

Q: This year, we are celebrating the 40th anniversary of ISMRM. You organized one of our society's early meetings, i.e., the 1987's SMRM meeting in New York City. Can you tell us something about that meeting?

David Hoult: Do you really want to know about this? It wasn't very pleasant, actually. I mean, I was asked to do the meeting. I accepted. People like Paul Lauterbur, Thomas Budinger, and George Radda asked me to do it. But when it came down to actually doing it, it was a nightmare. It ended up with, I think, only \$125 in the bank account at one point. Not my fault. Then the secretary resigned when the meeting was coming up. There were massive problems with unions in the hotel. In particular, the unions demanded that they would not allow others to do some work. For example, the electricians had to man the slide projectors. Not surprisingly, the slide projection was a disaster. I ended up typing and retyping most of the manuscripts *myself*, which involved incredibly long hours of work to put it all together. When we progressed into the meeting, we finally managed to get the finances into some decent order. But I had no sense of accomplishment at the end of it whatsoever. I just felt completely, totally exhausted by the whole thing. The last straw was that people insisted on giving me a fancy limousine to get to the airport. I was exhausted, and the limousine's suspension was broken. I was just about to throw up. As far as I was concerned, that meeting is something I would rather not remember very many details of.

Q: How did these early meetings look like? How different were they compared to today?

David Hoult: I don't remember that there were any sort of parallel or education sessions. The meeting itself was the education – it was sufficiently small. The main competitor in those days was the Experimental NMR Conference (ENC), which was just about everything, including improvements in techniques, methods, and so on. The first SMRM meeting in Boston was a fledgling meeting. It was very unusual to bring a mix of basic scientists and people involved in medical research into a single meeting. There were about 400 people in the Boston meeting, which was quite impressive. I don't think anybody expected that number. There was beginning to be a lot of interest in MRI, which was then an offshoot of NMR spectroscopy. It was true! Much of the preliminary work that led to MRI had been done in the NMR spectroscopic field. It didn't come out of nowhere, it evolved. So, it was a relatively small conference. You were able to find the people that you wanted to talk to. You sat down with them, just talk and talk, exploring wild ideas.

Q: How much research was on the clinical side, and how did the clinical research evolve?

David Hoult: That depends on your definition of "clinical". With the modern understanding of clinical MRI research, you really need to have a scanner, right? Well, scanners didn't exist as

such, not as what we know today. There were instruments that were built mostly at home. There were a few beginning companies like Disonics. But most of the investigations were using small magnets looking at peripheral things like hands with what you would call appalling quality today.

It was just the beginning of the exploration. And that exploration was an ongoing process. It started in the 1950s, well before imaging. There was always this interest by people in using NMR spectroscopy for investigating physiological and biological concerns for medical purposes – not *clinical* purposes, medical purposes. I think that's the key distinction. We are, after all, the I.S.M.R. in *Medicine*. Images had been produced by 1960 at NIH by a man called Kudracev using a very crude method. Researchers in Japan produced images in 1972/73. If you want to call a 1-dimensional (1D) projection imaging, that has been in use since 1952. I used 1D projection as a graduate student at the end of 1960s, when we were investigating the homogeneity of the first superconducting magnets in Europe. When we were looking at the B_1 homogeneity of the coils, we would put a linear gradient on. So, there's a huge history that goes back. It's not a sudden leap. Lauterbur's paper came along, which extended the 1D method to 2D. That was really the major change, from methods of getting 1D information to an efficient method of getting 2D information. But X-rays could do that. The real challenge when applying to the human body was, of course, dealing with the third dimension.

As I said, I had been working in Oxford with the first superconducting NMR magnet in Europe. By sheer good luck, in a chance conversation over tea in the afternoon with another group, we realized that it should be possible to *do in vivo* NMR spectroscopy. We should be able to get information, for example, out of a muscle. The rest is history. We got *in vivo* NMR signals from frog muscle (Hoult et al., "Observation of tissue metabolites using ^{31}P nuclear magnetic resonance," *Nature*, 1974). We were immediately very, very heavily into that. I think it's fair to say that paper was the forerunner of the use of magnetic resonance spectroscopy (MRS) in humans. After we published that paper, every muscle physiologist in the country wanted to get on the machine that we had. You must realize that it was a *wide-bore* of about 2.5 cm in diameter!

Q: How did you get into the field of MRI?

David Hoult: First of all, I was a radio amateur as a teenager. I got my radio amateur licence. I was passionately interested in electronics. I went to Oxford and did a degree in physics specializing, though, in electronics. One of my tutors was a gentleman called Howard Hill, who worked with the professor of physical chemistry, Rex Richards, who later became Sir Rex Richards. And by the way, he got his knighthood for his service to NMR, the most unusual citation of a knight I've ever heard of. He was a giant in NMR in Europe. Howard worked for him but was

leaving to Varian, who had just begun to produce superconducting magnets. Rex wanted somebody who knew electronics, but also a physicist to work on the use of superconducting magnets and the spectrometer from the ground up, trying to analyze the whole thing. So, I went into the physical chemistry department and soon realized that there were massive challenges there, certainly enough for far more than a doctorate. About a year into it, Rex really was fed up to the back teeth with being full professor of physical chemistry, and decided there was a future for NMR in biochemistry. He resigned from his position and moved the entire group into the biochemistry department. That was *terra incognita* – completely unknown what we were going into. But it worked out. And that's how I began to get involved and had to interact with medical problems because I was in a biochemistry department – an eminent biochemistry department with a Nobel Laureate, Rodney Porter, heading it.

Nobel Laureate Dorothy Hodgkin, who was in another department, interacted closely as well. All this background there and out of that interaction, here was me building this machine and building the electronics. It was all homemade. Almost every single thing was homemade. There were things like frequency synthesizers, which were gigantic boxes. No computers at that point. Recorders were used for recording free induction decays (FIDs). You carried them over to the computing lab. You got a spectrum of a 1000-point FID in a day or two days later. Computers cost a dollar a bit, *a bit!* So that's fundamentally how I got into it. We finally, after a tremendous number of problems, got the magnet working, got the instrumentation working, had a full understanding of it, and made all sorts of innovations in the instrumentation.

Paul Lauterbur published a paper closely followed by another paper from the Mansfield group on how to get slice selection, which changed the whole perception of the field. But there was just one problem: I could see intuitively that the papers were wrong! There was another problem: I had just got my doctorate, how could I tell Lauterbur and Mansfield, two full professors, that they were wrong? I had to do an experiment. However, the MRI machine was besieged by physiologists. It was very difficult to get time on the machine. So, it took a long time to do it. Eventually, in 1975 or 1976, I set up an experiment and was able to show the original method didn't work. I further showed that if you made an echo by reversing the gradients then you really could get slice selection. But there was no hurry about this. This was just academic interest. This oddball idea of getting pictures of the body was considered a minor offshoot of NMR.

Paul Lauterbur told us that he was coming to Europe from Stony Brook in the summer. Paul came to the lab. I showed him what I'd done. I said, "This paper of yours on slice selection, I don't think it's right and let me show you." So, I was kneeling down to get at some of the things on the probe

and so on to get the machine working, and showed my experiment to Paul. Now, Paul, as you know, was a big man, right? There was me kneeling down, and Paul looming over me, imitating my British accent, "You're telling me I've been a bloody fool, aren't you?" Imagine, there were this senior professor and a young postdoc. How did you reply to something like that? It's like my life in my hands. I looked up at him and said, "Actually, yes!" Paul laughed and said "You're absolutely right! Let's collaborate." That was just how we established a very firm friendship and collaboration from that point on. We sent the manuscript out, no hurry for publication, to the *Journal of Magnetic Resonance*. But it got lost in the mail. It took about two-and-a-half years to get it published because we had to resend it a year later when we realized what was happening. Can you begin to see the lack of any pressure to publish?—It was far more important to publish something that was serious, deep, and right, rather than the latest increment. Anyway, that was how I got involved in the field of MRI. But, unfortunately, Rex decided that NMR spectroscopy was far more important than getting pictures could ever be. He's not the only one who chose that either. If I wanted to carry on with imaging. It was quite clear I had to get out of Britain. The field was way too crowded there. I went to the NIH and carried on doing research on this rather esoteric topic.

Q: You mentioned a funny story about superconducting magnets. What was it?

David Hoult: We were working with the fledgling Oxford Instruments Company. They were working out of a basement initially before they managed to get some sort of production line working. We struggled and struggled with the magnet. We eventually found out that we had to remove the joints in the superconducting wires and pull them out of the strong magnetic field to get them to work. So, on the top of the magnet, there were a set of poles where the wires came up. One night we got the superconducting magnet working. We just put a little sign on the magnet saying "Magnet On" despite that the magnetic field inside was 7.5 tesla. The next morning when I walked to the lab, I heard an old man, the cleaner, screaming "There's a ghost! There's a ghost! Help!" I stopped him and held him. He was shaking and kept saying there was a ghost in the room. I said, "Show me." So, we went down to the room where he said: "It grabbed it." There, attached to the superconducting magnet were his mop and his bucket of water for cleaning the floor. And we learned that you had to be careful with the magnet. We had no non-magnetic tools. They didn't exist then. So, you had to be doubly careful.

Q: Can you give some advice to the new researchers in our society on how they could make new groundbreaking work?

David Hoult: That's a really tough question. When you are in a very mature field, doing groundbreaking work is a very difficult thing to do. You know, when it's a new field, you've got the

cream on the cake that's relatively easy to scoop out. My advice is that you've got to be really certain that you understand the subject from the bottom up. Let me explain what I mean by that. The goal of an undergraduate is quite frankly passing exams.-It's not supposed to be, but those are your main goals. What do you have to do? You have to memorize, memorize, and memorize. Then, you will pass the exam. But, as you move into research as a graduate, that mentality will not help you. You really have to understand the subject to a deep level on your own terms not just on what the textbook says because textbooks sometimes skip things. What's easy for the author of a textbook may be difficult for you. The next piece of advice is: don't specialize too much. Butler once said the definition of a specialist is somebody who knows more and more about less and less until he/she knows everything about nothing. So, make sure you understand the subject. Then get different viewpoints. You come in from different sides, and that will give you insights.

Q: What are the biggest challenges in your career? How did you overcome them? What advice you can give to the new researchers of our society?

David Hault: The biggest challenge I had is when you cross a discipline, it can be very difficult to convince people, who have got a considerable background in their own field but not a sufficiently large one in yours, that there are things that are simply not correct. It can be particularly difficult if those people are very eminent. It's a real problem that you face when crossing disciplines. You have to be very careful yourself that you don't fall into that trap. Let me give you an example, which is magnetic resonance imaging supposedly using radio waves. This is so indescribably wrong from a classical physics point of view, or from an electrical engineering point of view. But when you approach the idea from the view of quantum mechanics, and you're so steeped in quantum mechanics that you don't really know the classical theory, obviously this has got to be right because you've got energy levels with transitions, so you must be able to get emissions from them. Then you've got Nobel Prize winners saying this. How do you counteract it? What can you do? The problem is there is a pecking order in science, isn't-there? Theoretical physicists, are arguably on the top of that. Engineers come relatively low down on the pecking order. My advice to anybody in that situation is you've got to do an experiment to prove your point. So, I did the experiments with a very talented undergraduate from Memorial University, who was working with me at the Canadian National Research Council for the summer. We proved it experimentally and I proved it theoretically as well. But it took a lot of time for that to sink in and to convince people.