

Magnetic Resonance in Medicine *HIGHLIGHTS*

Elizabeth Morris

Equity, Diversity and Inclusion

**2021 Young
Investigator Awards**

*Meet the I.I. Rabi and
W.S. Moore YIA finalists*

Tim Leiner

President's Interview

Editor's Picks

Mark Henkelman

An interview by Elliot McVeigh

Jean Chen

Udunna Anazodo

Julien Cohen-Adad

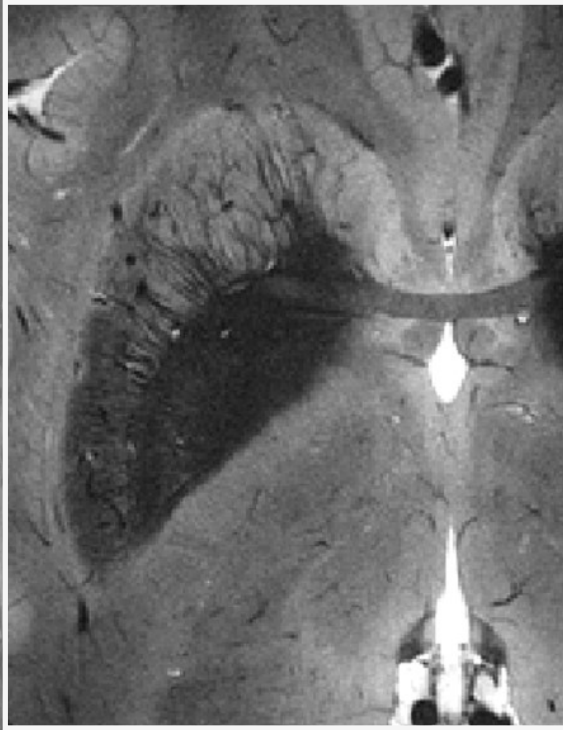
Canadian Researcher Profiles

ISMRM



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January - November 2020



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Diffusion MRI is commonly limited by image artifacts and low SNR. In DWI, the SNR can be improved by spiral acquisition which reduces echo time. Normally this leads to strong image artefacts, which can be avoided by using field monitoring to track actual k-space trajectories. Shown at *right* is an example of these types of results - high resolution single shot diffusion with high SNR.

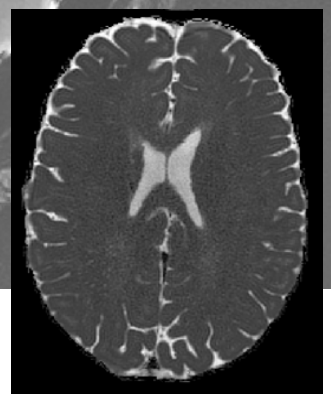
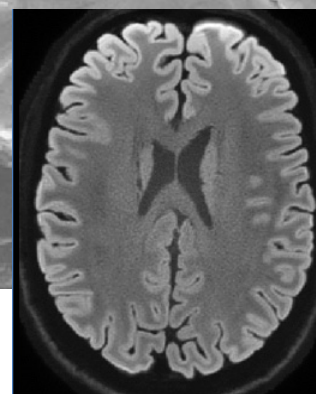
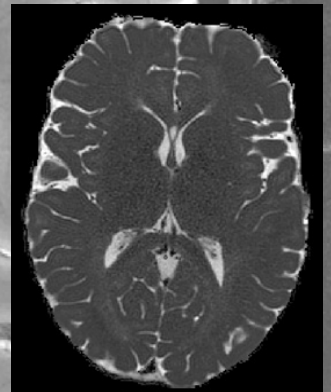
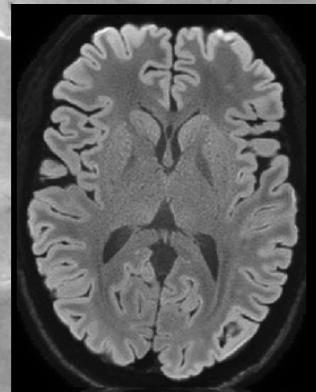
Courtesy of Klaas Prüssmann and group, IBT ETH Zurich and University of Zurich

right: $b = 1000$ spiral diffusion acquired at 0.8mm in plane nominal resolution, TE = 44ms

Courtesy: of Yoojin Lee, IBT ETH Zurich and University of Zurich DOI: 10.1002/mrm.28554 (adapted image)

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Welcome to *Magnetic Resonance in Medicine Highlights*

Many of us are now into our second year of COVID-related restrictions, with significant impact to our personal and professional lives. The 2021 ISMRM Annual Meeting, which was to be in Vancouver, has been converted to a virtual format and this issue of *MRM Highlights* will again be distributed electronically. However, despite the challenges and disruptions we have all faced, we are excited to bring you the 6th volume of this magazine, which includes new interviews and highlights from papers published in *MRM* over the past year.

• • •

This magazine features an interview series with several Canadian MRI scientists, a reflection of the planned Vancouver meeting. Elliot McVeigh interviewed the recently retired Mark Henkleman for *Highlights*, and we followed that up with interviews with three of Canada's next generation of MRI scientists: Jean Chen, Udunna Anazodo, and Julien Cohen-Adad. We continue with the tradition of the ISMRM President's interview with Tim Leiner, and also conducted an interview with ISMRM EDI Officer Elizabeth Morris. We are also delighted to continue showcasing the amazing early-career talent in our society with profiles of the 2021 ISMRM Young Investigator Award Finalists, for both the W.S. Moore and I.I. Rabi awards. Finally, the magazine will feature the online Q&As curated by the *Highlights* Digital Content team.

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I would also like to introduce the newest member of the *MRM Highlights* editorial team, Maria Eugenia Caligiuri, who joined us this year as *Highlights* Magazine Deputy Editor. Together with Mathieu Boudreau and Atef Badji from the Digital Content team, and *MRM* Editor-In-Chief Peter Jezzard, we're really proud of the original content *Highlights* has been able to put forward, and the magazine that has resulted from it. We also thank the volunteer contributors that have worked on the *Highlights* interviews and Q&As, the ISMRM Central Office, and the team at Wiley who have all helped put this magazine together. We hope you enjoy reading it as much as we enjoyed making it!

Mark Chiew
MRM Highlights Magazine Editor

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Equity, Diversity and Inclusion: Elizabeth Morris

INTERVIEW BY MARIA EUGENIA CALIGIURI



Elizabeth A. Morris

Elizabeth A. Morris, Chair of the UC Davis Department of Radiology, is also ISMRM's Equity Officer, a new position established by the Society's Board of Trustees. After her appointment in 2018, she created the ISMRM's Equity, Diversity and Inclusion (EDI) Task Force. In this interview, we discussed the major accomplishments of the Task Force, as well as the challenges she has encountered along the way.

MRMH: What is the overarching mission of the EDI Task Force? Which actions do you routinely manage?

Elizabeth: Our primary goal, obviously, is to reduce discrimination. And by this, I mean discrimination on the grounds of gender, race, religion, sexual orientation, age, or ability. I believe there is also an educational role, of having people understand that each

of us is different, and that differences have to be appreciated and respected. Diversity is a positive thing; it brings together different opinions and experiences, and any organization is probably going to be more successful with a diverse team rather than with a very homogenous one. Within ISMRM, it was a gender issue that was at the origin of this whole EDI adventure. It was also recognized that we didn't have a lot of women speakers or moderators at the meetings and that's when the Women@ISMRM committee was started, to create awareness around this issue. But after that, we started thinking that this was a much bigger problem of equity, diversity and inclusion. This is why ISMRM decided to actually create an ad-hoc officer, encompassing women and women's issues, but also looking at gender, sexual identity and all other discrimination issues.

MRMH: How did you select the task force members?

Elizabeth: Since the beginning, we wanted a representation from all different groups. I worked with Roberta Kravitz (Executive Director of ISMRM) and Karla Miller (Vice Equity Officer), who know the membership very well. We developed a list of potential members, and I then asked people if they were willing to be on this task force. It was really interesting, indeed, trying to figure out who was going to represent each category. Take sexual orientation, for example: very few older ISMRM members are out, while quite a few younger ones are out. We wanted broad representation from both generations. The processes of choosing people was not easy, and it showed how careful people sometimes feel like they must be in their professional lives. We are aware that this might not be the most diverse way of making a committee, which is why going forward I would like to have people self-nominate if they want to be part of the task force.

MRMH: How has the role of Equity officer evolved and changed since your first appointment in 2018?

Elizabeth: The decision about creating the position and the task force had a top-down approach. It was proposed by the leadership; however, what I'd like to have is bottom-up approach. And ISMRM provides the right context to perform this change: what I love about this Society is that the members really run it - they give input and have amazing ideas. What I would like to see in the future of the EDI task force is something similar to what has happened with the Secret Sessions, which really made ISMRM more accessible to its members. That, to me, was magical: seeing all these passionate and enthusiastic people wanting to make the Society better for everyone. It was a very touching moment that made me really happy and proud to be a part of the ISMRM.

MRMH: Were you impressed by any Secret Session in particular?

Elizabeth: There were two 2020 Secret Sessions that really impressed me. One was the "Getting Involved with ISMRM", which also resulted in a plan for the ISMRM Mentoring Working Group, led by Sola Adeleke and Thomas Lindner. Their aim is to establish empowering mentor-mentee pairing, and get students and early career researchers the support needed to achieve their full potential. Another one that I appreciated was about "MRI: Making Research Inclusive". Jodi Watt (a task force member) was among the organizers, and it really succeeded in its objective of facilitating a respectful discussion about increasing inclusivity in the research environment. Jodi is now working with the chapters, to address inclusion and get more people involved with EDI activities at a more local level. This is the kind of activity that I want the Task Force to foster. We're here to facilitate ideas and energy from the membership.

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I think the biggest accomplishment is that we have created awareness regarding EDI. Having incorporated that awareness into the Annual Meeting Program Committee (AMPC), where EDI has become an important topic now, I find the program to showcase a more diverse selection of speakers and moderators.

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The ISMRM EDI Task Force in 2019.

MRMH: That's really inspiring. What has been the biggest achievement of the task force? Have you made changes in the way ISMRM operates?

Elizabeth: I think the biggest accomplishment is that we have created awareness regarding EDI. Having incorporated that awareness into the Annual Meeting Program Committee (AMPC), where EDI has become an important topic now, I find the program to showcase a more diverse selection of speakers and moderators. There's a big push to not only have the meeting gender-fair, but also to be representative of the overall society, making sure that we have inclusion from not only North America and Europe, but also the rest of the world, particularly Asia. We also moved the needle on awards. The first year after our inception, we had an all-female slate of gold medal and distinguished service medal winners due to massive efforts by Kar-

la Miller and Margaret Hall-Craggs soliciting nominations.

MRMH: What will the task force focus on in the coming years?

Elizabeth: Actually, the challenges of being an Asian academic will be the focus of our forum at this year's Annual Meeting. In the US we had black lives matter, and now we're facing issues of Asian discrimination. We're going to have Professors Pek-Lan Kong, from Hong Kong, and Caroline (Lindy) Rae, from Sydney, to make a sort of Pacific Rim, linking Australia and Asia and promote awareness, as Uduenna Anazodo has done with Africa. Another great initiative has been that of the Parents Working Group, where Lars Kasper, Kathryn Keenan, Shella Keilholz and Efrat Shimron have done an amazing job advocating for parents. They made headway by changing the policy of allowing children to be brought to the venue, at least in the poster

hall. ISMRM used to be a complete no-children event, which is not okay, as it discriminates against parents, especially young female scientists. For the highly anticipated Sydney meeting we had started the stipend program to support costs for bringing children and someone to take care of them. The Parents working group put a lot of work into the Sydney meeting, having local contacts, suggestions of kid friendly outings and all this stuff. And then of course the pandemic arrived which unfortunately extinguished all the efforts!

MRMH: What was the greatest challenge you encountered to date? And how are you dealing with it?

Elizabeth: I would say the greatest challenge is that I'm impatient and I want things to be done fast. But ISMRM is a big organization, and in order to move the needle, the needle sometimes has to go slower than I'd like. It's



While there's a lot of other societies that have an EDI committee, I think it's really hard to find another society like ISMRM. We're big. We're diverse. We have members all around the world, we have MDs, we have MD-PhDs, and we have PhDs. This inherent diversity enriches you.



more of a personal challenge, but I really want to move that needle. I'd love to see the change happen, to realize things that are not going to be flashes in the pan.

MRMH: In 2018, you released an interview for ISMRM, which ended with a powerful statement regarding the shift you wished to see in our Society: "I'd like for the Society leadership to embrace this idea and be the ones actively promoting Equity Diversity and Inclusion. I want ISMRM to be an example of how a Society can create environments for individuals or groups to feel respected, welcomed, supported and valued so that their voices can be heard and they can fully participate in the ISMRM. We will be stronger for it." Are you seeing this shift taking place in the Society?

Elizabeth: Unfortunately, again, COVID has slowed most of our initiatives, but I think the last ISMRM was definitely a more inclusive meeting. Maybe that had to do with the fact that it was virtual and that more people could actively participate. I felt like I have heard more voices; for example, in the sessions I found that there was a lot of engagement, and that was one of the really positive things that the virtual format has brought. EDI is all about engagement, we want people to engage, participate, and we want their input. In the future, I think hybrid meetings are the way to go, especially for inclusion.

MRMH: In the last MRM Highlights issue, we had an infographic showing that male members of ISMRM outnumber female members by 2.5 times, and this is particularly true within Full Members. What do you think could be done to encourage women to continue their path in the Society, especially given that Full Members have access to leadership positions?

Elizabeth: To me, this is actually a STEM issue with women, which has its roots in the inability of middle and high school to engage

girls and women in STEM programs. In ISMRM, we have women coming into the society as students, and of course we would like to retain them and have them be active engaged members. However, as time progresses to a stage of life where family planning becomes an interest, it is difficult to consistently engage people, as it coincides with childbearing years. If someone desires a family there will be the inevitable time for maternity/paternity leave. Thus, it's important to have flexibility in the work situation as well as the promotion process. It's critical to find a situation where the potential parent knows that they will be supported. Often, there is a plateau in productivity that occurs where one is going from assistant to associate professor due to competing family interests. Investment in communication, mentorship, and trust from leadership during these years can make or break a career. Personally, I was helped through that period: when I had my kids, my chair was supportive (luckily, she was a woman), and that seriously meant the world to me. It allowed me not to have to sacrifice one for the other.

MRMH: Gender inequality is a big issue, but it's certainly not the only biased aspect that the EDI task force deals with. Can you give us a few examples of unbalanced situations that might go unnoticed?

Elizabeth: There are a lot of different types of disability, and many of them aren't visible. If someone's in a wheelchair you can see that, but there are also neurological or psychological disabilities, such as autism, learning deficits, not being able to process auditory input, visual impairment. We must aim at having different ways of learning to satisfy all needs. I think being aware of people's disabilities is also part of the committee mission, and in this regard Hamied Haroon has been such a fantastic advocate for members with disabilities. For example, he brought to our attention that Paris was very hard to access, because of

cobblestone streets, and he couldn't go very far. These kinds of things are really important to take into consideration when choosing sites for meetings, or when considering going virtual. We also must take into account that some countries are not accepting of same sex couples. That's why I want to see hybrid meetings to take place, so that we can increase participation from all sides.

MRMH: What can we learn - if you have any experience - from other scientific societies in terms of EDI?

Elizabeth: Good question! While there's a lot of other societies that have an EDI committee, I think it's really hard to find another society like ISMRM. We're big. We're diverse. We have members all around the world, we have MDs, we have MD-PhDs, and we have PhDs. This inherent diversity enriches you. What we really need to work on are the Inclusion and the Equity parts. For example, we need to increase participation of underrepresented categories among the Awards nominees.

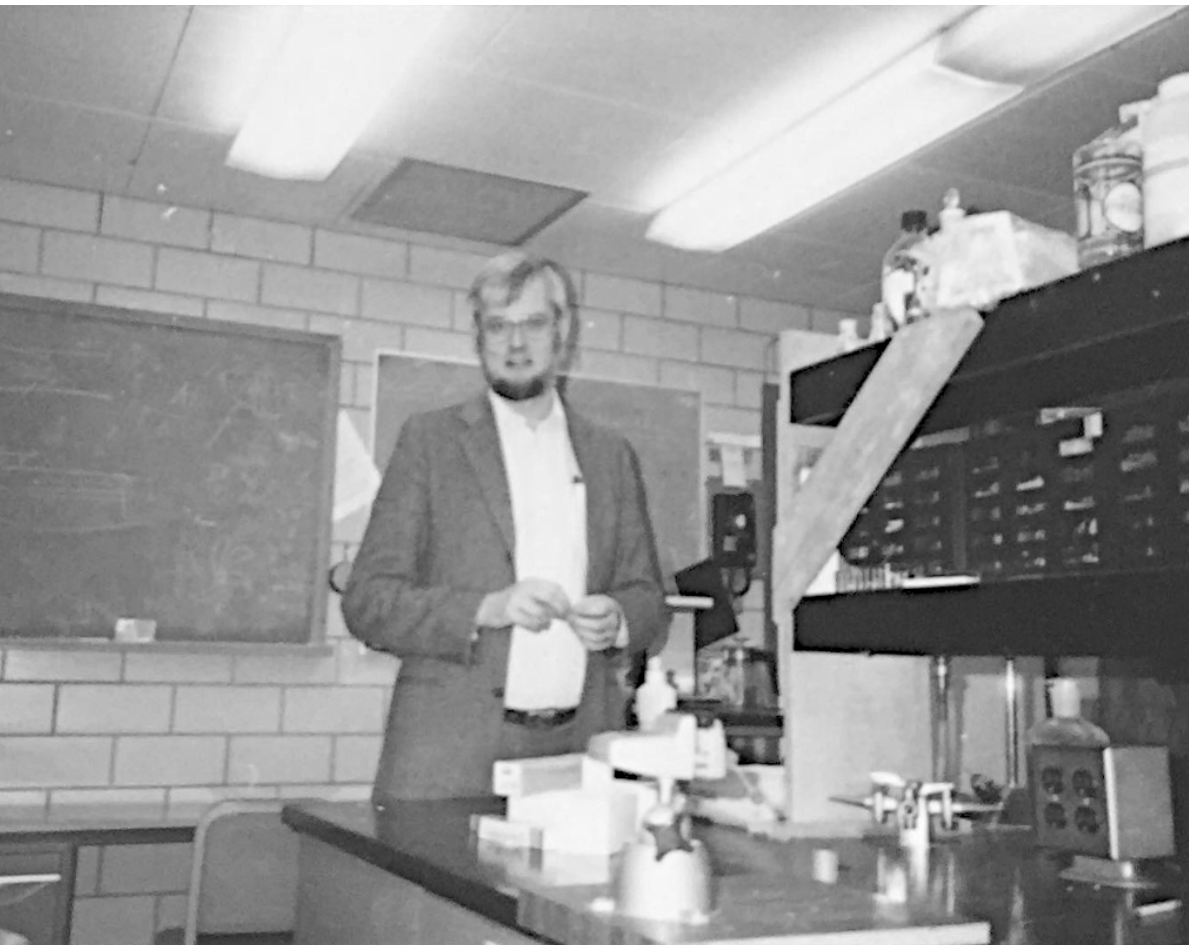
An important thing to recognize is that we are all biased. We wouldn't be human if we weren't. Part of EDI training is to recognize your biases and create some awareness around that. As an EDI task force, one thing we are going to do, when COVID lets us, is to train everyone in ISMRM leadership, or anyone that has an important role in the Society, on bias. Krishna Nayak is currently working on methods for unconscious bias training. One thing he recently proposed is a "how diverse is your universe" exercise, a questionnaire on diversity followed by a group discussion. As soon as we can meet in person, we will hopefully move this initiative forward. In the meantime, educating yourself on your biases with online programs is possible.

MRMH: Thank you so much, Dr. Morris, this was such an inspiring conversation.

Elizabeth: Thank you! It's been a joy talking to you about the task force! ■

Of Mice and Men on the Frontier of MRI in Canada

INTERVIEW BY ELLIOT MCVEIGH



Mark in the lab at Princess Margaret Hospital.

COURTESY OF ELLIOT MCVEIGH

“
So I went to Toronto, and I think mostly for patriotic reasons.

–Mark Henkelman

”

Elliot McVeigh: How’s life in Toronto these days?

Mark Henkelman: Well, it’s locked down pretty tight, and we’re basically stuck inside. It’s been a quiet winter - very little snow. I have been up to the cottage several times.

Elliot: I wanted to say congratulations, Mark, on the Order of Canada. That’s phenomenal, and brings me to my first question - over the course of your career you’ve set up these really great centers, you must have had opportunities to look at major jobs and potential centers south of the border, in the US. I can imagine lots of places that would be interested in getting you. So why did you stay in Canada?

Mark: Well, I’m a patriot. But seriously, when I left Van-

cover, I was offered a job at Harvard, and in the process I asked Toronto for a letter of recommendation. Harold Johns phoned me and said, “If you’re leaving, come and see us, we can give you a better offer than Harvard”. So, I went to Toronto, and I think mostly for patriotic reasons. Now, way back, I applied to graduate school in physics at all of the top schools in the United States. I was accepted to every one except Princeton. But then Vietnam came along, and no one would guarantee that I wouldn’t be drafted. So I didn’t go to the States, and it’s worked out incredibly well for me.

Elliot: I agree 100%, and it’s part of the reason why I think the Order of Canada is an appropriate award

Elliot, Mike Bronskill, Adrian Crawley, Mark, and Hal Dunlap at the 1985 SMRM meeting in London.

“
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—Mark Henkelman



COURTESY OF ELLIOT MCVIEGH

because you obviously had the potential to use a lot of resources down in the US, and instead, you chose to develop the resources up in Canada. It brings me to another point - you became the VP of research at Sunnybrook Research Institute, and subsequently built the Mouse House (Mouse Imaging Centre). So it seems that instead of taking traditional academic leadership jobs, you chose to build things. Instead of taking a job as a dean or a department chair, you built a new center or an entirely new research institute. Was that on purpose? Or was that just how it worked out?

Mark: I think you've got it right - I am inherently a builder. I like to make things that weren't there before. For Sunnybrook, we had some problems with Princess Margaret Hospital, and we wanted more space. It was actually Mike Bronskill's suggestion that we approach Sunnybrook. And there was a kerfuffle and I ended up as vice president. I agreed to give Sunnybrook eight years, which I did, and then I took a year's sabbatical. And then I decided I wanted to do something different. I wanted to build something else. And Stuart Foster and I just sort of said, "Let's quit imaging humans, let's image biology".

Elliot: Can you tell us about how you actually got into MR research?

Mark: I wrote 10 grants to work on MRI before there was any MRI, and had been turned down. The usual story was, "he's a smart guy, but he's got no experience in this and we're not sure it'll work." Finally, I said, well, damn it, we'll get some experience. So we grabbed this five ton magnet from the medical sciences building, got it cranked up and got some experiments done. And

from then on, 80% of my grants were funded.

Elliot: Oh, come on. That's a blessed life there, Mark, you worked hard. But that is pretty good.

Mark: I feel incredibly blessed. The province of Ontario had a Premier's Council on health, and they wrote this report. It had a section on MRI, which they knew nothing about, and it got sent to me for review. And I rewrote it totally, it was a good thing because they'd have been embarrassed had it gone through. But it also had an appendix on the end by a Catholic theologian on the ethics of high tech medicine, which infuriated me. It said, "you shouldn't introduce anything new in medicine if you can't make it available to everybody." And I put a big red X through it and said instead, "if you don't know whether it works, you should buy two of them and mandate two places to look at it for two years. And then if it works, you can ask about how to deploy it." Apparently, the committee was very impressed. Six months after that, I had a phone call from the Premier's office saying "that thing you were talking about, can you give me a one page write up?" This is 10:00 in the morning, and he wanted it by 2 PM, because the Premier wanted to put it in the throne speech. So I got my secretary to type it up, I put in my pocket and rode my bicycle across to the government buildings. The only time I've ever been in the government buildings. And sure enough, the next morning, the Premier said, "we're putting one of those things (MRI systems) into Princess Margaret Hospital."

Elliot: Remember those early days, and those trips we took to Technicare?

Mark: I was thinking of one of the first times. So we got this Technicare machine, a 0.15 T resistive magnet, un-

stable as hell. Everything was wrong with it. But it was a good learning tool. We went down and we met with Waldo Hinshaw, who was in charge of their shop.

Elliot: That's right. Remember we did a noise power spectrum of the background, and showed him all of the filters they were using, and they were like "how'd you get that?" I still enjoy those moments, actually, when you have the companies in the room and you pop up stuff you've measured from their scanner. Especially in CT, because they're not that happy about having all of these hairy things revealed. But, if you know what you're looking for, you can measure them.

Elliot: I tell students this story about you, and your back of the envelope calculation you made once. MR was just getting started, and you estimated that in order to actually have this work in humans, you would need, you know, a magnetic field that's like, 10,000 the Earth's field and the magnet would have to be the size of a truck. Therefore, this will never work.

Mark: Yes, I recall where that happened. It was a talk that Lauterbur gave in Ottawa. He imaged a lemon, and it took him 10 hours. And it took him 20 hours to reconstruct it. We were sitting around with beers afterwards, and I said, "Yeah, it's a cute idea, but not going anywhere."

Elliot: If you consider what it means to have been a scientist over the last 30 years or so, do you feel it's

changed? The volume of literature, and the pace at which science changes.

Mark: 50 years - I graduated 50 year ago... When I was asked to give my first talk at Princess Margaret Hospital on MRI, I went to the library and I got all of the papers. And I understood seven and the last one I've never understood.

Elliot: Peter Mansfield's interferometry explanation?

Mark: You got it. But yes, it's explosive. But I still think the experience of science is something that is wonderful. We had a little kid visiting us at the cottage, and we had peanuts over on the railing. And squirrels were coming by and picking up the peanuts. And I said, if you take the shells off the peanuts, will they like them better? So she shelled a bunch of them and said, "we're gonna do an experience. And I love that. Isn't that what we've been doing all along? Yeah, we call them experiments." But we are asking questions, and we feel really good. Because we're engaged. We're finding out about the world.

I don't think that's going to go away - a bit too bad that there's so much technology and you have to deal with companies, and there's lots of money and there's lots of politics. But fundamentally, we're asking questions to which we want to know the answer. And that's incredibly satisfying. And sometimes it's useful.

Elliot: I remember that you had this behavioral pat-

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It was a talk that Lauterbur gave in Ottawa. He imaged a lemon, and it took him 10 hours. And it took him 20 hours to reconstruct it. We were sitting around with beers afterwards, and I said, 'Yeah, it's a cute idea, but not going anywhere.'

–Mark Henkelman

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Giles Santyr, Adrian Crawley, Elliot, Scott Hinks, Mark, Mike Bronskill, and Peter Hardy at the 1986 SMRM meeting in Montreal .



COURTESY OF ELLIOT MCVIEGH

Mark and colleagues
in front of a Technicare
MRI scanner (0.15 T,
resistive magnet) at
Princess Margaret
Hospital in 1986.



COURTESY OF ELLIOT MCVEIGH

“
.. I think it is the
Mouse Imaging
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different

–Mark Henkelman

”

tern, where it seemed, regardless of what was going on in the lab, you never seemed to be overwhelmed or in a rush or anything like that. Usually by five o'clock, you got up and left, and you used to leave with this little folder. Inside the folder would be two papers, maybe. I'd be working in the hallway and say “see you tomorrow Mark”. And when you come back the next morning with that same folder, I knew damn well those two papers had been read. I tried to emulate that as best I could - know what it is you plan to do, or get it to the right size, so that you actually do it, so that you actually read those papers before you come back tomorrow.

Mark: I always wanted at least one paper with me, because I might have a half an hour. But I didn't need a briefcase full. I read copiously.

Elliot: Looking across your career, what's the thing that stands out? A specific contribution to the field - a favorite paper or discovery or method, something along those lines. Does anything in particular stand out to you?

Mark: There were about 10 years of basic MR development, lots of odds and ends, magnetization transfer and that sort of stuff, which was all very good science. But I think it is the Mouse Imaging Centre that I feel is my claim to have done something really different. Nobody had ever thought of that before. I didn't even know where it was going to go. But it took off far better than I could have expected. And it's well recognized around the world.

We got involved with this mouse knockout consortium,

which is a huge international effort. It's knocked out all of the mouse genes one at a time, and it's now made 22,000 different strains of mice. And it's maybe halfway through sequencing them. Our contribution was to say, if you really want to know what's going on, image them. And because that made us realize you can't do it one mouse at a time at an hour apiece, if you're gonna do it. You've got to scale it out, which sort of drove some of the technology features.

Elliot: I find it it's fascinating the relationship between genetics, behavior and morphological change in brains. Especially when the morphological change from MR distortion is not insignificant. There's a challenge there, right? The difference between distortion and actual morphology, and understanding the underlying physics so that you get all that right.

Mark: Jason Lerch showed that learning and memory results in morphological change. We've done lots of experiments, and it works. It always works. But we still don't know why - that bugs me. It's remarkable, people would never believe you could measure a 1% change. But once we did, a lot of people are now using it around the world.

Elliot: Quick question - how do you know that a mouse has autism?

Mark: It shows up in our behavioral measures. There is a three cage system, where on the right hand side, you have a strange mouse in a little internal cage. And on the left hand side, you have a Lego piece, also in a cage. And you put the test mouse in the middle. And you see where they spend most of their time. For what we

call an autistic mouse, it's about 50/50. Whereas a normal mouse spends 90% with the other mouse sniffing around. There are other tests, a whole battery actually. But that's the one that's most impressive, and actually remarkably robust.

Elliot: And what about missed opportunities?

Mark: Bob Balaban and I ran an MT workshop way back. And I was asked by somebody who said, "If you do the saturation on the left, or do it on the right, is there a difference?" And I said, "No, it's a symmetric line shape. So it looks exactly the same." And I was pretty adamant and a little pissed. This guy said, "No, no, we measured it". And I basically said, "you screwed up." But that must have been the CEST effect, so I remember that distinctly as one clear blunder.

Elliot: Are there any other thoughts you have Mark on where you see MR going? Have you been keeping watch on what's happening across the whole field?

Mark: I mean, the AI stuff I find intriguing. I started to fuss with that a bit, but I didn't have the right tools. In fact, I think the whole of imaging is going to be redone again, with much more sophisticated computing, less measured data, and more AI for getting answers. I don't know what that will look like, but it's clearly happening. And when I try to read about it, I haven't a clue what the hell is going on.

Elliot: Well, you know, I think one of the things is I'm not sure anyone does. But you can't argue with the performance numbers, even though it just rips out the core of my beliefs in signals and systems. You have

this crazy net that has, you know, millions of degrees of freedom, and it learns how to control itself. Are we going to drift away from people modeling signals, to "I don't really care if I'm going to model the signal, I just want this machine to perform as well as a human".

Mark: I think we'll reach a point where we don't even care what the raw data is coming in, and then we'll wake up and say, we've got to go back and figure out what is the real, important measured data. And then we can be as sophisticated as we want with the math. But if we don't get that input right, we'll start writing fairy tales.

Elliot: So what's what's next for you, Mark? What are you going to do?

Mark: Well, I thought I would retire and travel. But the virus had a different idea. I'm a little lost at the moment. It's a very interesting question as to what the world will look like, when COVID is over, or mostly over. Will we have all our meetings like we're doing right now (over Zoom)? Where we have a lab that only two students go to and do stuff, and report back to us?

Elliot: I tend to believe that we won't, because all of us are craving to get back together. At least the kids in my lab are anyway. But just the additional communication facility of sitting together and having a whiteboard available is pretty significant. Compared to sitting on a Zoom call...

Elliot: OK, thanks Mark - you stay well, and next time I'm up in Toronto we should grab a cup of coffee.

Mark: Thanks, it was a pleasure! ■



COURTESY OF JASON LERCH

“
... we can be as sophisticated as we want with the math. But if we don't get that input right, we'll start writing fairy tales.
—Mark Henkelman

”

Mark in his office at the Mouse Imaging Centre (MICE).

MRI in Canada: Jean Chen

INTERVIEW BY AUDREY FAN

Jean Chen is the Canada Research Chair in Neuroimaging of Aging, Associate Professor at the University of Toronto, and Senior Scientist at the Rotman Research Institute, Baycrest Centre for Geriatric Health. She has been at the forefront of using imaging to characterize brain aging and neurodegeneration, and we were lucky to be able to speak with Jean about her career, advice on juggling academic and family responsibilities, and her aspirations of driving a van around Toronto with a low-field MRI scanner in the back.



Jean Chen

MRMH: Can you tell us a little bit about what your lab is working on now?

Jean: I've been at Baycrest and the University of Toronto since 2011. Since then, my research has really honed in on brain aging and the vascular contributions to resting state fMRI. We've also expanded into quantitative fMRI and diffusion tensor imaging to study neurodegeneration. That's more by necessity rather than by design, because to answer some of the questions in aging, multimodal approaches are increasingly essential.

MRMH: How do you learn a new technique or choose a particular modality to pursue?

Jean: One example is that we recently included EEG into our experiments because I felt there are certain limitations in the MRI measurements that are driven by vascular effects. On the one hand, we really want the vascular information for its own value, but on the other hand, to get to the ultimate goal of understanding the neural implications of the resting state fMRI signals, we needed something else. EEG was a natural alternative, which I was completely new in.

And I must say that my students and postdocs who invested time in this are really great. We learned some of the EEG topics together, and they also taught me things from their prior experience. Being a supervisor doesn't mean you have to know everything; it's life-long learning. Unless you admit to not knowing some things, you cannot grow.

MRMH: MRI is still the core of your research – what drew you to MRI in the first place?

Jean: My undergrad degree was in Electrical Engineering, so I took a lot of courses on computer programming and computer architecture. I found myself naturally drawn to signal processing during my studies at the University of Calgary. I did not start out as an NMR physicist, but thanks to one of my professors, Mike Smith, I saw a gap in the application of engineering principles in medical imaging, and decided to do a Master's degree with Mike and Richard Frayne focus-

ing on MRI of stroke. I thought this would be where I can bring my engineering skills to bear in medicine and make a difference in patient care.

Toward the end of my Master's, I got into MR physics and went through a tutorial on how to program a GE MRI scanner. I still remember the first MRM paper I read was a 1996 paper by Leif Ostergaard on dynamic susceptibility contrast perfusion imaging. I became very interested in MR physics and the brain, so I decided to move McGill to do my PhD with Bruce Pike, which involved a lot of sequence programming and brain physiology.

MRMH: What got you through the initial challenging parts of research?

Jean: I believe every PhD has highs and lows, and it's not really for the faint-hearted. There is no way to foresee how the project will evolve over the course of a few years, and towards the middle of it usually comes a low point. I think what got me through, besides the unwavering encouragement from mentors, is the fact that I'm pretty stubborn and I don't take failure for an answer.

The experience taught me to be resourceful in problem solving, and to appreciate the power of friendship. During my time at the Montreal Neurological Institute, I had a really great group of friends. My friends and I had a common habit of working till late everyday and oftentimes on weekends, and we would hang out afterwards. Really good for morale, and they were often the subjects for my scans!

MRMH: What scientific communities are you currently embedded in?

Jean: Up until recently, I was actively involved on the OHBM (Organization of Human Brain Mapping) Communications Committee, specifically on the blog team. I volunteered to write blogs about MRI and brain research, and I really enjoyed the team because there was a shared passion to communicate science to the public and in doing so, to bring international research communities together. My trainees and I take

pride in attending the meetings and participating in the ISMRM and OHBM every year.

In terms of local community, there is a large research community in MR imaging in Toronto and I believe it's home to the oldest program of its kind in Canada. At the Rotman Research Institute, I'm the only MR physicist. I work regularly with Baycrest colleagues who are neuroscientists or psychologists; they'd bring their questions and I'd try to tailor MRI acquisitions to answer.

MRMH: How do you effectively communicate with collaborators who are not physicists?

Jean: We are constantly trying to educate diverse groups of trainees so that basic MRI concepts will not be foreign to them. There also needs to be compromise. For communicating, if my collaborators are trying to learn my "language", I am also trying to learn their language.

In my lab, for some years we've had a self-teaching neuroanatomy learning program. I would come up with study material on neuroanatomy and neurophysiology to teach those concepts to physics and engineering students. We try to bridge that gap by knowing some of the biology. Every year, we also have neuroanatomy trivia, which we take quite seriously (laughs). Interacting with trainees is the best part of my job. We laugh together, and I learn so much from them. I always hope that the time they spend in my lab will make a positive imprint on their lives.

MRMH: How have you made your position work with two kids?

Jean: As a female PI, I was wary because having kids meant that you had to spend a lot of time on caregiving. Spending time with my children is something that I love to do, but I was worried that it might reduce my productivity. To a certain degree, that was the case – in my research trajectory, immediately after the birth of each child, there's a drop in the number of publications.

But I would say that the downturn was only temporary, because having children made me more efficient. I became more focused than before and created a strict time allocation so that I don't overwork and neglect my kids. In the morning, I try to get to the office very early, but I would also have to be out by four o'clock to pick the children up from school. From then all the way until bedtime, my time belongs to them. I highly recommended kids as a means of increasing efficiency (laughs).

MRMH: What advice do you have for junior researchers who are considering families?

Jean: First, I'd like to debunk the misconception that successful researchers don't spend much time with their families. My kids deserve my attention, but I also benefit from being with them. If I were having a bad

day at work, and I come home and see my kids, my mood instantly changes for the better. Seeing them reminds me of the essence of life, and reminds me I need to set a good example for them. Of course, sometimes they drive me up the wall, but most times, they bring out the best in me.

Second, to junior researchers in general, I would also say, don't be afraid to speak up. My close friends know that when I was a student, I was averse to speaking up because I felt like an imposter most of the time. I think there may be some gender differences in speaking our minds we should be aware of, but it's important to practice speaking up (politely, of course). My mentors, especially my postdoc advisor David Salat, helped me to come out of my shell and start debating. Nowadays if I see trainees are afraid to speak up, they remind me of myself, and I make provisions to allow them to feel more comfortable doing it.

MRMH: How do you envision yourself and the MRI field growing in the next 5-10 years?

Jean: I'm of the mind that most positive developments would be organic. I think we're going to increasingly embrace multimodal imaging and quantitative fMRI, because a barrier to our research is the fact that most of the information in neuroscience and clinical fields today is not quantitative. We have known the caveats for decades, but we have not been able to introduce many feasible solutions in those realms. I hope this can be tackled with accelerated imaging methods and increased computational power to fuel our signal-modeling ambitions. As an example, we are now particularly interested in gas-free calibrated fMRI.

From a hardware perspective, I'm really interested in low and ultra-low field MRI. When we study aging, it may be a researcher's dream to be able to go from location to location to study older participants from different communities and backgrounds. I have always dreamt of taking a milli-Tesla scanner in a van with us as we drive around the city or even the province. Low fields bring affordability, accessibility, patient friendliness, and a new bench-to-bedside concept, which has been taking shape in my mind since I started working at Baycrest.

MRMH: What's something fun you do outside of work?

Jean: Once the pandemic is over, I'd love to go to Legoland with my kids, just to let them release their energy and remember how life was before. On regular days, I really enjoy cooking and the chance to produce my favorite meal at the end of the day. One of my kid's favorites is saag paneer – it's an Indian dish which is one of my favourites to make on weeknights. I also recently started baking bread, which is surprisingly therapeutic for me.

MRMH: Thank you so much Jean!

Jean: Thank you! It's been a real pleasure! ■



Interacting with trainees is the best part of my job. We laugh together, and I learn so much from them. I always hope that the time they spend in my lab will make a positive imprint on their lives.

–Jean Chen



MRI in Canada: Udunna Anazodo

INTERVIEW BY AUDREY FAN

“
Now the biggest
hurdle is finding
the personnel
to run these
scanners,
well trained
radiologists
to interpret
the images,
and imaging
physicists
that can help
clinicians
use MRI to
solve relevant
problems.”
—Udunna Anazodo

Udunna Anazodo is an Assistant Professor at Western University and an Imaging Scientist at the Lawson Health Research Institute. We were excited to catch up with Udunna as part of our interview series on Canadian scientists, find out what she's been working on, and to hear her perspectives on accessibility considerations for imaging technology in our global research community.

MRMH: What are your main research interests and how do they intersect with the MRM community?

Udunna: My main research interest is to understand what biological mechanisms drive functional changes in cognition in late life. These mechanisms include inflammation, oxidative stress, and vascular dysfunction. The idea is - can we make imaging tools that are sensitive enough to detect subtle changes in drivers of cognitive change?

I look at this as a mind-brain and body problem because these mechanisms are ubiquitous biological pathways activated in nearly all tissues in the body in response to stress, trauma, infection, or injury. This makes it important to understand how the mind is influenced by neurodegenerative changes but also systemically by how the body interacts with the environment (physical, psychosocial, cultural, etc.). I use a heart-brain connection and cardiovascular disease as a model to address this research question. In cardiovascular disease, I want to use imaging to understand the impact of major cardiovascular events, such as infarcts or heart attack, on the brain and how this influences cognitive function. Is the effect of a heart attack transient or can it actually lead to long-term changes in cognitive function? Can we image the brains and hearts of ischemic cardiac disease patients shortly after a cardiac event to better predict cognitive outcomes?

MRMH: As a field, we're only just starting to make imaging links between the body and the brain. How is your lab pursuing this?

Udunna: My lab started with imaging vascular dysfunction, which can be done well using contrast and non-contrast MRI. The next link is inflammation and we are interested in how it interacts with vascular dysfunction to influence cognitive function. We use an integrated PET/MRI scanner to simultaneously image inflammation using TSPO – translocator protein PET



Udunna Anazodo

tracers and vascular dysfunction using MRI. The neat thing about TSPO PET tracers is that they were initially designed to penetrate into the brain to look for changes in microglia activity but they also bind to macrophages, so this allows us to link inflammation in the body to the brain.

We're going to link inflammation to vascular dysfunction in the heart and brain of ischemic heart disease patients, focusing on blood-brain barrier dysfunction in the brain and ventricular function in the heart. We are also going to ask how this heart-brain interaction affects brain networks (BOLD fMRI) and how it contributes to cortical and macrostructure (DTI) degeneration. If we can put all these parameters and puzzle pieces from the brain and body together, then we might be able to un-

derstand why some parts of the brain are more vulnerable to systemic changes than others and why some individuals are prone to cognitive decline and dementia.

MRMH: Are you going to follow the same patients longitudinally?

Udunna: Yes, the ischemic heart disease patients will be followed and imaged twice, 6 months apart. I am fortunate to have access to one of the largest and well-coordinated cardiovascular rehabilitation programs in Canada, which runs in the same building as the PET/MRI, actually a floor below from the PET/MRI suite. I think we are probably the only group in the world with this setup and with also immediate access to a cyclotron and radiopharmacy lab to make TSPO imaging tracers.

Cardiac rehab is a 6-month multi-intervention program and includes things like exercise, diet counseling, and cognitive behavioral therapy for mood disorders, and it's offered to patients as the standard of care here in Canada. We've seen that cardiovascular rehab decreases your risk for reinfarction and may prevent stroke, so we know it is good for the heart. But I demonstrated during my PhD that it is also good for the brain and may even reverse cardiac disease effects on the brain like gray matter atrophy, macrostructure integrity loss and cerebrovascular dysfunction. This gives us an opportunity to see if cardiac rehab, particularly the exercise aspect of it, modulates the inflammatory load and vascular dysfunctions in the heart and brain. This is something that could make cardiac rehabilitation an even more important clinical intervention in management of cardiac disease.

MRMH: If you're given an opportunity to go to Ottawa and make a pitch, what would you advocate for related to imaging research?

Udunna: It's striking to ask these questions on a population level because a lot of these mind-brain-body issues are affected by our physical and social environment. These environments are constantly changing and changing more rapidly than our bodies can adapt to. We know air pollution is just as deadly as smoking - it is the new tobacco and has been linked to rising rates of heart disease and dementia, globally. But we don't fully know how these changes in our environment are acutely and chronically changing our bodies to impact our brain and mind.

Because these health impacts are driven by adverse changes in the environment, we can't rely on centralized imaging facilities to understand this question. We have to take the lab to where the people are, to where the largest burden of brain and other chronic diseases are - to the poorer low-to-middle income communities. There are communities in Canada, especially indigenous communities, that experience poor physical environments who don't have access to 1.5 or 3 Tesla MRIs. So, to understand how the body interacts with the environment, we have to bring the lab to the people by

creating MRI technology including imaging sequences for low-field MR and portable scanners. So, I would encourage the government to invest in home-grown accessible imaging technology and research innovation in Canada and turn Canada into a global leader in production of high-value portable imaging technology.

MRMH: In your perspective, what are current barriers to make imaging more accessible?

Udunna: Cost is one, but lack of imaging expertise is equally an important barrier. I got firsthand experience seeing this when I visited Nigeria in January 2020 and went to a few hospitals and imaging centers, including those in key cities in Ibadan, Lagos, and Abuja.

The number of 1.5 T scanners in the region is growing, because they have figured out how to power the scanners continuously but also are increasingly able to secure financing to procure high field scanners. Now the biggest hurdle is finding the personnel to run these scanners, well trained radiologists to interpret the images, and imaging physicists that can help clinicians use MRI to solve relevant problems. As a community, we (the ISMRM) have an opportunity to provide advanced and multiparametric imaging capabilities to low-resourced regions as an alternative to PET or even CT. There are just 2 PET scanners in Africa, outside of South Africa and North Africa. Think about what this means for cancer care in the region. CT contrast, a staple in acute stroke imaging, for example, is not readily available in most African countries. I spoke to a neuroradiologist at Lagos University Teaching Hospital about imaging for epilepsy surgical planning and asked how they provide care in the absence of PET and sparse SPECT imaging for cases where standard anatomical MRI appear normal. She smiled and calmly said, if we don't see it on MRI, we don't operate, we can't do much beyond this. But non-structural lesions can be detected with sodium MRI, ASL perfusion imaging, and DTI,

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I want to use imaging to understand the impact of major cardiovascular events such as infarcts or heart attack on the brain and how this influences cognitive function.

-Udunna Anazodo

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Udunna pictured in front of a 0.36 T Mindray Open bore MRI system at the University College Hospital in Ibadan, Nigeria.



Udunna with radiologists, radiographers and a nuclear medicine physician in front of the Access to Basic Medicine Center (ABC), in Ibadan Nigeria - one of the growing number of private diagnostic imaging centers in the region with a 1.5T MRI.



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ISMRM can provide an inclusive space for collaboration and networking, which are very important in advancing MRI research and clinical translation.
-Udunna Anazodo

just as PET and SPECT can. Research into optimizing these techniques can be enabled in these communities through collaboration within ISMRM. MRI can be a cost effective and high value tool for low-resourced areas, if we can enable colleagues in these communities to gain the skills and training, they need to create their own solutions.

MRMH: How are you trying to bridge this with your efforts on the Equity, Diversity, and Inclusion (EDI) committee in ISMRM?

Udunna: Through the EDI initiative at ISMRM, I am working to raise awareness on the MRI challenges in low-resourced regions and provide opportunities for ISMRM members to partner with local experts on the ground to increase MRI access. The ISMRM Virtual Meeting in February (ISMRM Spotlights Africa: Doing Much With Little) highlighted important targets for those interested in working on this problem. Training being one target, but another is networking and knowledge exchange. ISMRM can provide an inclusive space for collaboration and networking, which are both very important in advancing MRI research and clinical translation. I plan to continue working with the EDI committee to make it more feasible for trainees and MRI experts in low-resourced communities to attend and present at ISMRM meetings and training workshops. I hope we can have more of these region-specific spotlight series in the future. Maybe the next one will spotlight unique imaging challenges and opportunities in Latin America or the Middle East.

MRMH: What can individual ISMRM members contribute to research in low-income areas?

Udunna: Within the African continent, there's currently no good funding mechanism to fund health research or enable imaging technology development. When funding exists, a lot of it is diverted to what is typically thought of as "Africa's problems", such as infectious disease. However, looking ahead, the rise in stroke, cancer,

and dementia burden will not be in Western countries, but rather is projected to be in low-to-middle income countries, including Africa. So how can an individual ISMRM member help with imaging research to address these complex health problems; 1) Train students from low-to-middle income countries and regions in your lab. A perfect example of this is Dr Johnes Obungoloch, who learnt to build low-field scanners at Penn State and now leads a dynamic biomedical engineering group at Mbarara University of Science and Technology in Uganda. For those interested in students from Nigeria, Ghana, Rwanda, Tanzania, Uganda, or Cameroon, I can help connect your lab to groups in the region. 2) Plan studies that include patients from these unique populations. There are local clinical experts in stroke, cancer, cardiac disease, and dementia in the region with no imaging expertise that ISMRM members can collaborate with. There are NIH funding programs that support this and local data collection helps increase local MRI capacity. Finally, 3) Develop MRI sequences and data analysis tools in an open-sourced and vendor-neutral manner, so these can be readily accessible.

MRMH: What are you looking forward to doing when we can travel again?

Udunna: Any time I travel, I tend to go to museums, especially museums of culture or art. I like thinking about what it is to be human, and how we've evolved as humans to get here. How do we as humans grapple with our changing environments (physical and social), and what were our human ancestors doing when the environment was different- more homogenous, or should I say more local, less global? I think that answers to some of these questions could be preserved in the works of arts and culture in these museums. I've been listening to Mike Duncan's podcasts on The History of Rome during the pandemic, but I am looking forward to going to museums again.

MRMH: Thanks for your time, that was a lot of fun.

MRI in Canada: Julien Cohen-Adad

INTERVIEW BY AUDREY FAN

Julien Cohen-Adad is a Canada Research Chair in Quantitative MRI, Associate Professor at the Ecole Polytechnique de Montreal, Director of the NeuroPoly lab, and a fixture in the spinal cord imaging community for many years. We had a great conversation with Julien on open-source software, his approach to mentoring, and his passion for shimming.

MRMH: What attracted you to MRI research?

Julien: I did my Master's with Pierre Jannin in Rennes, working on the issue of brain shift during neurosurgery. During my Master's, I was fascinated by how beautiful the images the MRI system produced were. But at the time, I had no idea how complicated this technology was. Then, in 2005 I had an opportunity to do a PhD with Habib Benali, who was in Paris at the time, and Serge Rossignol, who is an MD trained in neurophysiology. My mission was to develop analysis methods for functional MRI of the spinal cord.

MRMH: Why is it important to study the spinal cord?

Julien: The rationale for my PhD was spinal cord injury, when there is partial interruption of the tracts of communication between the neurons in the brain and neurons in the spinal cord. (Because there are neurons in the spinal cord!). We were interested in people with partial injury – and some showed improvement after several weeks of locomotor training on a treadmill. Why is that? How can we use non-invasive imaging to see the actual state of the injured spinal cord and optimize the training?

The preliminary fMRI results were disappointing, because the quality of the data was horrible. An out-of-the-box EPI scan simply does not work well in the spinal cord; it's "garbage in, garbage out". This is how I shifted my attention to MR physics and data acquisition, rather than focusing on data processing. This illustrates how things could shift during the course of a PhD, and it's healthy to revisit the problem at large.

MRMH: For your PhD students, how do you balance freedom with hands-on mentorship?

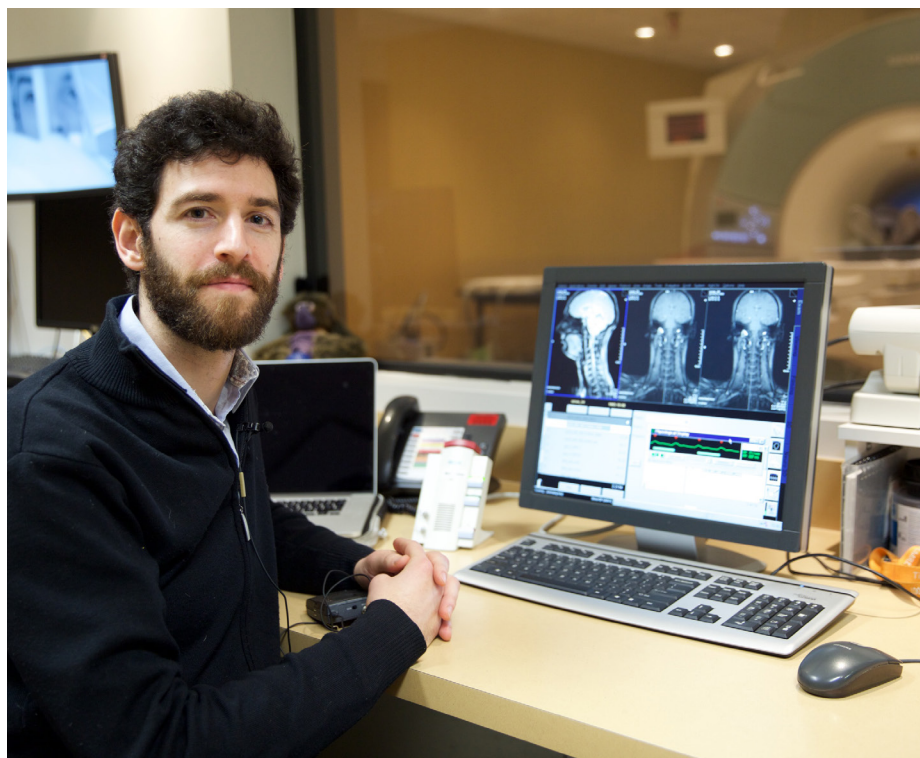
Julien: I have regular meetings and constantly try to treat everyone as equals, whether they are a fresh Master's student or postdoc or PI like myself. We are all equal and trying to solve a problem together, and that makes the discussion way easier.

At first, Master's students would address me with "vous" because in France, the "vous" and the "tu" forms are two different ways of addressing "you". The formality immediately creates a barrier and removes freedom in the conversation, which is not efficient for exchange of ideas. I'm really trying to facilitate communication so that students can think about research without any concerns other than solving a scientific problem together.

MRMH: How do you come up with ideas to overcome scientific problems?

Julien: I come up with my best ideas in the morning when I shower. And in general, going to conferences,

Julien in front of the scanner console, doing what he likes to do best: scanning!





2016 Christmas party in the lab.

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As MRI has become popular, I've also become increasingly aware of the reproducibility crisis in neuroimaging.

–Julien Cohen-Adad



attending talks, and talking to people are excellent ways to get ideas. These activities are very important to get immediate feedback on our ideas. I miss going to conferences in person because to me, the purpose of the conference is to just be among others – to confederate with people.

MRMH: When was your first ISMRM?

Julien: My first ISMRM was in Toronto in 2008. I remember being very excited about the free food events, and getting lost in the conference center. I also remember a funny anecdote: the conference center is divided into two distinct aisles. While passing through the first non-ISMRM aisle to go to the ISMRM aisle, I noticed that another parallel conference was happening at the same time. That conference was on beauty products. What struck me was the drastic difference in gender distribution between aisle 1 and aisle 2. Fortunately, the ratio at ISMRM has been changing since then. I realize this anecdote is very apropos as we're doing this interview on International Women's Day.

MRMH: How have you seen this representation evolve over time in Canada?

Julien: EDI (Equity, Diversity, and Inclusion) is present in all our committees, such as recruitment for fellowships and faculty positions. The main question, though, is how are these policies implemented?

I'm part of the "clan" that is more proactive and believe there are things that need to change right away. Affirmative action is a concrete action that could make that change. After things are more balanced, we can reconsider our policies, but I believe we need a few years of transition where we are highly proactive in EDI.

MRMH: How do you balance family and work?

Julien: When I started my academic career, I had no family responsibilities. Now I have a partner and a 4 year-old, and balance has been both a necessity and a

lifestyle decision. I have learnt to say no to new work opportunities, and to be less obsessed with trying to neatly align all the boxes when making figures for a paper or for a talk. I'm also quite obsessed with optimizing my workflow using productivity apps like Quiksilver and using keyboard shortcuts.

MRMH: Tell us about the balance between scientific disciplines in your lab.

Julien: I started my lab with a mix of engineering, neuroscience, and related fields, except one: open source software. Evolving in MRI academic research made me realize that software is the glue to everything. To do shimming, we need software. To process MRI images, we need software.

As MRI has become popular, I've also become increasingly aware of the reproducibility crisis in neuroimaging. My friend and colleague Nikola Stikov, with whom I co-direct the NeuroPoly Lab, is particularly sensitive to this issue. So, we took on the open science mission, and the development and maintenance of open source software came with this spirit. I love to code, and hiring professional software engineers to maintain the software ecosystem and implement good coding practices is critical.

MRMH: How have you sustained growth of your open source Spinal Cord Toolbox?

Julien: Our first methods to automatically segment the spinal cord and to perform image registrations were developed over 10 years during my PhD and later by my first student, Benjamin De Leener. When we announced the toolbox at the 2014 OHBM conference, there were maybe five users in the world. Now it's over 500 users. It's very rewarding to witness the community using our tools but it comes with a lot of responsibility. It takes a lot of resources to find excellent software developers (we have seven now) and about 95% of the effort goes



Lab members' brain scanned, segmented, 3D printed and turned into Christmas tree ornaments.

to maintenance. A general software developer has no idea what MRI is or what the NIFTI format is, so they need to communicate with our lab to get a sense of our users. It's an excellent experience for students to work with professional developers and see their tools being used by researchers all around the world.

I plan to continue developing open source packages, including a new shimming toolbox that we'll announce at this year's ISMRM.

MRMH: What is unique about working in Montreal?

Julien: I will probably annoy a lot of people, but I find Quebec to be a fusion between the US and France, where I'm from. There is a much-needed dose of pragmatism, brought by the Anglo-Saxon influence, into the Latin culture which I grew up with.

Montreal is a hub for both neuroscience and AI. There's a very cool initiative called Compute Canada, which provides all academic researchers free access to over 250,000 CPUs and 2,500 GPUs. It's also a hub for leisure - if you are a foodie like me, you will enjoy the many diverse restaurants. The art scene is also quite active, especially the street art, and finally the bilingualism brings a *je ne sais quoi* of cultural richness.

MRMH: How has the field changed since you started working in MRI?

Julien: It changed by +4T. (Sorry, this is an obvious joke.) More seriously, I see that shimming is gaining attention. I've also witnessed the increasing popularity of the word "quantitative", and frustration about the elusiveness of true quantitative MRI. There is an eternal debate between the "accuracy clan", which tend to be the physicists and the "precision clan", which tend to be the physicians.

Accuracy means: can we get the number right? This opens a Pandora's box of how you validate imaging, because for instance histology methods themselves can be questionable. Precision means: can we take the MRI method to another country, have another technologist model the data, and get the same results? We should question what we spend our time on and what adds value for clinicians.

MRMH: Looking ahead 5-10 years, what do you think

are the most exciting developments in MR?

Julien: Shimming. On the topic of quantitative MRI, I'm following the debate between accuracy and precision and curious to see who is going to win. Maybe both, if the research community does a good job in standardizing practices, and manufacturers "open" their systems more. With the deep learning tsunami, AI will definitely become more pervasive in our work, so we need to be aware how these algorithms are implemented. I do think that it will bring some good, notably for MR reconstruction and computer vision tasks.

MRMH: What do you do for fun when not working?

Julien: Spending time with the ones I love, playing piano, playing tennis, smoking pot, and answering questions for MRM Highlights!

MRMH: Thanks Julien, it was great speaking with you.

Julien: Thanks so much for putting this together! ■

Lab picture at the Montreal workshop "Toward a Super-BigBrain: Promises and Pitfalls of Microstructural Imaging" organized by Nikola Stikov.



Tim Leiner

INTERVIEW BY STEFANO MANDIJA AND CHENGCHENG ZHU

Tim Leiner is a tenured Professor of Radiology and holds the Chair in Cardiovascular Imaging at Utrecht University Medical Center, Utrecht, The Netherlands. As current ISMRM President, he shared with us his views on the past and the future of the Society, as well as his scientific interests and wishes to make ISMRM an always better Society to be a part of.



Tim Leiner

MRMH: When was your first ISMRM meeting and how many annual meetings have you attended since?

Tim Leiner: The first one I went to was Philadelphia in 1999, and since then I have attended all meetings in person, except for the last one, of course, which was virtual!

MRMH: Do you have any tales that you would like to share with us about your first steps in MRI research?

Tim: During my 4th year in medical school, I became interested in a research project where they needed someone to help recruit patients. It was a study focused on MRI of peripheral blood vessels in the abdomen, pelvis, and legs. I wanted to become a cardiologist, so I thought “this is interesting!”. I applied for that research position and I got it. Together with my supervisor, Dr. Kai Yiu Ho, we came up with this new technique to do MRI imaging of the peripheral vessels. Soon, we were spending evenings and weekends working on this technique, and he suggested to submit an abstract to the ISMRM conference.

MRMH: Do you remember your first ISMRM presentation? How was your research initially received?

Tim: This abstract was accepted for an oral presentation and so I booked a plane ticket to Philadelphia. I was both super excited to get the chance to present our results, but also scared to death of being on the podium in front of all these experts, who were much older and wiser than I was. But after talking to them, they turned out to be very friendly people. This is how I became part of the community of vascular imaging in the first place, and every year I attended ISMRM I got to know more and more people. I still consider the ISMRM Annual Meeting my primary scientific home.

MRMH: What was your first official role in the ISMRM? And which path led you to become this past year’s ISMRM President?

Tim: After my PhD, I went to work with Dr. Warren Manning in Boston. During that period one of my supervisors suggested that I show my interest in doing committee work at ISMRM. I mentioned this to a couple of people that I knew and after a while I got an invitation to chair a session. I got to know more and more people, and I kept letting them know that if they were

looking for committee volunteers I would be willing to help. From there I got into the Board of Trustees, between 2006-2009, and ever since I have always been involved with the ISMRM. Suddenly one day, I was asked if I wanted to run for President. I wasn't expecting that at all but I tried. I actually ran twice: the first time I lost to Pia Maly Sundgren. Then they asked me again, and I got elected.

MRMH: Is there anything you would do differently at this point if you could start over again? Do you have any advice for our members?

Tim: Looking back, personally I would not have done anything differently. I really believe that if someone wants to get involved in places like ISMRM, they just have to step forward, let people know that they would like to be involved. There are so many tasks and things that need to be done within the Society, so we are always looking for people willing to do things.

MRMH: How has ISMRM changed over the years?

Tim: One of the changes that I have seen happening is a downward trend in the number of doctors within ISMRM and I think it is a shame. One of my priorities is to try to reverse that. All the technical advances that are happening are fantastic. MRI is an incredibly powerful tool in modern medicine, and I am always amazed and full of energy when I see all the cool techniques that are being developed, but I think our field could be even more powerful if more doctors were involved, as they are the ones who know what the true clinical needs are. We need to bridge the gaps that the MDs feel exist in terms of diagnostic tools and techniques, especially in incredibly promising fields such as MRI for therapy and intervention, where there are no other techniques that can do this.

MRMH: What do you think is the cause of this decline in MD numbers?

Tim: MRI techniques are becoming more and more complex, and many physicians feel intimidated by all the technical details. Thus, they prefer to attend organ specialty-based meetings, where they learn about how the new techniques are used, without the load of technicalities. But I think if we involve these clinicians we can create something more than the sum of the separate parts, developing things that can be translated into clinical practice for the benefit of patients and patient care.

MRMH: Are there any actions being undertaken to reverse this trend?

Tim: One of the initiatives we are deploying in the upcoming meeting is to build a sort of clinical mini-meeting into the more technically focused ISMRM program. We will also try to involve clinicians by creating a recognizable clinical curriculum for them in these days. Hopefully, they will see all the cool stuff we are doing as a Society and decide to stay around in the coming years.

MRMH: Looking to the future, what are the emerging



Tim at the 2000 ISMRM Annual Meeting in Denver.

technologies that you think are worth investing in?

Tim: That's a difficult question and a little bit subjective. I am a cardiovascular radiologist and I look at the field through this lens. When I got started, the 1.5T systems were just becoming mainstream. From there, high and ultra-high field MRI systems have been developed, but to be honest, a trend that I see in cardiovascular imaging is actually people exploring low field imaging. And it is interesting because, from the work that I have seen, the images are more than good enough for clinical diagnosis of bread-and-butter cardiac conditions. I think that this trend might be very beneficial for MRI, because at low fields the magnets become much cheaper and many more patients can get access to cardiac MRI. I also think that manufacturers are looking into this with a lot of curiosity and I think there is a market for these systems as these smaller magnets can be also based in smaller facilities, and not only in big hospitals. I think that it has the potential to democratize MRI imaging for many applications and I am excited about this trend.

MRMH: What do you think about Artificial Intelligence (AI) in MRI?

Tim: That's a very big topic. I think AI has the potential to add value in all of the steps of the imaging process. From selecting patients for imaging, making use of the clinical information, to image acquisition, reconstruction, analysis and generating automatic reports and deriving prognostic information. Images used for clinical decision making also contain prognostic information that may not be relevant at first for making a clinical decision or answering a certain question, but could be useful for long-term monitoring of patients. I therefore think that all these steps will be affected by AI techniques and this will have a big impact on the way we will do MR imaging in general. We can already see it in other cross-sectional imaging techniques, e.g. CT, where there are commercially available scanners that have AI image reconstruction, so I believe this will

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Anyone that wants to contribute to ISMRM in a positive way should be heard. There should never be any barrier to that in a scientific society.

–Tim Leiner

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Tim at the start of his Postdoc in Boston, in 2002.

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We need to bridge the gaps that the MDs feel exist in terms of diagnostic tools and techniques. [...] This way we can create something more than the sum of the separate parts, developing things that can be translated into clinical practice for the benefit of patients and patient care.

—Tim Leiner

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come also to our clinical practice very soon.

MRMH: What about open access data allowing reproducible research and replication of results?

Tim: I think this is very important. On one hand, it may not be the most sexy topic, in terms of getting it published in Nature or other high-impact journals, but I think it is super important for the reliability of the field that we are as open as possible, allowing reproducibility studies on the data and algorithms that we publish. One of the things that I really like and I am looking at this with the journal editors is whether we can ask authors to publish manuscripts including datasets and code available for other researchers. I think by doing that, the chances for a novel technique or approach to be accepted will be much greater. As a clinician, we would never use techniques that are not properly validated and tested across different institutes. To have a clinical impact this is an essential step forward.

MRMH: ISMRM has been very committed to guar-

anteeing equality, diversity and inclusion among its members. What do you think the results of these efforts are at the moment and is there anything else that would be worth doing in this regard also in the upcoming meetings?

Tim: I think this is a very important topic and I strongly believe that anyone that wants to contribute to ISMRM in a positive way should be heard. There should never be any barrier to that in a scientific society. One of the things we have within ISMRM is an EDI officer, Elizabeth Morris, who is a dedicated person asked to make sure that all the committees and activities within ISMRM pay attention to this. As of 2020, about a third of our full members is female, while among trainees the ratio is less than a half. It is therefore our concern to understand why women do not stay with us for the long term. For instance, when people start a family and have children, women are often the ones bearing most of the burden. One thing we are trying to do is to make it easier for young parents to

attend the annual meeting by offering child care, for example, and trying to lower that barrier.

MRMH: Recently ISMRM has launched Sustainability Initiatives to reduce the environmental impact of the meeting (<https://www.ismrm.org/20m/sustainability/>). What do you think we can do, as individuals and as a Society, to contribute to facing the climate crisis? Do you think this new online format could be one possible solution for this?

This is a relevant question that we are continuously evaluating. In fact, in April we will have a strategic meeting with the leadership of the society to see all different scenarios in this regard. But what will be the future of our meetings? What we have learned during the pandemic is that the possibilities for coming together as a community online were better than expected. On the other hand, we hear a lot from our membership that they would like to get back together physically in one place. I think this will not go away, but what we can do is that we make sure to carefully consider the impact of doing this in terms of frequency of meetings, maybe coming together in different locations avoiding long travel, or even by providing online platforms for people to join meetings remotely from their home country. I think we will become more thoughtful about how this will take place but I also think we cannot totally replace getting together in person with an online conference. It is very difficult to replicate that surprise element of running into someone in the hallway and sitting down for a coffee, exchanging some ideas and catching up in an online meeting.

MRMH: What are the chances of having the next Annual Meeting in London in person?

Tim: It depends. If vaccination takes off, and most of the ISMRM member countries are well on their way, hopefully by the end of this year most of our members will have received a vaccination. There will be therefore good chances that the next meeting will be in person. But we are also looking at a hybrid meeting solution to include members that cannot travel because of institutional or country restrictions. It's likely this hybrid type of meeting will be a new type of format in the future.

MRMH: This is now the second year we are having the Annual Meeting online. Is there any activity devoted especially for new members who otherwise might not feel fully engaged in the community?

Tim: We will always have the so-called newbie reception for people attending for the first time, to welcome them in the Society. There they will have the chance to meet and talk with senior leaders in the field. This year will not be an exception.

MRMH: Is there anything specific you are looking forward to this year's Annual Meeting?

Tim: As a Society, we are doing fantastic work that has the potential to be highly impactful. In this regard, a priority that I have is to further improve how to explain

our work to the outside world, patients, funding agencies, doctors, and people who could potentially benefit from our activities. We will have a Presidential lecture by Simon Singh on this topic: 'Explaining science to the outside world' and I am really looking forward to this lecture!

MRMH: Over the last two years, we as a wider society have also been affected by the COVID-19 pandemic. What is the role of MRI in COVID?

Tim: The short answer is we don't know the role of MRI. The long answer is, I am involved with a group of cardiac imagers and we're writing an article about what MRI can do for COVID regarding heart disease. We know COVID can damage the heart, but we don't know the long-term effects yet, because COVID hasn't existed for that long. There are some case reports showing the heart disease was so serious that it even led to cardiac death. If there is evidence of heart damage by echo or lab test, MRI will be valuable to see what is going on in these subjects. Some patients have consistent symptoms, which is called "long COVID". They feel they are never recovered regarding their energy level, and maybe MRI can help understand the mystery. And I am sure we will see some abstracts in the coming ISMRM meeting and future meetings addressing these questions.

MRMH: Thank you very much for speaking with us.

Tim: Thank you, it was a pleasure. ■



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It is super important for the reliability of the field that we are as open as possible, allowing reproducibility studies on the data and algorithms that we publish.

–Tim Leiner

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Tim as a PhD student in Maastricht, in 2001.

2021 ISMRM Young Investigator Award Finalists

EDITED BY MARK CHIEW

Every year the Society nominates three finalists each for two Young Investigator Awards (YIA), and the winners are announced at the annual meeting. The W.S. Moore Award (JMRI) is given for original clinical research, whereas the I.I. Rabi Award (MRM) is given for original basic science research. As usual, we have an outstanding group of finalists, and we have the pleasure of showcasing them here in the Highlights magazine.

Caroline Colbert

W.S. Moore YIA Finalist

My interest in physics began as part of my undergraduate education in Nuclear Science and Engineering at MIT. An undergraduate summer internship at Massachusetts General Hospital convinced me to pursue a graduate degree in biomedical physics. Presently, I am a PhD Candidate in the Physics and Biology in Medicine Graduate Program at UCLA. My research is overseen by my co-advisors, Drs. Kim-Lien Nguyen MD and Peng Hu PhD. My research focuses on the development and validation of novel magnetic resonance imaging techniques

Caroline Colbert



for the diagnosis of ischemic heart disease using the iron-based contrast agent ferumoxytol. As part of my PhD research, I worked with my advisors and our collaborators to develop 3D printed coronary stenosis implants that can be used to create swine models of acute myocardial hypoperfusion. My group uses these swine models to develop and validate ferumoxytol-enhanced (FE) cardiac MRI techniques such as FE T1 cardiac stress testing. Most recently, our group has investigated a two-compartment fractional myocardial blood volume (fMBV) model

in healthy and ischemic swine. As part of this work, we adapted an existing principal component analysis-based image registration method for use in studies of fMBV and integrated it with in-house T1 and fMBV fitting code to create an end-to-end data processing pipeline for generation of fMBV and T1-reactivity maps. We hope that in the future this tool can be further adapted for other parametric mapping applications. Going forward, our group plans to investigate FE T1 reactivity and fMBV mapping as part of a clinical study in patients with ischemic heart disease. We are also interested in investigating the applicability of fMBV mapping to other myocardial pathologies.

NOMINATED PAPER:

“Estimation of fractional myocardial blood volume and water exchange using ferumoxytol-enhanced MRI”

Fractional myocardial blood volume (fMBV) provides insight into myocardial ischemia severity beyond what is provided by myocardial blood flow (MBF) alone. Multi-compartmental modelling can be used to quantify fMBV from contrast-enhanced cardiac MRI. True intravascular contrast agents eliminate the need to model contrast leakage into the extravascular space. One such agent is ferumoxytol, an ultrasmall superparamagnetic iron-oxide nanoparticle approved for the treatment of iron deficiency anemia. Ferumoxytol is only marketed in the United States and its diagnostic use is off label. We hypothesize that ferumoxytol-enhanced (FE) T1 MRI can be combined with a two-compartment model to quantify fMBV as a proxy for myocardial perfusion.

We implemented and tested a two-compartment water exchange model for fMBV quantification. Nine healthy swine and one swine model with single-vessel coronary stenosis underwent MOLLI T1 imaging at

3.0 T following multiple individual ferumoxytol infusions. Published fMBV values range from 5% to 12% in human, swine and canine studies using the iron-based intravascular contrast agents ferumoxytol and NC100150. In our healthy, normal swine subjects, we found fMBV and water exchange values within this range of published results.

Elevated fMBV has been proposed as a compensatory response in the setting of regional myocardial hypoperfusion downstream from a significant coronary stenosis. In our single swine model with artificially-induced single-vessel coronary stenosis, we generated a quantitative pixel-wise fMBV map of the left-ventricular apex in order to look for elevated fMBV downstream from the coronary stenosis. This map showed regional differences in hypoperfused relative to perfused regions. This study demonstrates the feasibility of fMBV estimation using multi-dose FE-MRI with a two-compartment water exchange model. fMBV derived from FE-MRI may have the potential to provide a unique means of assessing myocardial perfusion.

Dengrong Jiang

W.S. Moore YIA Finalist

I grew up in a beautiful city named Guilin, which is famous for its scenery of karst topography. While enjoying the splendid views, I had always wanted to be a scientist. I spent my childhood savings on scientific magazines and learned to build simple optical systems using convex lenses. So, the first imaging modality I worked on was actually “optical imaging”. In my undergraduate years in Tsinghua University, I worked on X-ray CT for a year before I met my favorite modality: MRI. In 2012, I joined Dr. Kui Ying’s group as an undergraduate researcher and worked on compressed sensing image reconstruction and MRI temperature mapping.

Pursuing my enthusiasm, I joined the Biomedical Engineering Ph.D. program at Johns Hopkins University (JHU) in 2013. Under the mentorship of Dr. Hanzhang Lu, my Ph.D. work focused on developing MRI techniques to measure cerebral oxygen extraction fraction (OEF), an important parameter for the brain’s energy metabolism. I extended the scalability of our method across multiple MR vendors, revealed the physiological underpinnings of normal OEF variations, and also developed a rapid technique to measure OEF in a particularly challenging population, newborn babies. After earning my Ph.D. degree in 2019, I have been a post-doctoral fellow in the Department of Radiology at JHU.

My current research pertains to the technical development and clinical applications of MRI methods to quantify brain physiology. Continuing my Ph.D. work, I am developing techniques to assess regional OEF to gain better sensitivity and specificity to brain diseases,

surpassing previous global OEF measurements. I work closely with clinicians on Alzheimer’s disease and have shown that OEF can be useful in etiology-based diagnosis of cognitive impairment. I also work with neonatologists on hypoxic-ischemic-encephalopathy, a leading cause of neonatal disability and mortality, and have found OEF correlates with clinical indices that can predict patient outcome. In addition, I am actively disseminating our techniques, which have been utilized in over 40 institutions around the world.

NOMINATED PAPER:

“Brain Oxygen Extraction Is Differentially Altered by Alzheimer’s and Vascular Diseases”

Cognitive dysfunction has become a major health problem for society, affecting over 50 million people and costing one trillion dollars globally. Alzheimer’s disease and vascular cognitive impairment, as well as their concurrence, represent the most common types of cognitive dysfunction. Treatment strategies for these two types can be very different. However, there exists a considerable overlap in their clinical symptoms and neuroimaging features, and we still lack effective tools for their differential diagnosis. Cerebral oxygen extraction fraction (OEF) reflects a delicate balance between neural (e.g., oxygen consumption) and vascular (e.g., blood flow) function. Therefore, we hypothesize that, if the brain is characterized by neurodegeneration while the vascular functions are relatively intact (i.e., Alzheimer’s disease), OEF will be diminished due to reduced oxygen consumption; on the other hand, if the brain mainly suffers from vascular diseases (i.e., vascular cognitive impairment), OEF will be elevated due to abnormally decreased blood flow.

In this work, we included 65 elderly subjects with mixed Alzheimer’s and vascular pathology. We used a non-invasive and rapid (1.2 min scan time) MRI technique to measure the subjects’ OEF levels, and investigated the relationship between OEF and clinical diagnosis (cognitively normal, mild cognitive impair-



Dengrong Jiang

ment or dementia), vascular risk factors, cognition and amyloid burden. We found that, when evaluating the whole group, OEF was lower with more severe cognitive impairment but was higher with greater vascular risk factors. Further analyses on subgroups of participants showed that in individuals with low vascular risks, lower OEF was associated with worse cognitive performance and greater amyloid burden. Among cognitively impaired individuals, higher OEF was associated with greater vascular risk factors. These findings suggest that OEF is differentially affected by Alzheimer's (decrease OEF) and vascular (increase OEF) pathology and may be useful in etiology-based diagnosis of cognitive impairment.

James MacKay

W.S. Moore YIA Finalist

I am a clinical academic radiologist based in Norwich in the UK. Both my clinical practice and research focus on musculoskeletal MRI, in particular imaging of osteoarthritis (OA). My current research aims to develop and implement advanced MRI acquisition and analysis methods for knee OA and related conditions such as anterior cruciate ligament injury.

My work to date has shown that the incorporation of quantitative MRI and PET-MRI biomarkers of OA can both improve our understanding of disease pathophysiology and potentially aid the development of new

treatments by providing more relevant and responsive outcome measures in early phase clinical trials. Under the mentorship of Professor Andoni Toms, my early work focused on the use of texture analysis to quantify subchondral bone disorganisation on knee MRI and the use of ultrashort echo time imaging to assess integrity of the osteochondral junction. This led to my doctoral work at the University of Cambridge under the supervision of Professors Fiona Gilbert (Radiology) and Andrew McCaskie (Orthopedics) where I evaluated the suitability of a panel of candidate quantitative

clinical trials and experimental medicine studies. Towards the end of my PhD I was awarded an OARSI (Osteoarthritis Research Society International) scholarship to enable me to spend some time at Stanford University with the groups of Feliks Kogan and Garry Gold. Here I combined previous work developing dynamic contrast enhanced MRI to quantify synovitis with sodium fluoride ($[^{18}\text{F}]\text{NaF}$) PET to quantify subchondral bone metabolism. This enabled us to demonstrate the association between these two parameters for the first time in vivo.

Following completion of my clinical training, I moved to a new position in industry with AstraZeneca. Here my responsibilities include the implementation of imaging in late phase clinical studies and supporting the development and qualification of novel imaging biomarkers which can enable more efficient trial design in future.

NOMINATED PAPER:

Three-Dimensional Surface-Based Analysis of Cartilage MRI Data in Knee Osteoarthritis: Validation and Initial Clinical Application

Background: Conventional MRI outcome measures for cartilage in knee osteoarthritis (OA) clinical studies lack responsiveness and require time-consuming manual analysis.

What we did: We validated and clinically implemented a novel semi-automatic approach termed 3D-Cartilage Surface Mapping (3D-CaSM). This enables spatially corresponded analysis of both cartilage morphology (thickness) and composition (e.g., T2 mapping). Validation was performed using cadaveric knees and high-resolution peripheral quantitative CT (HRpQCT). Clinical implementation was done in one observational and two interventional studies (total $n=59$).

What we found: 3D-CaSM reduces analysis time for a single knee by >10 fold compared to conventional manual segmentation (15 minutes vs 3 hours). Agreement for cartilage thickness measurement with gold-standard HRpQCT was good (mean bias [95% limits of agreement] = 0.06 [-0.43 , 0.56] mm) and comparable to expert manual segmentation (-0.13 [-0.64 , 0.38] mm). In the observational study, the number of participants demonstrating significant changes at 6 months was 13/14 with 3D-CaSM vs 1/14 using standard methods. Use in interventional studies has allowed identification of focal regions of statistically significant change in cartilage composition in response to exercise and changes in cartilage thickness following knee joint distraction not detectable by standard methods.

Why this matters: 3D-CaSM is a valid tool to assess changes in cartilage morphology and composition over durations relevant to both early and late phase clinical



James MacKay

imaging biomarkers of knee OA for use in early phase

trials in OA. Improved responsiveness of 3D-CaSM could permit smaller, shorter duration trials. Work is ongoing to assess association with symptomatic progression in large observational and interventional studies.

Beata Bachrata

I.I. Rabi YIA Finalist

I am a post-graduate student of Medical Physics at the Medical University of Vienna. My main interest is the development of new MR imaging techniques. Currently, I am working on the development of a new fat-water imaging technique called SMURF.

I finished my bachelor's degree in Biomedical Physics at Masaryk University in the Czech Republic in 2015. That was my first encounter with MRI. I was fascinated by this technique and was keen to learn more about it and was lucky to find a masters' project with Simon Robinson at the High Field MR Centre in Vienna, in the use of functional MRI data for Quantitative Susceptibility Mapping. That involved programming for online MR reconstruction, which was entirely new to me at the time. In hindsight, I think the fact that I got those methods to work online was the reason Simon offered me a PhD developing an idea he had for simultaneous imaging of species with different resonance frequencies. By that time I had some experience with reconstruction but I realised it was going to be a very challenging project. Nevertheless, I've really enjoyed all aspects of it – RF pulse design, sequence programming, careful testing at the scanner, protocol optimization, image processing and evaluation. It has also given me the opportunity to propose solutions to some of the problems which weren't obvious at the outset, like the fast spatial-spectral pulses needed for 2D and slab-selective 3D imaging, and to bring new ideas to the project as the possibility to correct for the fat-water phase disparity. Due to the complexity of this project, I also gained experience in the use of lots of tools and got a deeper understanding of the MR physics involved. I'm now keen to make sure that this method makes the transition to basic research and clinical practice.

NOMINATED PAPER:

“Simultaneous Multiple Resonance Frequency imaging (SMURF): Fat-water imaging using multi-band principles”

SMURF is a new fat-water imaging method that is analogous to Simultaneous Multi-Slice imaging. Using spectrally-selective dual-band pulses, we simultaneously but separately excite fat and water. The fat signal is shifted in the image domain by applying CAIPIRINHA phase-cycling to the fat band, making it possible to sep-

arate the fat and water images using parallel imaging techniques.

The presence of fat gives rise to artefacts in MR images. If both fat and water should be imaged, SMURF provides an alternative to the Dixon approach, which unlike Dixon does not need a multi-echo and high receiver bandwidth acquisition – making it very flexible. SMURF also achieves similar fat-water separation quality, even with higher reliability, to Dixon, which is already being improved for 35 years since its development.

The chemical shift of fat is problematic in a number of body regions. In our paper, we demonstrated that SMURF works in the breast, knee and abdomen. The first area we would like to pursue is breast imaging, because of the intermingled fat-based and water-based structures. It also looks promising in musculoskeletal imaging, where chemical shift displacement prevents a reliable assessment of cartilage thickness and integrity. We are also applying SMURF in Quantitative Susceptibility Mapping, in which the presence of fat leads to errors in field estimation and therefore susceptibility. Recently I have transitioned SMURF to 7T and applied it to QSM in the head and neck – work which we have presented at the 2019 QSM annual workshop and the ISMRM 2020, both of which were well received – being awarded the best overall presentation prize at the QSM workshop and, at the ISMRM, a Summa Cum Laude Award and selection for the highlights session. Finally, although we present SMURF as a fat-water imaging method, we see potential in simultaneous imaging of other chemical species, such as phosphocreatine and inorganic phosphate, measured in studies of muscle metabolism, and hyperpolarized ¹³C metabolites.

Keshav Datta

I.I. Rabi YIA Finalist

I received my Ph.D. in Electrical Engineering from Stanford University under the supervision of Prof. Daniel Spielman. As part of my thesis work, I developed novel techniques for metabolic imaging using hyperpolarized carbon-13 compounds. The highlights of my



Beata Bachrata

work include 1) deriving the theory behind the initial asymmetry in a hyperpolarized sample of [1,2-¹³C] Pyruvate, and explaining its time-evolution using Redfield theory and three relaxation processes in the context of quantitative imaging, and 2) demonstrating that in vivo measurement of lactate to bicarbonate ratio is a predictor of survival post treatment with anti-VEGF therapy in a rat glioma model, thus establishing a vital imaging tool for measuring the Warburg effect. Partially funded by a NIH Predoctoral National Research Service Award (F31), my work resulted in 3 journal publications and 13 conference abstracts, winning two awards.



Keshav Datta

Under the mentorship of Prof. Daniel Spielman and Dr. Shreyas Vasawala, Department of Radiology, Stanford, my current research interests include clinical translation of hyperpolarized imaging methods, developing deuterium metabolic imaging techniques to study tumor metabolism and neurodegenerative diseases, and developing methods for eliminating motion artifacts in MRI using deep learning.

I am passionate about teaching MR Spectroscopy and Imaging related topics, and enthusiastically mentor several graduate and undergraduate students. As an active member of the Stanford Radiology Diversity Committee, I am deeply committed to, and have participated in many initiatives to promote diversity, equity, and inclusion. It is a great honor to be selected as a finalist for the Young Investigator Award and I would like to thank the ISMRM committee for this opportunity. The ability to utilize quantum mechanics to manipulate nuclear spins in a magnetic field to form images never ceases to fascinate me and I look forward to a career dedicated to advancing this field.

NOMINATED PAPER:

MRI of [2-¹³C]Lactate without J-coupling artifacts

Imaging a J-coupled nucleus, for example a ¹³C attached to a ¹H, poses significant challenges. In addition to reducing the SNR, the peak-splitting induced

by the coupling causes ghosting and blurring artifacts, depending on the k-space trajectory. We propose two novel techniques based on the idea of quadrature detection to resolve these artifacts during imaging. While the solutions are applicable to any J-coupled nucleus, we present them in the context of imaging [2-¹³C] Lactate, a metabolic product of [2-¹³C] Pyruvate that plays an important role as a biomarker in assessing various diseases and evaluating treatment responses. Metabolic imaging using hyperpolarized [2-¹³C] Pyruvate has the potential to probe two important pathways in cellular metabolism simultaneously, glycolysis and Krebs' cycle, but has been limited due to the difficulties in imaging [2-¹³C] Lactate, and our solutions aim to eliminate this impediment.

The evolution of J-coupling during imaging applies a cosine weighting in k-space that nulls certain spatial frequencies. The two strategies described in our work to eliminate the J-modulated artifacts, use the same underlying principle of combining the in-phase and quadrature components to recover the signal free of J-coupling artifacts. In a two-shot method, we show that the complex combination of the quadrature components, acquired 1/2J seconds apart (where J is the coupling constant in Hz), compensates for the missing information in k-space and results in artifact-free images. The second method utilizes a long, single-shot narrowband radiofrequency pulse to combine the cosine and sine components during excitation and eliminates the effects of J-coupling. The key contribution of our work is the use of product operator formalism to derive the evolution of coherences in the presence of J-coupling as well as chemical shift to show that the combination of in-phase and anti-phase doublets resolves the peak-splitting during image acquisition.

The solutions presented in this work pave the way for imaging J-coupled nuclei, and we hope that in the context of hyperpolarized metabolic imaging, the possibility of simultaneously imaging glycolysis and oxidative phosphorylation, improves our understanding of cellular metabolism and leads to exciting discoveries.

Nan Wang

I.I. Rabi YIA Finalist

My journey in MRI research begun in the Department of Bioengineering at UCLA, and in Biomedical Imaging Research Institute at Cedars-Sinai Medical Center in the fall of 2015, when I became a PhD student of Dr. Debiao Li and got the opportunity to work with a group of talented MR scientists. The power of MRI to capture pictures inside the human body noninvasively with exquisite soft tissue contrasts and rich information about structural integrity and functional mechanisms attracts me very much. It is also a perfect combination of my

interest in math and physics and my enthusiasm to contribute to medicine and healthcare. With the guidance, support, and numerous resources provided by Dr. Li and BIRI colleagues, I learned basic MRI physics and its clinical utilities, found my own research interested in advanced image reconstruction, DCE, and quantitative MRI, and begun to make my own small contribution in this magical field of science by developing advanced techniques applicable to clinical practice.

My major focus has been the development of an advanced DCE MRI technique using the MR Multitasking framework, which accelerates the acquisition by exploiting the high correlation along and across multiple image dimensions using a low-rank tensor model. The novel Multitasking DCE technique has achieved motion-resolved dynamic T1 mapping with a temporal resolution of around 1 second, adequate anatomical coverage, and sufficient spatial resolution. The high-temporal-resolution T1 quantification allows for the improved depiction of contrast kinetics and evaluation of the underlying vascular properties; the coverage and spatial resolution are flexible and can be adjusted to fulfill the characterization of multiple organs and diseases; the ability to resolve physiological motion and bulk motion enables co-registered DCE quantification without extra burden for breath-holding on patients. The Multitasking DCE technique has been applied to characterize carotid atherosclerosis, pancreatic cancer, and breast cancer with promising results. It produced high-quality DCE images and quantitative DCE maps representing vascular properties. This quantitative DCE information is capable of differentiating diseased tissue from normal and has the great potential to allow for early diagnosis and timely evaluation of the therapy response.

Graduated as a PhD in 2020, I continue to be a post-doctoral scientist in BIRI, to develop advanced, further accelerated MRI techniques, as well as to push forward the applications of these techniques for real clinical benefits.

NOMINATED PAPER:

“Five-Dimensional Quantitative Low-Dose Multitasking Dynamic Contrast-Enhanced MRI (LD-MT-DCE): Preliminary Study on Breast Cancer”

DCE MRI is the key technique in the screening, diagnosis, and monitoring of breast cancer and bears a great potential to evaluate tissue vascular properties. However, technical challenges have prevented existing DCE techniques from fully realizing this potential. One major difficulty is to simultaneously achieve entire-breast coverage, high spatial resolution, and sufficient temporal resolution to capture both the spatial

variation and temporal kinetics. Clinical DCE protocols usually adopt 1-mm spatial resolution with compromised temporal resolution of >60 s per phase, obscuring vascular information. Another concern is the risk of gadolinium (Gd) retention in the human body such as in brain and bone; although the long-term clinical consequences of Gd deposition are unknown, the benefit vs. risk of Gd-based imaging can be controversial, especially for screening.

To address all the limitations and concerns, we proposed a low-dose Multitasking DCE (LD-MT-DCE) technique, which accelerates the acquisition using a low-rank tensor model to exploit the high correlation along and across different image dimensions. LD-MT-DCE performs dynamic T1 mapping with whole-breast coverage at a spatial resolution of $0.9 \times 0.9 \times 1.1$ mm³ and a temporal resolution of 1.4 sec in one 10-min continuous scan using only 20% of standard dose (0.02 mmol/kg). The high-temporal-resolution T1 mapping allows the evaluation of the kinetic parameters representing perfusion and vascular properties crucial for disease diagnosis and monitoring.

The study on 20 healthy subjects demonstrated that the kinetic parameters estimated by LD-MT-DCE were repeatable and agreed well with the estimation of standard-dose MT-DCE. The experiment on 7 patients with triple-negative breast cancer indicated that the image quality of LD-MT-DCE was excellent and comparable to the standard-dose clinical DCE. The diagnosis made on LD-MT-DCE matched well with the clinical standard. The kinetic parameters also showed significant differences between malignant tumors, benign tumors, and normal breast tissue.

The preliminary results demonstrated that LD-MT-DCE is a promising technique for the diagnosis and characterization of breast cancer. By reducing Gd dose to 20% without losing diagnostic accuracy, LD-MT-DCE should significantly improve the benefit-risk ratio of DCE MRI. The kinetic parameters provided by LD-MT-DCE contain rich information in the tissue vascular properties and bear the great potential to further improve the diagnosis of monitoring of breast cancer. ■



Nan Wang

Pharmacokinetic modeling of dynamic contrast-enhanced MRI using a reference region and input function tail

INTERVIEW BY MATHIEU BOUDREAU

EDITOR'S PICK FOR JANUARY

The January 2020 MRM Highlights interview is with Zaki Ahmed and Ives Levesque, researchers at McGill University in Montreal, Canada. Their paper is entitled "Pharmacokinetic modeling of dynamic contrast-enhanced MRI using a reference region and input function tail". With a new year (and a new editor-in-chief) come new beginnings: as of 2020, MRM Highlights interviews will no longer be selected MRM Editor's Pick articles. Instead, the MRM Highlights treatment will be reserved for papers that demonstrate reproducible research practices. Accordingly, this paper was chosen because in addition to sharing their code, the authors shared scripts that reproduce every single figure from their article (even the supplementary figures).

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Cancer likes
blood and so,
thanks to the
tracer, we get
to see affected
regions
-Zaki Ahmed

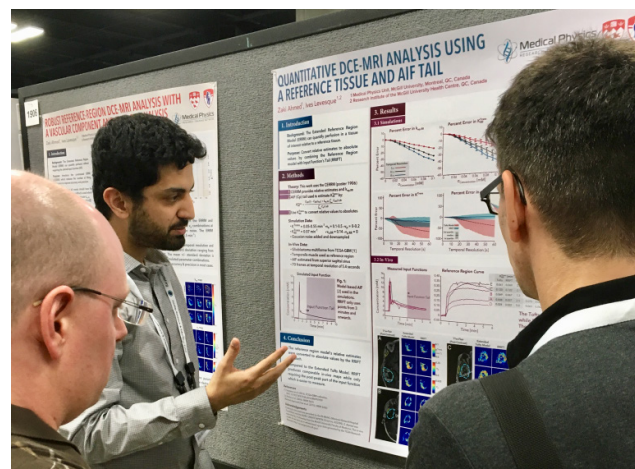
MRMH: To start with, could you tell us a little bit about yourselves?

Zaki: I did my undergrad at the University of Windsor where I studied medical physics. Then, for my masters, I came here to McGill where I joined Ives' lab. I decided to stay with him to do my PhD, and that is what I'm currently working on.

Ives: I first came to McGill as a graduate student. This is also where I studied with Bruce Pike for my masters and did my PhD work in neuroimaging, which focused on white matter imaging. I then did a postdoc at Stanford, where I learned about image reconstruction and 7 Tesla imaging while being advised by John Pauly and Brian Rutt. I came back to Montreal to take up a faculty position in the Medical Physics Unit, where I started the MRI Methods Research group.

MRMH: Could you give us a brief overview of this paper and the work you've done here?

Zaki: So, DCE-MRI involves injection of a tracer followed by a rapid series of scans in which we are able to see the arrival and the uptake of the tracer in tissue. Cancer likes blood and so, thanks to the tracer, we get to see affected regions. But to get quantitative information, we need to know a blood vessel's contrast-time curve (the arterial input function), which has a very rapid



Zaki presenting his poster on RRIFF at ISMRM 2017.

peak followed by a more steady-state tail. To measure the rapid peak, you need a rapid scan, even if this is at the expense of image quality. But it's a bit of a Catch-22, really, because blood vessels are small, so if you sacrifice image quality it's hard even to see them. Our work initially focused on the reference region model, in which healthy tissue (e.g. muscle) is used as a reference, but that technique only gives you semi-quantitative results: ratios of quantitative DCE values in the tumor relative to the muscle. So, in this paper, what we proposed was to use the latter part of the input function, the tail (so called because it's flat), as this would allow us to get away with using a slow scan. One of the benefits of this technique is that even with a slow scan, you still get good fully quantitative maps.

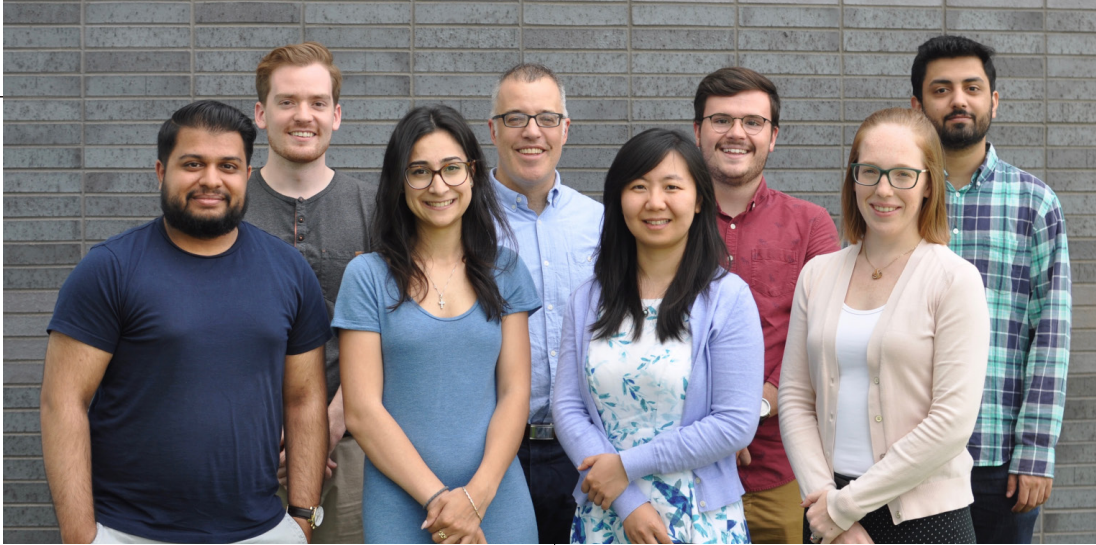
Ives: The first time I spoke about this work to a group

Ahmed, Z, Levesque, IR. Pharmacokinetic modeling of dynamic contrast-enhanced MRI using a reference region and input function tail. *Magn Reson Med*. 2020; 83: 286–298.

<https://doi.org/10.1002/mrm.27913>

<https://blog.ismrm.org/2020/01/24/qa-with-zaki-ahmed-and-ives-levesque/>

<https://blog.ismrm.org/2020/01/31/reproducible-research-insights-with-zaki-ahmed-and-ives-levesque/>



The MRI Methods Research Group in 2019.

outside our university, I was met with little bit of disbelief. For those who understand the quantitative Tofts model and more advanced DCE models, one intuition is that the Ktrans variable (the transfer constant, which is the flow of blood plasma per unit volume of tissue) is strongly determined by the initial part of the enhancement curve. And so the widespread thinking is that you need high temporal resolutions in order to collect those dynamics and measure Ktrans. In reference region modeling, you get Ktrans relative to the reference region. This work is sort of a backdoor calibration method that enables you to get back to the absolute Ktrans by considering the integral of the pseudo steady-state contrast agent concentration. It's a nice trick, which Zaki thought of, that circumvents the need for temporal resolution while still giving you absolute parameters.

MRMH: Why is this work important?

Zaki: At present, quantitative DCE-MRI is prevalently a research technique, because it requires a fast scan but also high resolution with low noise, and this makes it really difficult to perform clinically, especially in certain cases, like breast tumors. There are some groups that are working on acceleration techniques to make these scans faster, but most clinics don't yet have access to these. Our technique lets you get these quantitative maps from low temporal resolution data using conventional imaging protocols; this should make them more widely accessible.

Ives: My view is that although the development of fast 4D high-resolution acquisitions will continue to progress in the coming years, at some point the frames are going to be so close in time that SNR may become more of a limitation. This analysis method lets you acquire the necessary images while retaining good SNR.

MRMH: Let's just touch on the topic of sharing your code. Few people share code along with their papers. This might be, for example, because they're afraid of getting scooped on future work, or because they feel their code isn't clean enough to share. Did you experience some of those anxieties before deciding to share your code with your paper?

Zaki: Feeling that your code is not clean enough is pretty par for the course in academia! As regards the code I shared now, I felt that way about several files that I

wrote. You have to weigh up the costs and benefits of refactoring a lot of code that might not be essential. As for the fear of being scooped, that was never on my mind. Code sharing is frequent within the DCE-MRI community. In particular, last year at ISMRM there was the Open Source Initiative for Perfusion Imaging (OSIPI), where we got together and discussed good practices for sharing code. I think I feel most anxious when things actually work; that makes me a bit suspicious, because usually they don't! [chuckles] So my biggest worry is that I may have made a mistake someplace in the code. But even if there is a mistake, it's better for the work to be shared; that way, it might be found by someone else. Surely, that is better than to publish something that's wrong but can't be verified.

MRMH: That's the way science should work, I would say.

Ives: Yes, I agree with you, it's the way science should work. You need to have a good dose of humility. What's more, if you open up your notebook to someone and they say it's solid, then you have more confidence moving forward. ■



“
If you open up
your notebook
to someone
and they say
it's solid, then
you have more
confidence
moving forward.”

—Ives Levesque

Zaki with fellow students Véronique Fortier and Stella Xing at ISMRM 2017.

Deep learning how to fit an intravoxel incoherent motion model to diffusion-weighted MRI

INTERVIEW BY TOMMY BOSHKOVSKI

EDITOR'S PICK FOR FEBRUARY

This month's MRM Highlights Pick interview is with Sebastiano Barbieri, Oliver Gurney-Champion, and Harriet Thoeny, researchers at UNSW Sydney in Australia, Amsterdam UMC in The Netherlands, and Hôpital Cantonal Fribourgeois, University of Fribourg in Switzerland. In a recent paper, they presented a deep learning approach for fitting an intravoxel incoherent motion (IVIM) model to diffusion-weighted MRI. They showed that their method is more efficient than the alternatives, and produces smoother parameter maps. This paper was chosen as this month's Reproducible Research pick because as well as sharing their code, the authors also shared a nice demo in a Jupyter notebook.

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As a radiologist,
I think IVIM
maps are
more visually
appealing.
—Harriet Thoeny

MRMH: Can you tell us a bit about yourselves and your backgrounds?

Sebastiano: I work on machine learning applications in the healthcare domain at the Centre for Big Data Research in Health at UNSW Sydney, and my background is in mathematics and computer science. I received a PhD from Jacobs University in Germany and the Fraunhofer MEVIS Institute for Digital Medicine. More recently, I completed a biostatistics degree at Macquarie

University in Sydney.

Oliver: I'm currently an assistant professor at the Amsterdam University Medical Centers, affiliated with the University of Amsterdam, where I work on the development and implementation of quantitative MRI. However, most of the work for the paper was done during my time as a postdoc at The Institute of Cancer Research in London. Sebastiano and I got to know each other after I read his paper on Bayesian IVIM fitting and decided to



Oliver Gurney-Champion (left), and Harriet Thoeny (right). Not pictured: Sebastiano Barbieri.

Barbieri, S, Gurney-Champion, OJ, Klaassen, R, Thoeny, HC. Deep learning how to fit an intravoxel incoherent motion model to diffusion-weighted MRI. *Magn Reson Med*. 2020; 83: 312– 321.

<https://doi.org/10.1002/mrm.27910>

<https://blog.ismrm.org/2020/02/21/qa-with-sebastiano-barbieri-oliver-gurney-champion-and-harriet-thoeny/>

<https://blog.ismrm.org/2020/02/28/reproducible-research-insights-with-sebastiano-barbieri-oliver-gurney-champion-and-harriet-thoeny/>

contact him by email. Since then we have collaborated on multiple projects.

Harriet: I am a full professor of radiology at the University of Fribourg in Switzerland. I have many years of experience in quantitative MR imaging with diffusion-weighted MRI as my main focus. Sebastiano and I worked together for several years at the University of Bern. I think we made an excellent team because Sebastiano was always there to answer my difficult clinical questions.

MRMH: Can you give us a brief overview of your paper?

Sebastiano: The paper is about fitting IVIM parameters to diffusion-weighted MRI. To some extent, this is a mathematically ill-posed problem: a small variation in the input can have a large effect on the computed output. Many of the traditional methods used to compute IVIM parameters have been found to be insufficiently accurate, which has hampered the application of these methods in clinical practice. For this reason, we proposed a novel approach for IVIM parameter fitting based on deep learning. We found that this method led to competitive results in terms of accuracy and visually improved parametric maps on patient data.

Harriet: IVIM is a very useful method because it provides information on diffusion and perfusion simultaneously. In radiology, it would be very beneficial to have a method for obtaining information without administering any contrast agent. There are various clinical applications where it would be extremely helpful to use this method because it provides reproducible results; diffuse kidney disease is an example.

MRMH: What type of deep learning architecture did you use in your study?

Sebastiano: We used a feedforward backpropagation multilayer perceptron, which has been around since the 80s. It consists of an input layer, which takes the diffusion-weighted signal measured at different b-values, a series of hidden layers, and an output layer, which contains the estimated IVIM parameters. However, since this network actually forces the input signal to be represented in a more compact manner using the three IVIM parameters, it can also be seen as the encoder part of an autoencoder architecture.

Oliver: It's a kind of auto encoder-decoder network, but in order to force the compressed signal in the bottleneck of the network to represent the IVIM parameters, we have replaced the decoder with the IVIM model. With this, the network then is forced to learn what IVIM parameters best fit the presented signal. The nice thing about auto encoder-decoders is that they can be trained without ground truth data.

MRMH: You note that the parameter maps generated by the model are surprisingly smooth in homogeneous tissue. How might you examine this further?

Oliver: This smoothness is interesting because the network does not know which voxels are neighbours in the image. It takes each voxel as a single independent input and predicts the IVIM parameters. It turns out that the parameters from the same tissue actually get similar values; the fact is that, although it sounds like this should be the case, in conventional IVIM fitting you actually often get very noisy maps with a lot of speckle; our approach mitigates that while otherwise having very similar parameter values. In the future, we would like to investigate whether the predicted IVIM param-

eter values are unique or whether there is a correlation between them. Additionally, we would like to look into a test-retest analysis and compare this to the effects of treatment response.

Harriet: As a radiologist, I think IVIM maps are more visually appealing. For day-to-day radiology tasks, the use of quantitative data is not always necessary. Instead, the information they provide can be used qualitatively. By simply examining parameter maps, it is possible to make inferences that are very useful clinically. For example, in the follow-up of a tumor, you can evaluate a treatment simply by looking to see whether it has produced a difference in the perfusion and diffusion map.

MRMH: You offer suggestions on how this method for IVIM fitting might be incorporated into clinical software despite the need for repeated training on different acquisition protocols. Do you foresee any other issues that would need to be resolved before its clinical use would be a viable option?

Sebastiano: One of the challenges with deep learning methods in general is that, depending on the initial random initialization of the network, you'll often get different models. This is because the optimization algorithm will get trapped in some local minimum of the cost function instead of finding the global minimum. This generally isn't an issue, since these minima appear to be mostly equivalent. However, sometimes training may go wrong, and therefore I believe that there is a need for additional quality checks after training. I don't know whether this could be taken care of in an automated manner or whether radiologists would need to do it.

Oliver: This was a feasibility study where we have shown that this method worked well in the tested volunteers. I imagine such methods need thorough testing before widespread clinical use. That being said, if we compare our method to the alternatives (e.g. least squares of Bayesian approaches), our parameter maps look promising. What is also promising about our approach is that it is really fast. We could make it even faster if we accelerated it on a GPU, which is straightforward for deep learning. Also, you could pre-train the model on simulated data and have some basic start that guarantees you're close to some optimum instead of training with a random initialization. This might also further improve its generalizability. I think all of these approaches could help to get the method to the clinic faster. However, this was a first feasibility study. That's how I feel, at least, or maybe Sebastiano had big ideas for commercializing it?

Sebastiano: [laughs] I'm not so interested in commercialization. I, too, see this as an initial feasibility study. The method has to be evaluated prospectively in a larger cohort before we can actually start thinking about releasing it for daily clinical use. ■

“It’s a kind of auto encoder-decoder network, but in order to force the compressed signal in the bottleneck of the network to represent the IVIM parameters, we have replaced the decoder with the IVIM model.”

—Oliver Gurney—

Steady-state imaging with inhomogeneous magnetization

INTERVIEW BY AGAH KARAKUZU

EDITOR'S PICK FOR MARCH

For this month's Editor's Pick, we interviewed Shaihan Malik and Daniel West from King's College London (KCL) about their paper "Steady-state imaging with inhomogeneous magnetization transfer contrast using multiband radiofrequency pulses". This paper presents an implementation of inhomogeneous magnetization transfer (ihMT) that uses nonselective multiband RF pulses to simultaneously saturate the off-resonance spins and excite the on-resonance ones. This work demonstrated exemplary reproducible research practices; not only did the authors share the code related to their work, but they also wrote excellent documentation to accompany their software.

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As regards
phantom
imaging data
and simulation
results, we just
put everything
available online,
because there's
no reason
not to!

—Shaihan Malik

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MRMH: Can you tell us a bit about how you got involved in MRI research?

Daniel: I did a physics undergrad degree here at KCL, and this is where I became interested in MRI. Right now, I am mainly interested in quantitative MRI methods for myelin imaging. So far during my PhD, I've worked on multicomponent DESPOT and ihMT.

Shaihan: I've been doing MRI work since about 2003. I did a PhD in image reconstruction and then a postdoc in parallel transmission, during which I worked on a 3T system. This, unlike 7T systems, isn't a field strength that uses parallel transmit a lot. I still work a great deal in parallel transmit; we just installed a 7T system here at King's College. But then we started this second strand of research into quantitative MRI and surrounding techniques. That's been going on for about the last five years. I'm enjoying the strictly physics part of MRI the most.

MRMH: Your paper has a pretty comprehensive title! Can you unpack it a little bit to prepare our readers for the rest of the interview?

Shaihan: ihMT is a really unique contrast mechanism, which I first came across a few years ago at ISMRM. If you jump straight in at the deep end, with a normal MT effect, you are looking at transfer magnetization between free water and semi-solid substances using a single off-resonance pulse. With ihMT, you apply the same amount of power at two different frequencies, equally spaced on either side of the water resonance. You may



Shaihan Malik

think that this is the same as applying all of the power either at the positive or at the negative frequency. But, the ihMT means that in some tissues applying RF power in that fashion gives you a different result from just having a single off-resonance frequency. The spin system is not following the normal equation that we would have used to describe it.

Daniel: This paper offers an alternative method for generating ihMT contrast. In the literature there are sequences where you have a preparation phase of multiple RF pulses with either a fixed or alternating frequency offset, followed by multiple gradient readouts. Our sequence applies multiband pulses, simultaneously exciting the free water and saturating the semi-solid component. Normally, these things are performed separately, but this method does them both at once allowing you to build the effect into regular steady-state sequences.

MRMH: Your group applied multiband pulses to stabilize quantitative relaxometry measurements. How does that relate to ihMT?

Shaihan: The idea of using these non-selected multiband pulses actually comes from that work. The idea

Malik, SJ, Teixeira, RPAG, West, DJ, Wood, TC, Hajnal, JV. Steady-state imaging with inhomogeneous magnetization transfer contrast using multiband radiofrequency pulses. *Magn Reson Med*. 2020; 83: 935–949.

<https://doi.org/10.1002/mrm.27984>

<https://blog.ismrm.org/2020/03/20/qa-with-shaihan-malik-and-daniel-west/>

<https://blog.ismrm.org/2020/03/27/reproducible-research-insights-with-shaihan-malik/>

was to collect multiple images using spoiled and balanced sequences with different flip angles, and then to fit the signal equations to estimate T1 and T2 values. But, depending on which combinations of flip angles we choose, we get systematic errors. When you change the flip angle, you either have to increase or decrease the amplitude of the pulse, or change the pulse duration. This changes the amount of RF power in the sequence and alters the magnetization transfer effect.

We came up with the solution of using non-selective multiband pulses. Let's say you start with a high flip angle. As you decrease the flip angle, you add additional RF power at sidebands, which are quite far away, a few kHz off resonance. They don't do anything to the water signal, but they add extra power to saturate your semi-solid. So, all of the measurements you make in your variable flip angle sequence have the same



Daniel West

RF power, which makes your quantitative maps much more reproducible.

MRMH: What do I need to do to allow my SPGR sequence to collect ihMT data? How practical is this?

Daniel: We obviously need the mechanism to generate the ihMT contrast. On the basis of what is reported in our paper, including our two- or three-band multiband pulses would be enough, and then you would have your SPGR readout after each of these pulses. So, it's just the pulse that allows you to generate the contrast.

MRMH: Can we use the exact same pulses that you designed?

Malik: Our GitHub repo actually contains software to make those pulses!

MRMH: That's great! What are some of the immediate implications of this work and where do you see ihMT going in the long term?

Daniel: I think the key feature of ihMT is myelin specificity. That's its selling point compared with standard MT methods. Recent histology studies showed that ihMT performs better compared with other MT and water imaging methods. For the next steps with ihMT,

we could look into demyelinating conditions such as multiple sclerosis, and into infant development.

Shaihan: The method in this paper is probably not the most effective for generating ihMT contrast. Steady-state sequences give us simple signal relationships, which are quite useful for doing quantitative MRI. We really use them as a demonstration of how ihMT fits into what we already know. But if you want to get more ihMT contrast, people have shown that it's better to alternate between saturating and then leaving it to recover for a while and then saturating it again.

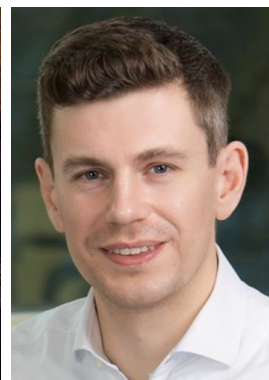
MRMH: I can't help but feel enthusiastic when I see a version control commit hash in a paper! Where else do you think MRI research can benefit from version control and open source?

Shaihan: This is not the first study where we've shared version control commit hashes in the resulting paper. It is something that we really try hard to do consistently. As regards phantom imaging data and simulation results, we just put everything available online, because there's no reason not to! A barrier, though, is the sequence code and the fact that we all have different scanners.

MRMH: Can the absence of collaborative pulse sequence development cause issues? Are you using any open communication channels for sequence development?

Shaihan: I think there are more parameters that can change the signal than the ones we normally report, and that can be a problem. An obvious simple one is the RF spoiling phase that you use in SPGR. Every manufacturer has a different phase increment value. We recently published another paper about this in relation to our CSMT technique, where we applied the same multiband pulses across different vendor scanners (Philips and GE). We showed that if you don't do anything, and just use the native scanner protocols, you get really different answers for the T1 and T2 mapping.

Daniel: Personally, I've only done bit sequence programming on a Philips 1.5T scanner. There are some online forums and stuff around for our scanners where we can talk about our implementation and get ideas from people. I guess that's the only communication channel that's currently available to us. ■



The other co-authors of the paper, from left to right: Rui Teixeira, Tobias Wood, Joseph Hajnal.

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I think the key feature of ihMT is myelin specificity. That's its selling point compared with standard MT methods.

–Daniel West

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Artificial neural network for myelin water imaging

INTERVIEW BY MATHIEU BOUDREAU

EDITOR'S PICK FOR APRIL

April's MRM Highlights Pick interview is with Jieun Lee and Jongho Lee, researchers at Seoul National University in South Korea. Their paper is entitled "Artificial neural network for myelin water imaging", and it presents a deep learning approach aimed at generating quantitative myelin water imaging maps. This work demonstrated exemplary reproducible research practices: not only did the authors share the code related to their work, but they also shared their trained deep learning networks.

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I feel like we
have entered
a different
research era
in terms of
reproducibility.

—Jongho Lee

”

Jieun Lee



MRMH: To start off with, could you tell us a little bit about yourselves and your background?

Jieun: I'm currently a master's candidate at Seoul National University and my background is in electrical and computer engineering. My research has focused on myelin imaging and applying deep learning in the field of medical imaging.

Jongho: I'm an MR physicist by training, with experience in developing pulse sequences and reconstruction algorithms. My interest in machine learning research

started in the last few years, and was prompted by the fact that many of my students were really excited about the potential of applying machine learning for medical imaging purposes. The nice thing with deep learning is that you can use it at the level of research, such as using the neural network as a black box to fit different models and see how it compares with well-established data processing algorithms. The use of neural networks in the MR physics field is still in an early stage, and this research by Jieun is one example of applying a neural network to replace traditional data processing.

MRMH: Could you give us an overview of your paper?

Jieun: What we proposed in this paper is to apply deep learning to generate quantitative myelin water imaging maps from T2 acquisition data. Multi-echo spin-echo data were used to estimate myelin water fraction. We explored three different artificial neural networks to produce myelin water fraction, and each one showed

Lee, J, Lee, D, Choi, JY, Shin, D, Shin, H-G, Lee, J. Artificial neural network for myelin water imaging. *Magn Reson Med.* 2020; 83: 1875–1883.

<https://doi.org/10.1002/mrm.28038>

<https://blog.ismrm.org/2020/04/17/qa-with-jieun-lee-and-jongho-lee/>

<https://blog.ismrm.org/2020/04/24/reproducible-research-insights-with-jieun-lee-and-jongho-lee/>



Jongho Lee

highly accurate results compared with data fitted conventionally. The deep learning method we proposed is interesting because of its computational efficiency; when using the deep learning algorithm, networks take less than a second to process. This reduces the processing time by a factor of 10,000 when compared with the conventional fitting method. We examined both healthy control and multiple sclerosis patients in this study, so it has shown great potential for myelin water imaging applications.

Jongho: Conventional data processing can take several hours, and you really don't know whether your acquisition is of good quality until after the subject has left. If the patient moved during the scan, you have lost the chance to redo it. Part of the motivation for this work was to find a way of speeding up the data processing to real-time levels, so that we can generate the images right after the scan.

MRMH: Jieun, do you have any advice for new graduate students who would like to incorporate deep learning into their project?

Jieun: A really helpful thing for me in the beginning was looking at code and datasets that others had shared. I learned a lot by exploring other people's work. It helped me gain a deeper understanding of deep learning, and find tricks on how to improve the performance of the artificial neural network.

Jongho: I think that's a really good point for early stage researchers. In deep learning, there are so many variables that you can control, such as the artificial neural network architectures, the depth of the neurons, or the size of the networks. There are no golden rules to follow for this technology that will point you in the right direction, it's a very exploratory process. But when it works, it really works well and it's very exciting when it

gives you the right result. However, it can take weeks or months of challenges before you are successful.

MRMH: It seems like you've benefited a lot from people sharing their code. From your perspective, how can sharing code and data along with papers help reproducible research?

Jongho: I feel like we have entered a different research era in terms of reproducibility. Before, we used to write a paper and people could reproduce the experiments by following the steps as described. This has changed for deep learning research. We cannot reproduce the results without a trained network or data because the performance of a network depends not only on network architecture, but also on training data. With no data or trained network, it is difficult to compare one's results with those of others. I believe sharing is becoming a common practice for research.

MRMH: Was that your motivation to share your code and trained models?

Jieun: We hope that by sharing our code, it will make our work more reproducible. Another benefit is that it also opens the door to constructive criticism that we can benefit from. When I initially presented this work at ISMRM, someone asked me for the code and I was able to quickly share the GitHub link. He then gave me some feedback on my code that I later incorporated.

MRMH: What do you enjoy doing when you're not in the lab?

Jieun: On vacation, I definitely love to go on a trip. After work, I like to relax by doing pilates and hanging out with my friends, but unfortunately those options are out at present, due to the current coronavirus epidemic. Hopefully the situation will get better soon and I will be able to socialize with my friends in person again.

Jongho: I really enjoy traveling, so that's out too at the moment! I was very excited at the prospect of visiting Sydney again, but that opportunity now seems to have gone. Hopefully we will recover from all these challenging events soon, and get to see people not just online but in person at events like ISMRM. ■



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The deep learning method we proposed is interesting because of its computational efficiency; when using the deep learning algorithm, networks take less than a second to process. This reduces the processing time by a factor of 10,000 when compared with the conventional fitting method.

–Jieun Lee

Jieun with co-authors of the paper, from left to right: Dongmyung Shin, Jieun Lee, Doohee Lee.

Portable and platform-independent MR pulse sequence programs

INTERVIEW BY AGAH KARAKUZU

EDITOR'S PICK FOR MAY

Authors of the featured paper in front of the first gammaSTAR compatible scanner. From left to right: Cristoffer Cordes, Daniel Hoinkiss, Simon Konstandin, Matthias Günther.

Leveling the development of pulse sequences is far from a bed of roses. Moreover, product sequences often leave researchers in the dark about implementation details that can contribute to differences in multicenter studies. The authors of the May MRM Highlights pick propose a powerful yet lightweight software solution, gammaSTAR, which was recently described in MRM in a paper entitled "Portable and platform-independent MR pulse sequence programs". We sat down with Cristoffer Cordes and Matthias Günther from the University of Bremen and Fraunhofer MEVIS and discussed how their gammaSTAR software might pave the way for unified, vendor-neutral and collaborative pulse sequence development.

MRMH: How did you get involved in MRI research?

Cristoffer: I started my academic career studying mathematics in Bremen, my home town. I like to work with abstract and theoretical concepts and that's why I chose

mathematics to begin with. Then I went to South Carolina for a year to do a master's degree in a medicine-related field. When I returned to Germany to do my PhD, I got interested in a fascinating field that suited my interests perfectly, namely MRI simulation! So, my PhD topic was decided, and it later translated into the gammaSTAR framework.

Matthias: My history with MRI dates back 25 years. I was doing my German diploma thesis in a completely different field, particle physics. Although this topic was very interesting from a theoretical perspective, its application was less exciting. One day a friend of mine asked me whether I might be interested in a completely different field, MRI. I thought I could at least give it a try. At the time, my wife said "you will get bored after six weeks", but I'm still working on it now and I really don't think I'll ever get bored with it. It is very exciting working in this field.

MRMH: What led you to the idea of developing a vendor-agnostic framework for pulse sequence programming?

Cristoffer: During my PhD, I had one big problem: I had the textbooks, but I did not have the sequences. I wrote my software to calculate theoretical signals, but found it virtually impossible to get it on the scanner easily. This is how the gammaSTAR project came about. Pulse sequences tend to get really complex over time and hard to maintain. I get real joy from trying out new ways of dealing with this complexity.

Matthias: My struggles came when we started working on arterial spin labeling (ASL). We were trying to introduce this really neat technique into clinics. This meant a lot of collaborators using our sequences. At a certain point, due to vendor and version issues, we found ourselves having to provide 8-9 different versions of our ASL sequences. As a result, it was not always the same MRI physics being played out on different systems. Even



Cordes, C, Konstandin, S, Porter, D, Günther, M. Portable and platform-independent MR pulse sequence programs. *Magn Reson Med.* 2020; 83: 1277– 1290.

<https://doi.org/10.1002/mrm.28020>

<https://blog.ismrm.org/2020/05/29/qa-with-cristoffer-cordes-and-matthias-gunther/>

<https://blog.ismrm.org/2020/06/05/reproducible-research-insights-with-cristoffer-cordes-and-matthias-gunther/>

though the results looked similar, we were still getting differences. Eventually, we decided we needed to separate MRI physics from the hardware implementation, and that's why we decided to develop gammaSTAR.

MRMH: What advantages does gammaSTAR offer users and developers?

Cristoffer: With gammaSTAR, you can dive directly into a sequence. You can see the calculations from protocol to final pulse shape, and get instant feedback if you change one of the input parameters. All that is possible without installing anything on your computer! All you need is a modern web browser; you don't even require internet access or access to our servers, because it's all self-contained. The framework is really efficient thanks to graph structures, to the point that it even enables real-time imaging.

Matthias: You need a few hundred kilobytes to describe a full-fledged sequence. Furthermore, you can easily make it part of the DICOM header. With this piece of information, you, eventually, can take an image from a Siemens scanner and run exactly the same sequence on a Philips, GE or a Bruker system. It is a really huge effort to save all the MR physics in a relatively tiny container.

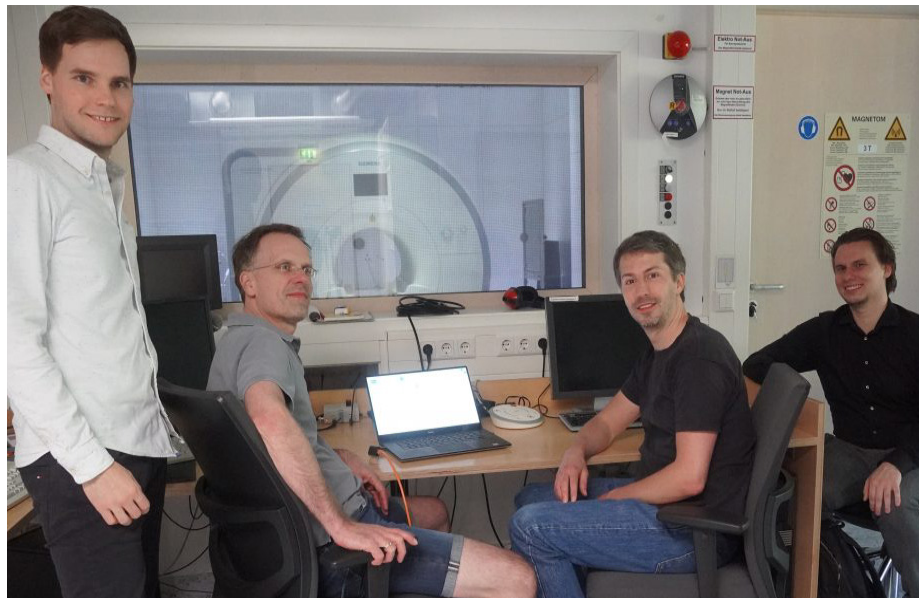
Cristoffer: We designed gammaSTAR to work on the scanner without having to compile a sequence. The sequence can still be changed after being loaded on a scanner. It can be adapted to cope with different hardware limitations. You can also change various other parameters such as slice positions and resolution or certain preparation modules.

Matthias: With a web browser interface, we can really start to think about collaborative sequence development. The web-based technology of gammaSTAR makes it much easier to jointly develop sequences.

MRMH: Could you describe the process of developing a new gammaSTAR sequence? What do I need to run it?

Cristoffer: If you want to develop a gammaSTAR sequence, the best starting point is a sequence that already exists. Then you can add to that, parameterize it and connect it to your scanner. It will likely fail at the first try (a standard event in any pulse sequence development process) if you connect it right away. Therefore, you first need to debug it and run some checks to see whether all the events are physically feasible from a hardware point of view. Then you can export it to a JSON file and place it in a certain directory in your scanner workstation. If the runtime still passes after you hit the start button, you will obtain your measurement. You can choose to use the native reconstruction framework, or open alternatives. We've tried Gadgetron and it works nicely.

Matthias: The gammaSTAR driver is a sequence that interprets the JSON file to run the hardware. Right now, this driver is implemented similar to a research sequence, and therefore requires a research license. Of



course, the ideal solution would be for the driver to be legally part of the product of the manufacturers on all systems.

MRMH: How do you see publicly available pulse sequence descriptions facilitating reproducibility in MRI research?

Matthias: In publications you can't adequately describe in all details what you're doing and how the sequence works. This is their main limitation. When you try to implement something from another publication, you therefore find this to be really difficult. There are too many degrees of freedom and many different ways of implementing something, and much of this is not specified. Yet this information can make a huge difference to the outcome.

Cristoffer: Currently, many techniques cluster around a specific vendor and a specific set of people who have a research agreement, and that research only takes place within this small cluster. Obviously, this is not good from the perspective of communicating pulse sequence development and many opportunities are missed due to this problem. Maybe we can repeat the success of the ISMRM Raw Data format (ISMRMRD) for pulse sequences. I hope to see an increase of related discussions at the ISMRM Annual Meetings.

Matthias: We have three vendor-defined sub-communities in MRI. Within each community, it is relatively easy to share code. But, if you want to compare your method to existing state-of-the-art techniques, it is almost impossible to do this across sub-communities, because you would have to re-implement them. This is a problem I hope we can get rid of some day. We should be able to download pulse sequences from the web and run them on our scanner regardless of what brand we have. ■

Authors of the featured paper, planning the next gammaSTAR features. From left to right: Daniel Hoinkiss, Matthias Günther, Simon Konstandin, Cristoffer Cordes.

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—Matthias Günther

FatSegNet: A fully automated deep learning pipeline for adipose tissue segmentation on abdominal dixon MRI

INTERVIEW BY EMILIE MCKINNON

EDITOR'S PICK FOR JUNE

June's MRM Highlights Pick interview is with Santiago Estrada and Martin Reuter, researchers at the German Center for Neurodegenerative Diseases in Bonn, Germany, and the A.A. Martinos Center for Biomedical Imaging in Boston. Their paper is entitled "FatSegNet: a fully automated deep learning pipeline for adipose tissue segmentation on abdominal Dixon MRI". This work demonstrates exemplary reproducible research practices: not only do the authors share the code related to their work, but they also distribute Dockerfiles to provide a reproducible and shareable computing environment for their code (i.e. a Docker container).



prospective cohort study (<https://www.rheinland-studie.de/>). However, most abdominal adipose segmentation methods to date have been hard to generalize to a large population due to the variability of the abdominal cavity. We therefore set out to create a method that was more robust.

Martin: Our lab's core research agenda is artificial intelligence (AI) method development for structural MRI with a focus on neuroimaging. This is the first time we have ventured into body MRI.

MRMH: What are the main take-home points of your paper?

Santiago: We have developed a fully automated pipeline for the reliable and accurate quantification of different fat tissue volumes from Dixon MRI. By using our 2D-Competitive

The DeepMI lab. Top (left to right): Prof. Martin Reuter, Leonie Henschel, Emad Bahrami-Rad, Kersten Diers, Christian Ewert. Bottom (left to right): Saikat Roy, Dr. David Kugler, Santiago Estrada, Clemens Pollak.

MRMH: Could you tell us a little about the journey that led you to MRI and how you got interested in this project?

Santiago: I study biomedical computing and this project was an interesting topic for my master's thesis. Visceral and subcutaneous adipose tissue have been related to metabolic disorders and could be potential biomarkers for neurodegenerative diseases. Therefore, the segmentation of these tissues is of great interest to the Rhineland Study, an ongoing population-based

Dense Fully Convolutional Networks (CDFNet), we have introduced an element of competition among features in order to improve selectivity. Most convolutional neural networks methods calculate lots of features, and in those cases the networks can get really computationally heavy. Another important contribution of our work is that we have validated the method really well with respect to accuracy, reliability, and sensitivity to known effects on a big unseen dataset.

Martin: That's right! There are two main points: one is that it's a complete pipeline. It not only takes an image and segments it, but also finds the region of interest consistently across subjects. Second, as Santiago said, is the validation aspect. It's really important that these methods are validated thoroughly in order to perform well in real-world applications.

MRMH: Can you explain, in simple terms, the added value of the CDFNet?

Estrada, S, Lu, R, Conjeti, S, et al. FatSegNet: A fully automated deep learning pipeline for adipose tissue segmentation on abdominal dixon MRI. Magn Reson Med. 2020; 83: 1471–1483.

<https://doi.org/10.1002/mrm.28022>

<https://blog.ismrm.org/2020/06/19/qa-with-santiago-estrada-and-martin-reuter/>

<https://blog.ismrm.org/2020/07/03/reproducible-research-insights-with-santiago-estrada-and-martin-reuter/>

Santiago: Basically the CDFNet is the core of the whole pipeline. It introduces local competition which lets us reduce the number of parameters and reduce the size of the network. A smaller network size requires less memory and is less prone to overfitting.

Martin: Dense blocks have been invented before which introduce something like shortcuts. The traditional approach, however, concatenates the features and every time you do a shortcut the network grows larger. The effect of our local competition is that only the strongest signals can pass through. The result is a leaner, slimmer, and more robust architecture that outperforms the previous methods.

MRMH: **Your method introduces a novel 2.5D approach to segmentation. What is the added benefit of this and how common are discrepancies between the segmentations in the different slice directions?**

Santiago: We adopted this approach because our images are not isotropic. We have high resolution in the axial plane, but you can see that there is important information in all directions. We have segmentation probabilities for each direction and normally people would just average these, but we decided to use a network to aggregate the views.

Martin: Santiago explained that perfectly. The problem with the different resolutions is that you do not know how much you can trust each view. So, one new aspect we introduced is that we let the network learn which direction to trust more, and this can vary spatially. Our advanced 2.5D network architectures have been shown to outperform traditional 2D and also 3D architectures, and seem to represent a good compromise between the large memory requirement of full 3D vs the low spatial context of 2D or 3D patch-based approaches. Sometimes the views do disagree, but these might be regions of uncertainty and it could be helpful to output this as a marker of quality.

MRMH: **FatSegNet is optimized for the Rhineland Study, but could it be used for other abdominal MRI sequences?**

Santiago: We have found that if you have Dixon images, the tool is able to generalize but might need some fine-tuning. What people could choose to do is to include the sequence of the Rhineland Study since it is only 40 seconds long, and our method is expected to work directly on those images.

Martin: Certainly, it would be best to include the Rhineland sequence. If you have already acquired data, you might need to fine-tune the network. We used 33 subjects (1700 slices in axial view) to train the deep learning models. For fine-tuning, a lower number is probably sufficient, but if the resolution changes, you would need to re-train the system from scratch.

MRMH: **Talking about the number of training subjects, how did you settle on 33?**

Santiago: We started with 20 cases and saw that it was working but the results were not generalizable to all cases, and so we asked our collaborators to label some more data.

Martin: Yes, it's always difficult to know how good you really are. We took the cases where the network didn't work well, had them manually segmented, and added them to the training set. That way you can select the training cases to span a wide variety of body shapes. And, of course, final validation needs to be performed on a variety of cases that were not used in training.

MRMH: **This was your lab's first non-neuroimaging project. How did you find the experience of venturing into the abdomen?**

Santiago: Actually, it is easier to know what you are looking at! I am not a medical person, yet even I can see that a liver looks like a liver, and a kidney looks like a kidney, etc.

Martin: In the abdomen, you have such high variability. Brains are always more or less the same and there is not a lot of movement; in that sense I think neuroimaging is easier. But Santiago is right, most people are probably more familiar with the appearance of the structures in the abdomen.

MRMH: **What have you been up to since this paper was written?**

Santiago: I am now doing my PhD at the intersection between Martin's group and population science (Prof. Bretelet) on deep learning in large cohort studies. Currently, I am working on olfactory bulb segmentation. This is a really tiny structure that's often overlooked and could play an important role in characterizing early stages of dementia.

Martin: One other project in my lab has been the development of a full-brain segmentation pipeline, called FastSurfer, that is capable of segmenting a brain MRI into close to 100 structures in under 1 minute with two orders of magnitude speedup. The core of this network is similar to the network introduced in this paper. More on our research can be found on our webpage <https://deep-mi.org>.

MRMH: **Do you have anything else you would like to share with the MRI community?**

Santiago: Deep learning has some clear advantages; for example, if you have a random error in your ground truth, the network will not learn it and random mistakes will be removed from the data.

Martin: I think there are three points I'd like to share: First, deep learning is now overtaking traditional approaches, sometimes even with respect to generalizability, which is surprising. Second, very large manual training data sets are not always necessary. Finally, manual ground truth can be wrong. So don't always blindly trust ground truth! ■



The effect of our local competition is that only the strongest signals can pass through. The result is a leaner, slimmer, and more robust architecture that outperforms the previous methods.

–Martin Reuter



A novel gamma GLM approach to MRI relaxometry comparisons

INTERVIEW BY PINAR S. OZBAY

EDITOR'S PICK FOR JULY

This MRM Highlights Pick interview is with Rohan Kapre and Angelique Louie, researchers at UC Davis, USA. Their paper is entitled "A novel gamma GLM approach to MRI relaxometry comparisons". In their paper, they proposed a gamma generalized linear model with identity link (GGLM-ID) framework for analyzing MRI relaxometry data and compared it with other models, like ordinary least squares (OLS), showing it to perform better, in terms of precision and accuracy, in relaxivity determination. Looking ahead to future work, they hope this model will prove to be a valuable framework to unify the analysis of MRI relaxometry data both for in vitro and in vivo (clinical) studies. The authors also made some of their code available, and created a nice user-friendly dashboard with R Shiny.



Rohan Kapre in front of the Sydney Opera House during a trip to Australia; Angelique Y. Louie next to a glass sculpture on the UT Southwestern Campus by the artist Dale Chihuly titled "Southwestern Seay Tower".

Kapre, R, Zhou, J, Li, X, Beckett, L, Louie, A. A novel gamma GLM approach to MRI relaxometry comparisons. *Magn Reson Med*. 2020; 84: 1592–1604.

<https://doi.org/10.1002/mrm.28192>.

<https://blog.ismrm.org/2020/07/23/qa-with-rohan-kapre-and-angelique-y-louie/>

<https://blog.ismrm.org/2020/07/31/reproducible-research-insights-with-rohan-kapre-and-angelique-y-louie/>

MRMH: Could you briefly outline your backgrounds and explain how you got into the field of MRI?

Rohan: I completed my undergrad in bioengineering in 2017 at UCLA. I had heard about MRI, or more precisely NMR, in an organic chemistry class. I was very interested in physical chemistry and the engineering side of that field. Later, as an undergrad, I started working in a lab performing cell density mapping based on T1/T2 contrasts, and continued from there. That led me to join Prof. Louie's lab at UC Davis, where one of our goals is to investigate the cellular uptake of different contrast agents via MRI relaxometry.

Angelique: My training was in lasers and optical imaging, but as a postdoc I worked for a chemist on a project to develop cobalt chelates as enzyme inhibitors. I developed a way to apply these as zinc finger transcription factor inhibitors. As that project was wrapping up, I was offered the chance to move to a different project in the lab to develop activatable MRI contrast agents, and the rest is history!

MRMH: Could you tell us the story behind the work, how the idea for this work evolved?

Angelique: It's an interesting story! It began when Rohan was assigned to work on a project to evaluate nanoparticle degradation by VSM and SQUID. As part of this, he had to do a number of relaxivity measure-

ments. He wanted to understand how relativity measurement works, so he set about probing exactly how the instrument (and its users) were coming up with their relativity values. He found that the relaxivity plots that are standard practice for calculating these values were prone to greater degrees of error at the higher concentrations. This set off what I think was the beginning of a real love affair with statistics for Rohan. The next thing we knew, he was doing many calculations and researching other methods to use to analyze the data, and this is what evolved into this paper and resulted in him getting a double M.Sc. in Biostatistics!

Rohan: What I liked about contrast agents and relaxometry was the quantitative nature of the measurements. While working on this project, I realized, while measuring relaxometry, that errors were propagating with higher values. I was taking stats classes at the time, where they talked about OLS (ordinary least squares) assumptions, and I realized our data didn't meet these. This led me to think that there must be a better way of doing it.

MRMH: Could you briefly summarize your method and its advantages over the traditional weighted least squares approach?

Rohan: The method can be seen as an iterative weighted least squares (IWLS) method. The biggest advantage is that the weights do not have to be set beforehand. This lends flexibility to the method as opposed to standard WLS, which we also explored. In comparison to a log transform, the GGLM method avoids distorting the linearity between relaxation rate and concentration. From MRI theory we also know relaxation rates are additive on the original untransformed scale, and GGLM adheres to this. Furthermore, though we mostly focused on GGLM-ID, the GGLM method can be used with 3 different link functions: identity, inverse (the default), and log links. It is possible that a different link function may be a better choice depending on the exact application. An advantage of the default inverse link, for example, is that it does not directly require one to invert the T2 data to R2 (which in some in vivo applications may potentially distort the data), but is instead applied to the expectation. On the other hand, in situations (with qualitative predictors) where comparisons involving ratios between R2 values are desired, one could use a log link. The usual log transform to compare ratios can be shown to be slightly biased. The choice of link function also adds to the flexibility of GGLM overall.

I should also mention that GLM is an already defined function in R, and should be in MATLAB and Python, too, so we didn't really invent it, simply discovered that it is useful for fitting MR quantitative data such as R2/T2.

MRMH: What was the biggest challenge in the implementation?

Rohan: For reproducibility purposes, I made an interface for relaxivity measurements using R Shiny. Cre-

ating a user-friendly and open-source dashboard was challenging and required me to learn some new skills. But once I had found a similar interface that I could adopt for my work, things got better and it worked really well. It was challenging to figure out how to implement the non-default identity link on R2 for GGLM so we decided to just use the default inverse link (GGLM-INV) on T2, which in the paper performs almost just as well. The dashboard can be found here: https://rokapre.shinyapps.io/GGLMINV_interface/

MRMH: What other projects involving GGLM-ID are you currently doing or planning?

Rohan: We have been doing a longitudinal in vivo study in mice. It concerns molecular MRI with the use of contrast media in mouse tumors. This study actually involves extending some of our findings to the area of gamma generalized linear mixed models (GGLMMs). Mixed models are needed to account for correlated responses in the mice over time. Another ongoing project is a cell (macrophage) study. There, we are comparing four different nanoparticles, and recent results based on residual data show that GGLM-ID is the best choice among other models. In both these studies, we are comparing the T2/R2 response to different contrast agents, and all of our predictors are categorical. Thus, this framework is applicable more broadly to MRI relaxometry studies beyond simple relaxivity calculation.

MRMH: Do you have any ideas on how you might improve the current model?

Rohan: One weakness of the current GGLM model is that it does make the assumption of an approximately constant coefficient of variation. This may be true for many but not all MRI relaxometry datasets, especially complex in vivo studies. In a different longitudinal mouse study than above, we found that both GGLMMs and log-transformed LMMs (linear mixed models) struggle at T2 values very close to 0 ms, and a regular LMM can even predict unphysical negative values in this regime. One way to improve upon this is to develop a GLM/GLMM where the variance function is estimated from the data itself, though this would require a large sample size. For now, a possible workaround solution is to use something called generalized estimating equations (GEEs), which are robust to variance misspecification. Moving forward, I also think we could definitely explore a way to incorporate our findings with deep learning neural networks. GLMs could be seen as one layer of the network, and we would need to include a loss function for gamma deviance, which could be minimized via gradient descent rather than iterative WLS. Our training set could be any quantitative measure, such as R2 or T2 values. Many biomarkers have a constant coefficient of variation, so a neural network using the gamma deviance loss could be useful for predicting these biomarkers based on raw MRI relaxometry images. ■

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concentrations.
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beginning of a
real love affair
with statistics
for Rohan.

—Angelique Y. Louie

Myelin water fraction estimation using small-tip fast recovery MRI

INTERVIEW BY JESSICA MCKAY

EDITOR'S PICK FOR AUGUST

For our August 2020 MRM Highlights Pick interview, we talk to Steven Whitaker, Jon-Fredrik Nielsen and Jeff Fessler from the University of Michigan. Their paper is entitled "Myelin water fraction estimation using small-tip fast recovery MRI". Steven started MRI research as an undergraduate and is currently a PhD student in electrical and computer engineering. Jon-Fredrik is an associate research scientist who designs steady-state pulse sequences and is passionate about "vendor agnostic" pulse programming, which is a framework for rapid prototyping of sequences across vendors. Jeff came to the University of Michigan 30 years ago as a postdoc who worked on many imaging modalities. His career evolved from there and, inspired by Doug Noll, he got involved in MRI research about 21 years ago.

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I've been benefiting from open source tools for my entire career, and I feel that this is a way of giving something back.

—Jeff Fessler

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MRMH: To start off with, I'm curious to know if you used Jon-Fredrik's vendor-agnostic pulse sequence framework for this work?

Jon-Fredrik: We did! The framework is based on MATLAB so that the user can design the sequence, preview it in MATLAB, and then export it to the scanner. This approach is closely related to—and compatible with—the "Pulseq" environment, and together these frameworks allow the same sequence specification to be played out on both GE and Siemens scanners. We hope to implement sequence drivers for other vendor platforms in the future.

Jeff: I have never written a pulse sequence myself, but I have had many students use the tools that Jon-Fredrik developed. Collaborating with these guys makes it so much easier to try out different sequences.

MRMH: There is a ton packed into this paper. Can you



Steven Whitaker



Jon-Fredrik Nielsen

break it down for us?

Steven: The goal was to develop a method using small-tip fast recovery (STFR) to estimate the myelin water fraction (MWF). First, we designed the STFR sequence parameters by minimizing the Cramér-Rao lower bound (CRLB) of our MWF estimates. After acquiring the data, we used a supervised learning algorithm called PERK (parameter estimation via regression with kernels) to estimate the voxel-by-voxel MWF. Another important aspect is that we used the three-compartment model with chemical exchange to simulate the training data.

Jeff: At a high level, the standard method for MWF imaging is a multi-echo spin-echo (MESE) technique that is just too slow to be used routinely in the clinic. By using a steady-state sequence, we hoped to greatly reduce the scan time, as we showed in the paper.

Steven: It has also been shown that myelin water experiences an additional off-resonance. We included this

Whitaker, ST, Nataraj, G, Nielsen, J-F, Fessler, JA. Myelin water fraction estimation using small-tip fast recovery MRI. *Magn Reson Med*. 2020; 84: 1977– 1990.

<https://doi.org/10.1002/mrm.28259>

<https://blog.ismrm.org/2020/08/21/qa-with-steven-whitaker-jon-fredrik-nielsen-and-jeff-fessler/>

<https://blog.ismrm.org/2020/08/28/reproducible-research-insights-with-steven-whitaker-jon-fredrik-nielsen-and-jeff-fessler/>

in our model, whereas it is typically ignored in other techniques.

Jon-Fredrik: The myelin frequency shift is a source of contrast that we employ by adjusting the flip angle and phase of the second RF pulse. For historical reasons we call this a tip-up pulse, but really that's a misnomer in this context because we are using it to alter the contrast in a way that is informative of the MWF.

Jeff: I'm learning here too! You're right, it's only a tip-up if we happen to be aligned. I'll have to read this interview and learn more about the method [laughs]!

MRMH: Can you explain more about your optimization?

Steven: We optimize the set of STFR scans in order to minimize the CRLB of MWF estimates. The tip-up in this STFR sequence introduces T2 weighting. We cycle through different flip angles and tip-up phases (as determined by the scan optimization) so that, for each location, we get a mixture of T2-weighting, T1-weighting,



Jeff Fessler in Hawaii at a previous ISMRM.

and sensitivity to the frequency offset. You need some mixture of flip angles and phase of the second pulse to make sure that you are sampling each voxel multiple times along this curve.

MRMH: Is the underlying objective to optimize the SNR?

Jeff: It's not that simple. Let me draw an analogy with diffusion imaging. If you want to maximize SNR, you should just set $b = 0$. To estimate diffusion parameters, you have to collect some scans with larger b -values, even though those have lower SNR. Analogously, we need a diversity of contrasts. There might be higher SNR in some of the images than others, but overall, we want to achieve the best possible precision of the MWF estimation.

MRMH: That makes a lot of sense to me! Has STFR been used for this purpose before?

Jon-Fredrik: No, it has not. This is a very different application of STFR which I really like. I think of STFR as a Swiss army knife, in the sense that it's a general tool for

altering the contrast. Steven came up with a really nice way to exploit that for this application.

MRMH: Have you learned anything in the course of this work that you wish you had known when you started?

Jeff: I wish we had known the importance of exchange when we started. The reviewers of a paper we submitted with another student pointed out the importance of exchange, something that we hadn't considered, so Steven rolled up his sleeves and started working on it. In this case, we really benefited from the expertise of the reviewers.

Jon-Fredrik: It's one thing to know about it, but it's another to know if it will really impact your estimation. It's a bit of a philosophical issue – maybe a method that is semi-quantitative is good enough.

MRMH: You provided a lot of code and data for readers. What was your incentive to do that, and how would you like other researchers to use your work going forward?

Steven: I look at it from the perspective of a new MR researcher. When I came here, one of the first things I did was to reproduce figures from STFR papers as part of my learning process. I coded everything from scratch because that is how I learn, but it was nice to have code from previous PhD students when mine wasn't producing the same results. I like putting the code out there so that if someone else wants to do similar research, they can use our code as a starting point. I see it as a learning tool for other people.

Jeff: I've been benefiting from open source tools for my entire career, and I feel that this is a way of giving something back. I always use LaTeX to write my papers, and I use Unix/Linux for most of my work; this work was all done in Julia. I'm paying back by contributing to science. Plus, the taxpayers have paid for this work so I think it should be open to the community at large so that everyone can benefit from the work they help support.

MRMH: What are the obstacles for translating this work to the clinic?

Steven: The main hurdle is getting whole-brain MWF maps within a reasonable time. We need to accelerate with undersampling and develop a reliable reconstruction algorithm.

MRMH: It seems that one advantage is that your approach is quite generalizable.

Steven: With Jon-Fredrik's work on vendor-agnostic sequence programming, we are getting to the point where it shouldn't matter what system you have. At this point, it should be enough to make sure the optimization includes the tissue characteristics and frequency offset for the field strength you are scanning at.

Jeff: Having said that, it would still be fairly simple to redo that optimization for a different field strength. ■

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It has also been shown that myelin water experiences an additional off-resonance. We included this in our model, whereas it is typically ignored in other techniques.

–Steven Whitaker

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RARE two-point Dixon with dual bandwidths

INTERVIEW BY NIKOLA STIKOV

EDITOR'S PICK FOR SEPTEMBER

This MRM Highlights Pick interview is with Henric Rydén and Stefan Skare, researchers at the Karolinska University Hospital and Karolinska Institutet in Stockholm, Sweden. Their paper is entitled "RARE two-point Dixon with dual bandwidths". They used dual readout bandwidth to eliminate dead times as a means of improving SNR in fat/water separation imaging. This paper was chosen as this month's Reproducible Research pick because, in addition to sharing some of their code, the authors also shared some nice interactive versions of their figures.

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Most pieces
of code will
likely not be
reproducible in
50 years' time,
whereas the
paper can be
expected to be.

—Stefan Skare

MRMH: To start off with, Henric, how did you get into MRI and how did you end up working with Stefan?

Henric: My interest in MRI began when I was a medical physics undergraduate student in Gothenburg. In 2010, the ISMRM annual meeting was held in Stockholm and because a professor of mine helped organize it, some of us got the chance to go. After attending the conference, I started talking to researchers from the Freiburg group, as I had noticed that this group was well represented at the meeting. As a result, I ended up working with Thomas Lange for half a year. Later on, just about the time I heard that Stefan was coming back to Sweden, a clinical position opened up in Stockholm. I applied and got the job, and after working there for several years, decided to do a PhD under Stefan's supervision. Actually, I will be defending my PhD thesis in September.

MRMH: Good luck with that! And Stefan, I only know you from our time at Stanford. How did you end up in the field of MRI?

Stefan: My links with the Karolinska Hospital date back to '94, back when we had only one MRI scanner for the entire hospital. Now we have 25, I think! My interest in MRI started during my time in the hospital physics program, when I decided I wanted to do my thesis work in MRI. At Karolinska I did a little bit of support work



Henric Rydén

for staff, a little bit of research, and then also my PhD in 2002. I was then invited to do a postdoc with Roland Bammer at Stanford.

MRMH: Could you explain what fat/water separation is and why the Dixon method is important?

Henric: Fat/water separation is a technique where you acquire both water and fat signals and then separate the two retrospectively during reconstruction. The fact that

Rydén, H, Berglund, J, Norbeck, O, et al. RARE two-point Dixon with dual bandwidths. *Magn Reson Med*. 2020; 84: 2456–2468.

<https://doi.org/10.1002/mrm.28293>

<https://blog.ismrm.org/2020/09/18/qa-with-henric-ryden-and-stefan-skare/>

<https://blog.ismrm.org/2020/10/02/reproducible-research-insights-with-henric-ryden-and-stefan-skare/>

it's a fat separation and not a fat suppression technique means that it is possible to model the signal from fat in more advanced ways, and in turn this allows you to account for chemical shift effects. It also allows you to inspect the signal from fat itself, which in recent years has shown some promise for clinical use, for example for musculoskeletal imaging and in multiple myeloma.

MRMH: What are dead times in the context of fat/water separation, and why are they a problem?

Henric: Basically, when you are designing a sequence that will allow you to separate fat and water, you often have to reckon with specific requirements in terms of the echo times or dephasing times. You also have to shift the spin echo readout to achieve chemical shift encod-



Stefan Skare

ing. But the problem then is that you end up with gaps in the sequence, where you are waiting for this chemical shift to appear. And it is that dead time that is our problem, because you end up spending very little time actually sampling the signal. It all comes down to efficiency, especially since SNR is the important currency in MRI. And so, our paper focuses on this aspect for single TR fast spin echo sequences, also known as RARE.

MRMH: I guess dead times account for about 30% of the duty cycle for that sequence?

Henric: Yes. The dead time, if we're talking about a spin echo sequence, is twice the desired shift. If you want to have a shift of one millisecond at 3 Tesla, then you have a dead time of two milliseconds for every refocusing pulse. And so, the dual bandwidth method we propose in the paper allows us to use all the available acquisition time in order to acquire the signal. Essentially, the question we asked ourselves was whether we could somehow place the acquisition window across the entire available acquisition time and then make the waveforms accordingly, rather than the other way around.

MRMH: And Stefan, from your point of view, how did this project evolve from an idea to the final paper?

Stefan: I have to say that Henric's project plan for his thesis was entirely his own. He's been very explorative and curious, and takes the time to turn every stone, also to ensure that I can follow! He's probably the most independent PhD student I have seen so far. It's rather fun to watch someone go through that journey by themselves, but it also means that, as a supervisor, you sometimes find yourself having hard time to catch up [chuckles].

MRMH: You shared code and some interactive figures along with your paper, so I'm curious to know where you stand on reproducibility in research.

Stefan: One thing I've been wondering is whether the links to code and to interactive plots should be considered as permanent as the papers themselves. If that is the case, then journals should probably take the same responsibility for those as they do for the papers. Most pieces of code will likely not be reproducible in 50 years' time, whereas the paper can be expected to be.

Henric: I myself wonder what it actually means for something to be reproducible in research. I think it is a question that may have a different answer for every paper. In the case of our dual bandwidth paper, I think it is actually the sequence itself that you need to be able to reproduce. Of course, it would be nice to have data available, too, so that you can reproduce the figures and everything else, but what's really new here is actually the sequence design. So, in this case, making our research reproducible was more about sharing the plots of the sequence. But for other papers, it may be more important that the data itself be reproducible. I think we should be having this conversation a little bit more in our field. ■

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The fact that it's a fat separation and not a fat suppression technique means that it is possible to model the signal from fat in more advanced ways, and in turn this allows you to account for chemical shift effects.
”

–Henric Rydén

Quantification of myocardial perfusion using simultaneous PET-MRI

INTERVIEW BY NIKOLA STIKOV

EDITOR'S PICK FOR OCTOBER

This MRM Highlights Pick interview is with Frank Ong and Miki Lustig, researchers at Stanford and Berkeley, respectively. Their paper is entitled "Extreme MRI: Large-scale volumetric dynamic imaging from continuous non-gated acquisitions" and it was chosen as this month's Reproducible Research pick because, in addition to sharing their code, the authors also shared a demo of their work in a Google Colab notebook.

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It's Extreme in the sense that we're trying to reconstruct a large-scale dynamic image dataset while pushing reconstruction resolution to the limit.

-Frank Ong

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MRMH: So, Frank, how did you get involved with MRI, and how did you end up working with Miki?

Frank: I started doing work in MRI when I was an undergrad at Berkeley. Miki was teaching a digital signal processing (DSP) class, where he would introduce a lot of examples using MRI, and I found the close relationship between MRI machines and the Fourier transform really amazing. I reached out to Miki in 2011 and asked if I could do some research with him, and that decision basically led to my career. Currently, I'm at Stanford working with Shreyas Vasanawala and John Pauly.

Miki: I actually remember things a little differently. I well remember teaching that undergraduate DSP class, and also that there was this one person in that class that was just nailing every exam and every assignment, and that was Frank. At some point I decided to write him an email to ask if he was interested in doing research. He expressed an interest, and so we set up a meeting with Martin Uecker, who was working with me at the time. We discussed possibly doing a combined flow and Bloch simulations. The next meeting, Frank actually showed up with the simulations for the entire project! One thing led to another, and he ended up having a paper by the end of his undergraduate studies. So obviously, I was pretty keen to have him as a graduate student. Frank has been an amazing graduate, with his PhD work resulting in this paper. Frank is now getting ready to go to the job market — he would be an incredible faculty. So, if any of the readers are on the recruiting committee in their institution.... They should be carefully paying attention!

MRMH: Miki, how did you get into MRI?

Miki: Well, when I came to Stanford, I didn't know what



Revolving doors: Frank (now at Stanford), wearing Berkeley regalia and Miki (now at Berkeley) wearing Stanford regalia.

I wanted to do, since electrical engineering is such a vast area. I ended up taking a class with Dwight Nishimura and learned about MRI, and my reaction was: this technology is really unbelievable! Around that time, I also started working as a TA for John Pauly, and that led to me working with him in MRI. Every time I think about MRI, or teach it, I find the topic incredible. I cannot believe nature has given us this! It's such an exciting and broad topic. And within this field you can do so many things, such as signal processing, computation, hardware, biology, physics, all the while staying within a single community. I think that's what really is remarkable about MRI.

MRMH: Moving on to "Extreme MRI", what's extreme about it, Frank?

Frank: It's extreme in the sense that we're trying to reconstruct a large-scale dynamic image dataset while pushing reconstruction resolution to the limit. Just to give you a sense of the problem at hand: the image datasets I'm talking about would be in the order of 100 gigabytes if we didn't do anything special with them. So, this

Ong, F, Zhu, X, Cheng, JY, et al. Extreme MRI: Large-scale volumetric dynamic imaging from continuous non-gated acquisitions. Magn Reson Med. 2020; 84: 1763–1780.

<https://doi.org/10.1002/mrm.28235>

<https://blog.ismrm.org/2020/10/23/qa-with-frank-ong-and-miki-lustig/>

<https://blog.ismrm.org/2020/11/06/reproducible-research-insights-with-frank-ong-and-miki-lustig/>



To do extreme research, you need extreme (ly good) collaborators!

work allows us to have a compression factor in the order of 100, albeit using a lossy compression. What's extreme is both the reconstruction challenge and also the memory and computation requirements. We wanted to see whether we could actually reconstruct an ungated dynamic acquisition at these high resolutions, because the underlying dynamics are not periodic or repeatable.

MRMH: Miki, care to add to that?

Miki: I think Frank is understating what's extreme about this work. I've always been interested in the whole idea of compressive sensing to speed up acquisitions. But the issue here is with dynamic imaging. While you can do 2D dynamic MR imaging with no problem, 3D has always been extremely difficult. And when you start doing constrained reconstruction with 3D dynamics, then you're limited not just by the algorithms or models, but also by the ability to actually compute and store the data on computers. So, there's a lot of thought that needs to go into doing that. And Frank came up with this amazing model making it possible not only to represent the data compactly, but also to store it compactly. This model lets you reconstruct really large data sets with amazing temporal dynamics. When he showed the whole body of a baby imaged using DCE-MRI, I was blown away by it.

MRMH: So, Miki has a long history of sharing code and making it easy to run, starting with his compressed sensing work. What did you decide to share for this work? And why did you decide to share it in the way you did?

Frank: Yeah, there's definitely a culture in his lab to share code and make sure almost everything is reproducible, which is partly a result of Martin Uecker's presence in the lab. Therefore, it was perfectly natural for me to decide to upload all my code and almost everything that I could share. I used Google Colab to host these demo Jupyter notebooks, and the reason I chose this service is because they provide GPUs for free (up to an allocated computation time limit). For the dataset, I used Zenodo, which now allows you to upload unlimited amounts of data.

MRMH: Miki, why is open science an important part of your lab culture?

Miki: Because, in my view, it's a key component to producing reproducible research. You can claim something in your work and show it in a paper, but if nobody can reproduce what you're doing, then what's the point?

I think that ensuring the proliferation of the method you're developing is really important. Even if you have a good method, if it's too complex to do or you're expecting other people to reimplement it from scratch, that will discourage others from using your work. In short, giving them the ability to do exactly what you did in your paper is critical for the proliferation of your work. And so, in the process of doing this paper, Frank also created this Python package called SigPy, and I am very happy to see it being used by a lot of people and institutions.

Nikola: Are there any clinics doing "Extreme MRI" at the moment?

Frank: A less extreme version is actually currently in operation at the Stanford Children's Hospital, where I know it is being used for some of the DCE scans. It's at a lower resolution than what we've shown in our paper, and the reconstruction time is therefore in the order of 15 minutes with four GPUs. But there's still a long way to go before we can deploy in a clinical setting exactly what I've described in the paper, because the reconstruction would take hours.

MRMH: To finish off, I wanted to touch on one aspect of Miki's PhD, which was on compressed sensing. At some point during our PhDs at Stanford, we were at a cafe with some other folks and we were talking about how many papers we'd written so far. At the time you were 3 or 4 years into your PhD and you still didn't have a single paper out. Then you got the compressed sensing paper published, and it's now the most cited paper in MRM. Why did you wait so long to publish? What made you wait, and how did the whole compressed sensing story come together?

Miki: Well, I started the work around 2003 or 2004, working with Dave Donoho, Jin-Hyung Lee and John Pauly. And after a short little while, we actually had some pretty good results. Yet, even though we'd been presenting this work in conferences, I found it pretty hard to narrow down the narrative of the paper. The compressed sensing theory was developed first by mathematicians, and so I think it was simply that it took us some time to work out how to explain it in a way that would allow any MRI layperson to read the paper and grasp what's actually going on. And I think that has been our main contribution, explaining this work really well and also providing the code to reproduce it. And all that took a considerable amount of time, and a lot of iterations. ■

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You can claim something in your work and show it in a paper, but if nobody can reproduce what you're doing, then what's the point?”

—Miki Lustig

B1 inhomogeneity correction of RARE MRI with transceive surface radiofrequency probes

INTERVIEW BY MATHIEU BOUDREAU

EDITOR'S PICK FOR NOVEMBER

This MRM Highlights Pick interview is with Paula Ramos Delgado and Thoralf Niendorf, researchers at the Berlin Ultrahigh Field Facility (B.U.F.F) in Berlin, Germany. Their paper is entitled “B1 inhomogeneity correction of RARE MRI with transceive surface radiofrequency probes” and it was chosen as this month's Reproducible Research pick because, in addition to sharing their code and data, the authors also provided exemplary documentation in their GitHub software repository and inside their code.

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No matter what
kind of science
you're doing,
it's all about
reproducibility.
This is, indeed,
how we give
back to society.”

—Thoralf Niendorf

MRMH: To start off, could you tell us about yourselves and your background?

Paula: I did my undergraduate degree in telecommunications engineering in Spain. Afterwards, I decided to go to Germany to do a Master's of Science in photonics. In my second semester there, I took an elective course in biomedical imaging. The professor (Prof. Jürgen Reichenbach) explained the topic of MRI with such passion that it really left me thinking “Wow!”. I realized that this field offered a perfect combination of physics, engineering, electronics, image processing — everything I was interested in! And so, I asked him if I could do an internship in his group, and he said yes. After that, I moved to Bremen to attend the Fraunhofer Institute, where I worked with Prof. Matthias Günther and team, and also did my internship and Master's thesis. I then saw an advertisement for this PhD position at the Berlin Ultrahigh Field Facility, and Professor Thoralf Niendorf and Dr. Andreas Pohlmann invited me to do my PhD here. And so, here I am!

Thoralf: I have been a member of ISMRM since 1992. My career has evolved through different stages, and included positions in academia and industry. Currently, I am head of the Berlin Ultrahigh Field Facility, primarily focusing on 7T MRI in humans, and also preclinical imaging at 9.4 Tesla. My background is in MR physics, but the development of applications to better understand diseases, and also the biology behind them, is where my heart really lies. I also recently decided to channel



Paula Ramos Delgado while on holiday in Perú (taken in Cuzco) a couple of years ago. She is very much looking forward to traveling again after this pandemic is over!

much of my passion and dedication into multi-modalities, multi-scale imaging, also focusing strongly on synergistically connecting imaging with data science.

MRMH: Could you give us an overview of the paper?

Paula: So, the use of surface RF coils is common practice both in clinical and in preclinical MRI. This is typically done with the volume coil for transmit and a receive-only surface coil. But recently, the market has seen a growing interest in transceiver technology (dual transmit and receiver coils). The caveat for transceive surface coils is that they have an inhomogeneous B1 field, and so they don't provide the right signal intensity for quantification. So, to image X-nuclei in future applications, you need a method

Delgado, PR, Kuehne, A, Periquito, JS, et al. B1 inhomogeneity correction of RARE MRI with transceive surface radiofrequency probes. Magn Reson Med. 2020; 84: 2684–2701.
<https://doi.org/10.1002/mrm.28307>
<https://blog.ismrm.org/2020/11/20/qa-with-paula-ramos-delgado-and-thoralf-niendorf/>
<https://blog.ismrm.org/2020/11/27/reproducible-research-insights-with-with-paula-ramos-delgado-and-thoralf-niendorf/>

to correct the B1 bias. This is typically done with an analytical signal intensity equation that relates the signal intensity to the flip angle and T1. But for complex sequences like RARE, the very long train of echoes makes this strategy impossible, because there is no analytical signal equation. And so, in this paper, we implemented and validated three different B1 correction methods for complex sequences for which no analytical signal equation is available such as RARE. One is a sensitivity method that was previously established as an intensity correction for surface coils; another is based on a signal intensity model, instead of an equation, to correct for B1+ inhomogeneity, and the third is a combination of both that and the sensitivity method. We showed that image homogeneity improved tremendously using these techniques. We validated the quantification and T1 contrast, and showed that they reduced the errors to under 10%. We're very happy with the results.



Thoralf Niendorf with Max-Delbrück – Nobel Prize Laureate in 1969, eponym of their institute and pioneering bicycle enthusiast – on his bike.

Thoralf: I got excited about this project for three reasons. The first is that I've been interested in RARE imaging since the time of my PhD thesis. The second is that we are now designing, evaluating, validating and applying several versions of multi-transmit receive RF arrays for human MRI at 7T. And third, I always like to balance preclinical studies with clinical studies, and Paula's project is a very nice example of how this can be done. It was so lucky we found Paula, who is and was the right person to address this specific issue and find a solution for it, which she did elegantly here.

MRMH: Why is this work important?

Paula: Like I said earlier, the number of transceive surface RF coils is increasing, both for clinical and for pre-clinical MRI. So, I really hope that anyone using these will consider the work we did here. I have spoken with many people who have transceive cryoprobes, and it really pains me every time they say they can't use their coils for quantitative measurements. It really is my hope that, moving forward, people will be able to use their transceive coils (which have incredible SNRs) to boost their applications, especially quantitative applications.

Thoralf: Yeah, I think Paula's work is a major forward leap towards parametric mapping with transceive coils, including quantification. Paula has shown, by example, how to approach this for T1 mapping. Meanwhile, we have also applied her technology for fluorine MRI, which has very low sensitivity but very high specificity.

MRMH: What advice do you have for people who would like to get started with this technique?

Paula: When I started, I wanted to use the best B1 mapping techniques. But in the end, I think just using what you already have available is good enough for most people and most applications. We ended up using a double angle method for B1 mapping, which works quite well, even though it may not be on a par with more modern techniques, like Bloch-Siegert shift. I would also recommend trying our hybrid method for B1 correction first, because it yielded the best results for us, but of course the sensitivity correction is very accurate and easier to implement.

Thoralf: My advice is really simple, and it's not meant to sound arrogant. I really would urge people to read the paper. It was written to read like a recipe from a cookbook, and Paula and her team put a lot of effort into describing every single step in great detail. Our ultimate goal was to promote reproducibility, and for this reason, the team also decided to make the code and data available through GitHub. We believe that this is the best way to disseminate the results, but also to share the technology with other sites.

MRMH: Is there anything else that you'd like to share with our readers?

Thoralf: I'd just like to reiterate that the idea of reproducibility is really close to our hearts, and we really have tried to walk the talk here and live up to the mission of reproducibility. I recently had a conversation with the head of our PhD and postdoc offices here, and it became very clear that no matter what kind of science you're doing, it's all about reproducibility. This is, indeed, how we give back to society. I might even go so far as to suggest that journals like this one should, in the future, move away from encouraging voluntary sharing of code and data and instead make it a mandatory requirement, because we firmly believe that this really is an essential "ingredient" for achieving reproducibility. I understand why it's been voluntary up to this point, but I would love to see it become mandatory in the long run. ■

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especially
quantitative
applications.”

–Paula Ramos

CONTRIBUTORS

Mark Chiew

Magnetic Resonance in Medicine Highlights Magazine Editor

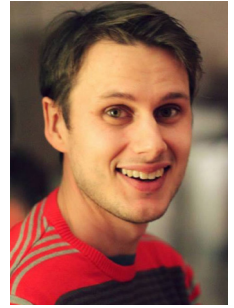
Mark is an Associate Professor at the University of Oxford. His research interests include the development of acquisition and reconstruction techniques for highly accelerated and robust neuroimaging. As for things that don't involve large and expensive magnets, Mark also enjoys eating noodles, wearing sandals, and spending time with his family.



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Magnetic Resonance in Medicine Deputy Editor for Science Outreach & Highlights Online Editor

Mathieu is a research fellow at the Montreal Heart Institute, after having completing his PhD at McGill University. His current research interests are in developing open-source software for quantitative MRI techniques and other related image processing tools. In his free time, Mathieu enjoys cooking, hiking, and making grad students feel anxious about not having a proper backup of their computers.



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Magnetic Resonance in Medicine Highlights Magazine Deputy Editor

Maria Eugenia is a Post-Doc at the Neuroscience Research Center of Magna Graecia University in Catanzaro, Italy. She completed her PhD and part of her post-doctoral experience working at the Institute of Molecular Bioimaging and Physiology of the National Research Council. Her work focuses on advanced methods for multimodal MRI fusion and on their application in the field of neurological disorders and healthy brain aging. Maria Eugenia is the proud mom of Federico (a tiny human) and Pulce (a not-so-tiny cat), and in her free time enjoys listening to music, binge-watching TV series with her husband, and being a crazy-cat-lady.



Atef Badji

Magnetic Resonance in Medicine Highlights Q&A Editor

Atef is an MD, currently working toward her PhD in Neuroscience at the University of Montréal. Her research focus is on the quantitative evaluation of pathological states of the brain using MRI. Among her specific goals are the understanding of the white matter changes in the elderly, as well as the understanding of the natural course of multiple sclerosis. In her free time, Atef enjoys writing, eating chocolate, and watching Big Bang Theory with her husband.



Tommy Boshkovski

Tommy is a PhD candidate in the NeuroPoly lab at the Institute for Biomedical Engineering at Polytechnique Montréal. His research focuses on introducing quantitative myelin metrics to the study of brain dynamics. Tommy is a contributor to the ISMRM online education program, as well as to the ISMRM blog, MR Pulse. In his spare time, he enjoys watching sci-fi movies and medical TV shows.



Audrey Fan

Audrey is an Assistant Professor in Biomedical Engineering and Neurology at the University of California, Davis. She leads the Functional Advanced Neuroimaging Lab to develop new MRI and PET methods that enable understanding of brain pathophysiology in stroke and dementia. Audrey has a deep passion for teaching, and strives to help trainees utilize research skills to create impactful biomedical tools that help patients. She believes there is a strong link between the beauty of art and science, loves Chinese brush painting, and has years of volunteer experience at art museums.



Agâh Karakuzu

Agâh is a PhD student in Biomedical Engineering with NeuroPoly Lab at Polytechnique Montréal. His research is centered on developing a reproducible quantitative MRI platform, with a particular focus on neurocardiology. He is an open science enthusiast and plays an active role as a science communication contributor for several platforms including MR Pulse and OHBM blog. He enjoys graphic designing, skiing and exploring specialty coffee.



Stefano Mandija

Stefano is an Assistant Professor at the University Medical Center Utrecht, Junior Fellow of ISMRM, and Chair of the ISMRM Benelux Annual Meeting Committee '21. His research topics range from fundamental and methodological MRI research to clinical development of quantitative MRI methods and biomarkers for MRI diagnostic and therapy. In particular, he works on the characterization of tissue electrical properties for radiotherapy treatments efficacy assessment using MRI. He is also co-leader in the European STOPSTORM consortium for MRI-guided cardiac radioablation using stereotactic radiotherapy and supporter of the Prep2GO consortium for MRI-guidance of spinal cord neurostimulation. In his free time, he likes sporting with friends, travelling, and visiting his family back to his home country, Italy.



Jessica McKay

After getting a Ph.D. from the University of Minnesota, Jessica joined the Body MRI Research Group at Stanford University as a postdoctoral fellow. Her research focuses on improved detection and characterization of breast cancer, including the development of high quality and resolution breast diffusion weighted imaging (DWI). Jessica loves contributing to the MRM highlights initiative to broaden science communication and collaboration. She also enjoys all types of skiing: cross-country in flat MN, water skiing on the lake, and downhill in the CO Mountains.



Emilie McKinnon

Emilie is an MD-PhD Candidate at the Medical University of South Carolina. She is currently finishing her PhD which focused on the application and development of diffusion MRI techniques at high b-values. In her free time, Emilie plays competitive roller derby for the Lowcountry Highrollers and for the South Carolina state team. In these circles she is better known as Waffle, named after the delicious treat from her home country Belgium.



Pinar Özbay

Pinar joined the Advanced MRI group at the National Institutes of Health in 2017, right after obtaining her PhD at ETH Zurich. During her PhD, she worked on novel contrast mechanisms for brain imaging, particularly quantitative susceptibility mapping at high field MR systems. At the NIH, she has been widening her interests towards fMRI, i.e. investigating fMRI signal characteristics during wake and sleep, together with physiological and EEG signals. She enjoys painting, stone carving and pilates, and is still discovering new coffee spots in DC.



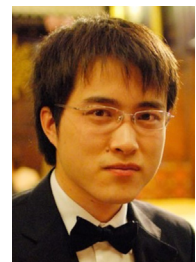
Nikola Stikov

Prior to joining the faculty of École Polytechnique (University of Montréal), Nikola completed his post-doctoral training at the Montréal Neurological Institute, and his BS, MS, and PhD degrees at Stanford University. A son of a sports journalist, Nikola has made journalism his hobby by periodically contributing pieces on science and film to newspapers and blogs in his home country, Macedonia. His career and his hobby are finally united in Magnetic Resonance in Medicine Highlights.



Chengcheng Zhu

Chengcheng is an Assistant Professor of Radiology in University of Washington Seattle. He got his PhD in University of Cambridge in the UK, and did postdoc training at UC San Francisco. His research area is cardiovascular MRI of stroke and aortic aneurysms. He has been with ISMRM since 2010 and was an ISMRM junior fellow in 2017. Outside work, he enjoys music and singing, badminton, basketball, skiing and family time.



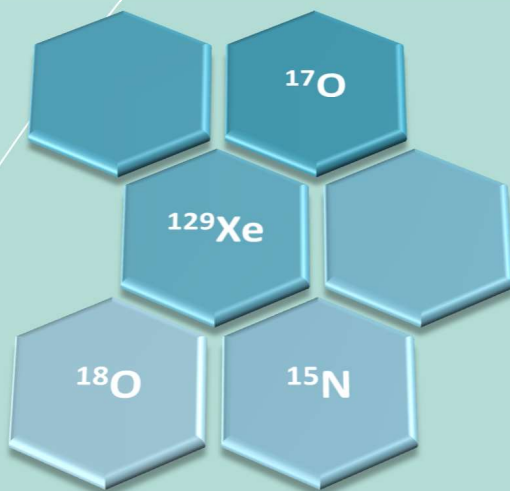
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See you in London 2022!