



# Understanding Your MRI

Presented by:

Jill Conway, MD, MA, MSCE

## **Kyle Pinion:**

Well, good evening and welcome to the Multiple Sclerosis Association of America's live webinar, Understanding your MRI. I'm Kyle Pinion, Vice President of Mission Delivery for MSAA and your host for tonight's program. On behalf of MSAA and our presenter, we greatly appreciate the opportunity to keep you updated on this very important topic. And please know we hope you and your family are staying safe and healthy in these uncertain times.

As you may know, MSAA is a national nonprofit organization in service for over 50 years dedicated to improving lives today for the MS community. I wanted to take a moment to give a briefer than brief overview of our services. If you've called us before, you've likely already connected with trained and compassionate helpline specialists who have a social services or counseling background and are familiar with MS. Helpline specialists can assist people living with MS and their care community with identifying helpful MSAA program recommendations as well as other resources available from the broader MS support community.

I will also note that MSAA's Cooling and Equipment Programs are available to individuals who might be experiencing financial or insurance barriers to accessing tangible items that can help to manage some of the symptoms of MS. Examples of products available through these programs include items such as cooling vests to help those experiencing heat sensitivity and/or seated four-prong walkers for mobility support. And of course, we also have the MSAA MRI access program also for those who are experiencing financial barriers to accessing their cranial or C-spine MRI for a diagnosis of MS or to track disease activity. What a timely topic to talk about today. For information about eligibility criteria, applications, or just more details about these and other MSAA programs, please visit the MSAA website, pop us over an email or give us a call. We'd love to chat with you.

Also, just a brief reminder that the discussion being presented tonight is for reference and informational purposes only and does not constitute formal medical recommendations of any kind. For any personalized recommendations, please be sure to consult with your medical professional. And for your friends and loved ones who couldn't join us, tonight's program will, of course, be archived to our web site very soon. For our Q&A session, please type your questions into the chat box and we'll address them at the end of the presentation. Also, if you're having any technical issues, please type those concerns into that Q&A box as well.

Finally, at the conclusion of tonight's program, you'll be asked to complete a short survey. We would be so grateful and appreciative if you complete the survey before closing out of the meeting window. Your honest and open feedback on our programs is vitally important and helps shape future programs, just like the one you're watching tonight.

With that said, I'm delighted to introduce you to our presenter for tonight's presentation, Dr. Jill Conway, the director of the MS Center at Novant Health in Charlotte, North Carolina. Dr. Conway earned her medical degree from the University of Illinois and completed her neurology residency at the University of Pennsylvania. Dr. Conway completed a two-year multiple sclerosis fellowship with a clinical research focus at the University of Pennsylvania. Dr. Conway has a long-standing interest in clinical ethics and clinical research ethics and has served on Carolinas Medical Center's Ethics Committee. Her recent research interests include cognitive function in multiple sclerosis, treatment of mood disorders in MS, new and emerging therapies, Neuromyelitis Optica, and issues related to women and multiple sclerosis. Dr. Conway is also, I'm very proud to say, a member of MSAA's Health Care Advisory Council.

This has been a program I've wanted to present in this format for quite some time. Dr. Conway had kindly brought this idea to me many, many years ago. The idea of presenting more information about the MRI and helping patients understand what an MRI looks like and what an MRI read is like. And the program was so successful in person that we absolutely must had to do it on a webinar. So, I'm so delighted to be able to do that.

And certainly, if you haven't had a chance, please also take a look at the Motivator Magazine article from I believe it was summer 2018 that covers a lot of the great information that will be talked about tonight. We'll make sure to put a link in the chat box as well for that. But with that said, Dr. Conway, I'm going to turn this over to you. Thank you so much.

### **Jill Conway:**

Thank you so much, Kyle. I appreciate that lovely introduction and I want to make certain I have control, so I need to share my screen here... Perfect.

So, I am delighted to have the opportunity to present on this topic and I appreciate MSAA for giving me this chance. I feel like I tried to put together in this talk a source of information that is what I wish someone had explained to me when I first started to study neurology, and I was very new at trying to understand MRI. And I feel like if every patient who's just diagnosed could understand more about what the MRI is and why people like me ask people with MS to get MRIs, then it would perhaps take some of the sting out of how difficult it is to pay for MRI and how unpleasant it can be to lay in that machine. But there really is crucial information that we get from that. And I'm going to go over that in a lot more detail.

So what I want to cover today is to understand the role of MRI in how we diagnose MS, learn how MRI can be used to monitor whether or not a treatment is working, explore the range of MRI findings that we see in MS; really get a sense for what is mild or MS on MRI and what can be more severe, and then finally examine how MRI changes relate to future disability. So what I'm going to do is present information about each of those things and then at the end, I have three cases that I'm going to go through to demonstrate a little bit how I think about MRI in treatment.

So the first thing I want to say is that when people get MRI's, we very often see evidence of white spots or hyperintensities is the official word. And there are lots of reasons that people develop spots on MRI that are not MS. So the first thing I want to communicate is that every

spot on an MRI is not necessarily related to MS, nor does it diagnose MS. So, when we try to think about MRI, we think about where the spots are, we think about how many there are, we think about other conditions a patient might have. And we put all of this together to try to get clarity about a diagnosis.

Other things that can look like MS on an MRI include things that we think of as MS mimics. So anyone I see who's coming to me and I'm concerned about me, I'm going to rule out some of these mimics and that includes other diseases that create lesions on MRI that look very similar to MS, like neuromyelitis optica, something called anti-MOG disease, which is a separate antibody that we can test for. An acute syndrome that can cause MS-like lesions but is not an ongoing chronic disease called ADEM. There are infections that can look like MS, and that includes Lyme disease and HIV, but there are many others as well. Anybody I'm evaluating for MS is going to get a syphilis test, and I always try to be clear that it's not that I think someone has syphilis, but that's really part of the workup for many neurologic conditions.

There are genetic causes for changes in white matter that can look like very severe MS. They tend to be more confluent changes in the white matter that is kind of the whole area can look impacted rather than separate spots. But sometimes that can be confusing, especially early on in a genetic condition. There are other autoimmune inflammatory diseases like lupus, or something called Sjögren's disease, or something called sarcoid or Behcet's disease. All of these end up with spots that can look like MS. And then the more common causes of spots are what we would call nonspecific, which I think is really just a measure of age-related changes in the brain. I sometimes say to patients that your skin doesn't look like it did the day you were born. Your brain doesn't either. And so as we age, sometimes there's the accumulation of small white lesions in the brain. They tend to be smaller than what we see in MS, but they are definitely present, and they can be in locations that are hard to tell apart from MS.

And so, I'm looking at the whole patient when I am evaluating this. Someone who has a lot of risk factors for vascular disease, has more white spots associated with aging. That SVID here at the bottom of the screen stands for small vessel ischemic disease, and that is damage to little blood vessels. And that damage happens more often in people who smoke, who have diabetes, who have high blood pressure, who have high cholesterol. And so, if I'm talking to someone who's 70 years old and they have a long history of multiple other conditions, I would expect them to have a number of lesions in the brain that may look like MS, but are probably from a different process.

So how do we tell when we're looking at an MRI whether the lesions or white spots that we see are MS? First, we look at lesions in particular locations. So not all lesions are in locations or are in a size that is typical of MS. We also look for other clues. So one of the other clues is to do spinal fluid. And about 95% of MS patients have antibodies in their spinal fluid. And so that can be helpful confirming information when we have an MRI that looks potentially like MS and then we also have spinal fluid that looks like MS.

And then finally, we look for symptoms. And in MS, especially early on in the disease, the symptoms tend to be specific. So it's very common for me to start with numbness in one hand and then it goes away or loss of vision in one eye and then it goes away. Those sorts of situations are much more likely to be MS than someone who has symptoms everywhere, because, again, in MS, the symptoms occur because of changes in the brain and spinal cord and especially early on in diagnosis, there tends to be not that many changes and so there doesn't tend to be completely global symptoms where... I sometimes will have someone say, I looked this up on the Internet and I have every symptom. That tends not to be typical, especially

in early MS. Now, someone who has MS and who has had MS for a long time may have many symptoms associated with MS, and that may include fatigue or feeling really weak when you're overheated. But that doesn't tend to be how MS presents initially.

So what is an MRI? MRI stands for magnetic resonance imaging. And the important part about that is that first term, "magnetic", because MRI does not work with radiation. So a CAT scan and an X-ray use radiation and therefore cause radiation exposure which can be damaging when people are exposed to too much radiation. That is not true for MRI. MRI is a magnet that helps these protons in the body, so protons are hydrogen nuclei, they're part of water molecules, align when they are exposed to a field. All of the nuclei sort of face a direction. So what happens in an MRI is that that magnet pulses, when you're in the MRI, you hear the clicking sound and then it moves and then you hear a different sound and it goes on and off. That's a magnet turning on and off. And as it does that, it creates an effect in tissue where these hydrogen ions line up in a particular direction. And that helps us create a picture of the tissue based on the behavior of those hydrogen nuclei, because what that does is allow us to know how much water content is in a particular kind of tissue, and that allows us to create a map of what the tissue looks like.

When we are in that machine and that clicking is happening, the MRI is taking a series of different image types. So every time you hear sort of 60 or 90 seconds of click, click, click, click, click, and then it stops. And then you hear sort of the machine move and then it starts again. That is a different series, looking at tissue in a different way. So some kinds of the way tissue is looked at is a slice through you cross-sectionally, so like that. So that's called axial imaging. So it's it's a cross-section as if you just took a big axe and cut your head right through. Sagittal imaging goes sideways. So you sort of start at one ear and then you go through the head and then you come to the other ear. And then coronal imaging is front to back. So MRIs take pictures of you essentially sliced and diced where you can look in any of those different planes and you see slightly different things and the architecture looks different. And sometimes you can get a better view of things when you can look at it in more than one direction.

So again, as the machine is making this clicking, that gives us different pictures. And these pictures, which I'm going to show you in a minute, highlight different aspects of brain anatomy. So the first kind of image we look for is called T1, and T1 gives you a picture of the brain that looks like it would if you just sliced it open. And I'll explain what that means. Gray matter is gray, white matter is white. T2 highlights pathology. It makes things that aren't normal kind of show up as bright light, that can include tumor, it can include MS lesions, it can include strokes. So lots of different things will show up as bright on a T2 image, even if you can't see it on a T1 image. And then because in a T2 image, all the fluid in your brain, and again, I'm going to show you pictures in just a second, all of the fluid in the brain is white on a T2 image, and the lesions are white, too, and that makes it really hard to see the difference between the lesion and the fluid. And so there's a special image called FLAIR - "fluid attenuated inversion recovery" is what that stands for, and that makes the fluid black. And then the lesions or stroke or scars pop out and you can see them quite clearly.

So that is the first image I look for when I'm looking at an MRI and it's the first image I look for to see what MS lesions look like. And then there's also a way to take an image when you put gadolinium contrast in the IV, and that shows the breakdown of the blood-brain barrier. So I'm going to show you what each of those looks like.

We're going to start with T1 imaging. Now, this is a particularly good image because it's from a research level machine that's a high magnet strength. So your typical commercial MRI isn't quite this good, but this is a slice through the head. It's axial, right? So it's a slice through the head

cross-section. The gray matter of the brain is this gray strip around the outside. The white matter is the lighter areas on the inside. And as I said, T1 imaging shows us the brain as it would look, so if you just sliced open the head, it would look very similar to this. The gray matter on the outside is slightly darker, the white matter is slightly lighter. And then there's a lot of gradations in the brain, there's layering effects, and you can see some of that in this MRI. So this is a very typical appearance of normal brain in a T1 image.

This is a T2 image. And a couple of things have changed. So if we go back to T1, these areas that are black are fluid. And so there are some fluid filled areas and the fluid shows up as black on this kind of image. When you move to a T2 image, there is fluid. This area right here is a ventricle filled with fluid. This area around the outside of the brain is fluid. That's the cerebral spinal fluid. So if you've ever had a spinal tap, they're taking this fluid out from the back. It all circulates around through the brain and around the spinal cord, and the fluid is white. Now, if you can look really closely, you will see that the outside gray matter here is actually lighter than the white matter. So one thing that happens in T2 imaging is that the white matter becomes darker and the gray matter becomes lighter. So this is not how the brain would look if you took it out of the skull. This is a particular kind of image that highlights special things, but it inverts some real-world relationships. And then this, these white areas, are lesions. But as you can see, because this fluid is white and the lesion is white, it's actually a little bit difficult to see where the fluid ends and where the lesions start. And so that's one of the limitations of T2 imaging, is that the fluid is white and it compromises our capacity to see the white lesions.

So this picture shows us the other two images I talked about. So we're going to start with this one. This is a T2 image. So if you look at the gray matter around the outside, it is lighter and the white matter is darker. That's the definition of a T2 image, but a T2 image also has the fluid as bright white and this has the fluid as dark. So this is what we call a FLAIR image. It is the best image for seeing lesions on MRI over time. This doesn't tell us whether a lesion is happening right now. It only tells us that these are scars from the past. So these white areas are scars typical in appearance of MS. And this is what we call a FLAIR image. It's a T2 image with the fluid made as black. So it's specially converted with some software.

Now this shows us all these spots and if I look at this spot, I cannot tell you if that spot happened yesterday, 20 years ago, or two months ago. This only shows me evidence of scar from the past, which is these white areas. Most of the time these lesions will stay present in the brain. They don't go away. Occasionally, someone will heal well enough that you can't see a lesion anymore.

But if I want to know if this lesion is happening now, I can give IV contrast. So IV contrast, or gadolinium, is put in the IV, circulates around through the blood vessels that go into the head and those blood vessels should keep what's in the blood vessels inside and not let it leak out into the head. So your brain tries to protect itself from noxious chemicals or from outside influences by not letting anything that's in the bloodstream get into the brain and things like alcohol diffuse through the blood-brain barrier, which is one reason alcohol has an impact on brain function. Gadolinium will not normally get through the blood-brain barrier as long as the blood-brain barrier is intact. But if I am having an MS relapse, so that my brain is inflamed and I am creating one of these spots by white blood cells coming into the area and attacking myelin, the blood brain barrier in that area gets leaky. And what that means is that when you put the contrast in and circulates around, when it gets to the area in the blood vessels that are leaky, it leaks out and it shows you that area as bright.

So if we come to this image, this is the same MRI as this. This is a FLAIR image. This is a T1 image with contrast. This is a vein filled with contrast in the back of the head, you can see it's lit up. And when we get into the brain, we see this lesion here. We come over here and it does not light up. So this lesion is old. But if we look at this lesion and we come over to where that is in this brain, it's lit up with contrast and this lesion is lit up with contrast. So these two lesions are happening at the time the MRI was done, and it takes about 4 to 6 weeks for contrast enhancement to stop. So if someone's having a relapse and they're having a new lesion and you do an MRI within about 4 to 6 weeks, you should see this contrast enhancement. So when we talk about MRIs as being enhancing, that's what this means. Sometimes this is referred to as disease activity. So this is evidence of a disease that is currently happening, not something from the past. So we call that enhancing or active, or contrast enhancing, sometimes.

Okay. So we went through the major types of views that we get when we do an MRI. And this is a little bit more detail about some of these. So this is also one of these T1 images and it does not show us the spots as bright. Right? If you come here, you lose all the spots that are bright, you don't see them anymore. But sometimes in a spot like this, when you come over here, you see a black area. And that is what we're seeing on this image. These are called, unfortunately, I don't like this name, but they are called black holes. So they are sometimes called T1 black holes, and that is an area of brain that has really been damaged so significantly by an attack that some of the tissue underneath has really been lost, and you can't see the architecture of that tissue anymore. So black holes are associated with increased disability, and they're associated with increased difficulty with cognition.

And so these are especially concerning to someone like me when I'm looking at an MRI and I really want someone who is making multiple black holes like this to be on very powerful therapy so they stop having lesions, because these are basically lesions that were created and they've healed really poorly. They have had permanent damage done to the brain rather than a decent amount of recovery. And then this is with contrast. So if you look over here, this lesion right here is contrast enhancing. All of these other areas are old lesions from the past.

So this is a view of kind of a very typical MS patient. If we think about what lesions look like in MS, the most common description is ovoid. So the lesions tend to be oval shaped. Perpendicular to these ventricles. So the black fluid is fluid filled ventricles in the head and it is very common for MS lesions to be aligned perpendicular to those. So they tend to sort of come off sideways from these fluid filled ventricles and they also tend to be about a centimeter in diameter. And this spot here, in this spot here is also about a centimeter in diameter. So sometimes you will see on an MRI report, it will say something like there are periventricular ovoid lesions that are perpendicular to the ventricles in a pattern typical of MS. And that would refer to lesions like this that are... fit that description in terms of where they are, the shape they are, the size they are, and how they're oriented.

So this is another typical MS, but this is someone who has more lesions. So again, here's our fluid ventricles. And so here's a slice right above that. So you're above the level of the eyes sort of slicing right through the forehead. And this is a very typical MS lesion. Right periventricular ovoid and perpendicular to the orientation of the ventricle. So it's at a cross angle there. This kind of pattern where you see... you look out here, you don't see any lesions. You look out here, you don't see any lesions. But near this ventricle and right above it, you see these lesions that are, again, perpendicular to it. That is very typical of MS. If I were walking through the room and I didn't know anything about this person and somebody showed me this picture and they said, Is it MS? I would say yes, because it's very typical.

This is the sideways view. So we were looking at cross-sections. This is the brain sliced left to right. And when you get to the center of the brain, so here is the nose and here's the lips. And this is the center of the brain. And this black area is the fluid filled part. Those periventricular ovoid lesions stick up from the fluid, and it almost looks like fingers projecting out from the ventricle. And these are called Dawson's fingers. And it's really the radiological sign of MS. If you look this up in a book, what indicates MS, Dawson's fingers, which is this appearance, it's these sort of oval projections from the top of the ventricle.

This is somebody who has a little more MS. So you see more of those projections. These, again, are very typical pattern. The other thing that can sometimes happen in MS is that this area of the brain thins a little bit and this fluid filled area enlarges a little. We don't really see that happening in this patient, but that can happen, especially in more advanced MS.

You can also have lesions in the spinal cord, and this is a sagittal section. That means, again, cut through right to left. So this is right through the center of the chest. The chin would be up here. This is the front. This is the back. These are bones, these are disks. So when you talk about a slipped disk, it means this, this disk is poking out a little bit. It's not quite in place where it should be. This long gray string is the spinal cord, and the spinal cord should be gray and smooth and the same. This area is normal. This is a lesion. This is a lesion. This bright area is a lesion. This bright area is a lesion. Here's another one way down here and here's a little one here. So this is someone who has a number of lesions in their thoracic spinal cord and lesions in the thoracic cord can be associated with more trouble walking. So this is somebody I would worry a lot about. I would want them on very aggressive medication.

So that's MRI background. How do we use that in diagnosis? The major thing in MS is we are trying to establish that this is not a one-time event, this is an ongoing process. And one way we do that is by looking at MRI. So typically, we have thought of MRI in MS as requiring two things: separation in space, or dissemination in space, and dissemination in time. And what that means is that we want evidence of an old thing and a new thing that tells us this wasn't a one-time event. And there are other conditions that can be one-time events. Someone can just get optic neuritis and not have MS. We don't want to diagnose someone who just has optic neuritis with MS if they don't have MS. So one thing we do is we see whether the MRI changes over time. So if you have a lesion one day and six months later you have another lesion that gives us that criteria. The other thing that gives us that criteria is seeing lesion like this one that's not enhancing. So that's an old lesion and then a lesion like this one that is enhancing. So that's a new lesion. So you can have separation in time by having an old lesion and a new lesion at the same time.

The other thing we look for is separation in space. So we want people to have lesions in different parts of the central nervous system. So if somebody has again, optic neuritis, which is inflammation of the optic nerve three times, that doesn't mean that you have MS. You need to also have something else somewhere else in the nervous system. MRI helps us do that. We can see that there's a lesion in the optic nerve. We can see that there's a lesion in the brainstem. And that gives us what we call separation in space.

If there's anything I communicate today that sticks with anyone, I hope it is this. We have evidence that MRI matters in treatment. So I think there's two reasons to get an MRI when you have MS. The first is to diagnose it. We use those criteria I just showed you to diagnose MS. The second thing is to see if treatment is working. And MRI helps us by showing us that a treatment isn't working early before there's a lot more damage done. And then we can change to a different treatment and hopefully get a better result. So this is an old study and it was done

on some of the older medications, but what it showed was that if you started someone on a medication and then you did an MRI later and the MRI a year later showed the presence of new lesions, and you left them on that medication and you measured disability five years later, the more lesions people had, the more disability they had. So I think of MRI as a crystal ball that tells me what's going to happen in the future. If the MRI shows no new lesions five years later, 5% of people have worsening disability. Most people are exactly the same. If the MRI shows three new lesions, 83% have more disability five years later. So I want an MRI to see how someone is doing when they're on a medication. And the way I do this is six months after someone starts a medication, I get a new baseline and from there I don't want anything to change in the future.

So this is just a very brief background on the range of what we can see in MS. So this is a patient with very early MS. So if someone comes in and they have a symptom typical of MS and they have maybe some exam findings typical of MS, and they have this MRI, which shows only two lesions where we can see this. This is one and there's another one here that you can see a little better on this next slice. So this is two slices of a brain MRI on a patient that shows two lesions, but they're lesions that are periventricular ovoid, about a centimeter in diameter, perpendicular to the ventricle, and absolutely typical of MS. And so that would be enough for diagnosis in some circumstances.

This is another patient of mine who this was their first MRI at diagnosis. So they had never been diagnosed with MS before. And instead of having two little lesions, they have lots of damage. So all of this white area should not be there. And here you can see multiple lesions. Some are, what we call, subcortical, out near the gray matter. Some are confluent because it's so many different lesions that they've almost run into each other. There is extensive damage and there's a little bit of atrophy of the brain. And this was at diagnosis. So someone who had maybe had symptoms and hadn't gone to see anyone, maybe didn't have symptoms and attributed whatever they were feeling to other things, but they were diagnosed quite late, which is much more difficult for treatment purposes.

This again, new diagnosis with somebody with very confluent lesions. All of this white area is abnormal. It is, again, evidence of these discrete lesions, but there's so many that you really can't tell them apart and they're almost running into each other.

So what makes somebody have aggressive disease? There are some risks that we know about that are typically found in people with more aggressive disease. One thing that notes that this is somebody we're going to worry extra about is more relapses in the first year or two after diagnosis. So if somebody had a relapse and maybe didn't get diagnosed with MS and then they come in with another relapse five years later, that's actually a good prognostic sign because they went so long between relapses. If instead, while somebody is trying to get diagnosed, they have a relapse and two months later they have a different relapse, and two months later they have a different relapse, that makes us worry about them in the future. We worry about everyone, but especially worry about them.

Men tend to do a little worse with MS than women, so we worry about men sometimes more, and we think about more aggressive therapy, potentially earlier. People who have darker skin tend to have a harder time with MS. So this is also true for people with darker skin that we want to treat aggressively very early to try to minimize any possible damage. People who have spinal cord disease tend to have more disability as time passes. So we want to treat those folks very early and aggressively. People who breakthrough therapy. So if you're on a therapy and you have new lesions anyway, that's a negative prognostic sign that that makes us more concerned

for the future. And then finally, the number of T2 lesions at baseline. So that MRI I showed you at diagnosis with all of those lesions is going to make it likely that that person does worse than the person who just had two lesions at the time of diagnosis.

So this is kind of a range for how terrible things can look. And my goal in doing this is that I feel like always when I'm showing a patient their MRI in an exam room, they had an MRI last week, I bring it up on the screen, we go over it together. I sometimes see someone who has three lesions and they're very upset about that and they're very worried and they think that it's three, it's terrible. And I always wanted to be able to show someone a range of what this looks like. And it is typical for someone who has two or three lesions to have a better time with their MS than someone who has an MRI that looks like this. So this MRI shows us multiple enhancing lesions. All of these areas that are surrounded by brightness. This ring around the spots, those are enhancing lesions - here, here, here. So just in that one slice of MRI, I can see multiple active lesions. In the next slice, there's maybe ten more active lesions. Here, here, here, here, here, here, here. This is a catastrophe in terms of being the neurologist for this patient. This is horrible treatment failure. So either the patient isn't on therapy, isn't taking therapy, or the patient is not on the right therapy. So this is what we try to avoid when we treat MS, we try to avoid any enhancing lesions. When you see many like this, it's a treatment failure and we need to do better.

This is one of the worst relapses I've ever seen as a neurologist, and I've been doing this for a while. But each one of these areas that are white is an active lesion. And again, just in this picture I'm looking at, I can see probably 30 active lesions, and this is two slices. So an MRI goes size, slice, slice, slice, slice, up through the head. So there's many other slices. This patient had 100 active lesions, which is an emergent catastrophic-type relapse.

Sometimes people who have MS get larger lesions than what we have been talking about. So typical lesions are about a centimeter in diameter. This is a ruler, and between two hash marks is a centimeter. But sometimes people have larger lesions and they're so large they almost look like tumors. And this is referred to as tumefactive MS. So this is a patient who presented with only a few lesions, but they're quite large, they're much larger than one centimeter. And this area, if you can see, there is a breach here because the patient was actually biopsied. So they had a brain biopsy trying to see what this lesion was. And when it was looked at under a microscope, it looked like MS. So tumefactive MS can have larger lesions. It can come on very suddenly and dramatically, but it can also respond quite well to treatment.

Okay, so that's the background. And in the last few minutes, I just want to go through cases, kind of illustrating how I would use what I've just discussed in Clinic Day. So the first case is a 32 year old who was diagnosed with MS in 2006. She had an MRI done for recurrent headache. She had pain in multiple locations refractory to treatment. So she had surgery for neck pain and she was on many pain medications, including narcotics, without much benefit. And she had been diagnosed with MS and put on therapies and she didn't feel like the therapies were helping her. So when I first saw her, she had actually not had a spine MRI and she had not had a spinal tap either. Neither one of those things had been done when she was diagnosed and put on therapy.

So when I first saw her, this was the brain MRI that I saw. And this is again two slices cross-section through the head, through the forehead. This black area is the fluid filled area. This is one slice above it. You see the remnants of the fluid as you come above it. And this is the brain, and this person has multiple small spots. Here's a little spot. Here's a little spot, here's a spot. Here's a spot. Here, here, here, here, here. So what's different between these spots and what

else I've shown you tonight? They're smaller. They aren't in the same location. They are not next to the ventricles. They are not perpendicular to the ventricles like a big spot like that. They are only a few millimeters in diameter, and there aren't that many of them either. And these spots are typical of what we call small vessel ischemic disease or nonspecific lesions, and they're much more common in people with a strong headache history as she had. So people with migraine often have spots like this. So when I saw this patient, I actually ordered the MRI of the spine. She had no lesions in the spine. And I also ordered a spinal tap, and she also did not have the changes in her lumbar puncture that would typically be associated with MS. So I think this is a misdiagnosis of MS and what she really has is what we would call nonspecific lesions or small vessel ischemic disease.

Now, this is somebody with very mild small vessel ischemic disease, but you can have people with more severe changes in the brain that are age related changes. And so this is somebody who's going to be older, they're more likely to have cardiovascular risk factors, more likely to have high blood pressure, high cholesterol, diabetes, smoking. And these lesions, they have many of them, but they aren't in the right location. And generally speaking, they're smaller than an MS lesion. Not all of them. This is big enough. This is big enough. But it's not in that periventricular, next to the ventricle area and it is more dispersed through the head. And it's also more typical in locations where we see what we call vascular disease or small vessel ischemic disease. And that tends to be, I sometimes refer to this as deep white matter. So it's not right under the gray matter, which we call subcortical, which can happen in MS, and it's not next to the fluid filled ventricles; it's not periventricular. It's just kind of dotted in the center of the white matter. So that is more severe, nonspecific or vascular disease aging changes, not MS.

So that's one case, right? The kind of range of things that can look like MS that aren't MS. This is a second case of a 63-year-old woman who presented to me with an MS diagnosis, and she had vertigo and she was dragging her right leg. She had some leg pain. She had fatigue for many years. Her MRI was pretty suspicious for MS. She had a spinal tap, but the spinal tap had a lot of white cells in it, which can indicate inflammation. And that is unusual in MS. So people with MS might have a little bit of increased cells, but it should really be below 50. And she had more than that. She did have the antibodies that are typically associated with MS in her spinal fluid. So she had a positive spinal tap for MS.

This is what her MRI looked like, and she has some of these periventricular ovoid lesions. And she also has some enlargement of her ventricles. And when you take the sideways view, you can see that she has that, what we call, Dawson's fingers, this very special appearance of these lesions coming up from this fluid filled ventricle area. So I looked at this MRI and I thought, I think you have MS. And I heard her story and it sounded like primary progressive MS. But I was really bothered by her spinal fluid because she had too many cells and I was afraid that there was something else I was missing, but I couldn't find anything else. And so I ultimately told her I agreed. I thought she had MS.

A couple of years later, she presented to the emergency room with some acute changes and was struggling to walk. And her MRI looks like this. This is an MRI with contrast and this area around her brainstem here is all lit up with this thickening of the coating around the brain called the meninges. So this is like a meningitis and there's thickening and inflammation involved in these areas, and MS does not do this. And so at this point, I no longer think she has MS and I am worried that she has something that does tend to do this called sarcoidosis, so that was one of the MS mimics that we talked about.

This is her neck. So sliced through this way, this is her spinal cord. And do you see these white lines that almost look like somebody took a magic marker and put white lines up around? That's that's thickening of the coating around the brain and spinal cord. And that, again, is very typical of sarcoid and not typical of MS.

So she had an extensive work up. It was all negative. She had a brain biopsy that didn't show sarcoid. But ultimately, I believe she had sarcoid. It is another autoimmune inflammatory condition that can mimic MS in the brain. It can cause thickening of the coating around the brain. It can cause optic neuritis, just like MS. It can cause spinal cord lesions like MS. And I have treated her for many years. And she finally developed a skin lesion that looked like sarcoid, and it was biopsied, and it was sarcoid, but it wasn't clear that this was sarcoid for many years after I first met her. And this is one of the things that mimics MS, and it's sometimes very challenging.

And then the last case I want to mention is just what we do when we use MRI to try to help guide us when somebody has pretty aggressive MS and we're trying to get good control over it. So this is a patient who developed initial symptoms at age 14, and he had multiple symptoms in the first year, including double vision and left arm numbness and difficulty with balance. He was diagnosed and started on therapy. His initial exam was almost normal. Most 15-year-olds look pretty good, even if they have changes on their MRI.

So his diagnosis was quite clear. He had positive spinal fluid for the antibodies. He had multiple lesions, he had four enhancing lesions, and he also had spinal cord lesions. So he gets started on a therapy and six months later we check another MRI to see if he has... his disease has calmed down or if he still has active disease. And six months after therapy, he still has enhancing lesions. So the therapy he's on is not working and it's not doing what we need it to do, which is really shut off all this disease activity. So on his MRI six months later, he has a bright spot there, a bright spot there, a bright spot there, and one there. So that's multiple enhancing lesions and that means we have treatment failure, so we need to do better.

So we went back and we started him on a new medication and he continued to have relapses through the first year. That medication didn't work either. And then, I mentioned some of the markers of aggressive disease, so here's lots of things to worry about. He's male, he has multiple spinal cord lesions. He has failed therapy. He has enhancing lesions on multiple different therapies. And so in order to try to minimize disability in his future, he ended up getting different medications. And so we kept going through different medications until he was on a very aggressive therapy that finally stabilized him. But it took a while, and this is how we use MRI both to monitor treatment effect, but also it can be helpful to help us plan treatment effect.

So one reason this young man ended up taking medications that weren't maybe strong enough for him is that he was a minor when we were having these conversations and his parents were very afraid of side effects and they would not consent for him to be on certain other medications. And so he actually came to my office the day he turned 18 and switched to a different medication because he could then make that decision for himself. And ultimately, we got control of his disease. But the MRI showed us along the way that we weren't doing well enough.

So in summary, how do we use MS? We use it in both diagnosis and in monitoring, and it is easier to prevent new lesions than to repair them. So we want MRI to help guide treatment so we know what kind of treatment to use. And then we want to make certain that the treatment is working by monitoring MRI. We want to look for enhancing lesions. So new enhancing lesions predict poor outcome and we don't want to see those. So my goal for anyone is I start a therapy,

I get an MRI six months later, I don't want that to show any disease activity. It might show new lesions because lesions might have happened before the therapy worked, but at six months it should be working. So there should be no disease activity. And then from there, I never want that MRI to change. I want it to be exactly the same because that tells me that we have the disease under the best control we know how to do currently.

It is very common to have MRI lesions. It is more common than relapses. So in clinical trials, people have about ten lesions for every symptom they have. What that means is that this is a crystal ball to the future. We want to catch a change on MRI when there's only been one new lesion before somebody has a relapse, before they have more disability. So it's an early indicator of what might happen three or five years from now. I like to do an MRI six months after any change of therapy to make certain it's working. And then if there's active disease, I would switch therapies and I would find an alternative.

And with that, last thoughts: MRI is a useful tool in diagnosis. There's lots of causes of lesions that aren't MS related. It can be useful in monitoring MS on treatment, and the initial MRI can help us make treatment decisions so that we take a more aggressive therapy and potentially higher risk from the therapy early on if the MRI indicates that there are markers for aggressive disease. And with that, I will say thank you very much and I am happy to answer questions and I will turn it back over to Kyle.

**Kyle Pinion:**

Thank you, Dr. Conway. And yes, we have so, so many questions. So many questions, which I'm happy to say. Unfortunately, we don't have a lot of time to answer a lot of them, but I'll try to get to a couple. And, certainly, thank you for such an amazing presentation. I want to say that before we even get to the questions, I think this was just so enlightening and interesting and just so vital for people living with MS to have a better understanding of how disease course is measured.

Now, here's the first question. I think this has been asked a few times, so I'm going to try to put my own spin on it: does the location of a lesion, is it indicative at all of the type of function that is affected or a symptom of the disease?

**Jill Conway:**

Yes, it can be. So if you have a lesion in the optic nerve, it's likely to cause vision problems. If you have a lesion in the brain stem, it can cause double vision or vertigo. If you have a lesion in the spinal cord, it can cause numbness in your hands. But most new lesions in the brain do not cause any symptoms. Ten new lesions for every symptom people have in clinical trials. Most of those periventricular ovoid lesions I was showing don't cause symptoms. So we try to catch the MRI change early to prevent more lesions in locations that would give people symptoms. So some lesions are associated with symptoms quite clearly. Some are not.

**Kyle Pinion:**

Thank you very much. In terms of the frequency in which someone living with them needs to get an MRI, I know in the diagnostic process, obviously, it's quite sooner, but for someone who's been living with MS for a number of years, how often should they receive an MRI?

**Jill Conway:**

So I, you know, if you had asked me this question 10 or 15 years ago, I would have said, because there can be so many lesions people don't know about people should get an MRI every year. But some of the newer medications are so powerful and change on MRI is so rare

that I do this less frequently these days. And so if I have somebody who's been on good therapy, I had a six month MRI, they were fine. I did another one a year later, they were fine. I very often will go two years between MRI's. And we image the brain more often than the spinal cord, and the reason for that is that most new spinal cord lesions do cause symptoms. Most new brain lesions don't. So people can have a lot of brain change and not know it. Most of the time, if somebody has a new spinal cord lesion, they call me, they say I get a shock when I put my head forward, both my hands are numb, I'm dropping things. And that indicates a cord lesion, and then we would do an MRI of the spinal cord.

**Kyle Pinion:**

Terrific. The question of aging in MS is one that I think is being asked quite a bit, and not just in this program, but many of our programs. So I'll ask this one that one attendee has asked us: do senior citizens with MS tend to have less MS lesions as they age and therefore don't need to be on a DMT any longer?

**Jill Conway:**

Yes-ish. So the immune system ages with us. And because MS is an autoimmune disease and it involves the immune system attacking us, as the immune system gets weaker as we age, it attacks us less well. Now, on top of that, most of our medications suppress the immune system and have an increased risk of infection. That risk increases as people age. So when we look at treating MS, there's a benefit risk profile of whether it's worth it to treat. And for somebody who's 25 and having lots of enhancing lesions and they have a minimal risk of infection, of course it's worth it to treat. It's very important. For someone who's 75 and may have a higher risk of infection and may not be having new lesions, then it's probably not worth it to treat.

This is very individualized. I have 78-year-olds on very powerful medicines who are having relapses and I have 50 year olds who aren't. But generally, we question whether about 60, whether some people can come off medication. And there was just a study released at the recent consortium meeting that did suggest that the risk of relapse was not high in most people when they stopped medication. So they actually did a study and they left people sort of in the 60 age range on medication and they took some people off and 5% of the people on medication had a relapse, 12% of the people off had a relapse. And what that means is that most people, if they stop medication about the age of 60, won't have relapse. So this is a conversation I have with people. And whether we stop a medication depends on someone's MS, depends on what they're on, depends on the aggressive markers, depends on where they are in their MS, how long they've had MS. All of those are questions that we think about on an individual basis.

**Kyle Pinion:**

Excellent. That's a great answer. Thank you. The question of brain volume and brain volume loss, does that play at all into treatment decision making and outcome measurements for people living with MS currently?

**Jill Conway:**

Yes. So, you know, when we don't want that brain volume loss, we know it's associated with changes in cognition and more disability. And so we want to prevent it. There are some good studies on some of the newer medications that there is benefit on reducing that volume loss when people are on these therapies. And some of the newer trials also have outcome measures looking at cognition. So that's one of the things that is measured in various ways, trying to show that if we treat MS, we impact both the volume and the cognition that goes with it. And I think we

have adequate evidence to suggest that if we treat early and aggressively, we really minimize both the cognitive changes and the atrophy.

**Kyle Pinion:**

Excellent. There's a couple of situational questions I wanted to ask you about that I thought quite interesting. First things first, someone has said that a 3T MRI showed many more lesions in their scan two years ago. Do you think it's important for a patient to continue getting a 3T scan, even if it is quite far away from where they live?

**Jill Conway:**

So it's a great question. It depends a little on the particular situation. So if a 3T is a more powerful magnet, you can see more. When you compare a 3T scan to a scan done the year before on a 1.5 Tesla magnet. It's very hard to compare because sometimes you see changes and you don't know if those changes were there before. You'll often see a radiology report that will say something like "allowing for differences in technique and software and scanning capacity, I don't think there's any change between this." But it's really hard to tell. It's like if you got a much better camera and the new camera shows you a detail you didn't see before, do you know if that was there or not? You can't answer that if all you can compare it to is something more fuzzy. So I think it's helpful to have the same imaging every year to be able to see changes. And so picking an MRI and doing that one, I think is helpful. Spinal cords are hard to see. I feel like 3 Tesla is very helpful in a spinal cord, less helpful for me in a brain MRI.

And then finally, I would say it partially depends on the situation too. So if there's concern that there's a lot of change and someone's 62 and they're thinking about stopping therapy, it might be very helpful to have that additional information. If somebody is 25 years old and they're on the most powerful therapy I can imagine, and you're doing the best you can anyway, then you probably aren't going to make big changes based on a tiny thing that was seen on the 3 Tesla compared to the 1.5. So for me it would partially depend on the situation. Generally speaking, the better the picture, the better. But you also have to compare to prior and it's useful to compare the same MRI the next year.

**Kyle Pinion:**

Outstanding. So another question is, I've been told I have a lot of black holes, but it seems the number doesn't have as great an effect on my disability as one would think considering the number. Why is this so?

**Jill Conway:**

Oh, well, I mean, I think that's a bigger question, is why do some people have more disability than others? And I think there's a lot of different things that play into that. So sometimes people have more reserve, is what we call it, right? So sometimes people who had a brain that was functioning very well, they managed to function even despite losing some areas due to black holes or due to lesions, sometimes when we look at where a lesion is, black holes that are in that periventricular area don't cause nearly as much damage as a black hole that's in the spinal cord or a black hole that reflects damage to an eye where you might lose vision or you might lose mobility. So sometimes people have more capacity to work around. Sometimes people have the rest of their brain is healthier. This is one reason why smoking really helps people progress faster and have more damage with MS, because the rest of the brain is less healthy, so it's harder to recover. Sometimes people who take really good care themselves seem to

recover better from a relapse, even if you can see it on MRI. Sometimes the person looks fabulous. And so there can be a lot of different reasons for that.

**Kyle Pinion:**

And I'm going to try to make this the last question, since we're a little over time, and I do want to make sure our East Coast friends get to bed at a good hour. Alternative options for people who can't get in the MRI machine. For example, someone who sent in this question said that they have a defibrillator and that prevents them from being able to utilize the MRI machine where they live. They just can't get one. What would be the potential for monitoring their disease course in that scenario?

**Jill Conway:**

So you have to do it without MRI. So, you know, this is a tool, and that tool is not available in that situation. And so you might think that doing some cognitive testing every year might be helpful. It might be helpful to keep an eye on, you know, one of the things we monitor is gait speed, right? So you want to try to get other pieces of information that will help you assess the severity of the MS and how well things are going because you just can't MRI with a pacemaker. And so you lose this tool. But there are other tools you can substitute to try to give you additional information, but you won't get a picture like this because, you know, this does give us a lot of information and there are many situations where it just can't be done.

**Kyle Pinion:**

Well, thank you, Dr. Conway. These were... there were so many good questions. I wish I could get to them all, but I think we'd be here for another 30 minutes to an hour if I did, really. And it would just be... no one would ever get to bed. So I appreciate you taking over a little extra time here.

So that concludes tonight's webinar. And I would like to once again thank Dr. Conway for her insights into the MRI process and how the MS community can better process the scans their physicians are reading. I think we can all say we learned a ton about the subject. I sure did, and we are so grateful for your time and expertise.

As mentioned, tonight's webinar will be archived to MSAA's website, and we ask you to take a very brief survey that's coming up next. Your feedback is critical to ensure our programs are relevant and impactful. So please just take a couple of minutes to answer a few questions for us. On behalf of MSAA and Dr. Conway, we thank you so much for joining us. Thanks again Dr. Conway.

**Jill Conway:**

Thank you. Have a good night.

**Kyle Pinion:**

Goodnight everybody.