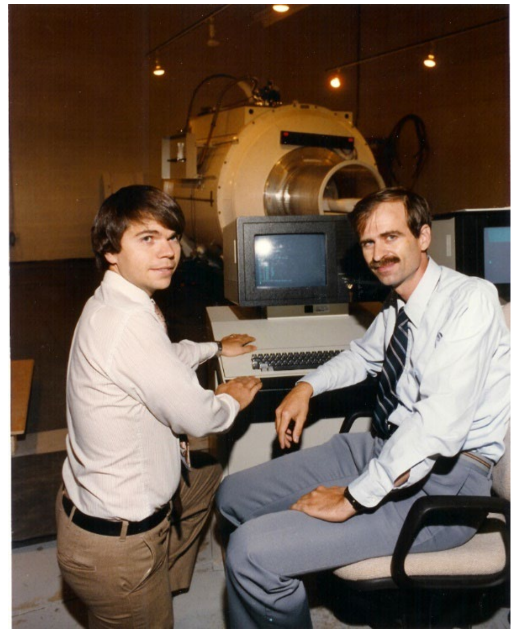
Q: How did you get into the MRI field? What was your educational background? Why did you choose MRI research?

Mark Haacke: Thank you for this opportunity to share some of these early thoughts with you and others at the ISMRM 2022. I graduated in high energy physics at the University of Toronto in 1978 and did a post-doc in the physics department at Case Western Reserve University (CWRU) with Les Foldy, who is famous for the Foldy-Wouthuysen transformation in relativistic quantum mechanics, and Bob Brown, a long time colleague and Distinguished Professor, until 1981. Interestingly, just before I left for my next job, Prof. Emeritus Robert S. Shankland donated his vast physics library to an auction at the university. I remember arriving late and there weren't too many books left but there was an old book in pretty good shape called NMR by Raymond Andrew, who, of course, was the first Editor of our Journal MRM. That was the first book published in NMR (MRI had not yet been conceived by Paul Lauterbur and Peter Mansfield). At this point, I didn't know that I was going to end up in the MRI field. In any case, I offered a dollar for it and no one else bid on it. I picked it up prior to heading to Pittsburgh for a two-year stint as a geophysicist with Gulf Research and Development Company from 1981-1983.

While there, I worked on several interesting projects; one of them was a pioneering concept of imaging trapped gas far below the surface of the earth using P and S waves. These two waves are longitudinal and transverse seismic waves and travel at different speeds. So, you can use that differential to do imaging. This is something that might be of interest to everybody, the students particularly. There was a very interesting work published, I think in Scientific American back about that time, on crabs deep in the ocean. These crabs basically can't see. The question was how can they possibly capture their prey if they can't see? It turns out that they have two sets of hairs on their claws, one of them sensitive to P waves and the other sensitive to S waves. So, in some way, nature invented imaging about half a billion years before we ever thought about it. That always fascinated me!

And the last project I worked on at Gulf was tomographic imaging in geophysics, which is really where I first cut my teeth on imaging. But, about that time period, 1983, the market fell out of the oil industry. Gulf Research ended up being sold, I think, to Chevron and much of the company moved south to Texas. When I saw the writing on the wall, I decided to come back to Cleveland, where my wife was studying for medical school and we had just had our first son, and I took up a job at Picker International. Picker had a long history in imaging including x-rays and CT and it was just beginning to enter the field of MRI.

At that time, an interesting group of people were there, including John Patrick, Gordon Demeester and none other than Neil Holland from Nottingham. They were gearing up to produce superconducting 0.5T systems from the early 0.15T resistive systems that had been the early mainstay.



John Patrick and Mark Haacke circa 1984

When I started, I was perhaps the 5th person in MRI there. We moved to a new building about a month after my arrival in 1983 and I recall a lunch with about 15 people. [Within a year there would be 150 people at this bustling MR division of Picker.] Given that there was but one table, I asked everyone to tell us something about themselves and how long they had been there. They all talked about their background and it turned out that no one had been there longer than two weeks. Surprisingly, I found myself the senior MR physicist present having been there just one month. That's how new MRI was in those days. There weren't really a lot of people in MRI at that time. Later, I asked Bob Brown from CWRU to join me for technical discussions and Bob quickly became an expert in MRI and to this day remains a good friend. We actually just celebrated his 80th birthday last October (2021) in Cleveland. He's been doing MRI pretty much as long as I have.

Another interesting thing about those times is that computers were dramatically slower and much, much less powerful than today. I remember Frank Bearden, a computer science expert, trying to speed up image reconstruction using the FFT. Computers were so slow in those days that it took several minutes to reconstruct the images. Computer speed was the real challenge of the day. I recall one time Frank came running back to say he had gotten the images to reconstruct in less than a minute using a special array processor. We had a big party that day. Computer memory was another problem. I started pushing for 3D imaging from the very day I arrived. We were only doing imaging with a matrix size of 128x128 (1/64 MB) in those days. But still the amount of data I had was increasing up to the level of many megabytes. We got a giant hard disk for data storage, which was about a foot in diameter and cost $2000 back in the mid 1980s. You have to realize that the value of such money has increased at least by a factor of at least 10 to date with inflation.

There was no way back then for us to find and afford a device with storage space as large as the thumb drives we have today (e.g., 64 GB).

By the way, I have about a TB storage space on my current computer. I still fill it up with data and constantly have to move my images back onto a hard disk. We've been doing something today called MICRO imaging. We've been imaging vessels using susceptibility weighted imaging (SWI) using an ultra small particle iron oxide (USPIO). We can now visualize vessels as small as 50 – 100 microns, i.e., the thickness of human hair and have recently published a paper imaging the vessels of the hippocampus *in vivo*. For this project, we sometimes use matrices as large as 4096 x 4096, i.e., 1024 times larger than the 128x128 images we acquired in 1980s.

Another challenge at that time was the gradient strength in the MRI scanners. When we started, we had only 6 mT/m! Finally, we got this up to 10mT/m by the mid-1980s. Even with these gradients, I recall having a student image the vessel wall of an aorta using a spin echo sequence with a resolution of roughly 80 microns. I think it took us about 4 hours to do that overnight. The data matched with the ultrasound impedance profile very well. Imagine what you could do today with 80 mT/m or higher! To the young students and faculty, I say to you, think outside the box to discover what is really possible.

In those days, with the gradients we had, I was developing Hybrid echo planar imaging (EPI) using oscillating gradients. The gradients were still strong enough to allow me sweeping through 5 lines in k-space. The resultant image reconstruction was very challenging because of the sinusoidal sampling trajectory in k-space. I had to develop a new method of phase shift reconstruction to avoid aliasing (now reconstruction times became even longer). So, we were doing that type of fast imaging at 1 cubic millimeter in 1985. Here is another important story for the students. You can be precocious in what you're doing, but it could be 10 years before the rest of the world catches up to you! That's because it's hard to take these methods and put them into the clinical environment, even if they work. There would be a lot of inertia and the companies might have to get FDA approval for these methods. So even if you publish a great paper, it may not get adopted unless you spend a lot of time trying to get the work to the next level. I think that's something to bear in mind. It depends how important what you did is and if you have the energy to follow through with it to make it commercially viable.

I remember doing 1mm isotropic 3D imaging of the brain in 1985. One day, while I was trying this fast imaging in the heart, Dr. Ralph Alfidi, Chairman of Radiology at University Hospitals (across the street from and partners with CWRU) saw me doing this when he came to see about buying an MRI machine from Picker. A week later he called me and asked me to join his Department back again at CWRU.

At that time, I had 6 or 7 patents already at Picker. Those two years were so fruitful because I had the entire field to myself to discover new things without a lot of competition. I was like a little kid on Sea Shell Island near Sanibel having all the best selection to choose from at my disposal. It was a lot of fun and a very dynamic time. At that point I knew I had already fallen in love with MRI, and that was probably what I was going to work on the rest of my life.

Q: When was your first SMRM/SMRI/ISMRM Annual Meeting? What is your memory of it?

Mark Haacke: My first abstracts were presented when I was at Picker in 1984 at the second annual SMRI at the Grenelefe resort, in Orlando. It was quite memorable because I had expected to go down there and be able to wear my shorts and go swimming. When I got there there was a snowstorm, and I was totally unprepared for that. Nevertheless, the meeting was inside of course. The meeting itself was quite broad given that there were only about 100 or so people there. It was more like a workshop than what we would think of as an annual meeting today. It was the coming together of an early group of people in NMR before they really knew NMR would explode. I remember a very famous fellow AV Lakshminarayanan who went by the name Lak because of his long name. He had been famous in CT for having created the M filter for Radon transform reconstruction and he was also at Picker when I first got there. And Bill (William) Moore from University of Nottingham was there, whom I met for the first and only time, as he died shortly thereafter. David Kramer from Technicare (a competitor to Picker) asked me a very interesting question. As you know, in the early days radial sampling was the norm. Then Cartesian sampling really came into play because (despite its own limitations) it was much easier to do and had less reconstruction issues than the Radon transform. David mused: “Do you think radial sampling and reconstruction will make a comeback?” Radial sampling has come and gone several times in the history of MRI. It has unique applications. One cool thing about radial sampling is that you can get any field of view you want by setting the sampling rate in the readout appropriately. That reminds me of a cute story, that Ian Young (I think) actually wrote a patent to be able to image elephants, which was called the MR Room.

At this time, my focus had been on fast imaging using Hybrid EPI imaging and also developing short TR imaging. The early pioneer of short TR low flip angle imaging was actually Ian Young. (Jens Frahm and Axel Haase were the ones who really pioneered its further development and adoption.) I had done some extensive historical searches on fast imaging at that time as an expert in the field regarding some patent litigation. What I found was really amazing. There had been even earlier work maybe late 1970s or early 1980s on fast imaging using steady state free precession (SSFP). I should make a comment here for those of you who haven't read the papers by Bloch and Purcell recently. You should go back and read them because those papers are so precocious. They have derived some formulas when they looked at the limits of continuous RF pulses, which match what we know about SSFP and are prescient to almost everything we were about to rediscover in the imaging world.

I also did a lot of work on water/fat imaging and published a review on this around 1986 that included the three-point Dixon method.

A third project that actually led to a breakthrough in MR angiography was developing a method to remove ghosting artifacts for resistive systems. In the mornings, when people first got to work early to scan, they got good results. But by around 9:00am and after, the results got progressively worse. The question was: "Why was that?" Well, that was because the resonance frequencies were changing, which, of course, led to ghosting artifacts or aliasing artifacts. It turned out that the power supply was not uniform and there was a surge in use of power that caused a temporal variation of the magnetic field. My job was to solve that problem. So, I figured out a way to map the frequency shifts and remove the ghosting artifacts by correcting the shifts. But that didn't last very long because we had literally within a few months switched over completely to superconducting systems.

However, that experience taught me a lot about removing sources of aliasing, or ghosting caused by motion or pulsative flow, as did the interpolation method I mentioned earlier about Hybrid EPI imaging. These things all fell together to look for a means to eliminate phase variation which is when I came up with the concept of flow compensation gradients, leading to the ability to do MR angiography. In the early days, if you actually did gradient echo imaging and even spin echo imaging, you couldn't see any blood vessels. And if you did, it was just a ghosting artifact from blood vessels.

After that, I have actually spent much of my academic life studying neurovascular diseases, using MRA methods and MRV methods (including SWI and QSM for example). I presented the first images of the pulmonary vasculature at the RSNA in 1986 using flow compensation gradients with a spin echo sequence. That was a major breakthrough. I knew that this was a critically important direction. It wasn't long after that I met James Potchen; we had barely started doing MRA. Sitting up in the bleachers watching a basketball game after one of the MRA Club meetings, we decided to write a book on MRA (the first of its kind about 1989) because within two or three years, everybody was studying MRA.

Maybe this is worth another story. Don't give up on your work if you know it is important. We almost all get comments and critiques from reviewers because the important thing is people see things from a different viewpoint, and that usually helps you improve the quality of your work. Don't be horribly disappointed. But in this particular case, I originally submitted our work on flow compensation for MRA to Radiology. The reviewers lacked the insight to realize how game changing this was and thought it was just another paper on correcting motion artifacts. Dr. Alfidi recommended submitting it to AJR and amazingly the editor himself reviewed it and the paper was almost immediately accepted for publication, literally within a few weeks.

As far as writing papers is concerned, be persistent. Take any reviewer's comments to heart and answer them all before you resubmit a paper, even if it is going to another journal; it is a great exercise in improving your work.

Q: How does one get involved in the society? What is your experience?

Mark Haacke: In 1987, I ran my first workshop. The topic was on fast imaging. I was lucky enough to get Peter Mansfield to come and many other famous people in MRI back in that day. It was a wonderful meeting, and I had lots of students involved in this project. It was a great success and led to an entire issue on fast imaging in the journal MRI. So that's one way I contributed to the field of MRI but not yet to SMRI. At that time, I had no real interaction with the Societies although I was becoming known in the field. A very interesting story for the young people is an event that took place at the 5th SMRI in San Antonio in 1987 headed by Gary Fullerton. Maybe there were about 200 people present but the meeting really took off in Boston in 1988 with more than 300 people attending. By that time MRI was becoming more and more popular. Gary always prided himself as pushing for more equal clinical participation and SMRI did a good job attracting the clinical researchers. SMRM was still viewed as mostly basic scientists.

After one of the sessions, I found myself exploring the environment and heard some voices in a small conference room. I walked by and saw Gary Fullerton at the blackboard. I paused as I passed the door and listened and discovered that they were planning the next year's meeting. So, I decided to be a little bit bold as young as I was at that point. I walked back to the entrance and knocked and said: "Excuse me, I hear you are planning the topics for next year. I have some ideas in mind, do you mind if I sit in on this meeting?" Gary was very welcoming and brought me into the room to participate in my first SMRI meeting planning session. This is the type of interaction that I hope our society has been doing a better and better job at over the years, i.e., welcoming young people to participate. Of course, at that point, I wasn't a total novice. I had been in the field for four years.

By 1989 I had been elected the next President Elect of the SMRI. In 1990 I was the only Canadian to become President in Washington, DC, (of the 8th annual SMRI) and, by 1991, I was President of the SMRI and already planning the merger of the SMRI with the SMRM.

Of particular interest to the ISMRM, in 1989 I ran on the platform of better education and merging the two societies of SMRI and SMRM into one. In 1990, I visited Herb Kressel then President for the New York SMRM meeting and we chatted at the reception in his Penthouse Suite. I can remember very clearly sitting with him, probably over a glass of wine, and talking about the potential to merge the two societies together and whether he could bring this to the SMRM Board. I had already brought it to the SMRI Board and we had voted that we wanted to do it. Luckily, Herb was very supportive of this. In 1992, the two Societies formed the joint Merger Committee and, after a five year effort from inception to closure, I became the first President of the new Society (SMR) in 1994 and Steve Riederer the second, while Herb was the first pro-tempore President just prior to the official start of the society itself. So that basically covers my first ten years in MRI.

Herb Kressel, Mark Haacke and Steve Riederer, the first three Presidents of the ISMRM in 1994.

Well, what comes after that politically is another saga left to the next generation.

Q: What is your experience in teaching and training students? Do you have any advice you can give to young MRI researchers on how to make new ground-breaking research?

Mark Haacke: As for graduate students, I was very lucky to have many bright students from CWRU. Zhi-Pei Liang, Gerald Lenz (who ended up going to Siemens), Labros Petropoulos (who went to Phillips), Ramesh Venkatesan (who's now in GE and running a center on MRI in Bangalore, India), and Jean Tkach (who is in Cincinnati) were a few of my first PhD students, followed by Todd Parrish, Fernando Boada, Cynthia Paschal, and Weili Lin. Many of these early students are heads of their own MRI centers, which is really great to see how far they have gone. Two of my early post-docs were Debiao Li and Dmitriy Yablonskiy. And, again, these names are probably very familiar. I was seen as accepting of both male and female students in those days. I had graduated a number of very good female students, Jean Tkach being one and Cynthia Paschal being another. Now I think I have trained close to 150 students, from high school students, to medical students, to master’s students, PhD students and residents, as well as mentoring many young faculty over the years. I think that probably makes me a great-grandfather or great-great grandfather in MRI relative to the history of those students!

Of course, teaching played a major role for me in the early days and even today. From that teaching came the book MRI: Physical Principles and Sequence Design, which students sometimes call “The Green Bible of MRI”. It took almost seven years to complete; basically 28 man-years of work, because there were four of us involved. I think we started in 1993 and continued to 1999 when we finished it. This book was possible thanks to Bob Brown’s tremendous interest in physics education, his love of teaching and his depth of physics knowledge in MRI. He's a superb teacher. You might recognize the name of Ramesh Venkatesan. He did his masters on an image reconstruction method. Then he started his PhD and began helping with some parts of the book, in the end extending his time as a PhD student by about a year, as did another young man, Michael Thompson, who was a student of Bob Brown. They are justly listed as co-authors of the book. Inside the text, there are sometimes a single image that represents the basic element of an entire Masters or PhD thesis. I am indeed thankful to those students for all the hard work they did and to Norman Cheng who also played a major role.

There is an insightful story about Ramesh. One day Ramesh timidly knocked at my door and asked if he could come in. He meekly said, “Prof. Haacke, I have something to admit to you. Although I got my Master thesis, and understood the equations I used, I never really understood the concept of why it worked. In helping to prepare the book, I now realize the fundamental reason why it worked!” He was very happy. One thing we tried to do in that text was to teach the fundamentals without skipping steps. Even today, I try to show people how to understand the Fourier transform not just as a mathematical equation but as a basic physical principle of phase. Don't just look at the math itself. Try to understand the fundamental concept behind it.

The early work we did still resonates today including the work on fast imaging (SWI, SSFP and Hybrid EPI (a precursor to CAIPIRINHA and waveSWI), MR angiography, and RF penetration, which was an area I began focusing on when I first went to CWRU. I received funding from the then famous Whitaker Foundation. This work too was with Bob Brown at CWRU. There are many well-known people who got Whitaker foundation grants, John Gore being one of them and many other early people in the field. By the way, such grants from the Whitaker Foundation led eventually to the introduction of the R21 awards when the foundation disbanded this research support.

One of our papers on RF penetration published in Physics in Biomedicine studied the dispersion relationship using a planar model, the real part being related to relative permittivity and the imaginary part being related to conductivity. This paper had hardly been quoted in the early days. Interestingly, many years later, a young man named Ulrich Katscher came up and talked to me at the ISMRM. He said, “Excuse me, Prof. Haacke, I'd like to talk to you about a conference we're going to have.” I said “Yes. What's that?” He said you published a landmark paper in electric tissue properties. I smiled and said, I did? Then, he said: “Well, everybody refers to this paper now because we're all doing 3D electric tissue properties, and we want to invite you to give the opening talk at our workshop in Korea.” And I thought, wasn't that very nice that this early paper really ended up leading to something important. So, you never know. You write your papers and you hope you've done something important. MRA and SWI of course have developed a life of their own over the years.

Perhaps the final story for the students, which is a very cute story of thinking outside the box and which is yet to find its next crusader, but likely will one day, is the work with Zhi-Pei Liang on constrained reconstruction. Zhi-Pei started with another Professor in Biomedical Engineering and came highly recommended to me. I was in the Physics Dept. at CWRU. Cecil Thomas asked me if I had the funds to take on another student, which thanks to Prof. Ralph Alfidi, I did. However, I was leaving on vacation and for a very rare time I spent two weeks at my grandfather’s cottage in Ontario. Just prior to leaving, I sat in my grandmother’s rocking chair thinking about going back to work and about the challenges of imaging. When that magic AHA struck me, that we don’t need to use complex exponentials as in the Fourier transform as the basis functions (which leads to Gibbs ringing) but rather we could use specific shapes instead as the basis functions. Sometimes it is a good idea to take a break and clear your mind so you can come back with a fresh perspective. With this in mind, I came back to Cleveland and met Zhi-Pei who then had no experience in MRI. He asked if I had any new projects.

When he came to visit me, we went to the blackboard in my office on the third floor in the Rockefeller Building (the upper floor held the famous Michelson-Morley experiment, that pivotal experiment that showed there was no ether) and I began outlining the concept of super-resolution (in some ways a pre-cursor to compressed sensing and/or something that could be married with compressed sensing). Well, when I said we could image to a fraction of a voxel and overcome the diffraction limit from an optics point of view, he looked distraught. Then I proceeded to show that as you go to higher resolution you lose SNR in FT reconstructed images but with constrained reconstruction you actually gain SNR as you continue to collect the data. Something still not really appreciated by the field today. By that time, he was more than distraught, he said: “Prof. Haacke this is totally against everything I’ve learned at University.” He turned and ran out of my office. I thought maybe I will never see him again. A week or two later, he came back and said: “I’ve been thinking this could be a very exciting project, can I be involved?” I think it was only about two years later we submitted a paper on this topic. That paper won the Sylvia Sorkin Greenfield Award in 1989 for the best paper in Medical Physics. That was all thanks to his enthusiasm of jumping into this project. And that was the beginning of many years of fruitful science and a long lasting friendship. Coincidentally, also about that time, a paper was published in Physical Review or Physical Review Letters by a Prof. Durbin on overcoming the diffraction limit in laser propagation by appropriately modifying the phase (I taught optics as well as MRI in those days).

With that story, I hope that it encourages and motivates students to look outside the box. But I have to close with one key piece of advice. Read, read, read; study the fundamentals until you know them inside out, in fact, until you know them so well that you can basically get up and give a lecture that your professor would have done. Think of what Ramesh Venkatesan said. Think of Zhi-Pei’s first reactions. You must have a solid fundamental foundation to be able to be creative. I thank my training at the University of Toronto, where I did my undergraduate in mathematics and physics and all the math and physics training I received at graduate school in preparation for a PhD degree in high energy physics.

Today, there have been major hardware and software advances in MRI. So much so that there is another whole open beach to explore. MRI is a magic place, where there is a symbiosis of the fields of chemistry, computer science, mathematics, physics and statistics and the marriage of these with the clinical interests in both studying the etiology of disease and diagnosing disease. I look forward to watching the next generations open new doors and make important new discoveries that will push the frontiers of this field and lead to better treatment of patients. Next year will mark my 40th year in MRI, and I am just as excited about it today as I was when I started in 1983.