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Imaging Advances in Stroke

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Advances in Stroke: Diagnosis and Imaging

Title: Imaging Advances in Stroke: Use of Advanced Neurovascular Imaging or Disruptive Innovation with AI?

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Non-standard Abbreviations and Acronyms

AI	artificial intelligence
ASPECTS	Alberta Stroke Program Early CT Score
CT	computed tomography
CTA	computed tomography angiography
CTP	computed tomography perfusion

FDA	United States Food and Drug Administration
MRI	magnetic resonance imaging

Introduction

The initial diagnosis of acute stroke has been driven by advances in breakthrough imaging technologies and more recently, disruptive innovation approaches to imaging data that have multiplied the global impact beyond the individual patient presentation. Reflection on the past year of advances in diagnosis and imaging may yield a list of interval scientific publications or more accurately, depict the incremental shift in the philosophy or conceptual application of stroke imaging as part of clinical practice in 2023. *Are the latest imaging advances in stroke related to the use of advanced neurovascular imaging modalities or to the application of disruptive technologies that include artificial intelligence (AI)?* Historical accounts of stroke imaging reveal a relative slowdown or diminution of novel or breakthrough imaging technologies, displaced by incremental or vertical refinements and horizontal expansion or disruptive innovation models of imaging applications across the stroke field. Disruptive innovation was defined almost 30 years ago in business theory and in the stroke field our focus is on disruptive innovations that leverage the variable definitions often interchanged for "AI". Iterative refinements in automated, real-time imaging pipelines and expanding applications to various stroke subtypes (e.g. hemorrhagic versus ischemic, proximal versus distal arterial occlusion, large core definitions, etiologic classification) provide vast opportunities to rapidly accelerate stroke imaging science. In 2023, the concept of "AI" arises in daily conversations, yet even within the niche field of stroke imaging far afoot from mainstream life there are innumerable references to "AI" on stroke imaging data. Unlike many years ago, stroke imaging publications now reflect routine clinical practice and not just the idealized, restrictive nature of prospective randomized controlled trials of therapeutic interventions. We briefly explore the current status of imaging in acute ischemic stroke in three clinical scenarios (large core ischemia, distal occlusions and basilar artery occlusion) to underscore that imaging advances in stroke relate predominantly to novel applications or disruptive innovation models of data use, not breakthrough technologies or even, the most advanced imaging modalities available on a global basis.

Chronology of Imaging Advances in Stroke

The history of imaging cerebral ischemia in humans begins almost a century ago with the introduction of cerebral angiography, yet the depiction of acute stroke with this technology was illustrated just over 50 years ago.[1] Within a few years, computed tomography (CT) and magnetic resonance imaging (MRI) were developed, providing the earliest images of

ischemic injury in brain parenchyma. About 30 years ago, diffusion-weighted imaging on MRI revolutionized the diagnosis of acute ischemia within minutes of onset. It has also been around 25 years since multimodal CT, with CT angiography (CTA) and CT perfusion (CTP), or the MRI equivalents have been used in conjunction with endovascular therapy for acute ischemic stroke. Automated processing of such acute stroke imaging data became available 20 years ago and AI algorithms for machine learning were inserted almost a decade ago. This chronology reveals a progressive shift from the focus on novel imaging hardware for imaging acquisition to software applications on resultant imaging data, to machine or deep learning of expansive datasets to precisely characterize specific imaging patterns in acute stroke. The relative slowdown in breakthrough technologies and expansion of disruptive innovation, seeking new applications in stroke and honing precision medicine, are strikingly apparent. Incremental innovation in delineating automated infarct core and penumbral measurements have been accompanied by horizontal translation of stroke imaging applications like automated arterial occlusion detection, aneurysm characterization, hematoma measurement and other features that rely on similar technology. The sole requirement for such automated approaches is availability of imaging source data, irrespective of human, expert clinician, or core lab interpretation, distancing any link with ground truth.

AI: Artificial Intelligence, Automated Imaging, or Applied Imaging?

AI is frequently invoked in current discussions on stroke imaging, yet the distinctions between *A*rtificial *I*ntelligence with machine or deep learning methods, *A*utomated *I*maging calculations using set formulas or scripted code, and *A*pplied *I*maging techniques for one type of stroke to another subtype, are almost never disclosed. AI machine learning has been used in only isolated steps of various computer-assisted diagnosis tools reviewed by the United States Food and Drug Administration (FDA) for stroke imaging. The “AI” designation is often used in scenarios devoid of machine learning. Furthermore, a 2022 FDA warning letter emphasized that such tools should not replace human interpretation of imaging in routine clinical practice.[2] These computer-assisted imaging tools are recommended to augment, yet not replace, diagnosis by human expertise where numerous other variables are considered in clinical context. Automated designations of “thrombectomy candidate”, “large vessel occlusion” or “suspected hemorrhage” on imaging results may be misleading or completely wrong in specific cases. A more rational strategy would be to provide probability estimates or confidence intervals on the automated, potential diagnoses. The ostensibly endless potential

for any of these AI definitions, however, is invigorating once large volumes of stroke imaging data are readily available. Even the seemingly magical prediction of CTP or CTA results from noncontrast CT is becoming reality with machine learning.[3] In the next few years, stroke imaging techniques, using rudimentary CT or MRI acquisitions, will be refined to yield patient-specific or precision medicine results based on demographics, presentation and co-morbidities.[4-6]

Real-World Data or Selective Clinical Trials on Stroke Imaging?

Applied imaging in acute stroke, as described above, is limited solely by the availability to transmit or process scans from anywhere around the world. This capability is increasingly global and the local imaging hardware has revolutionized the stroke field. The epidemiology of acute stroke, distinguishing hemorrhage from ischemia and stroke subtypes, has been rapidly transformed in geographies such as Mongolia or Papua New Guinea. Similarly, advanced neurovascular imaging, such as multimodal MRI before and after endovascular thrombectomy has been almost instantaneously established for routine clinical practice in places like Guadeloupe or French Polynesia. Wide variability in available imaging hardware or scanners undoubtedly exists, yet applied imaging is gaining traction in real-world data across the globe. Point-of-care CT and low-field MRI in various settings such as the prehospital phase, mobile stroke unit, or bedside will further accelerate this transformation. Acute stroke imaging was initially used to advance sophisticated therapeutic strategies like endovascular therapy, yet these "landmark" randomized trials from almost a decade ago now seem highly restrictive and far removed from real-world data. Applied imaging can now use routinely available CT or MRI to define how each stroke patient is distinct, how each imaging pattern reflects critical variables, to predict likely therapeutic response to specific drugs or devices and how therapeutic safety and efficacy of selective clinical trials may be generalized to the real world of routine stroke care. Future regulatory initiatives via FDA may simultaneously implement post-marketing surveillance with contemporaneous core lab adjudicated stroke imaging to mirror real-world data as prospective controls.

Clinical Paradigms – Large Core Ischemia, Distal Occlusions and Basilar Artery Occlusion

The imminent expansion of acute stroke therapies to large core ischemia, distal occlusions and basilar artery occlusion relates closely to recent stroke imaging advances. Each of these clinical paradigms does not necessarily require advanced neurovascular imaging or machine learning of AI, yet all three scenarios may depend on applied imaging of routinely available CT or MRI. Multimodal CT with CTA and/or CTP may be used to expand current indications for revascularization in acute ischemic stroke (Figure). The results of several large core trials will become available this year, utilizing a variety of CT and MRI approaches, including human or core lab adjudicated imaging and automated techniques. The key imaging questions will focus on how we define "large core" (CT/MRI, Alberta Stroke Program Early CT Score (ASPECTS)/perfusion, thresholds of ASPECTS/perfusion) with imaging. These potentially distinct imaging definitions of "large core" are not universally available around the world, are often unavailable in real-time medical decision-making, are inconsistently defined based on commercial software, and remain unvalidated, except in the isolated setting of early, isolated, complete occlusion of a proximal cerebral artery due to presumed cardioembolism. In the plethora of ongoing distal occlusion studies or randomized trials, imaging features will be critical as ASPECTS is irrelevant, Tmax perfusion thresholds unestablished, lesion sizes unclear and lesion evolution over time, previously undocumented. ASPECTS is irrelevant as only subsets or a few points of the 10-point scale can be applied in distal occlusions, whereas the established scale is completely extraneous in distal territories outside the middle cerebral artery. Tmax perfusion thresholds have only been studied and validated in proximal arterial occlusion, whereas the blood flow delay via pial collateral delivery beyond distal occlusions are shorter than the assumed Tmax>6 seconds definition of "penumbra". Distal occlusions encompass much smaller lesion volumes of brain tissue and the timecourse of ischemic evolution from penumbra to core remains poorly documented. Undoubtedly, core lab imaging adjudication of randomized trials for distal occlusion will provide such detailed evidence in coming years. For basilar artery occlusion, recent positive randomized trials and looming regulatory decisions provocatively ask whether any type of advanced neurovascular imaging is necessary.[7] The collateral routes, associated perfusion maps, lesion size, association with underlying etiology of occlusion, and timecourse of lesion evolution may not be relevant or critical in medical decision-making for evaluation and treatment of basilar artery occlusion.

Conclusions

In 2023, innovation in stroke and neurovascular imaging relies less on breakthrough technologies and increasingly more on disruptive AI. Incipient advances in the treatment of large core ischemia, distal occlusions and basilar artery occlusion will depend largely on imaging diagnosis through a variety of applied imaging approaches. The emerging big data era in stroke imaging will likely leverage global access to technology, diverse or heterogeneous clinical paradigms, instantaneous imaging transmission, archival of massive datasets, core lab annotations, detailed imaging calculations and true AI.

Disclosures

David S Liebeskind: Dr Liebeskind reports compensation from Cerenovus for consultant services; compensation from Stryker for consultant services; compensation from Medtronic for consultant services; compensation from Rapid Medical Ltd for consultant services; employment by UCLA Health System; and compensation from Genentech for consultant services.

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Figure 1: Multimodal noncontrast CT (left) with CTA (middle) and CTP (right) in: A, Large core proximal arterial occlusion; B, Distal occlusion; C, Basilar artery occlusion.