STATE UNIVERSITY
OF NEW YORK

DOWNSTATE MEDICAL CENTER

BIOPHYSICAL LABORATORY
• DEPARTMENT OF MEDICINE

September 17, 1969

George S. Mirick, M.D.
Scientific Director
The Health Research Council
of the City of New York
Department of Health
455 First Avenue
New York, New York 10016

Dear Dr. Mirick:

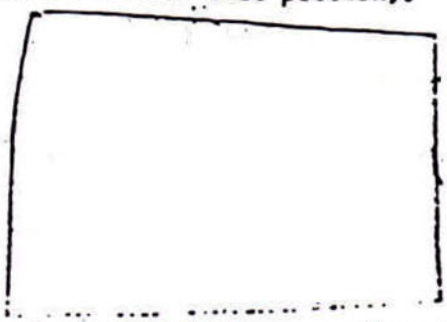
In accord with our telephone conversation of September 16, 1969, I am forwarding a letter describing the success of our "Pittsburgh Experiment" and the request for support it has inspired.

On August 21, 1969, Dr. Freeman Cope and I left for a small company (Nuclear Magnetic Resonance Specialties Corporation) on the outskirts of Pittsburgh with the remote hope that we could measure potassium by NMR spectroscopy and establish, once and for all, that cell potassium is not free in solution as usually supposed but organized in structured cell H_2O and complexed to fixed charges within the cell. Our hopes were remote since K^+ of any kind, cellular or inorganic, had never been measured by NMR and most experts seemed to agree that our prospects were grim. Grim, because out of all the nuclei on the atomic table, its resonance point was among the lowest. Consequently, its signal was expected to be much weaker than could be detected by existing equipment.

We banked our hopes on a superconducting magnet* that Nuclear Magnetic Resonance Specialties Corporation had agreed to make available to us for a few days use. If we could generate large enough magnetic fields, we had a chance. The superconducting magnet was rated for 50,000 gauss (the best of the commercially available electromagnets generate 25,000 gauss), which would permit us to receive the signal at 10 megacycles instead of 2, thereby amplifying our sensitivity 25 times. Other modifications such as the use of a signal pre-amplifier and a time averaging computer when taken together were estimated to produce an additional 10 fold amplification of signal.

Superconducting magnets make use of the absence of electrical resistivity of certain alloys (e.g. niobium zirconium, niobium titanium, niobium tin, etc.) at cryogenic temperatures (e.g. 4.3° Kelvin - achieved by immersion of the solenoid in liquid helium). Zero electrical loss is the result and it is possible to produce magnetic fields with an efficiency that approaches 100%. Conventional electromagnets dissipate most of the energy supplied to the windings as heat. Consequently the fields that can be generated are limited by the heat tolerances of the windings.

We completed the final assembly of the spectrometer and superconducting magnet in the early evening of August 30. At 2:30 A.M., we attempted to find the potassium signal in a saturated solution of K_2CO_3. Needless to say, we were jubilant when our first scan produced a resonance signal almost precisely where we expected to find it. The first NMR measurement of potassium of any kind had been made. (Attached below is a photograph of the K^+ resonance signal as it appeared on our oscilloscope - - an off-resonance beat pattern).



Additional measurements and some controls assured us that we had sufficient sensitivity to measure potassium in biological samples. Using Halobacterium Halobium, selected for its high intracellular potassium content, the first NMR measurements of biologic potassium were made the evening of September 6. Furthermore, the pulsed techniques in our spin-echo spectrometer provided direct evidence (T_2 relaxation measurements) that potassium was complexed to fixed charge groups, and or, solvated by highly structured cell H_2O as we had originally suspected. It is decidedly <u>not</u> in free solution as usually supposed.

Since the superconducting magnet was now needed for other measurements, and we had exhausted the time allotted us, it was at this point that the experiment terminated.

Since no spectrometer-superconducting magnet systems of the type we assembled are available commercially and since no one to the best of our knowledge and the knowledge of Nuclear Magnetic Resonance Specialties Corporation in the continental United States or abroad possesses such an instrument, neither we nor anyone else can pursue our findings. The experiment will remain suspended until someone can assemble the equipment we have described. (See attached manuscript).

Our findings usher in a major revolution in biology and we have only scratched the surface. To suspend our momentum at this point would be unfortunate indeed. Accordingly, I am writing to ask the Health Research Council for the support to equip my laboratory at the State University of New York, Downstate Medical Center, with a High Field Spin Echo Nuclear Magnetic Resonance Spectrometer, so that we can resume work as soon as the spectrometer is constructed. The quoted price for the finished instrumentation by Nuclear Magnetic Resonance Specialties Corporation is $89,000. Although they would prefer to receive the full sum on delivery of the instrument, they have agreed that, if necessary, they will accept a 3-year leasing agreement of $40,000 on delivery and $24,500 in the second and third year. A third alternative would be equally divided payments of $26,666 over a three-year period. Furthermore, if these terms are still too encumbering, I feel fairly

certain Nuclear Magnetic Resonance Specialties can be persuaded to accept a longer term lease-purchase agreement.

Hopeful that the Health Research Council can help us expand the exciting success of a project it has sponsored from infancy, I remain,

Sincerely yours,

Raymond Damadian

Raymond Damadian
Assistant Professor
Department of Internal Medicine

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P.S. I am enclosing a first draft of the manuscript we are submitting to Science for publication. I want to mention that our findings have powerful application in anti-cancer technology. Malignant cells have marked alterations in the physical structure of their protoplasm. To the best of my knowledge, it is generally true that all malignant cells have been marked by elevated cell potassium values and depressed Ca^{++} levels. I am very much interested in the potential of NMR spectroscopy for early non-destructive detection of internal malignancies. To the extent that our primary research objectives will permit, I will make every effort myself and through collaborators, to establish that all tumors can be recognized by their potassium relaxation times or H_2O-proton spectra and proceed with the development of instrumentation and probes that can be used to scan the human body externally for early signs of malignancy. Detection of internal tumors during the earliest stages of their genesis should bring us very close to the total eradication of this disease.

[Next article in the field of MRI by another person not published until 1973 (P.C. Lauterbur, Nature 2042, 1973, 190-191)]