Alzheimer's Disease & MRI Biomarkers for Disease-Modifying Therapies Transcript

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Introduction and Guest Background

Welcome back to the Reverse Alzheimer's Summit. I'm your host, doctor Heather Sanderson, and I'm so pleased to have Derek Snipes here today of psychometrics.

Dirk Stevens is the current chief technology officer at psychometrics, trained as a biomedical engineer. He obtained his PhD in medical image analysis in 2012.

After joining econometrics, he took different roles covering responsibilities in research and development, quality management, information security, management, marketing, sales management, management, and strategic partnerships.

Today, he is responsible for bringing new products to the market, demonstrating their clinical value and implementing them to be of value for the econometrics customers.

Derek, thanks so much for joining us today. My pleasure. Header. So as a clinician, I am really excited to learn more about what is on the cutting edge of imaging for Alzheimer's.

As you and I both know, dementia is much. It's much easier to prevent it and then to reverse it. And I think imaging has this really phenomenal ability to capture what we don't see, maybe behaviorally before it's manifesting as symptoms.

We can see it on a picture of our brains. So tell me a little bit about how you're doing that at ICA metrics. Yeah, that's that's really true. So with with imaging actually we can look inside the brain so we can actually look what is happening there.

And sometimes that is there are things visible there already. Years, maybe sometimes decades before clinical symptoms are present. And what we actually do is I take metrics.

We start from an MRI scan, an MRI scan that can be taken during the clinical routine practice. We analyze it with artificial intelligence and with the artificial intelligence.

We are going to look at such subtle changes that are almost invisible with the human eye to pick up the earliest signs of change compared to the healthy aging.

AI MRI Biomarkers for Early Alzheimer's Detection

Because in fact, that's what what is important, on imaging for dementia is to compare the MRI scan with MRI scans of a healthy aging population and try to depict the earliest signs of differences that might, lead us to an early diagnosis of, for example, Alzheimer's disease.

And so it also seems like it would make sense to have, like, a baseline for that individual where you're comparing not only to your the image of your brain to other people who are healthy, but the image of your brain to what it was previously.

So you could track change over time. Yes, absolutely. That's that's also very crucial as, there is a wide variation of humans, as you know, but the same holds for brains.

There is a wide variation of brains. Some people are born with the smaller brain, others are born with a larger brain. And there is this congenital effect that is actually not related to disease.

So some people just have a low brain volume. For for those we want to know whether that's because of it's congenital or because it's due to a disease.

And to get that answer, we need to follow up a patient over time and see how the brain is evolving. Is the brain. If the brain is shrinking faster than what we would expect for the same age and gender in a normal aging, then we know that there might be a disease active and we might have some clue to get a diagnosis for a dementia.

So then that brings up a good question that patients have asked me is okay. It says here that my hypothalamus is a little bit small or my hippocampus is a little bit large.

How confident can we be if we only have one image that it is related to a disease process? Yeah, that's that's again something that we need to be very careful of because as I mentioned, some people have a congenitally small hippocampus or hypothalamus and others might have a bigger one.

So there is this natural variation, same like with the length of people or the weight of people. So we need to be careful in, in, in the, in doing the interpretation.

But luckily there are some other signs. For example, if you look at the the region around the hippocampus, the hippocampus, as you know, the structure for for the long term memory, it is in a normal situation, there is not much, surrounding cerebrospinal fluid.

But in case of a pronounced Alzheimer's disease, we know that this the CSF space, the cerebral spinal fluid space is increasing. And it's that ratio between the hippocampus and that, CSF space that is around it.

It is a quite robust biomarker to indicate whether that patient has, Alzheimer's disease or not. And that is less dependent on congenital factors like the hippocampus on its own.

So we have some tricks to cope with it. But still we need to be careful in the interpretation. As mentioned earlier, it's always good to have a follow up scan and look also at the evolution of the brain shrinkage over time.

That makes a lot of sense. Okay, you're doing much more sophisticated analysis than just saying some brain region is this big, or there's this much volume in your cerebral spinal fluid.

You're going into ratios and comparisons and, and lots of other things that help you increase that confidence of saying there's something wrong or you're in the clear.

Absolutely, absolutely. We know that this is more sensitive and also more robust. So that's why we're doing those more complex ratios. But it also, means that there is some additional education to be done for the interpretation of the software because it's easier to interpret, like, hey, the hippocampus is smaller or harder, the whole brain is smaller than if ratio start changing.

It's not that intuitive anymore. So we need to do some education to get some, adoption of this new a biomarkers imaging biomarkers that are sensitive for the diagnosis of, Alzheimer's disease.

Let's jump into the tech then, because what we're doing now is an MRI magnetic resonance. And so there's no radiation is that right? That's that's correct.

Yeah. MRI works with, a very big magnet. It's one either in a one and a half Tesla or three Tesla. And this is an enormous magnetic field. If you compare that with the small magnets, that are used in the household, these are huge magnets.

And what they do is actually all the water molecules in your body are aligned in the direction of the magnetic field. And then what happens is there is some magnetic, there is some pulse sent to the area of interest.

For example, the brain. And that distorts this, this water molecules to be, aligned with the magnetic field and how

they relax back to their starting position that learns is a lot about the tissue properties.

This is called the magnetic properties of the tissue. For example, in the brain there is different property. There are different tissues present. There's for example, fluid that brings nutrition to the brain, but there's also the actual brain tissue, basically from the actual brain tissue, we distinguish typically the white and the gray matter.

And they each have different magnetic properties. And these intelligent devices have magnetic resonance imaging can can distinguish those, tissues. And based on that information, we we learn a lot on how your, your, your brain is, is organized and whether some parts of the brain are changing compared to last time or are different from a population or whether some of the mouth is there.

So this is actually the principle of an MRI scan.

Interpreting Brain Volume, Ratios, and Follow-Up Scans

And then with this particular MRI that we're talking about for detecting Alzheimer's and tracking the course of treatment or change over time is, contrast involved in that?

Yeah. That's, it's an interesting topic, actually, because, if we inject contrast, it's, it's it's basically a chemical substance that is injected, in the, in the blood vessels, and it travels all around the body, and it also comes into the brain.

And what is what the, the contrast is chosen to be, to have different magnetic properties than the rest of the brain tissue. And that's, causes a different signal, and therefore it can be easily distinguished.

So the contrast typically travels through the blood vessels. So the blocked vessels are easier to distinguish. But sometimes and so certain neurological conditions, for example, in multiple sclerosis there is a problem with the blood brain barrier.

And because of that problem there are there is also a contrast going from the blood vessels into the brain, causing some yeah, for example, inflammation in the case of multiple sclerosis.

So that's the reason why contrast is used in case of dementia. It is not frequently used because also there might be some safety concerns around contrast.

I think today we are quite confident that, if you have every. No. And then a little contrast, there might not be any health risks, but there are more and more concerns that if you have, a very regular basis, these contrast injections, there might be some accumulation of the contrast in the brain or in other organs.

So we should always be careful with the admission of contrast in the, in the in the blob to see more actually, because it's it has a, it has an advantage.

But if you compare that risks and there's benefits you typically would use not really contrast for patients with dementia. So it can be done. And for example it is done to exclude reasons of dementia that are cost for example by tumor.

The contrast will help to find the the tumor much easier. And also explain how activities so sometimes it's used but it's less used on a frequent basis.

In in dementia rate because balancing that risk benefit ratio, we want this information. This can be really helpful. And yet we don't want to put the patient at risk by having these repeated exposures to the gadolinium or whatever else could be in that contrast agent.

So with dementia, what you're saying is we can do these kind of repeat scans, look to make sure we're on track with treatment, look to make sure disease is in progression progressing or, you know, go ahead I guess determine

that it is that we need to change our treatment plan.

And we can do that without using contrast so that we're not accumulating that risk. Yeah, exactly. So, you know, here it is that the artificial intelligence comes into play.

Basically this such an image is like, I sometimes compare it with a breadth where you can slice the breadth in multiple slices. And that's actually also how the brain is imaged.

You image your brain in different slices, and each slice is reviewed by a radiologist to look at it. Whether it is something wrong or not, the beauty of a computer is that it can look in more dimensions than a human can read it.

So basically what the computer will do, it will think the whole breadth, basically the whole brain has a three dimensional volume, and it starts doing all kind of analysis on.

MRI Basics and the Role of Contrast

And that can help us to depict smaller changes than that is possible. By the by the human eye, for example, we know that for a human eye, it is quite challenging to see a difference of 5% between two structures.

So if a patient is scanned and it's any scanned again after a certain period of time, if the change is smaller than 5%, the human eye will will have challenges with it too, just because it's so subtle to pick it up.

But with the artificial intelligence, we are able to depict changes for for which are much, much smaller. For example, for the total brain volume average, every brain tissue that is inside the skull, we can can see differences up to 0.1 0.2%, which is small enough to distinguish between how in healthy person, healthy subject is aging, and compare that with the deceased person we know.

For example, unfortunately, that old rangers are shrinking at the age of 30. It is around 0.1% per year. At the age of 75, this is about 0.3% a year. So of course, when you want to see something meaningful in one year, you need to have a tool that can measure it with an accuracy that is lower than what the actual brain is shrinking, and therefore we need those AI tools to see that change because the human eye will not pick on to depict them will not be, it will not be clear to them.

So that's that's the reason why we are applying those AI tools on the imaging. And is the AI that developed already, or is this something that you are planning for in the future?

No. Yeah. The AI is is available. And this is also kind of the beauty of of AI and software. It is quite rapid to build it. And it can be put into like the clinical routine help radiologists, help neurologists, health experts all around the world.

Because it sees so much new data, it can learn from it and it can become smarter and smarter. And this measurement error goes down and down on down. So that's the beauty about the system.

So it is now, for example, to take our system as an example. It's now in the US market since 2016. And and it underwent several improvements over this time.

Of course there's luckily and I think this is a very good thing. There is a regulator, the Food and Drug Administration, the FDA, that looks whether every change is really a an improvement before you can put it into the clinical routine as a, as a company.

But the beauty is that it keeps on improving all of these tools. And at a certain moment it will be able to maybe depict changes that are so relevant that can also be, have, have the necessary accuracy to be quite certain about a certain, diagnosis, whereas now it's more of a, support for diagnosis.

Big decisions support too, rather than a decision tool. And of course it will always be a help for the physician, but at

some point it might be a bigger help.

So interesting, interesting changes to to come here as well. Very exciting. So if someone is looking at doing an MRI to measure these biometrics for someone and they're considering a diagnosis of dementia, maybe they even already have that diagnosis.

What would be required for the MRI? Like what things are necessary to be able to have more and get the full benefit from this potential technology? Yeah, it's it's of course important that the MRI machine is used in a good way.

We unfortunately see that in the real world. So in, in the data that are acquired everywhere around, everywhere in the United States, there is quite some variation in the quality of the data that is acquired by the MRI scan.

Today's MRI scans typically have the ability to do good MRI scans for for for dementia. I told earlier that it needs to be a good strong magnet, and if it's a strong magnet, it is typically able to to get good images.

And, basically what we, what we, would like to see is what we call a 3D image. That means, it should cover the full brain. And it's like the, the, the slices of bread that are acquired in such a way that the full breadth is present inside the image.

AI Precision, Clinical Adoption, and Scan Requirements

So sometimes it's, it's, it's like that, that half of the slices are, are thrown away and only a couple of slices are kept of the bread. And that's not good because then we miss information or the artificial intelligence information and algorithm misses information that is important to to quantify certain smaller structures like the hippocampus.

That's an important one. The second important one is also that with the, MRI scan, it is, a magnificent device because the pulses that you can send inside the brain to make the water molecules deviate from their standard position.

There are multiple ways to do so, and that gives different types of images. We call them a T1 weighted image or a T2 weighted image. And that gives us other information.

It gives us other magnetic properties. What we want to know typically for dementia patients is the T1 weighted scan, which is very good at distinguishing the different brain tissues.

As I explained earlier, the white and the gray matter. So we need a T1 weighted three dimensional scan in order to be able to use these AI, algorithms.

We can also use, T2 weighted imaging. These are other weighted imaging. And that's interesting to, for example, understand whether whether there are some vascular lesions which can occur in case of vascular dementia.

And this is one of the most common, differential diagnostic questions. But when a certain patient has Alzheimer's disease or vascular dementia, the two most common diseases causing dementia, and with the quantification and the assessment of the white matter lesions that can be extracted from a T2 weighted scan, we can also extract that with the artificial intelligence.

So long, long explanation to explain that with the MRI, if the MRI machine is good, we can acquire the images, that the AI needs. And we can help a lot with the differential diagnosis for patients with dementia.

I think that if a patient, say, who's listening, or watching at the summit right now, or, maybe a loved one of a patient who is suffering with dementia, if they were to go to a doctor and ask for this type of imaging, what would they ask for specifically?

I would recommend them to, to ask for, definitely a 3d T1 weighted image, which every MRI scan can do. And I

would also recommend them to ask for a volumetric quantification, because that is also sometimes how it's called.

Because AI is a little bit of a, a hype, the trendy name of, volumetric quantification. So more most radiologists probably know it more on their depth term.

And basically what it does is it asks the radiologist to quantify certain structures in the brain and basically also compare them with what is expected and depict the big changes from that.

And will this also be getting the this ratios that we discussed, some of that more advanced analysis? Yes, I would say so. So there is there there are different software packages on the market.

And some of them will do these ratios, others won't. But I would I would say the better packages do and I think this is something that is very valuable, especially if it's the first scan.

As I explained earlier, it can give already some clue, whether the patient is, affected by disease or whether it's just something that is part of the normal variation.

So a traumatic brain injury is one of the big kind of risk factors as people age in terms of developing dementia. And you guys offer imaging for TBIs as well.

How is that different from the type of imaging that you would get for dementia? Yeah. Well, that's that's very interesting. The because the field of TBI is, largely unexplored.

There are so many things we need to learn. We know at the moment that TBI is not really traumatic. Brain injury is not really a one time event. So obviously there is this event itself that causes damage to the brain, but it's actually the scalar.

So the events that happen after that damage that are very interesting. Some patients recover quickly from the from the from the brain trauma and might not have real symptoms afterwards.

But for others there is a start of a neurodegenerative process. So a process where the brain is dying or parts of the brains are dying and the interesting point is that we are now starting to understand the relationship between what's happening shortly after the traumatic brain injury and dementia later on onwards.

So for that reason, we are also investigating and spending a lot of effort in trying to build artificial intelligence models that can better quantify, better assess patients with traumatic brain injury, and preferably those with the mild traumatic brain injury because they are at risk of developing dementia for a portion of the population.

Whereas it's unclear for a clinician at the moment that it's happens. Which portion. Yes. And and basically we look at something that is called the white matter bundle, which is the white matter consists of connections between the the cortex of the brain, where all the functional areas are and everything else in the body.

And these bundle bundles, you can see them a little bit as a or ordered spaghetti bundles in traumatic brain injury they might get damaged. And with a technique called diffusion tensor imaging or more general diffusion imaging, we can learn more about the damage of those bundles.

And what we are developing and have developed actually, is an AI algorithm that can learn where the damage of those spaghetti bundles is occurring. And typically, if there is a certain amount of damage, it is it is the start of a neurodegenerative process and that can lead to dementia.

So what we try to do now is with patients with traumatic brain injury, try to measure what's happening in the brain, which of these spaghetti bundles are damaged.

Traumatic Brain Injury and Neurodegeneration Risk

And based on that, have an understanding whether there is a risk of further neurodegeneration and whether we need to look up for, for lookout for, for, for dementia.

And this is an interesting population because we can do a lot of interventions there. We might do, cognitive exercises or other, therapies at this point, because this is typically very early in the process.

It's only at the start of a new design process. So this is pointing to the importance of imaging very, very early in the process. But that's so exciting to me as well, because it means that you might be able to measure how well the treatment is going with in the absence of symptoms.

Right. You don't have to go back to okay. How fatigued are you? Are you not just are your pupils right. You can say, let's take a picture of your brain and let's look at these spaghetti noodles and see how disorganized they are.

And then apply some sort of treatment like exercises or oxygen therapy, hyperbaric treatments. What you the laundry phosphor do a colon and serum, a laundry list of things that I think of right away when there's been a TBI.

And if we do that when someone's 18 or 19 and having this TBI, then measure the changes on the pictures. Maybe we skip that dementia when they're 60, 70, 80 years old.

There is definitely a very, very big chance that that is that is working. And the beauty indeed is that the the what's happening inside the brain is typically so much earlier to the symptoms that will occur many years later.

So even if a patient with mild TBI has not really that much symptoms, it might be very important to treat the the patient early because it's the brain that needs to be preserved, because the brain that is preserved will keep this healthy life much longer later onwards.

And, to do so, we need end points. These are evaluation measures to define whether the therapy is working that are less related to long term outcomes, because that is is just way too long to wait for that.

And MRI and the derived metrics that we can assess from it are, are an intelligent way to do so. So it's definitely worthwhile doing and worthwhile investigating like that.

And as a clinician, I always wondered who in the absence of symptoms, are we done? Have we completed this process? Like did we fully treat it? Another time that imaging would be so helpful is sometimes we measure that people are getting better in some way, but they're not feeling it quite yet.

But when we can point to the picture, when we can point to the measurement and say, no, no, hang in there, keep doing the work because it is it is about to pay off.

Even though you're not feeling it, we can watch this picture and we can see it improving. That is such a motivator for people to to do the hard work of changing their lifestyle, their diet, some of these other things that we know are very impactful.

But sometimes just take a little while to reap the benefits. That's from a scientific point of view. That's absolutely true, but I'm super happy to hear from you that, yeah, that can also be a motivator for patients because actually it's so important that people can can follow their therapy to at the end, actually.

And there should be all kinds of like measures to, to keep them motivated. So, I'm happy to hear that that might be one. And that's definitely good. So what about cost?

A typical MRI typical image like this is do you know, in the US, if it's typically covered by insurance or if people are paid out of pocket, what that might look like.

Yeah. So the MRI image is, is typically covered by insurance. Might be an out-of-pocket expense there. And the, artificial intelligence analysis that comes on top of it is really nominal compared to the MRI price.

So typically that's also part of the whole package. And that really depends on, on center by center. Obviously the or luminary centers might, might ask a little bit more for that than an imaging center.

So there is there is some variation there. But it's it's it's a quite small cost compared to to the MRI scan itself. Got it, got it. So applying the AI to the images that are going to maybe be done anyways, isn't that it doesn't.

It adds a ton of value, but not a ton of cost. Exactly, exactly. I truly believe that. But, hopefully, I'm not the only one and things like that. So if somebody wanted to learn more about what all you guys offered psychometrics, how could they learn?

Well, we are, we're doing so much in the moment. But I want to maybe pick out one particular initiative. And that's, a website that that we have launched.

It is called ALS imaging.com ALS at ALS imaging.com, and it is a website that tries to summarize a lot of, how imaging in Alzheimer's disease is happening.

And it is, it's completely unbranded. It's all factual.

Cost, Resources, and Closing Remarks

It's with the strong clinical evidence. And I would definitely recommend everyone to have a look there and learn more about Alzheimer's disease and imaging, because, there is so much that we can learn from the imaging, especially in relation to therapies.

It will it will help us understand much better the therapies in the future as well. It will also in case at some point some medication will come on the market as a complement to the existing therapies.

It's it might also be of value there. And all of that information can be found there. And now of course from a commercial offering as a, as a company, I would also almost I would also be happy to, to refer you to a website, econometrics.com, where you can also find some nice blogs on the products and how they can help.

And there is also an opinion piece on how the world is evolving today on Alzheimer's disease and what the role of imaging can be. So there's definitely so, so much valuable information that it is out there.

Obviously, that's all coming next to the great content that, the patient organizations, are, are putting online. Also, the websites like, the one you, you have Doctor Tennyson is so valuable to have that content there to have an education because that's typically what we see as the main factor of good care, as a good education, good background.

If, if, if patients are informed, the likelihood of having a good outcome is just better. So I would definitely recommend to to all of this great content that is out there.

Thank you Derek I really appreciate that. And I told you before we started recording that I feel sometimes intimidated by the different imaging that is available.

And kind of unsure of how much it's going to influence my clinical course and the treatment. And so having access to this information, especially as it's changing so rapidly as the AI develops and as these things really mature, I agree that they're going to take a much bigger role in the clinical sort of the entire path.

Right. And in terms of diagnosis and treatment. And so I'm looking forward to that. And having, you know, having a little bit more confidence, in all of these pieces as the, the imaging and the AI on top of that start to inform what we're doing.

Okay. Fantastic to hear that. Yeah. So thank you so much for all of your insights and wisdom and for just kind of nerding out with the as to iron how MRI and imaging can be helpful in diagnosing and then preventing and

reversing Alzheimer's.

It was super excited to speak with you. The presentation's fantastic. Very great. And.