(Special Lecture I)

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The Rise of Human In Vivo Spectroscopy

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MRI and MRS are now fully integrated technologies, but it was not always so. Magnetic field gradients were the bane of traditional spectroscopy, so it was not obvious in the late 1970's that MRS could ever be compatible with a technique that could not exist without them. For us, the hint that chemical shift information was not destroyed by the MRI gradients lay in the observation of "chemical shift artefacts" which manifested as ghosts in a fluorine (^{19}F) MRI done at Nottingham in 1977 (1). Yet there was no compelling reason to do MRS on the body. What was expected of ^{1}H MRS, for example, were mundane fat and water peaks, while MRI had its own problems to solve.

The impetus for localized MRS evolved from phosphorus (^{31}P) spectroscopy studies that were ongoing independently in biochemistry laboratories: groups at Johns Hopkins and Oxford had managed to get live beating rodent hearts into conventional small-bore MR spectrometers and to monitor the energy metabolism under normal and globally ischemic conditions (2). So here was a possible major application: perform localized ^{31}P MRS on the heart or brain, and diagnose ischemia and infarction by measuring the primary energy pool, ATP. But alas, due to the low metabolite concentrations the sensitivity of this experiment was abysmal, 1000-2000 times lower than that of ^{1}H of water (3) in MRI which was still not established. A little relief was provided by the introduction of surface coils in 1980 (4), which provided localization for a study of regional ischemia and the effect of pharmaceutical intervention in the isolated in vivo rabbit heart (5). However, if MRS was ever to be performed on humans, a large bore high-field high-homogeneity magnet was needed.

In 1980 an order was placed for the largest NMR magnet that Oxford Instruments would agree to build for just this purpose. It was a whole-body 1-m bore system with a 2 T target field, and a 1.5 T minimum field, which was what was actually achieved. Smaller bore instruments that could accommodate an arm or a leg were also becoming available for human ^{31}P

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MRS, and one was used for the first patient MRS study, involving a muscular metabolic disorder, in 1981 (6). Meanwhile some very important problems in MRI were solved which had a major impact on localized MRS. For one, the negative refocusing lobe was put on slice-selective excitation (7), and for two, phase-encoding gradients were added as an imaging tool (8). Furthermore, for MRS, the lesson from the ^{19}F MRI and subsequent experiments, and from others was that spatial localization could be done with MRI gradients provided that the gradients were turned-off during acquisition. What followed directly from this realization was the chemical shift imaging (CSI) MRS method, using only phase-encoding gradient pulses followed by a long gradient-less acquisition period (9), and localized MRS methods employing slice selection (DRESS, PRESS, and later, STEAM), or combined slice-selection and phase-encoding gradients (10-13): the basic MRS localization tools we use today.

In 1982, MRI and MRS technologies were combined on the whole-body 1.5 T system permitting both anatomic and physiologic or metabolic studies on the same instrument (14). This was critical because the viability of MRS today depends on the essential role played by MRI in defining anatomically the regions of interest in the body for spectroscopic interrogation. It is also noteworthy of the intimate dependence of MRS on high-field MRI, that if high-field MRI alone were not competitive performance-wise relative to lower field systems, there would be far fewer high-field systems today, and consequently many fewer opportunities for clinical MRS. Thus, it is ironic that the advent of high field MRI systems is a direct result of the desire to perform human MRS, while localized spectroscopy is now only viable because of MRI.

Today, localized ^{1}H MRS is being used in clinical research studies of the brain in dementias, encephalopathies, ischemia, infarction, demyelinating disease, and tumors, to demonstrate neuronal loss and injury and other metabolic abnormalities, and in the prostate to identify cancer. We have recently adopted it to measure creatine in skeletal muscle (15) and in normal and infarcted human myocardium, as a potential marker for viability. MRS studies of nuclei other-than-hydrogen require broadband excitation and detection capabilities on clinical scanners: ongoing work in traditional areas such as ^{31}P and new interest in hyper-polarized gas MRI and sodium MRI, demand that these capabilities be maintained and supported. Another critical issue is to ensure that MRS benefits from the latest technological advances made for MRI, such as phased-arrays and high-speed techniques. For ^{31}P MRS we are continuing our efforts at quantifying energy metabolism in ischemic heart disease (16, 17). One goal is to determine whether combining every known technology, phased arrays, Overhauser enhancement etc, could make the technique clinically routine, by permitting direct imaging of ATP or phosphocreatine in the human heart or body, for example.

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