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5 KEY TRENDS IN NEURODEGENERATIVE IMAGING SHAPING CLINICAL DEVELOPMENT

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Neurodegenerative diseases represent one of the fastest growing medical challenges of our time. Defined by the progressive loss and degeneration of neurons in the brain and spinal cord, these conditions—including Alzheimer's, Parkinson's, Huntington's disease, and many more—currently impact an estimated 50 million worldwide. With age being the primary risk factor for most neurodegenerative diseases, this number is expected to rise as the average age of the global population and overall life expectancies increase with advances in medicine.

In addition to their devastating personal impact, neurodegenerative diseases produce an economic burden with high healthcare costs due to the need for inpatient care, long-term care, and informal caregiving. Today, treatment strategies are largely reactive, focusing on symptom management rather than proactive prevention. What's more, most diagnoses are made through exclusion and require significant time, resources, and diagnostics to reach a definitive diagnosis.

This is where neuroimaging has the potential to reshape this field. Advances could lead to earlier diagnoses, support more effective interventions, and ultimately shift care from late-stage management to early intervention and prevention to help improve patient quality of life and reduce the long-term economic burden associated with these chronic, progressive conditions.

NEUROIMAGING IN CLINICAL TRIALS: ROLE AND BENEFIT

A large challenge in the early stages of neurodegenerative disease is that many symptoms mimic the normal signs of ageing. As a result, diagnoses are frequently made by exclusion after symptoms begin to occur. This challenge is compounded in rare neurodegenerative diseases where small patient populations make it essential to extract as much high-quality information as possible.

Neuroimaging plays a pivotal role in overcoming those barriers, and the use of imaging can help lead to earlier diagnosis. Structural and functional imaging can reveal changes to the brain before physical signs and symptoms occur. By comparing affected and normal populations, imaging research helps build a pool of diagnostic information to catch diseases sooner and prepare treatment faster.

Neuroimaging can be performed using an array of modalities and focalized techniques. MRI, CT, and SPECT/PET are well-used and well-known tools due to their diagnostic impact for neuroimaging. Additionally, MRI is available for scientists and clinicians alike to track brain activity by measuring changes in blood flow but is potentially underutilized as a neuroimaging diagnostic tool.

As imaging techniques and technologies advance, clinical development in neurodegenerative disease is increasingly dependent on imaging biomarkers. The field is moving beyond markers of established neurodegeneration toward earlier biomarkers that signal disease before irreversible damages have occurred, which could enable a fundamental shift from intervention to prevention. Efforts are also being made to revisit trusted imaging modalities and test new techniques to gain more insight into the imaging and diagnostic capabilities of today's technology.

Advances in neuroimaging are the cornerstone of modern neurodegenerative clinical development. In this article, we explore 5 key trends shaping the neurodegenerative imaging landscape and how they are redefining what early detection and clinical trials look like in the years ahead.

5 KEY TRENDS IN NEURODEGENERATIVE RESEARCH

1. Devices

Devices are becoming increasingly sophisticated and helpful in assisting with counteracting the effects of neurodegeneration. With Parkinson's and other diseases characterized by tremors, besides devices that assist with daily living, there are now devices available that perform deep brain simulation to make up for the loss of neuron activity and normalize electrical impulses to help manage motor symptoms. These devices often go hand-in-hand with EEGs and other wearable brain activity monitors to assist with diagnosis, treatment, and daily monitoring for the overall assessment of brain health. As technology advances and clinical research continues to investigate, these devices can one day act as key predictors in changing brain activity and electrical signaling such as with epilepsy.

There has also been recent work on devices that alter the blood brain barrier to help better allow certain medications and drugs permeate into the brain. These drug delivery devices allow clinicians to better target therapies for the brain rather than use more invasive methods or treat symptoms with a broad-spectrum approach. What's more, utilizing new and minimally invasive techniques for treating the brain helps to fight disease progression, preserve normal function, and promote healthy compensation by targeting upstream effects of disease rather than downstream symptoms of pathogenesis.

Even wearable actigraphy devices and supporting equipment like smartphone applications can assist with the diagnosis and monitoring of neurodegenerative disease. Wearable devices can collect longitudinal data on walking patterns, gait, and tremors to better track and understand cognitive decline. This technology can also be used in conjunction with applications and software algorithms to catch nuanced changes in metrics like eye-movement and eye-tracking to further understand decline or disease effects on motor function and cognition. Overall, these devices can collect a wealth of data on daily living to help clinicians better understand disease progression, initial onset, and early compensation to more accurately and quickly diagnose neurodegeneration.

2. Non-Neuronal Cells

Non-neuronal cells, or glial cells, are in many ways like the immune system of the brain. Besides providing structural support, managing neurotransmitters, and producing cerebrospinal fluid, these cells —and in particular the microglia —act to repair damage and remove foreign objects from the nervous system. Research in this area is opening a number of exciting avenues by focusing on early preventative care rather than long term maintenance of disease after symptoms are present. What's more, imaging research has directly shown that non-neuronal cells and their dysfunction contribute to neurodegeneration and disease. These cells and their changes under disease effects can be monitored and further studied with imaging modalities like PET/CT or PET/MRI and DTI.

For example, as Schizophrenia has been considered a disconnection syndrome, researchers have investigated glial cells that focus on synaptic transmission and neurotransmitters. Researchers have found that degeneration or dysfunction of these cells occurs in patients with Schizophrenia, suggesting new avenues for therapy and highlighting the structural changes that occur to gray and white matter under this disease. DTI and sMRI in particular can assist researchers with tracking disease progression as the architecture of the brain changes.

Alzheimer's disease has also been attributed to the dysfunction of glial cells called pericytes, and still other neurological diseases like depression have been attributed to inflammation and the dysfunctional glial cells contributing to it. In addition to imaging that focuses on structural changes, these diseases can be further investigated for functional changes, such as with fMRI and Spectroscopy to track neurotrasnmitter markers, glucose metabolism, and overall levels of brain activity. Still other researchers are using imaging to investigate the effects that environmental factors and stress can have on the body over time, starting with maternal immune cells and the disruption of microglia. Collectively, this branch of neurological research highlights new avenues that can be explored with imaging to learn more about neurodegenerative diseases and their pathogenesis.

3. Multimodality Imaging

Multimodality imaging in clinical trials involves the use of multiple imaging techniques to gather more comprehensive data, develop a better understanding of the target disease, and better utilize tools for monitoring disease progression/treatment effectiveness. There are some initial compensation effects that occur throughout disease progression, so with a multiple modality approach, we can better assess what is truly disease effects versus the body trying to stay in an equilibrium.

Multi-modal imaging can provide more real-time insight, and complimentary effects occur with the intersection of collected data: some imaging modalities provide details on structure (CT, MRI), whereas others provide insights on function (fMRI, PET). Both approaches in the same study and at the same time provide greater insight into actual effects. For example, if a study is looking at disease progression in the brain and exploring downstream effects to muscle wasting, fMRI/PET in conjunction with MRI/CT can help investigate changes in the brain when tasks are performed.

Multi-modal imaging is most helpful when studying effects of treatment or safety/tolerability and helps obtain a larger amount of data to ensure a comprehensive view is captured. Medpace Core Lab (MCL) has extensive experience in the design and execution of clinical trials with multi-modality imaging. MCL can provide guidance to Sponsors to find the right imaging modality or the right collection of imaging modalities in order to streamline the collection of the data. The Core Lab further supports the analysis of imaging data for clinical trials, as well as regulatory compliance and quality assurance.

4. Injury

New research into injury and its long-term effects on the body are revealing insights about disease and pathogenesis. Injury, compared to disease, is a sudden effect on the body that requires rapid response for healing, recovery, and the systems return to normal/homeostasis. On the other hand, disease is a slow progression where the body's compensatory pathways are eventually overtaken. Maladaptation along with disease effects tip the scales and lead to widespread symptoms and health consequences. However, recent investigations into injuries such as traumatic brain injury and chronic traumatic encephalopathy have shown similarities between long term effects of injury and disease progression. In some instances, such as with head injuries or repeated head traumas, research has shown that these injuries can lead to neurodegenerative diseases such as Alzheimer's and Parkinson's.

In other instances, imaging research has directly led to treatment options and diagnostic tools for certain brain conditions such as stroke. In this scenario, time is critical to determine the type of stroke and therefore the best path forward for treatment and recovery. Without capabilities such as rapid CT or MRI, these treatments and other research efforts to improve stroke outcomes wouldn't be possible.

Collectively, the imaging and services that MCL provides helps to reveal new insights on not only rapid, emerging technologies for timely injury treatment, but also critical information and new treatment avenues for disease, its pathogenesis, and negative compensatory effects brought on by past injuries and trauma.

5. Emerging Technology

Artificial intelligence (AI) and machine learning (ML) are rapidly transforming the landscape of medical imaging in clinical research. While AI is still in the early stages of being incorporated into clinical trials, there are increasing submissions of drug and biologic applications using AI/ML components.

AI applications in medical imaging still require human oversight. So far, hybrid systems—where AI assessment and radiologist assessment are done in parallel to compare data variability, reliability, and other statistical measures—are seen as most accurate and reliable. AI can also be used as a tool to inform radiologists or other healthcare professionals and suggest more efficient or reliable options. For example, radiology AI models may help to provide suggested dosing and even tracers in the context of medical imaging to minimize exposure, maximize the window for good quality imaging, and improve treatment. This is particularly helpful to explore and improve upon therapeutic treatments for Huntington's disease where radiotracers are leveraged to track progressive brain cell decay with markers of metabolism, synaptic function, and neuroinflammation.

THE FUTURE OF NEURODEGENERATIVE IMAGING

Neurodegenerative diseases remain among the most complex challenges in clinical research, with a significant unmet need for innovative therapeutic approaches. Advances in neuroimaging continue to shape the future clinical research, enabling earlier diagnoses, more effective interventions, and a shift from late-stage management toward earlier intervention and prevention.

As a full-service CRO, Medpace offers a truly seamless clinical trial process for Sponsors of all sizes supported by experienced medical, regulatory, operational, and imaging experts. Our comprehensive CRO services are supported by our wholly-owned Central Laboratories, Bioanalytical Lab, Imaging Core Lab, ECG Core Lab, and Phase I Unit, as well as a Clinical Trial Management System that ties all study data together in a single platform. Through our proprietary image management software program for clinical trials, ClinTrak® Core Lab offers Sponsors a seamless integration of real-time central image collection, quality assurance, tracking, quantitative and qualitative analysis, data management, and image-related reporting with electronic database capture functions.

The MCL team brings together scientists, clinicians, technologists, project managers, and coordinators with deep expertise across MRI, CT, SPECT/PET, Ultrasound, and extensive experience using neuroimaging biomarkers in clinical trials. MCL remains at the forefront of innovations in the industry by exploring new ways to integrate emerging neuroimaging technologies into clinical research. By combining rigorous science with standardized and scalable processes, MCL continues to help Sponsors generate high-quality data and accelerate the development of therapies for neurodegenerative diseases.

Do you have an upcoming clinical trial that needs seamless execution? Contact our neuroimaging experts today to learn more.