

Visualizing the Progression of Multiple Sclerosis with Multimodal Video Microscopy

Storyboard

By Melissa Cory

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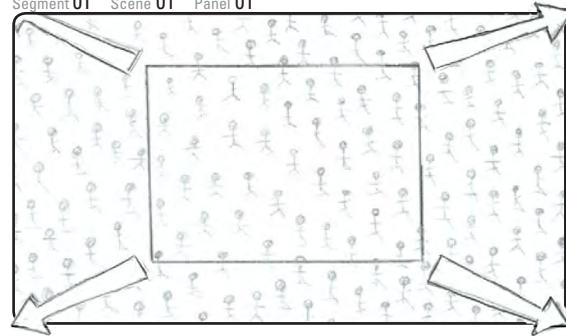
Audience

Undergraduate and potential graduate students in physics or biology.

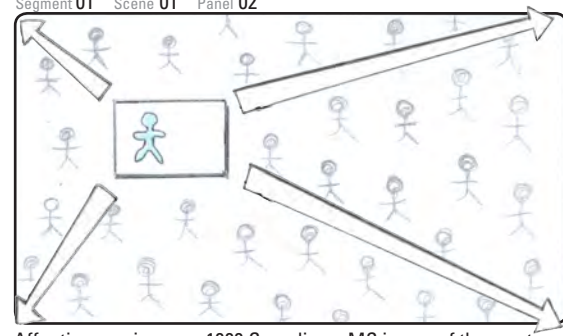
Message

With Multimodal Video Microscopy researchers can now look inside the spinal cord of a living mouse at the cellular level, and this is allowing for early detection of Multiple Sclerosis lesions.

Segment 01 Scene 01 Panel 01

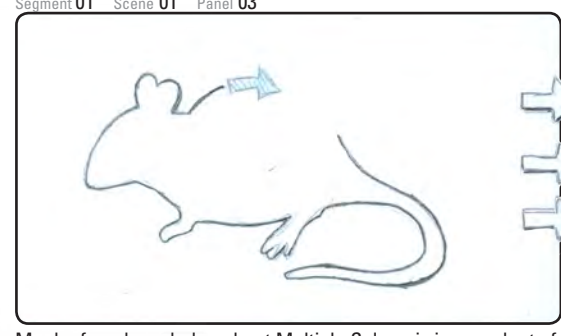


Segment 01 Scene 01 Panel 02



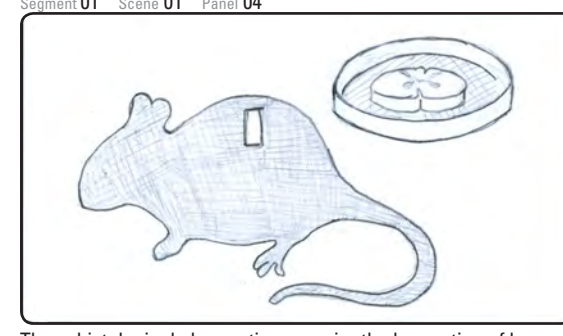
Affecting one in every 1000 Canadians, MS is one of the most prominent neurodegenerative diseases.

Segment 01 Scene 01 Panel 03



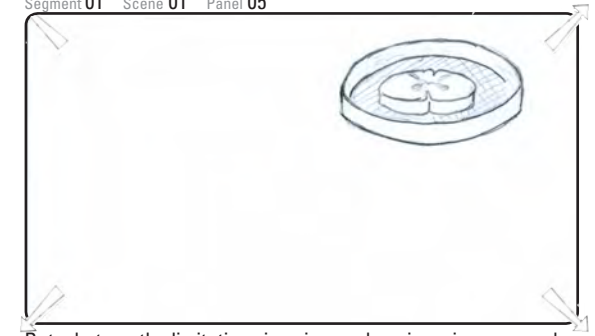
Much of our knowledge about Multiple Sclerosis is a product of cellular-level investigation into experimental mouse models.

Segment 01 Scene 01 Panel 04



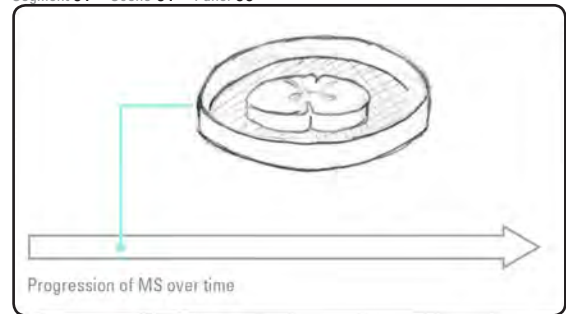
These histological observations require the harvesting of large amounts of nervous tissue at one discrete time point.

Segment 01 Scene 01 Panel 05



But what are the limitations in using such an invasive approach when it comes to investigating a disease such as MS,

Segment 01 Scene 01 Panel 06



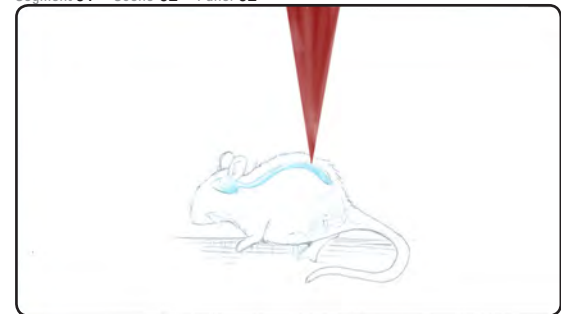
which progresses slowly over time?

Segment 01 Scene 02 Panel 01



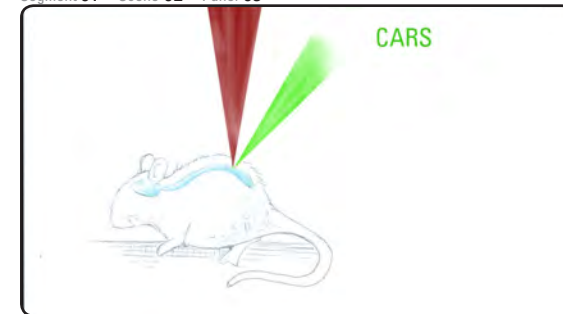
In order to probe this question, researchers at Laval University have created a hybrid microscope

Segment 01 Scene 02 Panel 02



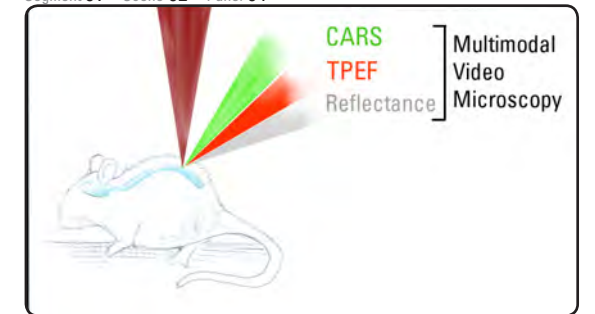
that is capable of imaging nervous tissue within living mice in a non-destructive way.

Segment 01 Scene 02 Panel 03



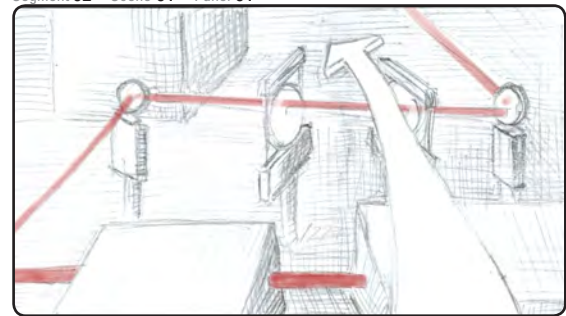
This microscope combines Coherent Anti-stokes Raman Scattering (CARS) microscopy with other microscopy modalities,

Segment 01 Scene 02 Panel 04



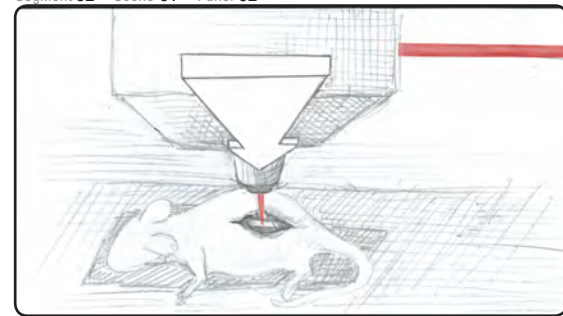
in a technique known as multimodal video microscopy.

Segment 02 Scene 01 Panel 01

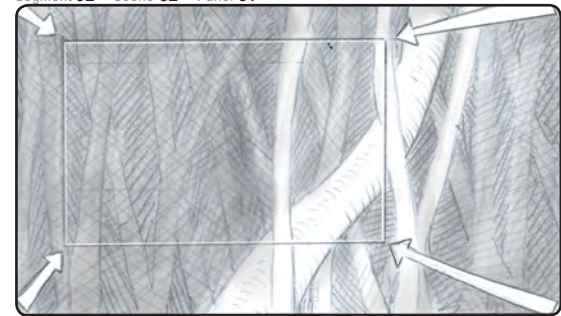


In order to understand the power of this new tool, let's take a look inside a healthy living mouse.

Segment 02 Scene 01 Panel 02

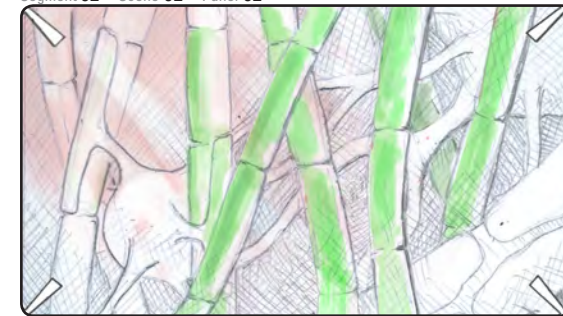


Segment 02 Scene 02 Panel 01



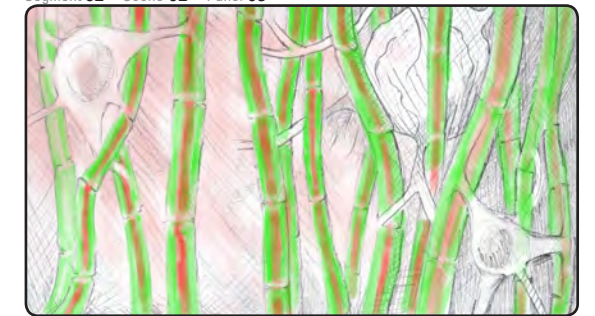
At first the dark neuronal environment is lit up using Reflectance Confocal Microscopy, which provides a rough orientation to the area of interest.

Segment 02 Scene 02 Panel 02



When the CARS channel is activated, an intact myelin sheath is illuminated in remarkable detail.

Segment 02 Scene 02 Panel 03



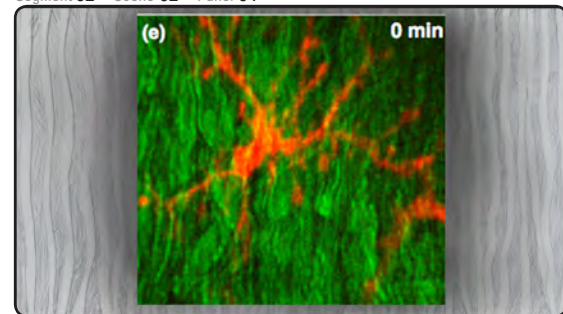
A Two-Photon Excitation Fluorescence (TPEF) channel can be activated simultaneously, revealing structures such as nerve axons,

Segment 02 Scene 02 Panel 04



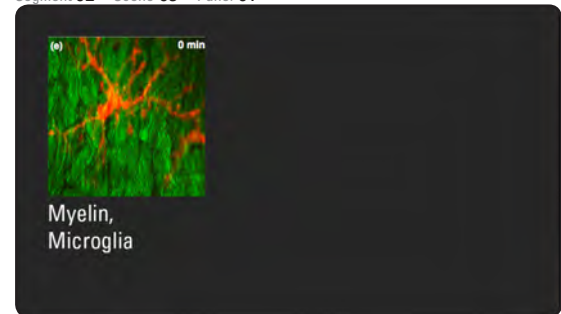
or microglia, that have been labeled in transgenic mice.

Segment 02 Scene 02 Panel 04



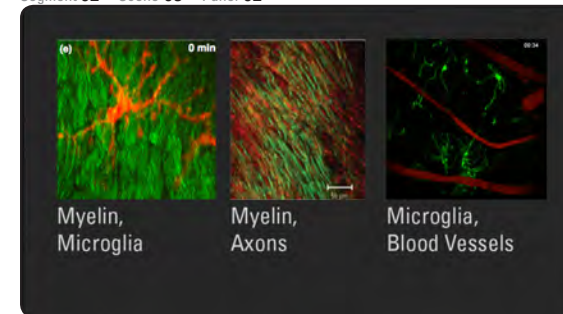
With video-rate collection speeds, it is even possible to view the dynamic processes of resting microglia in real-time.

Segment 02 Scene 03 Panel 01



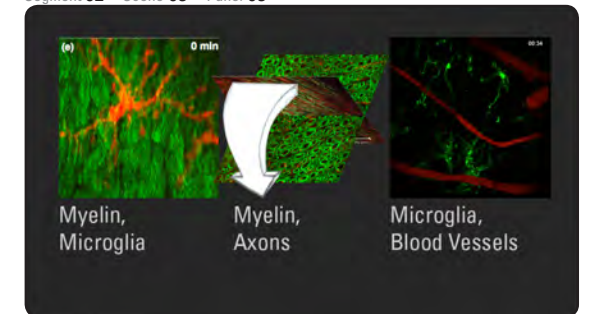
By using various combinations of CARS, Reflectance, and TPEF channels, multimodal video microscopy is sensitive...

Segment 02 Scene 03 Panel 02

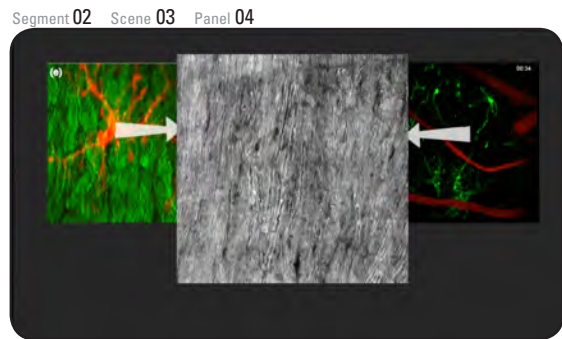


...to important relationships between different cellular structures.

Segment 02 Scene 03 Panel 03



It can also obtain multiple views.



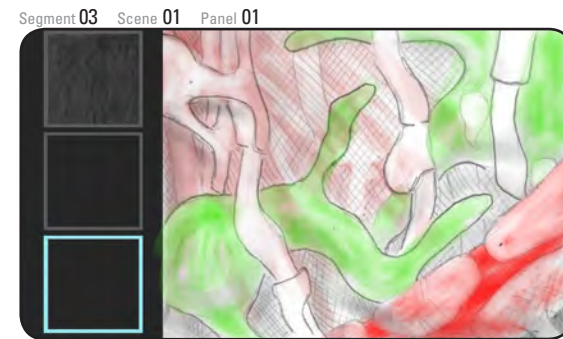
This versatility makes multimodal CARS well suited to investigating



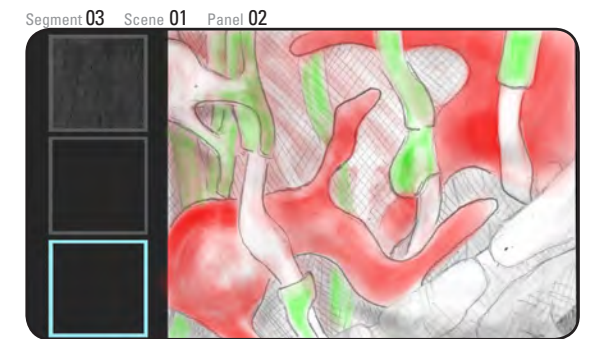
the complex pathophysiology of an active MS lesion. For example, if we were to look at the spinal cord of the same mouse



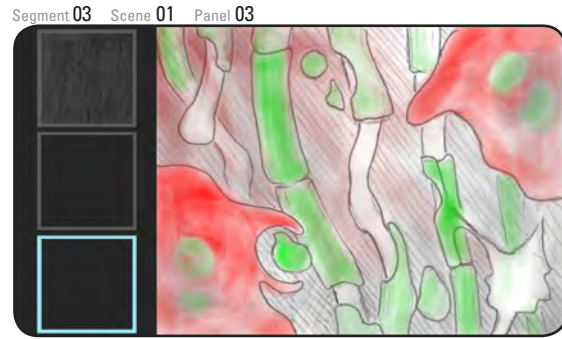
a few weeks after the induction of an MS-like autoimmune reaction, we would detect a greatly altered environment.



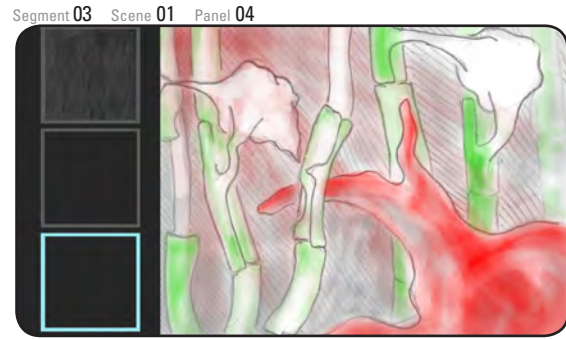
In this advanced stage of MS, a highly damaged blood barrier leads to chronically activated microglia,



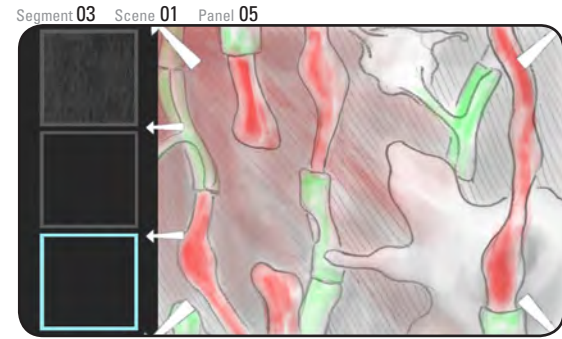
which facilitate the autoimmune response against the myelin-producing oligodendrocytes.



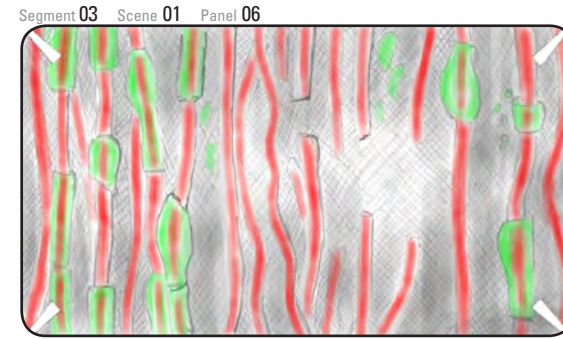
Free-floating myelin is engulfed by activated microglia.



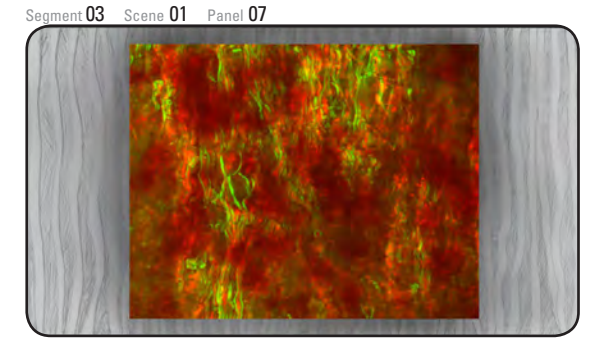
Damaged oligodendrocytes lead to a thinning or complete loss of the myelin sheath.



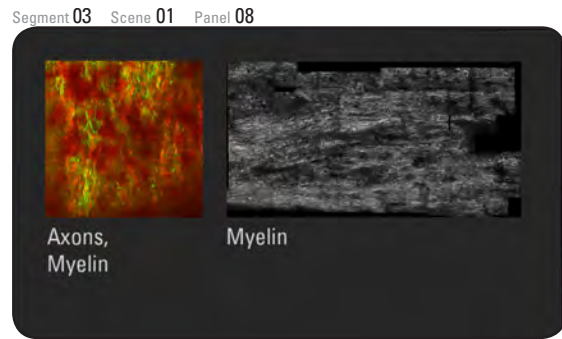
Even axons degenerate during the course of the continuing autoimmune attack.



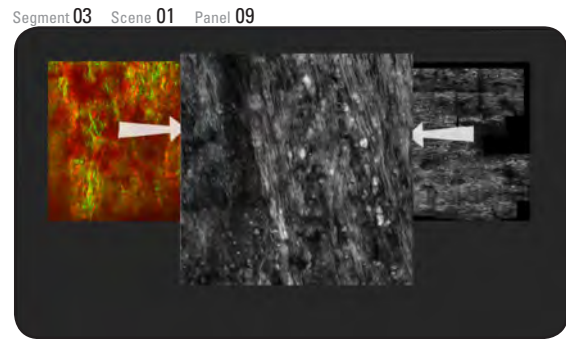
All of this results in greatly affected nerve conduction in the lesion area.



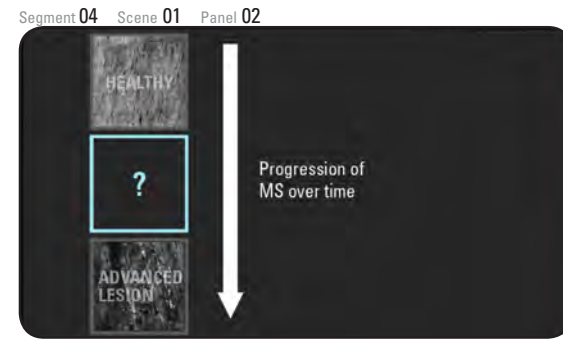
Advanced lesions of this magnitude have been heavily investigated, both microscopically,



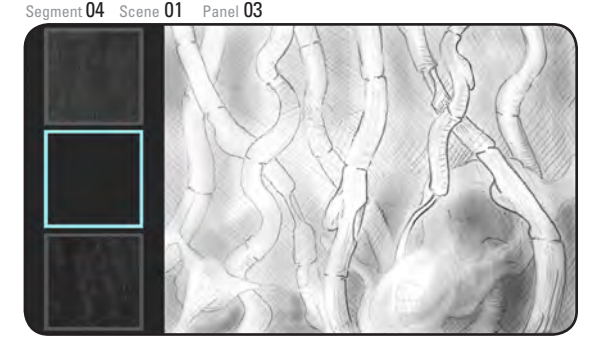
and on a more macroscopic level.



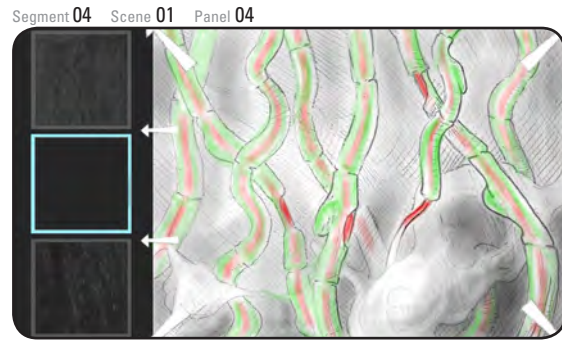
But understanding such an advanced lesion is only one part of the MS story,



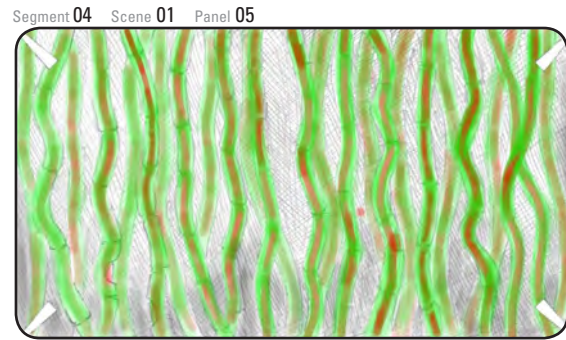
and what happens in the critical early stages of an attack is still not well understood.



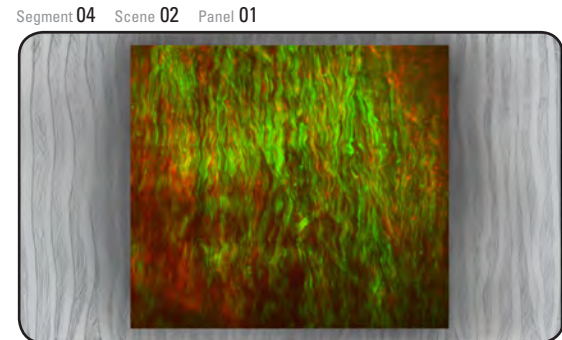
Imagine that we had begun our investigation into the same mouse much sooner after induction of MS-like symptoms.



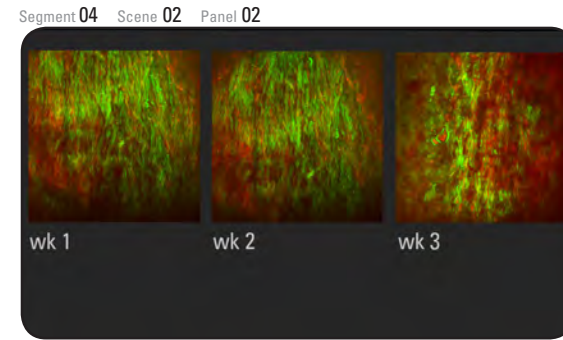
Excitingly, multimodal CARS is proving to be the first imaging method sensitive enough



to pick up on very small changes in axonal and myelin structure.



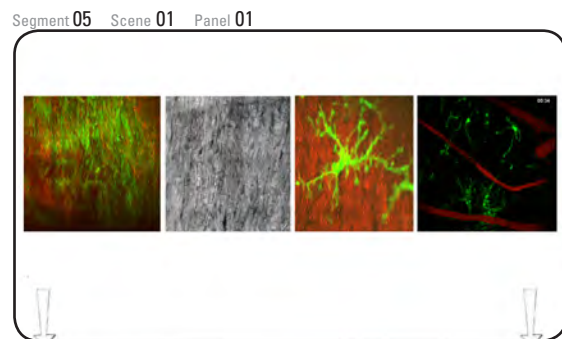
By obtaining multimodal CARS images from the same mouse at regular intervals,



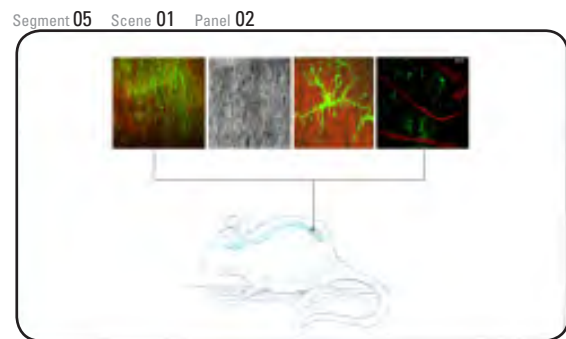
we are able to appreciate even very subtle increases in the tortuosity of axons and track a gradual decrease in myelin thickness.



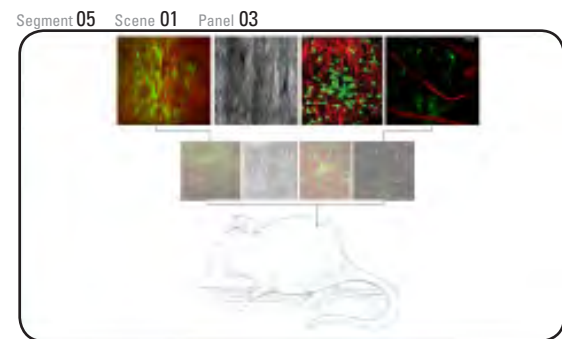
This makes early detection of lesions possible.



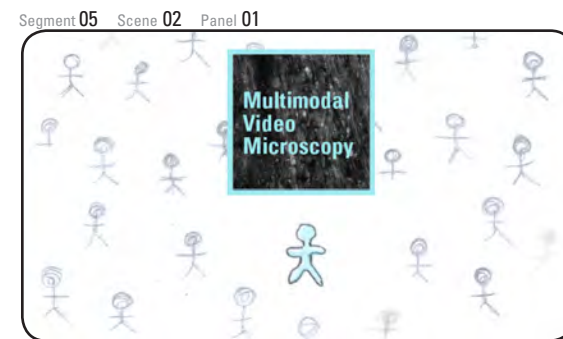
Multimodal video microscopy is the first in vivo microscopy method powerful enough to obtain comprehensive images of multiple cell types in the nervous system.



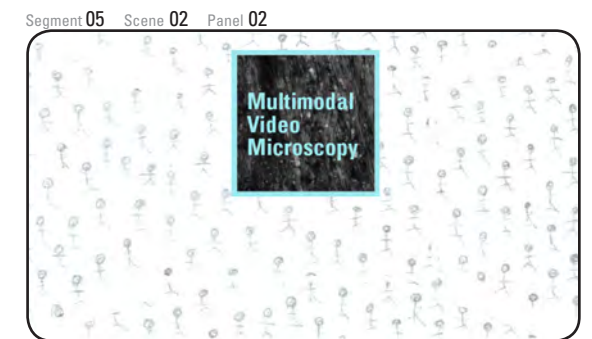
By remaining minimally invasive, this technique also has important practical benefits:



Much more data can be collected from a single mouse and time-consuming tissue processing does not need to be performed.



In order to develop effective treatment strategies for MS, a better understanding of what triggers these attacks is desperately needed.



Multimodal video microscopy can help revolutionize MS understanding by accelerating research and drug development.