Q: What is your background and how did you get into the MRI field?

Paul Bottomley: I studied Physics at Monash University in Australia. For the Bachelor of Science Honors degree, which takes an extra year, we had to do a research project and write a short thesis (analogous to a Master's degree in the USA). Essentially all the research in the Monash Physics department at that time involved measuring physical properties of metal alloys at liquid helium temperatures, which seemed to me to have little relevance to the real world. All, except for a project on using NMR as a probe to see how anesthetics work. I wanted to do something useful or relevant, so this project seemed to best fit the bill. Many small molecules (chloroform, halothane, Nitrogen, N_2O, Xe) are anesthetics and also form clathrate compounds with water. In these compounds, the water molecules form hydrogen-bonded cages around the anesthetic molecule. The gas pressure at which these clathrates are stable is directly proportional to the partial pressure required to produce anesthesia. This observation by Linus Pauling in 1961 led to his hypothesis that the formation of these structures blocked conduction pathways, mechanistically producing anesthesia.

So, in my Physics Honors project I used NMR to look at the water mobility in Xenon clathrate. I wrote a first-author paper on this work which was published in Molecular Physics. That got me a 1^{st} class BSc Honors degree in 1974, which came with an automatic qualification to be admitted into a PhD program in Australia. But I wanted to travel, so I applied to universities in England, Canada (Vancouver) and the USA (Harvard). One letter was to Professor Raymond Andrew who was the chairman of Physics at Nottingham as well as being famous in NMR for his book and the invention of magic angle spinning. He said he was just starting a new project on NMR imaging, and offered me a position as a PhD student working on the project. He also offered me financial support as a 'Demonstrator' (or Tutor) in Physics, starting in 1975. The UK had the same Honors system as Australia and I am sure that having published in NMR already as an undergraduate was an important factor in Andrew's decision. I accepted the offer and joined the original Nottingham group of Raymond Andrew, Bill Moore, Waldo Hinshaw and Neil Holland. I only became aware of Peter Mansfield's MRI group after I arrived in 1975 (I attended Mansfield's lectures on quantum mechanics).

The only other place that responded with potential financial support was University College in London, but that was not NMR-specific. Universities in the US required that I first do a Master's degree before I could be accepted into their PhD programs, and I wasn't going to do that, having already qualified.

Q: Why did you choose MRI research as your career?

Paul Bottomley: "MRI" or "MRI research" was not a career when I started. We created it :). Originally, I wanted to be a Chemist, but that required rote learning of all the types of chemical reactions which was very boring. I switched to Physics as the path of least resistance because I got good marks, and because you could derive everything from just a handful of equations and didn't have to bother with all the memorization. Also, I suppose I was fairly OK with applied math and calculus.

Q: When was your first SMRM/SMRI/ISMRM meeting?

Paul Bottomley: I attended the first meetings of both SMRM and SMRI which were held in 1982 and 1983. I was a charter member of both societies.

It should be noted that there were two very similar MRI symposia in the 2 years prior to 1982, whereupon the 1982 SMRM might be considered the 3rd annual meeting. These were:

1. The Nuclear Magnetic Resonance Imaging Symposium, Nashville, USA, 26-27 October, 1980, with proceedings published in J Comp Assist Tomogr 1981; 5: 296-298. This was hosted by Leon Partain et al.
2. International Symposium on NMR Imaging, Winston-Salem NC: Bowman Gray School of Medicine, Wake Forest University Oct 1-3 1982. The proceedings published in a book: Witcofski, RL, Karstaedt N, Partain CL, eds. NMR Imaging: NMR Imaging: Proceedings of an International Symposium on NMR Imaging. Winston-Salem NC: Bowman Gray School of Medicine, Wake Forest University 1982.

I gave talks at both these meetings. It was at this second symposium where discussions and agreements began in earnest to form the two societies (SMRM and SMRI).

Q: What is your memory of your first SRMR/SMRI/ISMRM meeting?

Paul Bottomley: I attended the 1st annual meeting of both SMRM and SMRI.

SMRM, 1st Annual Meeting, Boston 16-18 Aug 1982, in the Park Plaza Hotel

I chaired the session on instrumentation at this meeting. There may have been ~300 attendees. At this time, Bill Edelstein and I, working together at GE, were making head and body images on a 0.12T resistive system (initially presented at the Winston-Salem meeting), and we were trying to find a sequence and timing of TR, TE and other parameters that optimized contrast. We fixed a problem with T2 by introducing balanced read-out gradients to move the spin-echo to where it was supposed to be (before that you got an echo as soon as you turn on the gradient). However, we were still not getting the GM & WM contrast with partial saturation, which we should be seeing and others were seeing with inversion recovery. Bill started calculating contrast, and at some point, we realized the problem was with slice selection. We presented a paper comparing contrast with different sequences and introduced the "contrast-to-noise" ratio at the meeting (also publishing it in JCAT). The conference paper was:

1. "Edelstein WA, Bottomley PA, Hart HR, Leue WM, Smith LS, Schenck JF, Redington RW. Signal noise and contrast in NMR imaging. In: Scientific Program, Society of Magnetic Resonance in Medicine 1st Annual Meeting, Boston, MA, Aug. 16-18, 1982. Berkeley CA: Society of Magnetic Resonance in Medicine, 1982 p. 52-53.

SMRI, 1st Annual Meeting, Colorado Springs CO, Feb 14-18 1983, Broadmoor Hotel

I remember feeling like we'd struck gold. At this meeting, we introduced 1.5 Tesla MRI which basically blew away all of the low-field work (at 0.3T or much lower) in terms of image quality, SNR, spatial resolution etc. On top of that, the current "wisdom" of the time was that MRI at 1.5T was not possible. I remember being in a kind of glowing daze for the entire meeting–basically, over the moon. I had just gotten the first "holy shit" 1.5 T images that I presented in my 2012 Mansfield Lecture two weeks earlier, and this was the first presentation at a scientific meeting. We gave 3 papers:

1. Bottomley PA. Medical imaging by nuclear magnetic resonance. In: Society for magnetic Resonance Imaging, first annual meeting, Program and Abstracts, Feb. 14-18, 1983, Colorado Springs CO. McClean VA: SMRI, 1983.
2. Bottomley, PA, Hart HR, Edelstein WA, Schenck JF, Smith LS, Mueller O, Vatis D, and Redington RW. Head imaging and spectroscopy at 1.5 Tesla. In: Society for magnetic Resonance Imaging, first annual meeting, Program and Abstracts, Feb. 14-18, 1983, Colorado Springs CO. McClean VA: SMRI, 1983.
3. Schenck JF, Hart HR, Bottomley PA, Edelstein WA, Hussain MA, Redington RW. NMR imaging at very high fields: issues and theories, results and conjectures. In: Society for magnetic Resonance Imaging, first annual meeting, Program and Abstracts, Feb. 14-18, 1983, Colorado Springs CO. McClean VA: SMRI, 1983.

In addition, I gave an invited talk, "Principles of NMR imaging"; a Physics Tutorial; and chaired the Advance Lectures Session.

The Hotel had a nice big open swimming pool, in a courtyard, with posters or exhibits at one end, although there was other indoor space with exhibits. Among other things, Philips presented their invention of the CD for data storage (and music!), which was a revolution at that time. The CD was invented in 1979 but 1st shown publicly in late 1982, just a few months before the meeting. I had never seen them before. I waxed enthusiasm to my boss at GE about it. He said: "Oh yeah we looked at that, but the digital dots used for the encoding grow over". After the meeting I went skiing for a day. There were trainee sessions at this meeting and I participated. The lectures were organized into: introductory lectures, advanced lectures, contributed papers, and tutorials. I still have the program.

Q: What were the challenges 30 years ago VS now that the field evolved?

Paul Bottomley: The challenges were that MRI instrumentation was a work in progress. The best field strength to work at was unresolved. SNR was basically a black art: you couldn't calculate it analytically, and mostly you didn't know where it went. Image contrast could be calculated but not predicted because of what you got when you turned on the B1. There were no self-shielded gradient coils so eddy currents precluded techniques requiring phase sensitivity. Oh, and no

phased arrays. The MRI pulse sequences and localization protocols were not fully worked out. The clinical applications were unclear. What was the killer App? …and we didn't even have Apps. It was great! Being right at the ground level of the technology, everything we did was exciting and could have direct impact on clinical systems. But of course, that is partly in hind-sight: at the time you typically don't know if a problem is solvable, or where it will lead.

Q: Would you give some advice to young/new MRI researchers on how they could potentially make new ground-breaking work today?

Paul Bottomley: Do something different. In science it always looks like all the "good stuff" has been done. If you want to do something ground-breaking, you need to head off in a different direction. It is choosing that direction that counts. When MRI started, the focus was on advancing the instrumentation and methodology. Now we are 50 years later and it is unusual in the imaging field that so many ISMRM members are still focused on that. But it must be recognized that the returns are smaller. The best question to ask when you start a project is, "what will I have if I am successful beyond my wildest dreams?" If the answer is a tiny gain in SNR or a different reconstruction or a label for a particle that has no reason to go into a person, but it will take you 2 or 3 years, then maybe it's time for a different direction.

Also, researchers often adopt a forward engineering approach. We have a method, we work on improving it to move forward, or we look for an application of it. Instead, try a reverse engineering it. Ask: "what actually do I want to end up with?" For example, maybe you want to use MRI to diagnose Alzheimer's disease with 99.9% certainty from a single exam. You want to become the gold standard. OK, so you look at the current gold standard and see what it's measuring. Then you take everything you can think of that is linked or can be linked to that, make a protocol to measure it all, and see where you get. If you fall short you can throw in other common associated data. Such an approach, these days, is well-suited to machine learning, which we didn't have 50 years ago–so that's new, so do something with it.