. També em comentava un destacat directiu d'una important multinacional del món de la indústria sanitària, que des de la seva perspectiva, William Strauss era un autèntic «guru», ja que veia com la seva presència actuava com un catalitzador sobre les persones que estaven al seu voltant, i induïa la interacció intel·lectual i la generació de noves idees i nous projectes. William Strauss és reconegut, doncs, com un líder científic a escala mundial.

Personalment, recordo amb admiració, no exempta de nostàlgia, les sessions de les vuit del matí al seu departament de Boston. Amb una atmosfera amb una intensa olor de cafè, i sota la tènue llum dels projectors de transparències, residents, *fellows* d'arreu del món, i fins personalitats reconegudes en diferents àrees de la medicina, és a dir, tot el ventall del progrés professional i científic, discutíem en una actitud d'autèntica igualtat. Sota la seva intel·ligent moderació, l'aprenentatge es combinava amb la interacció intel·lectual, i donava com a resultat, cada dia, noves idees i nous camins per explorar. La necessitat de l'equilibri entre la creació intel·lectual i el

treball sacrificat del dia a dia al laboratori eren el missatge que ens vàrem emportar tots els que aquells anys vàrem tenir la sort de passar pel seu departament.

Des de Boston i ara des de Stanford, William Strauss manté viu el contacte amb tots els seus *ex-fellows* i col·laboradors. Això fa que per a nosaltres hagi estat fàcil d'establir des d'aquí una línia de col·laboració fructífera amb ell i el seu grup. Els darrers anys, la nostra col·laboració amb el seu grup ha donat lloc a la recerca específica que hem portat a terme pel que fa a la utilització dels anticossos monoclonals antimiosina en la detecció del rebuig cardíac, la miocarditis i la cardiotoxicitat, amb múltiples publicacions, tesis doctorals, beques d'organismes oficials i diversos intercanvis personals. Actualment també estem impulsant una nova línia de recerca cooperativa pel que fa a la detecció de plaques d'ateroma metabòlicament actives utilitzant diversos agents desenvolupats pel seu grup amb afinitat per aquestes plaques.

William Strauss té el perfil i totes les característiques adients per esdevenir doctor *honoris causa* per la Universitat Autònoma de Barcelona.

AN ABBREVIATED AND INCOMPLETE
HISTORY OF CARDIOVASCULAR
NUCLEAR MEDICINE
PER
H. WILLIAM STRAUSS

This is a scintillating story with a murky beginning and an ending that has not been written. It involves many dedicated people and illustrates the synergy between clinical needs, research goals, and technical prowess. Our story begins in the early 1920's and continues on through tomorrow.

Interest in understanding cardiovascular physiology fostered the major developments in instrumentation, radiopharmaceuticals and clinical applications of radionuclide imaging that ultimately gave birth to the field of nuclear medicine. One of the earliest human uses of radionuclides occurred in the mid 1920's, when Blumgart performed his pioneering studies of the circulation time in man. He injected radionuclides intravenously and observed its arrival in the other arm by the tracks made in a cloud chamber. As Blumgart applied this technique to study the changes in circulation time in health and disease, he needed a more sensitive and reliable detection device. To fill that need, shortly after the Geiger tube was invented in 1928, Blumgart adopted it for his subsequent studies of the circulation.

Similar rapid progress occurred forty years later with one of the first major clinical use radionuclides in cardiology, the radiocardiogram. Prinzmetal and his colleagues gave that name to a tracing of the transit of radiolabeled albumin through the heart and lungs recorded with a Geiger tube placed over the precordium. These measurements were valuable for the information provided about heart failure and cardiac output. As occurred with Blumgart, when a more sensitive radiation detector was described, it was immediately utilized to enhance the quality of the data. The sodium iodide scintillation detector was described by Hofstadter in 1947, and was immediately adopted to replace the Geiger counter for these determinations.

In 1952, Cassen developed the rectilinear scanner to record images of the *in-vivo* distribution of radioactivity in the thyroid gland. Shortly thereafter, investigators realized the potential of this device to record the distribution of radioactivity in any organ or system. Within six years of the description of the scanner, Rejali *et al* reported the use radiolabeled albumin blood pool imaging to detect pericardial effusion by noting the space between the cardiac blood pool and surrounding structures.

In the 1950's, the major radionuclide for imaging with the rectilinear scanner was ¹³¹Iodine, a nuclide with an 8 day half-life, that decayed with combined beta and gamma emissions, resulting in high radiation burden to the patient. The rapid growth of radionuclide imaging spurred research on short lived nuclides that could be administered in larger amounts yet result in lower radiation burdens. Richards and his colleagues at Brookhaven National Laboratories solved the problem by inventing the Molybdenum/Technetium generator. This system allowed the shipment of a column containing ⁹⁹Mo with its half-life of 67 hours. When needed, the daughter product, ^{99m}Tc, with its 6 hour half-life and pure gamma emission could eluted from the column. This allowed administration of doses about 100 fold greater than ¹³¹Iodine, but yet reduced the radiation burden to the patient.

The availability of a radionuclide that provided a high photon flux made it practical to image rapidly changing functions, such as the transit of blood through the central circulation. Scintillation cameras were developed in the early 1960's. An early application of these instruments was to record the transit of a technetium-99m tracer through the heart and lungs. Early applications of these imaging techniques included evaluation of congenital heart disease, valvular disease, and characterization of regional transit times.

The twenty-year interval beginning in 1965 saw the major advances in that led today's practice of cardiovascular nuclear medicine. In 1962, Bing and his colleagues described the use of Rubidium-84, a positron emitting radionuclide that localized in the myocardium, and coincidence counting to determine an index of coronary flow in man. The tracer was injected intravenously and the fraction of dose localizing in the heart was determined. This measurement was decreased in patients with myocardial infarction. In parallel with this, Ross and his colleagues at Johns Hopkins described their results from clearance measurements following intracoronary administration of Krypton and Xenon in the catheterization laboratory to determine coronary blood flow in normal and infarcted myocardium. As these studies were taking place, Gregg and his colleagues were perfecting the electromagnetic coronary flow probe for the measurement of coronary blood flow, and the microsphere technique of Rudolph and Heyman was applied to determine regional perfusion in animals with experimental myocardial ischemia. These determinations identified the degree of reduced perfusion that altered regional wall motion, the differences between endo and epicardial perfusion and defined the relationship between oxygen supply and oxygen demand.

In parallel with the developments in nuclear imaging, the cardiac catheterization laboratory had evolved from a place where pressures were measured in various chambers of the heart, to record information about coronary anatomy and global and regional ventricular function on cineangiographic film. It became apparent that «noninvasive» imaging techniques were necessary to allow repeated measures of cardiac function during the course of treatment, to determine how individual zones of myocardium were responding. These circumstances created the environment that resulted in the development of cardiac imaging procedures.

To quantify left ventricular performance the cardiology community settled on the ejection fraction. Ashburn and his colleagues described a method of calculating ejection fraction from images recorded during the initial transit of tracer through the left ventricle in 1966. This technique, though useful in patients with well maintained cardiac function, often produced poor images in patients with severe heart disease. In addition, only one or two measurements were possible with the initial transit technique. At this time, intensive studies were underway to evaluate new drugs to treat patients with acute myocardial infarction. An early goal of these studies was to determine if ischemic myocardium could be salvaged if drugs were

administered to reduce myocardial oxygen demand under circumstances of decreased perfusion. Defining the status of patients before they were treated with nitroglycerin or nitroprusside infusion, beta blockers, or high potency diuretics and monitoring their response to therapy then became important goals. These circumstances provided the environment that fostered the development of gated blood pool imaging. This technique, described by Strauss, Zaret and their colleagues, used a single crystal scintillation camera, a radiopharmaceutical that remained in the blood pool, and a technique of synchronizing (gating) the recording of data with the patient's electrocardiogram. The resultant images of the cardiac blood pool at end systole and end diastole were used to define the outline of the left ventricle at each phase of the cardiac cycle. These outlines were used to calculate the end diastolic volume, ejection fraction, and regional wall motion of the left ventricle. This information helped document the improvement in regional wall motion and ejection fraction that occurred following administration of drugs to unload the left ventricle in the early hours of acute infarction. This improvement suggested that some patients had myocardium in the zone of infarction that could recover, and set the stage for the current aggressive therapies used to reduce ischemia in these patients.

While regional wall motion measurements provide substantial information about the heart, they are only an indirect indicator of myocardial status. The pioneering work of Carr in 1963 demonstrated that an isotope of cesium concentrated in the myocardium to a sufficient degree to permit imaging. Initial investigations utilized ^{137}Cs , a radionuclide with low energy, which cleared slowly from the blood. Images were useful to identify areas of myocardial infarction involving the anterior wall as zones of decreased tracer concentration. Lesions of the posterior wall, however, were not well seen. A better radionuclide for myocardial imaging, potassium-43, was described by Poggendorf and colleagues in 1968. This agent had two important improvements over cesium: higher photon energy and faster blood clearance. The higher photon energy could delineate zones of acute infarction in any surface of the heart. In 1971, Zaret, Strauss, and their colleagues utilized the faster blood clearance of potassium-43 to detect myocardial ischemia. They reasoned that comparing images following injection of the radiopharmaceutical on two occasions, once during increased myocardial oxygen demand and the other at rest, would delineate zones of ischemia. Their pioneering studies in patients with coronary artery disease demonstrated the improved sensitivity of perfusion imaging to that of the exercise electrocardiogram.

Many investigators contributed to the advancement of myocardial perfusion imaging. Thallium 201 was described by Liebowitz and his colleagues, and quickly became the radiopharmaceutical of choice for these perfusion studies. The advent of single photon tomographic imaging, described by Keyes *et al*, allowed more complete data to be recorded, and enhanced the detection of lesions involving the posterior wall of the heart.

Quantitative techniques were developed to permit objective interpretation of these complex studies.

Since ventricular function can be influenced by many factors that occur during everyday events, it seemed worthwhile to record cardiac function as an individual went about their activities of daily living. This interest led Strauss *et al* to develop and validate a device for the ambulatory monitoring of ventricular function. After patients had imaging measurements of ventricular function, a small radionuclide detector was placed in a tight fitting vest-like garment and positioned over the patients left ventricular blood pool. Information about the changes in blood pool activity with each beat were recorded in synchrony with the patients electrocardiogram on a small tape recorder. After several hours of monitoring the tape was retrieved and analyzed for changes in cardiac performance. This instrument was used to define changes in cardiac function with walking, psychiatric stress interviews, sleep apnea, exposure to cold, episodes of anger, and during silent ischemia.

Another perspective on cardiac function could be gleaned from evaluating the substrates used for oxidative metabolism by the heart. Since the heart utilizes fatty acids, several groups of investigators had radiolabeled these agents in an effort to visualize the heart and study its metabolic efficiency. Fatty acid imaging was characterized by rapid uptake, initial high concentration, and rapid clearance of catabolized products from the myocardium. To overcome the rapid clearance, Livni, Elmaleh, Strauss and their colleagues synthesized a branched chain fatty acid that could not undergo beta oxidation. As a result, this agent concentrated in the heart but did not clear, allowing high quality images of the myocardium to be recorded. Changes in metabolism in areas of ischemia and myopathy were identified with this agent.

One of the most exciting developments in this field, however, did not involve the science at all. It involved people. Cardiovascular nuclear medicine attracted a cadre of highly motivated investigators from around the world. These individuals span many disciplines and continue to make great advances in radiopharmaceuticals, imaging devices, and in the clinical applications of these techniques. One major advance utilized radiolabeled antibodies directed against the heavy chain of cardiac myosin for the detection of acute myocyte necrosis. Many of the innovative applications of this radiopharmaceutical were developed here, at the Hospital de Sant Pau by Dr. Carrió and his colleagues.

The synergy of advances in instrumentation, radiopharmaceutical development, and the dedication of clinical investigators assure the continued growth of this field. In addition to antibody imaging some highlights of recent advances include metabolic imaging with the glucose analog Fluorodeoxyglucose to detect ischemia, beta receptor imaging with radiolabeled pindolol, peptide imaging for the detection of venous thrombosis and acute pulmonary embolism, and the direct detection of myocardial hypoxia with

radiolabeled misonidazole analogs. The quality of investigation, coupled with the array of clinical applications, marks cardiovascular nuclear medicine as a dynamic field with a scintillating future. The beat goes on.

CURRICULUM VITAE
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Academic appointments

Assistant Professor of Medicine, Johns Hopkins University School of Medicine	1972-1975
Assistant Professor of Environmental Health, Johns Hopkins University School of Hygiene and Public Health	1972-1975
Associate Professor of Radiology, Johns Hopkins University School of Medicine	1975-1976
Associate Professor of Environmental Health, Johns Hopkins University School of Hygiene and Public Health	1975-1976
Adjunct Clinical Professor in Nuclear Medicine, Massachusetts College of Pharmacy	1977-1992
Associate Professor of Radiology at the Massachusetts General Hospital, Harvard Medical School	1976-1982
Professor of Radiology at the Massachusetts General Hospital, Harvard Medical School	1982-1993

Hospital appointments

Associate Professor in Radiology, Division of Nuclear Medicine, Johns Hopkins University School of Medicine	1975-1976
Associate Professor in Environmental Health, Division of Radiation Health, Johns Hopkins University School of Hygiene and Public Health	1975-1976
Associate Radiologist, Department of Radiology, Division of Nuclear Medicine, Massachusetts General Hospital	1976-1979
Radiologist, Department of Radiology, Division of Nuclear Medicine, Massachusetts General Hospital	1979-1992

Editorial boards

Editorial Board, <i>Circulation</i>	1979-1984
Editorial Board, <i>American Journal of Cardiology</i>	1980
Editorial Board, <i>Journal of Nuclear Medicine</i>	1981-1989
Editorial Board, <i>Journal of American College of Cardiology</i>	1980-1985
Editorial Board, <i>American Journal of Cardiac Imaging</i>	1986
Editorial Board, <i>European Journal of Nuclear Medicine</i>	1988
Editorial Board, <i>The Journal of Nuclear Medicine</i>	1994

Grant support

NHLBI, Heart Imaging with Single Photon Imaging Agents PI: H. William Strauss, MD	1985-1991
Mallinckrodt, Inc. Research Myocardial Imaging Agents PI: H. William Strauss, MD	1982
Cambridge Research Lab Development of Radiolabeled Antibodies for the Imaging of Infectious Disease PI's: H. William Strauss, MD, and Robert Rubin, MD	1984
Capintec, Inc. The Vest PI: H. William Strauss, MD	1985
Johnson & Johnson Imaging of Inflammation and Infection	1985-1992

Original articles

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487
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Acte d'investidura com a
doctor *honoris causa* del doctor
H. William Strauss

4 de maig de 1995



Universitat Autònoma de Barcelona

1. El rector obre l'acte i diu:

Constitueixo aquest claustre, avui dia 4 de maig de 1995, per tal d'investir doctor *honoris causa* el professor H. William Strauss, i demano al doctor Salvador Alegret, secretari general d'aquesta universitat, i al padrí del doctorand, doctor Ignasi Carrió, que el vagin a cercar.

El padrí i el secretari general surten a cercar el nou doctor, que entra a la sala i és rebut a peu dret per tots els assistents.

2. El rector inicia la sessió dient:

Es declara oberta la sessió. Té la paraula el secretari general, que llegirà l'acord pel qual es concedeix el títol de doctor *honoris causa* al professor H. William Strauss.

3. El secretari general procedeix a la lectura de l'acord de la Junta de Govern.

4. El rector dóna la paraula al padrí:

El doctor Ignasi Carrió, padrí del doctorand, té la paraula.

5. El padrí llegeix el seu discurs i conclou amb les paraules següents:

Per tot això, Excel·lentíssim i Magnífic Rector, sol·licito que s'atorgui i confereixi el grau de doctor *honoris causa* al professor H. William Strauss.

6. A continuació, pren la paraula el rector, fa el lliurament del diploma al nou doctor i li imposa la medalla tot dient:

Heu estat designat doctor *honoris causa* per la Junta de Govern de la Universitat Autònoma de Barcelona i, com a símbol, us lliuro aquest diploma i us imposo la medalla de doctor *honoris causa*.

Us admeto i us incorpore al claustre de la Universitat Autònoma de Barcelona.

7. A continuació, el rector dóna la paraula al doctorand:

Té la paraula el professor H. William Strauss, el qual pronunciarà la lliçó magistral en aquest claustre.

8. Lliçó magistral del professor H. William Strauss.

9. Discurs de cloenda del rector.

10. El rector diu:

S'aixeca la sessió.