Dr. Alan Koretsky Interview

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Interviewee: **Claudia Wassmann**
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Dr. Alan Koretsky Interview

CW: This is Claudia Wassmann and today's date is July, Wednesday the 6th. I am doing an interview with Dr. Alan Koretsky.

CW: You came here as a post-doc first, maybe you can start with –

AK: I was a post-doc before there was the Imaging Center. So when I was a post-doc therewas very little brain imaging that I knew about. So probably the radiology department
had a low field MR system.

CW: When did you come?

AK: I left before the building that you're in was completed.

CW: So when did you come to NIH?

AK: So 1986 – I came in January '86.

CW: 1986, there was no – the center didn't yet exist –

AK: 1985, January 1985. The center didn't exist. Ted Becker was – it was all in the works and I only knew about it because my advisor Bob Balaban was part of the committee that was formulating how to put the center together, so yes.

CW: So can you describe a little bit what existed, what did you do?

AK: When I came I was mostly interested in metabolism, so nothing to do with brain imaging, the heart and kidney and we were doing magnetic resonance spectroscopy at the time. I come into this from the spectroscopy side of things and mostly interested in mitochondrial metabolism. We were isolating mitochondria and looking at perfused hearts studying metabolic questions.

CW: And you say you used NMR spectroscopy?

AK: Spectroscopy, yes we did not do any imaging. When I was here, Bob just got hold of a 4.7 Tesla animal scanner that could make images. So that was sort of the first generation scanner that those of us that were interested in metabolism – you know for the history, for brain imaging, it's an important group of people because almost all of the tools that came from functional imaging. The spectroscopy folks finally got our hands on imaging. So that had just arrived as I was leaving Bob's – it's a 4.7 Tesla small 30 cm pore system.

CW: Was it produced in collaboration with NIH or did NIH just –

AK: This was at NIH.

CW: It was at NIH.

AK: Yes, I was still at NIH as a post-doc. Was that scanner produced…

CW: Yeah.

AK: No, not as far as I know. You'll have to ask Bob. Bob, of course, would be a good person to talk to about all this, but at about the same time my colleague at Carnegie Mellon, Chin Ho was buying a similar system for Carnegie Mellon which is where I went to, and Kamil Ugurbil in Minnesota had a similar system. So there were a handful – Georg Deutsch at Alabama had it. So there were a handful of systems. I don't remember which was first but I think the manufactures decided they could do it. Typical with MR are the magnets – some says they can make the magnet and then other – the electronics get put on it and someone buys it. So this was an early one of that generation scanner.

CW: At that moment if you look back, would you have anticipated the development that these technologies took?

AK: For brain imaging yeah. There were a group of us I'd say in the late '80s that all were working hard on trying to image hemodynamic aspects of brain function. You know, of that group some were explicitly interested in cognitive things. You know we were interested in metabolic things, but there definitely was a group of three or four]labs that were aiming to measure something about regional blood flow in the brain in the late '80s.

CW: So when you say?

AK: We all thought we would be successful, sure.

CW: Yeah. So you were interested.

AK: We didn't know that it was going to flourish like it has, no.

CW: But at the time when you were here as a post-doc – I meant Ted Becker started – the in vivo center opened in '87, no?

AK: '80s?

CW: 1987 or ’88.

AK: Maybe they broke ground in ’87; I don’t think there was actually a physical structure here until ’88, but we – there was some discussion about that. Whereas Joe thinks – Joe Frank, who was here for most of that – everybody is little fuzzy on the details, but I think I left, because I got here early ’85 and I stayed – I think I left early ’87, March ’87 and they were building it because I had a bet with Bob about when it would be finished.

CW: What did you bet?

AK: I can’t remember what we bet or who won, but it was – I don’t think it was here yet. The ground may have been broken in ’87. So I bet equipment arrived in ’88. Kurt Munin [spelled phonetically], Kurt Munin – you must have heard Kurt’s name. Kurt might remember best since he was here for the equipment and he was hired to be the person to get the facility up and running.

CW: So you personally, you were using NMR spectroscopy and you were interested in metabolism and maybe just say a little bit about your own work.

AK: Now?

CW: Yeah.

AK: My work presently has become more and more interested in brain things and more and more interested in sort of wiring in the brain. So the metabolic interest has become a lower priority, just a small group. So mostly we are interested in developing the state of the art in brain imaging. New ways to get at brain function away from just watching blood flow and applying that to understanding plasticity in rodent brain – so most of this work is in rodents, you know detailed plasticity in rodent brains, so that’s the work.

CW: So you came back in to the NIH in 1999?

AK: I came back in 1999, yes.

CW: Yes and then you became the director of what has become the In Vivo NMR facility.

AK: Let’s be careful – that’s right. I’m director of what we now call the NIH MRI Research Facility which, originally, the facility and the center were the same thing and since then there’s a large cardiac imaging group that’s

grown, a large brain imaging group, continued radiology research group, a large animal facility, so the center sort of represents all those groups which are independent and within it, and maybe the smallest group in that, is the original facility which the facility always intended to offer MR to the NIH community as well to help advance the state of the NMR. It did so well in the early years that many groups had to build their own resources because the needed more than the facility could offer. So the center now encompasses all of sort of the research side of MRI – NIH, Heart Lung and Blood, NINDS, NIMH, Clinical Center. The facility still exists for the rest of NIH. So I direct that facility which is just a small piece of the Center. The Center is governed by a steering committee. The facility is governed by the same steering committee. Right now Bob Balaban is head, Bob took over for Becker.

CW: Okay so basically there are five big groups would you say?

AK: Heart, Lung and Blood, NIMH and NINDS somehow work together on the brain imaging, but within that there are at least two groups depending on how you break up groups. So let's say Heart, Lung and Blood, NIMH, NINDS, the Clinical Research Center so there are four.

CW: And the facility?

AK: And the facility is a fifth thing, yes.

CW: So within the facility what do you have now in terms of equipment?

AK: There's a 3-T human scanner, a single 3-T human scanner, and there's nine human scanners, so that's why the facility is small player, and it has what we call the mouse imaging facility which is not just for imaging mice. We image lots of different animals and that has – that's a whole little radiology department for animals that has now one, two, three, four MRI scanners, a micro-CT ultrasound equipment and a little bit of optical equipment for imaging animals all broadly used by the NIH community. So it's always been a strong – there's always been a component of animal imaging within the NMR Center. It's really grown a lot in the last five years or so.

CW: Is this all located here?

AK: Yeah it's all located here.

CW: Okay.

AK: Yes, Ted had the great vision of putting the NMR Center in an area where there was nothing around it; like all good things we grew to take up that area.

CW: Okay, so when you say one of your objectives is to develop the technology of brain imaging further, could you maybe mention some of the important projects that are going on now in the facility?

AK: Vis-à-vis brain imaging in the Center?

CW: In the Center.

AK: In the Center as a whole, because most of the progressive technology development is actually happening outside of the facility. The facility is really a place for other people to come apply to their own biological problems. So most of the interesting developments I think are – you know new MR developments are mostly in the other groups in the Center. So there's some good stuff in the facility, but a lot of the facility is to use things we know how to do to apply to a wide variety of biology. Biology is spectacular in the facility. So if you could say, "Can I could talk about new developments in the center," it's a more fun –

CW: Yeah sure.

AK: But one of the – in terms of MR developments, of course we continue to be early in moving to higher and higher magnetic fields so NIH was early in having a 3T scanner; we call it 3T-1. Peter Bandettini has a group that overseas that scanner and there are now, one, two, three, four 3T scanners here and we're looking for a place to site a fifth one, so that worked out – that's worked out very well. As part of the move to higher field we have a 7T scanner. It's been here for a couple of years. It's finally making some real nice images as well. That was I think the third or fourth depending on how you count a Tesla. So for a 7/8 Tesla it was the third or fourth in the world. None of them are operating routinely yet. I think we're hopeful that ours is the closest to – still early in that development and the images are looking better and better. So a move to higher field, mostly that gives us more sensitivity especially for functional imaging. Combined with that is there's been a big development of detectors here mostly headed by my colleague Jeff Duyn in our laboratory, which is to – instead of single detector to start using many detectors much like ultrasound uses. So parallel MR so there's been a big predominant detector, so from one to right now we're up to 16, and that will march on to some number, who knows? Combined that has increased sensitivity dramatically in the last few years.

CW: Are these collaborations where NIH scientists work with industry?

AK: This one was – yes this one was – you keep asking that. You're interested in that.

CW: Yeah.

CW: The 7T is collaboration with GE. They had never built one and we have had a lot of input. Not as much as we'd like because they've made some mistakes and they shouldn't have if they listened a little better, but that's collaborative in the sense that we're putting in a lot input although they would probably have made for someone else sooner or later. The coil development, that was all prototyped here, and it's interesting because it sort of starts in Heart, Lung and Blood with trying to get to 8 channels faster than industry had and then some of that expertise helped the NINDS group, Jeff Duyn's group, go to 16 channels and that – so prototyping that – the whole receiver system was built here and the coils were – the detector coils were prototyped here. There's a small company named NOVA in Massachusetts that has commercialized – I don't think there's any patent but they make a commercial product, which they're selling quite well. So that's a case where I'd say it was really a strong collaboration and that is it was prototyped here, they added what they did very well and it made a beautiful coil. So we're running 16 channels on the 3T, 8 channels on the 7T. So that's an exciting development because that increase in sensitivity is gone; if you counted the 1.5 Tesla five years ago as one unit of sensitivity, the 3T doubled that as expected to two units. The 16 element now depends on where you are in the head. In the center of the head it's another two and a half, so it's five fold better than the 1.5, and at the edge it's as much as another factor of two, so it's ten fold. So the 16 channel 3T coil has increased sensitivity ten fold in the cortex and about five fold in the center compared to 1.5T, and the 7T has doubled all that all ready. So we're five fold better in the center and close to 20 fold better at the surface and there'll be another factor of two I think. So we're talking 40 fold improvements in sensitivity in about a five or six year span. It's quite remarkable. Actually it's quite remarkable, and it's something that really lives here at NIH.

The hemodynamic information keeps getting more and more sophisticated and Peter Bandettini, Ogawa and Jeff Duyn have been looking at exactly what does BOLD fMRI mean and how does it localize and what are the temporal characteristics. So there's been a lot of refining of that notion of how to do brain imaging and the thing that we actually started in the late '80s, the blood flow measurements with arterial spin labeling that has been much slower to reach full fruition, and lately Ogawa specifically has beautiful whole brain blood flow images now at really for that measurement unprecedented resolution. You know about 1 to 2 mm resolution with a real number. So it's a quantitative number and –

CW: So what made that so difficult, well why did it go slower, you know?

AK: You know it's a funny thing. In principle it all could've been done 10 years ago. Why things go the rate they do I don't understand. That's a good question for you historians. In general I think the U.S. industry is very conservative. There are local groups who could have been able to do things that have shown that it would all work and in general for sort of widespread application, and so even the people that want to use it at NIH though it can be turnkey. It just takes a long time in the lab to build the equipment to work robustly, industry you can do it much quicker and they tend to be very conservative. So the MR industry in general, worldwide, has been, I think, extremely conservative in innovating. So that's why it's so long, but now the images look spectacular and I don't think it'll be that useful for – you know BOLD worked so well for cognitive sort of things, but for disease that's where I think it's going to be very important. So that's beginning to get used. You know there are four or five groups that are using that routinely. Those images look spectacular.

CW: Can you give an example what kind of disease they would look at? What would they apply it to?

AK: There's a hunt for both the combination of both the functional and the gain in sensitivity, there's a big hunt for changes in cortical – anatomy function at very high resolution and that's sort of starting or being most productive for MS. So multiple sclerosis, which is normally considered a white matter disease, there's also myelin and gray matter. So gray isn't all gray and white isn't all white and so pathologically it's been known that there's lesions in gray matter and no one has seen them yet in vivo, and Henry McFarland's group mostly with Ogawa are pretty sure they can detect anatomically and they're looking for blood flow changes associated with that. Wayne Drevets's group at NIMH is very interested in drug effects. So give a drug and then do a task and part of the problem with interpreting the fMRI, the BOLD responses, if you've change the baseline you may get a change in the hemodynamics that has nothing to do with the neural activity, so they wanted to know how blood flows changed and to make sure they correlate that. [Unitelligible] Alzheimer's similar they're using blood flow as a – you know they know what the resting blood flow for people before they do; it's not a functional test activation. Bill Theodore, I think, with epilepsy is looking at this, you know, comparing PET to MR blood flow measurements for epileptic localization of seizure focus about a handful things going on in the brain.

CW: So in the mouse imaging facility how many projects do they –

AK: So on the animal side there's a lot happening and the hard thing to do – you know I think a lot of that will impact biology, whether it will transfer to human use is always the challenge but the stuff that my group in particular has been doing we've been very interested in manganese, manganese is a beautiful MR contrast agent for Latimer [?] in his original paper showed that he could change MR signal with contrast agents and he used manganese as the contrast agent. So manganese will enter cells in a variety of different ways, a lot of enzymes need manganese. So there's great biology, so we've been sort of taking advantage of that biology to image things more specifically so manganese will accumulate based on activity just like calcium. So it's an MR monitor of calcium influx. It will trace, so when it's in a region of the brain it will move like a brain track tracer in an anterograde direction so you can track trace with it. Just a little bit of manganese in the brain and let it move until it's settled down just makes spectacular images, so we can see cortical layers and hippocampal layers; we can see things that we've never been able to see in MR. So we're real excited about manganese. Certainly for animal studies in our work, we're using it all the time for trying to understand things that change in animal brains. The systems monkey folks are beginning to use it, Barry Richmond and David Leopold – has a nice monkey MR system with the Center – not in the Center, across the driveway from the Center, so that it's closer to the monkeys. Whether it'll move to humans or not we'll see. There's toxicity issues, toxicity.

So that and the exciting project that I think a lot people are beginning to do is cell tracking, that is you can get enough iron oxide, very potent MR contrast agent, little particles of iron oxide. You can get cells to eat the iron oxide and then track those cell – cell migration and Joe Frank here, and my colleague at Pittsburgh, Chin Ho who I worked a little bit with this on, sort of been the two leading groups and it's something now that is being used by a lot of groups routinely. So Joe is still working very actively to try and translate that to clinical applications so that you can inject stem cells or lymphocytes and help them to see different diseases.

We – my group recently has been able to get very large particles into a neural stem cell, endogenous – stem cell is a strong word – an endogenous neural progenitor cell right at the sub ventricular zone that migrates to the olfactory bulb, so we can now see – we're pretty sure we can see single cells migrate – mostly they go to the old factory bulb. We make nice manganese maps of the bulb anyway, so we're going to actually, with the next generation experiments, going to ask if the cells either tell us where we should be looking for interesting changes in neural circuits or whether the cells are participating in interesting changes in neural circuits, but that's another – we're excited about that as well so cell tracking as well. Again, how it'll move to humans will depend on the agents and whether we can give them and I think that will – cell tracking somehow will

become very clinically important in our business so there's nothing slowing down about MR.

CW: Yes, are you still expanding the facility at NIH?

AK: The – well the facility expanded dramatically in the last five years you know thanks to mostly Bob Desimone at NIMH and Story Landis at NINDS so – and Bob Balaban – the animal imaging expanded also, that's Bob Balaban so the key – both administrative and scientific support. Will we expand in the next couple of years? So there's another 3T that NIMH and NINDS are looking to put somewhere. NIBIB is trying to decide what its intramural imaging program is going to look like and where that might sit, but I think one of the interesting new things that are developing is what's called an imaging probe development center. So that's just starting. That's part of the roadmap. That's one of the few intramural things in the roadmap and so that – and that's being modeled off of the original MR facility. So the administrative model is the same as the steering committee. I think Ken Lee [spelled phonetically] is head of the steering committee and physical space unfortunately it's going to be for at least the first few years off in Rockville somewhere because they need a lot of space where they can do a lot of chemistry, so it's hard to come by on campus right now, but it'll be a group of some number of chemists who basically people at NIMH will submit proposals and they'll make an imaging agent for that. So that's a new thing that, while it's not directly in the Center will effect the Center a lot, and a lot of the steering committee are people that participate in the NMR Center, so it's NMR Center influenced.

And that's actually also interesting is Ted – Ted was the genius at setting the place up administratively. The model has moved. I think the new neuroscience has got a lot of NMR Center aspects of it since NIMH NINDS knew a lot about how the NMR Center operated, so part of the goal of the new neuroscience center, which is trans-institutional like the NMR Center, more to be bottom-up and top-down managed like the NMR Center, that model has moved. So the Imaging Probe Development Center has more or less copied that model as well. So that'll be new. Whether the Center will expand physically I don't because, you know, building at NIH right now, budgetary and other reasons, make it hard to expand space right now. So I think the next couple of years things will be in terms of expansion a little quieter because of budgetary issues.

You know for the brain institutes, any time they recruit someone who wants to work on MS or neuropsychiatric problems; they all want to know where their imaging time is. So it's clearly an essential tool if you're any kind of brain scientist. We expect in the next few years, even if you're working rodents or monkeys, you'll need your MR system so…

CW: Oh yeah, what I was going to ask, when you came in 1999 the In Vivo Center moved from NIBIB to NINDS –

AK: No, not exactly – that was before. That was a year or two before me; two things happened former director of the facility Craig Moonin [spelled phonetically] left to go back to Europe and there was this transfer to NINDS.

CW: Do you know what the former institute was doing? It ended.

AK: I think the intramural program of NCRR ended. So the National Center for Research Resources had an intramural program and more or less that intramural program stopped. My understanding – I don't know. Bob Balaban and Storey Landis would know for sure, and maybe Ted knows for sure, but my understanding is the NCRR intramural program ended so all of the NCRR resources got transferred somewhere. Right? So a lot of it is in Mike Gottesman's office, now Office of the Director, in the bioengineering program. The NMR facility, NINDS was the major user of their 1.5 Tesla scanner at the time, and Storey Landis is notorious for wanting to work collaboratively with other institutes in a positive way, so I think she wanted to make sure the facility thrived not only for the interest of NINDS but for the interest of NIH, and everybody trusted her as well, and so she took it over. The other thing that happened is the neural imaging branch within NINDS, that the group in that ended – also ended. Takiro [spelled phonetically] Takiro have you heard that name? Takiro – I don't remember his first name. He died. He died, and so that opened up the lab. So that's – they recruited me for both jobs, director of neural imaging lab and director of the facility.

CW: And then the decision to create the – how do you call it? I say NIBIB but you spelled this acronym differently.

AK: Yes "NibBib" [spelled phonetically] is the way – N-I-B-I-B. "NibBib" is the way I think a lot of people say it.

CW: So NIBIB was created really as an imaging institute no?

AK: Imaging and bioengineering, yeah.

CW: Do you remember when the discussion came up to create such an institute?

AK: All political extramural – had very little to do with – at the time and I'm sure there's a written record of this. I wasn't privy to any of the details, but at the time there was another movement going on which was Harold

Varmus. When Harold Varmus was director he wanted fewer institutes. So it's funny, he was actually – there was National Academy of Sciences had a committee. Harold asked the National Academy of Sciences to look at NIH, were the number of institutes right or not? And they actually came out suggesting NIH shrink the number of institutes and at the same time, mostly in Congress, mostly if I understand it right, radiology, the U.S. radiology with connections in Congress were pushing for a new institute. So that won out over the notion that we should be administratively re-assessing the whole make up of NIH. That was all extramural and very political, very little to do with anything intramural, and they haven't yet started an intramural program. So we don't know how it's going to affect – if they start an intramural program.

CW: Is NIH one of the first in place in terms of science imaging?

AK: I think it's unique. It's why I came. It's why I came and what makes it unique is side by side I think you can find a handful of cardiac imaging groups as good as the cardiac imaging group, but only a handful, and you can find a handful of brain imaging groups as good as the brain imaging groups, but only a handful, and they're side by side strongly interacting, and there's unique ability to translate here to a broader biological community which is the role of the facility, which is unique. So, more or less, if we say we can do this there are people around who would like to see and vice versa, there are people constantly coming with good problems to help inspire new imaging experiments. So I think the MR Center is unique. There is no comparable place.

CW: Sounds like it's a fine place to work.

AK: Its impact has been big. You know it was early in the fMRI and not originating, but it did you know early in diffusion and the actual notion to make a tensor does originate here and other kinds of contrast are novel to here and cell tracking. This is, as I said, one of the two or three places that's developing that. Our own work with arterial spin labeling for blood flow and manganese had started in Pittsburgh but somehow it was influenced and it's back here now doing it. So yeah, I think it's a big impact.

CW: What do you think of the neural spin that they now created in France?

AK: Denny Libnah [spelled phonetically]?

CW: Yeah [laugh]

AK: We'll see. I hope it works. It's very ambitious. I am a big fan of the higher the magnetic field the better and you know there's this generation

of 7 to 9.4 Tesla magnets that 7 – 9.4 is all about the same. 12 Tesla is a nice big jump. I hope it works. I hope they make the magnet. It's great. It's expensive. It needs something like that to stimulate the technology. After they make the first one the cost will come down sooner or later so I think it's great.

Tesla scanner will be because it's probably – I don't know when they expect to have a magnet. You know I'm sure it's two, at least, if not three years to build a building and have a magnet; it's very exciting. Denny of course cut his teeth here so that's nice. So that's very exciting. Also on the animal side they're building very high field for a horizontal magnet, my own group has an [unintelligible] so that was one of the first two of those. So my group has always been early in trying to get whoever can make the highest field magnet that we could put animals in comfortably.

So we're at 11.7 Tesla now. I think they're going to go 16 Tesla. David Mostplaw [spelled phonetically] and with the EU project will try to get 16 Tesla and we hopefully will – as soon as we know the magnet can get made we'll jump right on. The interesting thing is the cost is extremely high, so when – and this is true for high resolution MR too. When the – we haven't ever hit that anytime anybody could improve the scanner there's been money to buy it. You know whether that will – because this is a big jump. This next generation is a big jump in cost. Everything else has always felt continuous to me. This is a big jump in price, so we'll see. We'll see. It's certainly going to take places like this conglomeration of people involved in France and when he thinks about the intramural program at NIH we could potentially gather the resources.

CW: I would like to look at how you keep records of what has been done here? Like administrative or the project that has been done.

AK: Oh Dana Carol [spelled phonetically] and I actually – you know there is a charter that – there is official documentation of the start of the Center and there've been changes and I've been – we need to re-write that charter for a lot of reasons, but I've been going through sort of minutes meeting. So I think we have a pretty good look at most of the administrative decisions that were made. You know I was looking for the SD minutes that transferred from NCRR to NINDS and there's all of the preliminary discussion but so far the official transfer doesn't show up in any of the scientific minutes so if you can find that I would love it. I haven't found yet. So administratively – scientifically that's hard. I mean the best thing to do is like I went to see Jeff – you know Jeff's office is right down the hall and when you said you were coming I thought you were going to be really interested in the details of the early fMRI experiments here. He was here and he said he wasn't involved in it. I said I didn't know that much about why did Bob Turner go to Boston and who was involved and,

you know, what was the early experiments on the – for the functional imaging here and, you know, we just looked up Bob Turner. We searched Bob Turner and I think there's this '93 paper that Bob Balaban and Peter Geiser about field differences. You know because they had their 4T. There was an early 4T here so it was easy for them to compare 1.5 to 4 Tesla. You know there's some CAT stuff and Leslie Ungerleider, very influential, then Bob Turner was involved in the *Nature* paper. So I think the best way to get at the science is just through the literature and if there's issues...

CW: Yeah but if I look at the literature – I mean so you've been involved so you know better. You can immediately say which paper was important and which one was not important. So it's easier if I have someone to talk to who can point me to the papers –

AK: So it depends on what aspect – so for the sort of BOLD fMRI – you know the big impact. Peter Bandettini whether or not Ungerleider '94 paper was as important as people at NIH think it was but that's a cognitive science question. You know, would fMRI have happened without NIH? There's no doubt about it, right? The early stuff was MGH, Minnesota and Pittsburgh was doing stuff. Did they influence it? Definitely. So for the functional imaging you know the other – the diffusion tensor tracking – Peter Basser and Denny. The diffusion, that also –

CW: Yeah I talked to Peter Basser.

AK: MTC, magnetization transfer contrast, which is an anatomical contrast agent with Bob. Well that still hasn't really borne fruit but I'm happy to help however I can.

CW: Yeah if we want to put it up on the web or – we have to make a choice. Do we present at exemplary or we present it for a specific type of – I cannot possibly put up everything, but I have to put up photos and so some things are easy, some things are difficult and then the earlier it gets the more complicated it is for me to locate what's important and what's not.

AK: Oh, I think that's – in terms of specific published work it's not so bad to figure out where it really stood; that's a different issue, but no, no that's no problem and you'll find functional imaging – you know if it's MRI broadly there are a number of things that are...

CW: Yeah I will work together – for the website I will work together with Ted Becker; he will do the NMR. So before the – before MRI because it has some prehistory where it was important in chemistry before it became important in medicine, and then I'm doing the MRI part of it.

AK: Yes, so but the stuff that happened at NIH early, you know, for BOLD based fMRI Bob Turner was a key guy, no doubt about it. For diffusion that's Denny – and Denny with Lihan and Peter Basser, who's here. Just in general, for anatomical contrast, MS has been – MS has been the great success for MR since the early '80s. Henry McFarland has, you know, sort of been involved in that so the impact on a specific disease that you can really get a handle on, maybe schizophrenia ten years from now we'll get a handle on, but MS there's been a lot of progress and Andrea along with Joe Frank have sort of lead the way through that whole history. And related to that there's magnetization transfer contrast, which is Bob – that's Bob and our profusion that you actually measure blood it sort of starts with us but Jeff Duyn here at NIH – they were very quick, Alan McLaughlin at NIBIB and Jeff Duyn were very early, and they were probably doing stuff before we were and we're at about the same time but they were very quick. So it's – Don, Alan McLaughlin and Peter Geiser who was another person who's now at Oxford hanging around through all that. So if you define it – what's new is cell tracking and manganese – you know there's the new stuff if you want to do that too. So if you could do five or six specific experiments that really NIH had a big impact it would be those.

CW: Yeah that would be wonderful. That's exactly what I would like to do and then I need to find like photos. So I don't know –

AK: Of people?

CW: Of people, of the building, of the machines, of experiments, of….

AK: You know it's funny because I'm not very good at that myself. I was amazed. I'm not very good and I was amazed at how little – I don't know, did she show our little – she has all the background. You know I was the one who said, "Oh where the hell is all the pieces of the paper?" I just want to admit that was for administrative record. I've got this little thing but it doesn't really have what you'd like, but we can snoop around. You told Carolyn – Carolyn, did you meet Carolyn?

CW: Yeah I'm going to meet with her next week.

AK: You know I have, it's not much – at least the physical – we got some over the [unintelligible]. That's new stuff. I have slides that showed the facility – we could probably get this back further. So I've got some of the layouts of the whole thing, which could probably be made into a nicer slide. This is what it was. That's pre-1999 and this is what's happened to it. I had the two slides one after the other, but I ended up trying to make them into [?] and we certainly could do a pre – so that was 1999 after cardiac had been built and the brain imaging was just building. So the

original facility was just this. So we could cut that out. You know we certainly could get – make a schematic of the original facility and show the original – this is an intermediate and even without the brain stuff you know just a cardiac. That would have been '95 – '90 – '91 / '92. I don't know when Bob built. This build out came in two pieces actually. This one and then this one. Whereas the original, there was this. That got expanded, this got added and there was a piece here, that's not yet there and a piece – I certainly could make that fancier to show the sort of development of the physical structure.

CW: Yeah and then you had all the other information, what kind of instrumentation was in it and so on.

AK: Either it's still here so we can take the pictures or there might be pictures. The real – the important scanner was the original 1.5 Tesla that sat there and that just lost a couple of years ago and we just upgraded it to 3 Teslas and I've got the other pictures of the magnet going out; I don't if there's pictures of the magnet going in.

CW: Yes.

AK: I can send those to you if want.

CW: Yeah that would be great.

AK: And your email?

CW: Okay it's wassmannc.

CW: I don't know is that a post-doc or someone who could sometime show me around so that I can physically see what this facility is about.

AK: We can go right now if want.

CW: Yeah, I would love to.

AK: You know I almost became a historian of science.

CW: Really.

AK: I was a chemist. I was at Berkeley. I was a little fed up with chemistry and I always had an interest in philosophy of science, and Berkeley had both a very strong crew of crazy, you know, philosopher of science prizes and what's his name the Mayan guy right now who's got so much attention. Plus the anti-Copernican revolution. Did you ever read any of that. Well anyways, so that was too philosophical for me but the history

of science was the good side; I was thinking about switching programs. I started reading the literature and it was too hard it took a professional historian to take all the fun out of history for me.

CW: That's true.

AK: I mean I wasn't ready – I couldn't get serious about it that way, right? It was good because it made me appreciate that you know to go deep into anything was going to be a lot of the trouble that I was having with science – but it was more fun in science than it was in history. It's sort of sad there isn't really a good history of magnetic resonance. I say it to Ted and he says, "Oh, I've got the encyclopedia." I said, "Yeah, but that's history by the people who did it so they all have their little blurbs and, you know, on some of these controversial issues the encyclopedia doesn't help." And sadly the primary people are all dead or dying.

CW: Yeah, so I'm trying to put this together.

AK: I know it would be ambitious to write a good history

End of transcript