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The Look-Locker Method in Magnetic Resonance Imaging: A Brief, Personal History

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In 1968, I was an Air Force lieutenant at the Aerospace Research Laboratories (ARL), Wright-Patterson Air Force Base (WPAFB), Dayton, Ohio, having finished my PhD in solid-state physics at the University of Pittsburgh. My thesis was based on measurements and theory of nuclear spin-lattice relaxation time (T1) in the rotating reference frame (T1ρ), applied to gypsum [1], and I was hoping to continue my NMR studies in my Air Force assignment. Indeed, I was allowed to do this because ARL functioned as a pseudo-university and in that vein the researchers were allowed to "follow their dreams" as long as the dreams had general relevance to Air Force needs and resulted in publications. I soon found that ARL was known as the "Ivory Tower" among the other laboratories on WPAFB, so I considered myself blessed. I was also blessed to have Don Locker, an expert in EPR and general equipment design, in the same laboratory. The NMR instrument I inherited was a Varian Model 4200B, of the CW variety, rather than pulsed, and in general CW instruments were used mainly for studies of lineshapes, not T1's. To measure T1, I had to apply a high RF field at resonance to saturate the spins (making magnetization M = 0), then move off resonance for time t while M built up to M(t), and finally sweep back through resonance to measure M(t). This procedure had to be carried out for several values of t, including one of at least 4T1 since we used the common approximation $M(4T1) \approx M(\infty)$. Then we could calculate T1 from $M(t) = M(\infty)(1 - e^{-t/T1})$. For T1 > 20 sec, or so, we could carry out the procedure by hand, but for shorter T1's it was necessary to automate. While thinking of the best way to automate, we realized that more information was available by sweeping the magnetic field back and forth through the resonance with a series of triangular waves, producing a sequence of magnetizations M_0, M_1, M_2,….M_n. During the time τ between each pass, M would partially recover, eventually reaching a steady-state value if n were high enough. After a waiting time T, the sequence of n passes could be repeated and averaged to improve signal-to-noise. The whole experiment could be carried out by simply adding a tone-burst generator to the magnetic-field sweep coils. The mathematical description of this process was not too complex, especially for $T \geq 4T1$, so Don and I measured several different kinds of samples and then published a paper on the method [2]. Not long after that, I realized that with a slightly more complicated analysis we could relate M_0 to $M(\infty)$, and this could result in considerable time saving since we no longer had to wait 4T1 for any of the points. A two-page paper on this improvement was published by Don and myself in 1970 [3], but neither paper seemed to generate much interest. By that time, I had satisfied my Air Force commitment but stayed at ARL as an onsite contractor sponsored by the University of Dayton.

About this same time a few researchers in various parts of the world began using NMR to image discrete volumes of nuclei in materials. The concept was simple: by applying time-varying, 3-dimensional magnetic-field gradients, only a particular small volume of spins in the sample would be in resonance at a given time. Of course, making this concept practical was extremely difficult, and it wasn't until 1973 that future Nobel Laureates Paul Lauterbur [4] and Peter Mansfield [5], working independently, managed to image some simple volumes. I remember that Don and I read Lauterbur's paper and concluded that it was quite interesting but would likely never have commercial viability. Wow, were we wrong! But in any case, the luster of ARL was beginning to wane, and in fact the laboratory was closed in 1975 because it was evidently too much of an Ivory Tower. Don and I ended up in different laboratories at WPAFB and I began doing electrical measurements, both of us leaving magnetic resonance behind. However, unknown to either of us, the seed we had planted in 1970 had begun to germinate in the 1990s. Indeed, time saving in medical imaging had become extremely important (e.g., consider a beating heart), and our technique was soon given its own name, "Look-Locker". I first learned of this on Oct 9, 2014, when Research Gate sent an e-mail stating that our 1970 paper [2] had been cited by M. Varela et al, in a paper "Cerebral Blood Flow Measurements in Infants Using Look-Locker Arterial Spin Labeling" [6]. Of course, I was quite shocked and thrilled and immediately e-mailed Don, who is now living in Seattle. Going online, I found that about 2300 papers (Google Scholar) and about 140 patents (freepatentsonline.com) contained the term "Look-Locker" [7]. On the other hand, there were only about 500 citations of the 1970 paper itself (Google Scholar), showing that the term "Look-Locker" had attained a life of its own. From a practical point of view, our 1970 basic research that occurred in ARL, the "Ivory Tower", has likely paid for itself many times over and possibly led to better health for many Air Force, Army, and Navy veterans. Moreover, I suspect there are many other achievements at ARL that have had similar histories. The cost of basic research is small, but the long-term payoff can be huge.

1. D.C. Look and I.J. Lowe, "Nuclear Magnetic Dipole-Dipole Relaxation along the Static and Rotating Magnetic Fields: Application to Gypsum", Journal of Chemical Physics **44**, 2995 - 3000 (1966).
2. D.C. Look and D.R. Locker, "Nuclear Spin-lattice Measurements by Tone-burst Modulation", Physical Review Letters **20**, 987 - 989 (1968).
3. D.C. Look and D.R. Locker, "Time Saving in Measurement of NMR and EPR Relaxation Times", Review of Scientific Instruments **41**, 250 - 251 (1970).
4. P.C. Lauterbur, "Image Formation by Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance", Nature **242**, 190 – 191 (1973).
5. P. Mansfield and P.K. Grannell, "NMR 'Diffraction' in Solids?", Journal of Physics C **6**, L422 (1973).
6. M. Varela, E.T. Petersen, X. Golay, and J.V. Hajnal, "Cerebral Blood Flow Measurements in Infants Using Look-Locker Arterial Spin Labeling", Journal of Magnetic Resonance Imaging DOI: 10.1002/jmri.24716 (2014).
7. For example, A.J. Freeman, P.A. Gowland, and P. Mansfield, "Optimization of the Ultrafast Look-Locker Echo-Planar Imaging T1 Mapping Sequence", Magnetic Resonance Imaging **16**, 765 – 772 (1998).