Deep Dive: Stroke Clinical Research

Accelerate your next stroke study with Medpace’s noted medical and regulatory experts, highly experienced clinical trial management teams, central labs, and core imaging labs.

As a therapeutically-focused CRO, Medpace specializes in the design and conduct of global trials in neuroscience clinical research, including stroke. We bring a global footprint, strategic medical, regulatory and operational leadership as well as fully integrated Central Labs and Core Imaging Services to accelerate stroke studies.

Highly relevant operational know-how and subject-matter expertise in neuroscience, advanced therapies, and associated antithrombotic and lipid lowering therapies

End-to-end suite of global imaging services seamlessly integrated into the overall structure of the trial

A well-profiled network of experienced stroke sites enable timely enrollment and high-quality conduct of trials

A wide range of relevant biomarker assays through our wholly-owned central lab network

**FOCUS ON STROKE**

Full-service Clinical Support for Drugs, Biologics and Medical Devices
Experience

Medpace has in-house neurologists, imaging specialists, and operational teams with relevant and recent stroke experience as well as backgrounds (and publications) in stroke-specific scientific research. We have designed and conducted numerous stroke detection and stroke prevention studies and our experience includes direct administration of drug to brain, either intraventricularly or intrathecally. Our biopharmaceutical and medical device experience spans:

- Advanced therapies including stem cell
- Restorative therapies
- Thrombolytic therapies
- Preventative therapies (Medpace is known for its deep expertise and experience in vascular research and development, including
  - Medical device therapies

Recruitment and Global Site Relationships

Recruiting patients for stroke studies requires a partner who has strong relationships with a well-profiled network of experienced stroke sites, and who can manage complex logistics, negotiations, education, and site maintenance to ensure success. Medpace has earned a reputation for managing highly complex studies and has the relationships to work with the complex and evolving referral networks (hub and spoke), community hospitals, comprehensive stroke centers, and other acute care settings to drive successful patient enrollment.

Medpace provides site training and certification processes to obtain reliable assessments on clinical scales including mRS, NIHSS & Barthel, PROs and QoLs.

Physician-Led Clinical Research

Medpace is unique in its physician-led approach to clinical research. The Medpace model gives you the advantage of early and ongoing insight and guidance from therapeutic experts throughout trial design and execution. Our highly experienced medical doctors provide strategic direction for study design and planning, train operational staff, work with Investigators, provide medical monitoring, and meet with regulatory agencies. In addition, our medical monitors work collaboratively with our global regulatory affairs experts to provide strategic guidance into the best pathways to accelerate approvals. See sidebar to learn more about the stroke experience and background of our Medical Affairs and Imaging doctors.
Meet our Stroke Experts

Richard Scheyer, MD  
Vice President, Medical Affairs, Neuroscience and Psychiatry

Dr. Scheyer, in his academic career, worked as attending neurologist in a stroke acute care unit and participated in successful landmark studies of antiplatelet agents in stroke prophylaxis. In his industry career, he has led efforts in management and reversal of anticoagulant and antiplatelet agents for stroke prophylaxis. In the acute care setting, Dr. Scheyer has worked on neuroprotective agents and has led programs for both enhanced thrombolysis and acute prophylaxis in patients with TIA or minor stroke. While at Medpace he has led efforts in prevention of acute complications following severe stroke. Throughout, he has worked on enhanced biochemical and imaging technologies for patient selection, treatment optimization, and outcome assessment.

Marco Tangelder, MD, PhD  
Senior Medical Director, Cardiovascular

Dr. Tangelder was an associate professor of clinical epidemiology, and has over 20 years of academic, pharmaceutical and biotech industry experience, mainly in the development of antithrombotic therapies for a broad range of indications. Dr. Tangelder is an expert in trial design and methodology, and has been involved in various stroke prevention trials, including regulatory submissions, totaling over 10,000 patients.

Thomas R. Thompson, MD  
Vice President, Medical Affairs, Neuroscience and Psychiatry

Dr. Thompson is board-certified in Psychiatry and Geriatric Psychiatry and has clinical development experience in numerous CNS indications including; stroke and post-stroke rehabilitation, Parkinson’s disease, depression, schizophrenia, bipolar disorder, anxiety disorders, epilepsy, and pain. Dr. Thompson has clinical experience treating post-stroke depression and industry experience in stroke and post-stroke rehabilitation. His drug development experience in CNS includes leading a project in stroke and motor recovery, the completion of an MAA, leading a sNDA and designing head to head studies in CNS.

James Vornov, MD, PhD  
Vice President, Medical Affairs, Neuroscience and Psychiatry

Dr. Vornov’s research during his academic career focused on mechanisms of acute ischemic injury both in animal models and in clinical trials, serving as an investigator in stroke trials. He directed development of compounds aimed at treatment of brain ischemia and other forms of acute CNS injury.

Imaging

Daniel O’Leary, MD  
Senior Vice President, Medical Affairs, Neuroimaging, Neurology

Dr. Daniel O’Leary is the former Director of Neuroradiology at the Brigham and Women’s Hospital and former Professor and Chairman of Radiology at Tufts University Medical School. He is a board certified neurologist, radiologist, and neuroradiologist. He is internationally known for his pioneering work in developing techniques for imaging atherosclerotic vascular disease. He has participated in numerous studies focused on identifying and quantifying risk factors leading to stroke and myocardial infarction. He is a Fellow of the Stroke Council of the American Heart Association.

Chahin Pachai, PhD  
Director, Imaging Core Laboratory (Lyon, France)

Dr. Pachai has been involved in the management of several stroke studies including thrombolytic and neuroprotective agents, secondary prevention drugs with focus on post-stroke dementia as well as clinical trials in small vessel disease indications such as CADASIL.
Medpace Central Labs Provide Safety and Biomarker Analysis

Medpace Labs provide consistency in methods and instrumentation across wholly-owned and purpose-built laboratories located in the US, Europe, China and Singapore. We offer a wide range of relevant biomarker assays for stroke and have the ability to rapidly establish and validate novel assays as needed. Over the past three years, Medpace has validated over 190 new biomarker assays based on guidelines from the Clinical and Laboratory Standards Institute (CLSI) and in accordance with CAP and CLIA regulations.

Below are key biomarkers used in stroke clinical trials.

<table>
<thead>
<tr>
<th>Type</th>
<th>Biomarker</th>
<th>Medpace Validated Assays</th>
<th>Medpace Lab Partner Network</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulation</td>
<td>• aPTT</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• D-dimer</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Factor Xa</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Fibrinogen</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• TAFI Ag</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PAI-1</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Platelet Count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Protein C</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Protein S</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PT/INR</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Thrombin Generation Assay</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• vWF</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>CHF / Atrial Fibrillation</td>
<td>• BNP</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ProBNP</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td>• CRP</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lp-PLA2</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• MMP9</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• VCAM</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Neuronal/Glial Injury</td>
<td>• S100beta</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• NSE</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Routine Safety Chemistry</td>
<td>• Glucose</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Gene Expression</td>
<td>• Various markers of gene expression being evaluated on exploratory basis</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>
Core Imaging Expertise for Stroke Studies

Imaging (CT and MRI) plays a crucial role to optimize the detection of patients who are more likely to benefit from a new treatment (eligibility), to monitor safety aspects such as hemorrhagic transformation during the acute and sub-acute phases, and to evaluate imaging-based secondary efficacy endpoints such as intermediary and final infarct size and post-stroke neurodegeneration (atrophy).

Medpace Imaging Core Lab provides an end-to-end suite of global imaging services to enhance and expedite biopharmaceutical and medical device development in stroke studies. A combination of imaging expertise and clinical trial experience ensure that imaging components are seamlessly integrated into the complex structure of the overall stroke trial. Capabilities include:

- Expedited imaging-based (CT/MRI) central eligibility evaluation using fully web-based image evaluation solutions coupled with Medpace’s IWR/EDC systems
- Imaging-based safety and efficacy evaluations based on the following parameters:
  - Hemorrhages
  - Infarct size: differentiation between acute and chronic vascular lesions using FLAIR/T2 and Diffusion Weighted Imaging (DWI)
  - Perfusion-weighted imaging (PWI) parametric maps such as Time to Peak (TTP), Mean Transit Time (MTT), Cerebral Blood Volume (CBV) and Cerebral Blood Flow (CBF) – an illustration is provided below. These maps are various ways to evaluate the severity of hypo-perfusion using an MRI examination including the injection of a gadolinium-based contrast agent. Similar maps can be generated using Perfusion CT.

Medpace can identify and qualify CT and MRI scanners to maximize the consistency and quality of image acquisition across the sites. If external hospitals are allowed to refer patients to the study sites, the screening scans performed at those external sites may be acceptable if they meet the minimum quality requirements to detect recent ischemic infarcts and hemorrhages as well as the localization and grading of the corresponding vascular occlusion.

ClinTrak® Imaging—a component of Medpace’s proprietary study management system—can manage and analyze Digital Imaging and Communications in Medicine (DICOM) images.
Specialized Medical Device Expertise

Medpace Medical Device (MMD) provides specialized operational and regulatory expertise for stroke detection and prevention medical device studies. MMD designs and conducts device and diagnostic trials in all stages—from single-center, first-in-human and feasibility trials to multi-center, full-service pivotal trials and large-scale, post-market outcomes studies.

Stroke experience includes embolic protection devices used in TAVR, LAA closure devices, and carotid stents.

A Full-Service Approach to Clinical Research

Driven by a full-service CRO model that coordinates and integrates all services for our clients, Medpace provides an accountable, seamless, integrated and efficient platform for executing clinical research—increasing quality and speed while significantly reducing the need for duplicate management oversight. Our disciplined processes, site relationships, and technologies enable us to execute even the most complex global studies, from first-in-human through post-approval.