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# HOW AI AND ML ARE TRANSFORMING THE FUTURE OF MEDICAL IMAGING IN CLINICAL TRIALS

Artificial intelligence (AI) and machine learning (ML) are rapidly transforming the landscape of medical imaging in clinical research. The global market size of AI in medical imaging was valued at $1.01 billion in 2023 and is projected to continue to grow.[1] The use of these technologies in clinical trials is also ramping up rapidly. This article explores our experience with AI for image analysis within the context of clinical trials that include imaging endpoints.

AI and ML can be described as a branch of computer science, statistics, and engineering that leverage algorithms to perform tasks and exhibit behaviors such as learning, making decisions, and making predictions. ML, a subset of AI, enables the development of models that are trained by data rather than explicitly programmed analytically.[2,3] Here we refer to these methods collectively using the AI label. One of the key features of AI is the use of neural networks, which can modify the weights of connections between nodes, mimicking the way the human modifies the synapses between neurons to encode memories and learning.

AI has been making progress for some time in clinical radiology, with mammography being one of the first applications approved by FDA as an adjuvant to diagnosis.[3] Today, ML algorithms enable training models that can provide initial diagnosis, which is then reviewed and approved by a radiologist. This process is designed to support and accelerate the work of radiologists, cardiologists, and pathologists. In clinical radiology, the U.S. government's Central Medical Services (CMS) plays a critical role in setting requirements. For a procedure to be reimbursed, CMS defines test codes and sets guidelines on the level of clinician involvement versus automation. Consequently, the use of AI for medical image diagnosis is effectively determined by the reimbursement levels.

While clinical radiology focuses on the detection and diagnosis of disease, clinical research is focused on quantitation of biomarkers of disease progression or response to treatment. Clinical trials are governed by the FDA, which determines what constitutes an acceptable clinical trial endpoint. 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. In 2021, the FDA saw more than 100 submissions of drug and biologic applications using AI/ML.[2] However, FDA has yet to approve an AI based solution for delivery of endpoints in clinical trials and draft guidance is still emerging.

While AI applications in medical imaging are increasing, they still require oversight of a certified physician. 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. As technology advances and larger datasets become available, particularly ones that reflect a diverse range of radiologists' viewpoints, AI may evolve to surpass current hybrid models.

## THE COMPLEXITY OF MEDICAL IMAGING

Medical imaging can include multiparametric data acquisition providing different information about disease response. This can present a challenge to clinical trial researchers in extracting relevant biomarkers for endpoints that accurately reflect treatment efficacy. Given the large volume of images collected in clinical trials with hundreds of patients and perhaps dozens of time-points for imaging follow up, systems to efficiently view and quantify a broad range of medical imaging are important. The management of these large datasets, along with the need to ensure data privacy, demands substantial storage and computational resources. Additionally, the large scale of data presents challenges for quality management and variability among data sets that must be addressed.

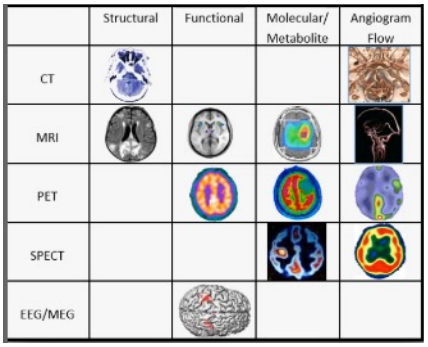


***Figure 1.*** *Example of the complexity of types of data in neuroimaging.*

Another challenge is the need for image co-registration. This arises when combining images from different modalities in the same patient, such as an abdominal CT scan and a PET scan. In these cases, scans may require alignment to ensure each pixel in one image corresponds to the same part of the body in the other image. Achieving proper alignment, or registration, is challenging in some regions of the body prone to movement, such as the abdomen, where breathing and patient position can create variations between scans. Also, image alignment between different patient visits may be important for measuring changes over time in a clinical trial that assesses response to treatment. AI has the capability of performing registration using unconventional methods such as CNNs and GANs. As it becomes more accessible for multi-modality data at separate imaging sessions, the accuracy of co-registration will improve the usability of such data in clinical settings and for clinical trial purposes.

As AI continues to evolve in medical imaging, it is important to have large and high-quality training data to train the algorithm for learning and achieving accurate results. Obtaining this training data can be difficult and expensive, as it requires respect for patient privacy and expert radiologists to annotate and classify images.

## BENEFITS OF AI/ML IN MEDICAL IMAGING

Harnessing AI in medical imaging for clinical trials offers many benefits aimed at achieving key objectives of all stakeholders. These benefits include increasing efficiency, improved consistency and accuracy, expediting enrollment, saving money and time, and more.

### *Consistency and Accuracy*

AI algorithms consistently deliver the same results, unlike human reviewers, whose interpretation can vary from one day to the next or have a level of uncertainty for a given image. The issue of variability is even more pronounced when different readers are involved. The accuracy of AI is another significant benefit, particularly when working with fine details like pixels and the differentiation between pixels, which can be difficult for the human eye to detect. In most cases, AI produces more detailed results, which can be further improved with additional training.

When Medpace Core Lab (MCL) selects central readers, we choose radiologists, pathologists, dermatologists, and professionals who have expertise around the disease indication and imaging modalities involved in the trial. These experts are highly skilled in reviewing images but may still need periodic updates on assessment criteria, particularly with quantitative measures. Once a ML model is trained, it does not forget or need a refresher. It retains information and can access it quickly, improving its performance with more data.

### *Expedited Patient Enrollment*

Expediting patient enrollment through faster eligibility decisions and more accurate data is essential in clinical trials. During the screening process, imaging and ECG data may be included as either an exclusion or an inclusion criterion. For example, patients may be required to have at least one measurable tumor for eligibility in oncology studies. Oftentimes a site sends images indicating a patient's eligibility, but the Sponsor requires a central lab to verify. This process can be time sensitive. Once the core lab receives the images, quality control (QC) is performed to ensure completeness, accuracy, and sufficient quality. This must be completed before the data is read by an expert.

This process can be expedited by a ML algorithm to conduct a preliminary eligibility assessment. By submitting the images to an AI program for tumor detection and size estimation through segmentation tools, we can quickly identify whether a patient meets the requirements, without the need for measurement of all tumors or co-registration with other modalities. This can accelerate eligibility decisions, while ensuring more reliable assessments that are beneficial to the Sponsor and documented for later audits or inspections.

### *Increased Efficiency to Reduce Cost and Time*

Conventionally, central review of imaging for a clinical trial has been performed by Core Labs using trained radiologists to review images to make measurements. Some applications can be labor intensive for the radiologist or technologist, such as drawing contours around tumors or organs and labeling images. This process can be slow depending on the availability of both the reader and the data. Improvements to imaging workflows—including automating data QC and performing preliminary image analysis for endpoints—can significantly increase efficiency and reduce the time required from imaging technologists and radiologists.

The time required for image review directly impacts the fees charged by central readers in a clinical trial. A radiologist can spend several minutes, up to an hour or more reviewing a single image per patient. With AI, quantification can be completed within minutes as soon as the data is available. By accelerating the image review process and providing more reliable, quantitative data, AI can help reduce costs. AI also minimizes the need for repeated reads and reduces the number of readers required, further driving down expenses. This acceleration in process and the ability to reduce variability makes AI a valuable tool in imaging for clinical trials.

## MEDPACE CORE LAB CAPABILITIES IN AI/ML

MCL uses secure image-based AI, including several applications that use models trained to recognize key features, to augment, and accelerate the quantitative analysis of medical images. MCL is a leader in the use of ML algorithms for medical imaging assessments in multiple areas such as:

1. Automatic organ segmentation and volume measurement of abdominal organs
    - MCL developed a deep learning-based model, and trained to segment MRI images for liver, spleen, and several abdominal organs to calculate and estimate the volume of the organs. MCL is actively using this AI model for measuring the volume of liver, spleen, and kidney in clinical trials that include changes in organ volumes as endpoints in response to treatment or disease progression.
2. Pathology: Scoring of liver biopsy specimens using the NASH Activity Score and CRN Fibrosis scoring systems
    - Digital pathology images are large, and it takes extensive time and effort to analyze those images by pathologists. MCL developed a neural network-based algorithm to automate scoring of liver biopsy slides according to these standardized scales, improving the turn-around time and reducing the cost while improving the reliability of these clinical trial endpoints.

3. Detection of infarcts and white matter abnormalities in brain scans[4]
    - MCL worked closely with a team in Paris Hospital, France who created a large trove of brain MRI data from many patients with CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) over the span of more than 10 years. This precious dataset was not well labeled, so MCL, with the help of multiple expert neuroradiologists from Paris Hospital, created new labels and segmentation of the white matter abnormalities. This data was used to train a model to accelerate the analysis of new image data sets and to provide insight into the progression of the disease in this large, multi-center trial.

4. Additional MCL AI capabilities
    - Segmentation model of CT scans for liver, lung, and colon tumor localization, detection, and quantification

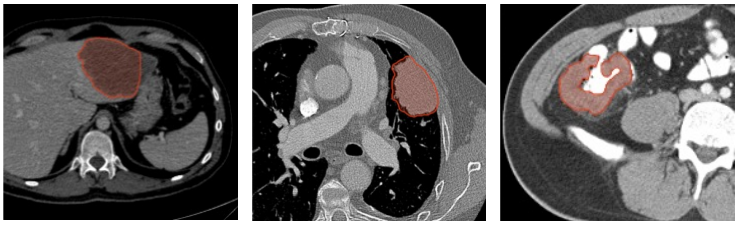

***Figure 2.*** *Liver, lung, and colon tumor AI-based segmentation*

- Quantitative analysis of muscle volume and volume changes over time, based on AI methods applied to MRI scans of legs and other body areas
- Identification, classification, and measurement of target lesions during treatment in oncology clinical trials using the RECIST 1.1 criteria[5]

## NAVIGATING THE FUTURE OF AI /ML IN MEDICAL IMAGING

New Medpace applications for AI in imaging are driven by Sponsor demand for specific imaging endpoints that can benefit from these tools. MCL has the expertise to recognize what ML tools to use and what training data should be applied to each specific solution. Our experts are skilled in providing secure, safe, and thoughtful use of AI in medical imaging. This is done through a strategic approach to AI involving the use of tools designed and trained for each application. These tools are implemented in a secure environment to protect confidentiality and prevent unauthorized access to data. All bespoke software developed at Medpace is subjected to a thorough validation process that includes Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ) according to industry standards. Results generated by AI imaging tools for clinical trial endpoints are reviewed and finally approved and signed by appropriate medical experts.

RECIST 1.1 response evaluation criteria for solid tumors is the only imaging endpoint that FDA officially accepts as a surrogate marker in oncology. MCL is automating the preliminary measurements and is developing multi-modality imaging training data to optimize those assessments. In the future, we expect to see more tools publicly available for such applications. Training data will continue to be a valuable commodity to achieve optimal performance of AI in medical image analysis for specific clinical trial endpoints. MCL and other groups are currently utilizing a variety of open-source resources to support these efforts.

The regulatory framework will play a critical role in shaping the future of AI/ML in medical imaging, providing guidance and ensuring the safe and effective integration of these technologies. As AI tools continue to evolve and become more advanced, we can anticipate updates to the FDA guidance and regulations of other healthcare agencies concerning these technologies. This evolving regulatory landscape will help define the direction and integration of AI tools in medical imaging in clinical trials.

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