The ARM Interview

The ARM Interview is a transcript of a webinar on the topic of digital pathology & augmented reality microscopy that featured Dr. Liron Pantanowitz, Director of Anatomic Pathology at the University of Michigan, Dr. Dan Rudmann, Global Lead for digital pathology at Charles River Laboratories, and Gabe Siegel, the CEO of Augmentiqs, a company that develops augmented reality microscopy (ARM).

The webinar was recorded on February 25, 2021, & was the continuation of a pre-recorded webinar discussing ARM technology, and its place within digital pathology.

Link to Part 1 pre-recorded webinar
Link to Part 2 Live Q&A recording

Viewers of the pre-recorded session submitted 6 questions, and these questions were presented to Dr. Pantanowitz & Dr. Rudmann who provided their answers. Following the question & answer session, Dr. Pantanowitz and Dr. Rudmann provided their concluding thoughts and predictions for both ARM and digital pathology.

While the questions presented by viewers during the first webinar are primarily focused on the pre-recorded webinar and ARM technology, the answers provided by Dr. Pantanowitz and Dr. Rudmann, who bring the perspective from both clinical and toxicologic pathology, cover many aspects of digital pathology; making the recording of the webinar and this transcript a valuable resource for any individual interested in digital pathology.

Topics Discussed in Each Question:

For questions on this transcript, please contact Gabe Siegel: gabe@augmentiqs.com

Question 1

“I work for a company that develops AI algorithms, and until this point we have focused on developing algorithms for WSI. The concept of deploying AI algorithms within the microscope is interesting, and appears technically easy to accomplish. However, I wish to hear your input on the actual need for such a solution and what algorithms in your opinion would be most advantageous to the pathologist for an AI company to develop.

As a second question, I also wish to mention several points that I believe WSI has an advantage over ARM, and ask for your input.

A) The use of AI on a WSI file has advantages over the glass slide, in that an algorithm can perform the analysis as soon as the slide is digitized. With ARM, it appears that the AI analysis can only be performed when the slide is on the microscope and pathologist is working. ARM seems to reduce the actual need for AI, as in the majority of instances the pathologist doesn't require AI, whereas with WSI artificial intelligence can be used to prescreen & prioritize the digitized slides prior to their being viewed by a pathologist which in my opinion is the gamechanger of using AI.

B) Furthermore, performing AI on a WSI file means that the algorithm takes into account the entire sample, whereas ARM is only the Field of View. Would you say that the quantitative results of the WSI file would therefore be more accurate than just the FOV? (Knowing that “more accurate” doesn’t necessarily result in a different diagnosis.)

C) There are certain pathology samples where a field of view is not enough to render a diagnosis. Prostate for example where we run algorithms on the entire WSI file. What is your opinion on these tissue samples like prostate?”

Dr. Pantanowitz:

I've 3 three separate answers to that multipart question.

The first thing is that when you're making AI for WSI you cannot use the AI unless you have WSI. The truth is most pathologists in the world have a microscope but very few have WSI. So, if you're making AI for WSI you are making it for probably less than 1% of pathologists around the world. One day we may get there, but this could be 5-10 years. What are we going to do in the interim?

The second thing is if you're making AI for whole side imaging, there's no reason you cannot apply the same AI to augmented reality microscopy. There are advantages to the WSI and I would say that actually one of the problems today with people making AI algorithms for whole side imaging, is they are making algorithms to replace the pathologists and not augment them, which is a huge problem. I think that ARM coupled with AI is probably the best solution we have now.

For example, I have a case of breast cancer that has extensive DCIS and only a small area of micro invasions. I'll bet that there are very few AI algorithms now that will get that right every single time. Exclude all the DCIS, diagnose that, and grade that, and then find the small area of micro invasion amongst them, and then separately grade that.

So, if you're going to try and implement a system to accomplish that, you need a highly sophisticated algorithm and I doubt you would get 100% performance on that.

However, if you add the pathologist to that equation, let the pathologist go find you the invasion and then deploy the AI. What's the grade of the DCIS? What's the grade of invasive cancer component? So, there's no reason why you cannot couple the pathologist with AI instead of having the AI replace the pathologist.

The third thing is if you know people building AI algorithms today for WSI, the main problem with that is that we're talking about very narrow AI - all they do is one task. I'm afraid that they don't really understand what we do as pathologists. What I do or what Dan does. There's much more that goes into interpreting a case and then reporting that an AI algorithm can currently do today. We are not at the point where we have super intelligent AI. These AI algorithms that are being built are very narrow that they could just do one thing.

For example, when I look at prostate cancer there are algorithms that are quite good at detecting prostate cancer, diagnosing cancer, grading it and so forth. What I do is in addition to that is that I'm ready for any rare variant that comes along my way. I'm also ready to diagnose not just carcinoma but other features in that case. What are the background granulomas or something else that's important?

That's why I think AI algorithms for WSI, while they're great, there's a long way for them to go before they replace us. I think ARM has a great role for coupling the AI with the pathologist and not eliminating us for now.

Dr. Rudmann:
Yes, totally. It’s wonderful how the preclinical space really just aligns that everything that was just mentioned.

While we have whole slide imaging capabilities at some larger facilities, easy access for people to be able to tap into those. I'll be honest, in toxicologic pathology 99% is still the glass slide. And even when whole slide imaging becomes more part of our industry as kind of the staple for our primary evaluation, there are still going to be a lot of consultants, a lot of smaller groups are just not going to probably do WSI just because of the logistics or cost and complexity. And so that's where ARM fits in.

So, I totally agree. It's the same picture in non-clinical pathology as it sounds like it is in clinical pathology which doesn't surprise me.

I also totally agree with the synergism. Think about it, when you're driving, you're driving a fancy Tesla car and it does the auto drive for you. You're sitting back and letting the car do everything… Is that better than you interacting with the car in a synergistic way to produce a better outcome? And that is a safe drive when you get there efficiently. I think it's the synergism. Because you've heard unfortunately the stories where people are falling asleep while they're letting the car drive themselves and then it leads to terrible accident. That's what we don't want to do as pathologists.

So, when you do the whole slide imaging in advance and then provide it to the pathologist, the synergism is not quite as much serious. Because you're actually you're looking at the pattern you're doing the pattern analysis real time. And then you're incorporating the AI as you are looking through the microscope, as your mind is thinking. It's almost like having another pathologist on a multi headed scope with you at the same time but instead of another pathologist it's a computer. The base and the basis of that computer is the ground truth of pathologists.

So, it's really a very interesting approach. I think that it's all about intended use. I think there's a place for whole slide imaging, there's a place for AI, where that can bring extremely good value to both our industries. But there's also a place for ARM and its considerations and again it's all about really how you want to use it and apply it.

Field of view for us in preclinical toxicology. You know we look at whole tissue section. Clinical pathology … much of it is biopsy, evaluation … for good reason. We at non-clinical pathology have access to the whole organ. Which is a benefit for us in some ways… but it's a lot more tissue to look at.

So, to be honest with you I think one of the things that we deal with in non-clinical toxicology it may be our clinical colleagues in human medicine don't have to deal with as much, as we… a lot of what we look at is normal. And because we are looking at a large tissue section, we're not looking at a biopsy coming out of mass.

So, I think for us maybe as whole slide imaging gets more incorporated, there may be some more advantages for a whole side image in AI approach for us for screening, than maybe how it would be in in the clinical world. So that may be where there's a little bit of a difference in the non-clinical in the clinical space.

I think ARM is equally intriguing and helpful for both bases, but possibly whole slide imaging AI screening approaches in a non-clinical environment, where we're trying to avoid false negatives and alert the pathologist to to abnormalities. There might be a little bit more advantageous for us than to the clinical pathologist colleagues. I would be interested to hear what you think about that but that's maybe the only difference I would say.

Question 2
"I understood from the webinar that ARM is not necessarily an expensive technology, yet unlike WSI (which our lab has acquired) an ARM would be required for each microscope while WSI can be a single system.

What I am interested in hearing is how in your labs you determined the cost-benefit of ARM."

Dr. Rudmann:

It's going be partly dependent on the structure of the organization. If you have a consultant practice, where you're the only pathologist & buying a whole slide scanner for yourself, it's just not a feasible economic return on investment. You know, (it's better) if you can access the system that works with your microscope you have already invested in. A system that can use ARM, and then you can apply tools and algorithms that we developed, that would be much more cost effective for that kind of single pathologist practice. In toxicologic pathology there is a huge area, there's a large number of pathologists at work as single consultant entities out there. To give them the opportunity to get advantages of ARM to help them in their practice would be very useful.

In my company Charles River, we have over 150 pathologists across the globe in multiple sites. Clearly for us, putting a single ARM unit on all 160 microscopes, I mean we could do it, but we could also take advantage of a network of scanners that can interact together, so then the return on investment changes a bit. Again, I'll tell you right now, that we are an unusual company. There's not a lot of companies that have 150 pathologists, we're probably the only company. Most companies have a few pathologists and maybe a dozen pathologists at the larger end.

So again, I think it's intended use, it's kind of based on the structure of your company, based on your needs. For instance, we looked at over 4,000,000 tissues last year. Is it realistic to scan all four million tissues? When really you only want to do image analysis and maybe AI on 10% of those. Is that worth the extra time and money? Or do you want to make it more ARM focused where the pathologist chooses what tool to apply the ARM to?

So, you save all that overhead of scanning, and the slide comes round the lab, it goes on the microscope with the pathologist and the pathologist has a toolkit of AI algorithm that he or she can apply on the microscope. Even in a large company that has to potential to scan a lot, do you need a scan at all to add value?

These are the types of discussions and things that people need to think about.

It's not as simple answer, but I hopefully gave you some perspectives on how it could be thought about differently with ROI.

Dr. Pantanowitz:

My perspective on this question is as follows. Many people underestimate how expensive it is to implement Whole Slide Imaging because they think that WSI is the scanner. In fact, the scanner is the cheapest part of the whole thing.

When you talk about as if the question actually says the WSI system is the scanner, then you need the image case management software, and the license, and perpetual maintenance on that. Then you need a server to at least host the images, and if you want to keep them for longer that's even more expensive. You need a digital cockpit for the person to work out where the viewer will work. If you want an FDA clear system here in the US then that there's quite pricey. And guess what, the scans don't scan themselves, so you have to pay a person to scan them, pay their benefits every year. When you scale that up it's more after each year and you need someone to manage all of that, whether you're paying a central IT or someone to manage that.

Actually, a WSI system is very expensive. To get started we're talking millions of dollars up front and then to maintain that operation.

Whereas today, every pathologist in the world has a microscope. If you're an anatomical pathologist in one form or another, you already have a microscope, so that's already done. Not every pathologist in the world has a WSI system, in fact, I think it's going to be more than a decade before everyone gets a WSI system. I'm talking in developing countries to. Today I could walk into any country in Africa where there's a pathologist practicing, they wouldn't be practicing with if they didn't have a microscope. So, they already have a microscope.

So, when we're talking about bringing the power and flexibility of digital imaging to every pathologist, the augmented reality solution now is a much more cost-effective solution to bring this technology including AI to everyone today. All they need to do is buy a system and get a computer to do the processing.

I think people underestimate WSI. And unfortunately, if you were saying you wanted to AI with WSI you cannot do AI without the WSI. You actually have to activate several millions of dollars and then only can you realize the benefit of AI. This (ARM) is a great work around that solves that problem now. If you, just as Dan said don't have the money, if you're even a single person, there's no return on investment for millions of dollars when you can just start using AI.

Dr. Rudmann:
Yeah, I think the other great thing about ARM is… OK, so us pathologists we're old souls. I don't know if you guys can see my microscope next to me. I'm a digital pathology guy, but guess what, my microscope is sitting right next to me. It's like a stuffed animal. I just I love it.

For us to expect all pathologists around the world to go from what we've been trained on and what we're used to using… we like to feel with a microscope, and focus rings, and to go WSI and AI, and still be effective and efficient, and even just accept, it is probably a pretty big objective.

But ARM is cool because you still have the light microscope, but again, it's like a multi-head scope in a way but with the computer. It is kind of a nice transition, and we can learn a lot from it too.

Another thing about WSI & AI is you're going to have a bunch of trainers that pathologies are going to be working with, such as computer scientists to make these AI algorithms using WSI. And then you're going to be giving these tools to pathologists at work. When you using the microscope using ARM, you feel like you're involved a little bit more. So, there's a little bit more interaction for the pathologist: not only using their scope. but also, in terms of tweaking how they need to use the eye to help them. I think that's got some value. That's different than the value you get from the WSI approach.

I don't think they are conflicting with each other. There are some limitations based on financials and other things for sure and totally agree that it is a huge infrastructure to build to do it right for WSI. I think they're complementary. I think that the ARM is possible for a lot of pathologists. It is a great transition into digital pathology.

Dr. Pantanowitz:
Dan, I'd like to add that you know this probably as well as any other pathologists, not every slide in the world is going to be able to be digitized. There are some that WSI just cannot focus on. There are old slides, their too thick, there are broken slides, someone patched them up. There's polarizable material on there that you just cannot handle with digital imaging today. Cytology material people complain about. You may need to put oil on a slide to look at.

So you know what happens to all of those slides? There are millions of those being looked at around the world, we just going eliminate those and all those patients? Or veterinary patients that you have to just exclude them from all the benefits? That makes no sense.

We need a solution for those cases that you just cannot digitize. I think ARM fills that gap. The current technology we have on the market cannot address that for now.

Question 3
"According to the 2018 Toxicologic Pathology study brought in the webinar, (Click here to access via PubMed) ARM can be used for real time telepathology for peer review. Yet it was also mentioned in the webinar that there is no guideline for validation and licensing. Can you please provide more details on this point?
Do you believe ARM or any other microscope camera with some screen sharing application can be used for telepathology? I am asking specifically for GLP studies & peer review, though I imagine there are similar requirements for clinical pathology.

B) As a second question, there is value in having a WSI file for telepathology. It enables me to view the entire slide. I believe there may be reduced value of the ARM approach where I can't see the entire slide?"

Dr. Rudmann:

The best practice of peer review in non-clinical pathology and toxicology is not raw data. It doesn't produce data. It's basically a consultation exercise, where there's a second pathologist that is interacting with the study pathologist who is responsible for the data and who is responsible for the final diagnostic decisions in the writing of the report. Anything that we use in the peer review is used to help them in decision support, to help them make a decision whether they agree or disagree with pathologists. It is not producing data; it's really just helping them make decisions. It's a different type of regulatory requirement.

If the peer review pathologist was trying to use as an example, wanted to quantify a specific finding, let's just say mitotic index, and wanted to report out a number using ARM of the mitotic index for a series of slides, that's different, because it's producing data. But if you're just using a system to help you make a decision, then it's a different situation. I think that the regulatory issues are different. That said, we obviously want to qualify the systems. We want to make clear sure these systems work well and that they meet specific requirements, because we don't want to give the decision support tools to pathologist that aren't useful.

Let me just give you a really good example. If I'm hitting the literature, and I'm reading, and I'm trying to use the literature to helping make decisions, I might avoid certain journals because their articles are not good. I don't trust them. I don't feel like they're going to provide good quality decision support material for me.

But I'll go to other journals where I know that I can rely on that information helping me to take decisions. It's the same thing right here. We want the pathologist to make sure that they can rely on these tools that we're building for them. Whether they're AI driven tools or just literature. The qualification will be very solid, but the GOP requirement is going to be different because it's not producing raw data that's for peer review specifically.

As for the second question, you can look at the whole slide with ARM. You've got the slide underneath the microscope then you move it around. You're going to get one image right away,

because you're going to need to look at your field of view, but that's the really powerful thing about it, because the pathologist will help get to the area of interest through their training experience, where they want to use the ARM to help them make a decision.

If you have a whole slide image, 95% of it is not interesting, and who cares what the artificial intelligence thinks about. There's only 5% of that huge file that really is of interest that would really help the pathologist make a decision. Someone could argue that even the other 95% is just wasted time and energy. I mean why waste your time scanning? Why waste your time building the infrastructure and scan that?

While if you have a slide or anything microscope and you have a trained pathologist that looks at the slide and says that she is really interested to see what the computer thinks about this part of the slide, here she goes right to that part of the slide, boom, gets to it and gives decision support. That is a key difference to think about. I understand people always think more data is better, but sometimes more details equals more time, less efficiency and distracting.

Dr. Pantanowitz:
I think in clinical practice, if you need to use telepathology to support your practice, you need to pick the right technology to fit that and not overfit back with expensive unnecessary technologies. So, if you have a situation where you do not have a skilled person on site, and someone just loading a slide in a box, they know nothing about pathology, then you need access to the whole slide and control of it.

Whether it's a whole side imaging system or robotic system that does microscopy and you can navigate. Those are expensive to buy an expensive to maintain.

But if you have a skilled person on site already like another pathologist or a technologist, then to buy a whole side imaging system or a whole robotic system is an overkill and it's unnecessary, kind of what Dan said.

All you need is that skilled person on site, who is actually doing the heavy lifting getting to the right area, but they just need some support - second opinion - right there and then advice on how to proceed. And so ARM is a perfect solution for that. You don't have to overfit the technology to address that specific needs. I think you know it's what you need, this provides a simple solution for that. It is not overly expensive and doesn’t waste of a lot of technology to maintain.

Question 4
"Can you provide more details about how you see this ARM technology being used for pathology education? In the school I teach at we rely heavily on WSI, and I imagine this is the case for most medical schools in the country."

Dr. Pantanowitz:
Most medical schools and actually allied health schools dental, etc. have gotten rid of microscopes. They are very expensive to maintain. And people don't include even the rare cases, because it's hard to find a rare cases and we certainly get a lot of recounts. Digital pathology has really been great from their point of view, whole side images. Can ARM provide similar functionality or education? I actually haven't thought about that because I haven't used it yet, but it definitely can.

Two examples.
Number one, if you are at a medical school where you could not invest in whole side imaging technology, or even if you have it, you could still have your teacher up front with your learners and you could broadcast to them just from one microscope. So everyone could see what's going on.

If you don't have someone who could teach you, at least then, if you have a microscope, many schools around the world have microscope still, you could introduce some self-tutoring AI. In other words, you could look at the slide.

But if the person cannot find the plasma cells or the eosinophils, then you turn on real time annotation. You can help learners with microscopes wherever they are. I haven't done this personally, but I certainly see the augmented reality microscopy can do that to assist with education.

Dr. Rudmann:
I agree, I think our veterinary schools and training programs are a little bit farther behind in the medical practices mostly just because of funding and size, and so there's probably a little more dependency on the light microscope then whole side imaging. Although the whole slide imaging definitely is being used for seminar types of learning and databases and those types of things and training. I think both could be very beneficial. I think the most important thing for us, that are really interested in pathology is to help transition our colleagues into it, because it's a big change for people. I think ARM can be kind of a nice transition and still have its own utility with its own space.

Question 5
“The technology seems pretty straight forward, ARM is a camera, a projector and a stage camera. Assuming the projector and stage camera are not used, is ARM any better than a normal microscope camera?”

Dr. Pantanowitz:
Augmented reality microscopy is a camera with added value. If you're going to buy a camera, why wouldn't you want to buy ARM? It's like I would tell someone why go buy a car with the Turbo if you never going to turn on the Turbo? Then don't go and by the car with the Turbo. But if you buy the car with the Turbo, then you get the benefit of driving with the Turbo.

I would say it is like buying a Turbo engine microscope. Turn on the Turbo and go for a ride.

Dr. Rudmann:
Yeah, exactly, basic cameras don't have the ability to integrate AI and machine learning in it. That's a real difference.

It is a telepathology tool or just a tool to take pictures for communication and presentations. ARM systems have the benefit of both. they are basically the computer assisted machine learning type of technology along with the digital camera technology.

Question 6
"In terms of reporting requirements for regulatory submissions, obviously more from the point of view of the CRO than a regulatory body, do you believe there is any potential for ARM?
In particular, data such as histopathology images, slide label, position of image on slide – what are your thoughts on including it with the rest of the documentation? And do you believe there are other aspects of regulatory submission that ARM could be beneficial to?"

Dr. Rudmann:
It's all about intended use. If you're using ARM as a way to produce data, a quantitation maybe a quantification, I think it is great if you look at just some of the papers that have been published on measuring Ki-67 for instance.

Let's say that you are doing a preclinical study and you want to measure Ki-67 and to quantify it. Yet, maybe, historically it's been more of a semi-quantitative method, that pathologists use or maybe they were just counting on a microscope slide. And then you use ARM for that instead and it quantifies Ki-67 readout, then you include that in a pathology report. That would be a raw data source for that pathology report. That would have to undergo as part of GOP study good laboratory practices, so you would have to go under undergo validation.

I'll be honest with you, we've been validating machine learning for decades. I've been at several companies where we develop machine learning algorithms that we've used as part of submissions to regulatory agencies.

There are well defined computer validation methodologies by the regulatory agencies. There's a lot of people out there that know how to validate systems, so it's really not a barrier. It's just a matter of do we need to validate or not. There's no reason to validate if you don't need to. If it's decision support, if it's just accessing the literature, accessing another pathologist, using computers to help you make decisions, that's one thing. If you're using to produce raw data, that's going to be the basis for pathology report & that's another thing.

Dr. Pantanowitz:
I am not an expert in this area, but I don't see why you couldn't track. You track the barcode, you track the GPS equivalent coordinates as you're looking at it real time, so it's not that all of a sudden now you cannot track anything - maybe not to the great digital extent, but there's no reason why you couldn't track slide, barcodes, GPS location, and so forth.

Concluding Thoughts & Future Predictions

Dr. Pantanowitz:
I was excited to see this introduction of augmented reality microscopy and I was happy to test it out for several projects. I'm still working on projects, exploring the use of this. My recommendation would be for pathologists out there, if you have a microscope slap on a turbo engine and give it a test drive. You'll be amazed by what you can do. You do not have to overcome that inertia of trying to get a slide digitized first, if you don't have that system.

I think it's a great opportunity for us to capitalize on what's happening now, whether it's just simple annotations, which we're doing now working with my fellow. We're just doing simple annotations which is so much easier in real time versus being able to run image analysis and we have done those Ki 67 slides.

It opens up the world for you on your microscope. You don't have to first digitize the slide even those difficult cytology slides or whatever that I have that I cannot easily digitize today. I can get going right away with my Turbo charged microscope.

Dr. Rudmann:
I agree. Automatically, the system provides just a non Turbo charge benefits which is just the ability to collaborate, ability interact, ability to capture images, this stuff that we can just do with basic cameras.

But it gives you an entry point which is a very reasonable entry point to start experimenting with machine learning annotations. I think really it is going to be the future for us in pathology. I don't see AI driven machine learning at all taking our positions. I think the pathologist will kind of adopt an AI machine learning as a tool in their arsenal, to be more impactful on medical science. So why not start now?

Why not to get involved with these type of systems which are a lot less expensive than a whole slide imaging system and are part of your experiment? Let’s build together the future of AI/ML and its impact on both clinical and non-clinical pathology. It's an exciting time for us.

I think this decade is going to be the most exciting ever for pathology in terms of its interaction with the computer. Let's make it happen. The more people that get involved the better. I know a lot of people can't get involved if they depend on WSI. So, for them the ARM is a great entry point. Don't buy it just to buy it though. The worst thing you want to do is buy an I7 computer when you need an I3. If you make the investment get involved and apply machine learning. A lot of companies, like Augmentiqs are very excited about partnering with us and there's a lot of other companies out there, interested in collaborations. Also there may be other people that are computer scientists who are interested in partnering with you. It's a great way for us to build relationships with computer engineers, computer scientists because if we let them do their own thing and we do our own thing then, unfortunately, our solutions probably won’t be the greatest, but if we work together our solution is going to be fantastic.