



Commentary

Artificial intelligence in stroke care: Deep learning or superficial insight?

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The concept of artificial intelligence (AI) has recently permeated almost every sector of daily life, including the rapidly evolving technologies and datasets of health care delivery. Each mode or type of technology, such as medical imaging, iteratively evolves each year and the resulting inter-related or multimodal applications multiply exponentially [1]. As health care technology, such as the electronic health record or diagnostic and therapeutic approaches expand, there is an ongoing demand for the continual process of leveraging, integrating and optimizing these synergistic advances. This modernization, or progressive refinement in optimizing the efficiency of existing technologies is devoted to eliminating inefficiencies and maximally utilizing the information embedded in every ephemeral event in routine clinical care. Such modernization is expected and not innovative, per se. In clinical medicine, as in other spheres of daily life, digital data is now amassing in distributed electronic health records and potentially voluminous clinical, imaging, laboratory and other datasets [1–3]. The recent expansion of imaging data in stroke is an ideal example, where data are universally acquired for all patients encountered, digitally preserved and thereby amenable to largescale computer algorithms for decades to come from around the world. Importantly, such informatics may yield insight far beyond the pace and extent of what we can accomplish as physicians in routine stroke care where every minute counts in patient outcomes. In this issue of *EBioMedicine*, Tang et al. provide an intriguing application of machine learning to MRI data in acute ischemic stroke to delineate the tissue fate of penumbral regions over time [4]. Importantly, they demonstrate that the typical time-based administration of intravenous thrombolysis may be successfully applied irrespective of time from symptom onset when advanced imaging enables AI via machine learning.

Tang et al. pooled the MRI data across seven centers, acquired within 9 h of symptom onset and focused on the identification of penumbral tissue as the target of intervention [4]. Measuring the size of the penumbra is a key goal of stroke imaging as treatments target such opportunities to offset potentially irreversible ischemic brain injury. The authors defied rigid time windows for intravenous thrombolysis and leveraged more sophisticated strategies to identify the potentially reversible penumbral zones of ischemia that are threatened or at-risk of ischemic infarction. They studied a cohort of 155 individuals, including 84 in a

training dataset. These populations are remarkably small in relationship to the expected task, yet they advantaged the power of independent voxel-based techniques to predict tissue fate in the brain after an ischemic stroke. Mismatch between hypoperfusion and core infarction or irreversible stroke damage in the brain, as defined in this study, correlated well with clinical outcomes at day 7 and 90 after stroke onset. The strikingly impressive AUCs for prediction of subsequent clinical outcomes in the validation dataset suggest the potential to utilize imaging, irrespective of time, in future clinical decision-making. The ultimate question, with this scientific paper, not dissimilar to most of the literature, is how likely this care paradigm for decision-making will perform in routine clinical practice, given the extreme heterogeneity of stroke cases encountered daily around the world.

Such machine learning methods engender several automatic or reflexive limitations [5–9]. Only MRI was used to define penumbra, whereas multimodal CT was not included. As a result, one cannot easily translate this imaging technology and mismatch paradigms, including the definition of core infarction or extent of ischemia. It demonstrates the potential of AI, but many philosophical and even more practical questions abound regarding future applications of this technique and related approaches to stroke imaging. The authors conclude their investigation with the panacea of all scientific reports, suggesting that future prospective trials should test their described methods. Unfortunately, in the majority of instances with this suggestion, prospective studies are never conducted, leading to publication bias and potentially misleading implications for clinical practice or the routine care of stroke. The reader and the clinician are left wondering, is this metaphorically, *deep learning* or simply *superficial* insight on the information that imaging can provide in acute ischemic stroke?

This innovative paper builds upon prior work in mapping tissue fate in acute ischemic stroke [6–9]. Most approaches, however, are predicated on key analyses that study highly selective paradigms or homogeneous clinical scenarios where basic protocols or algorithms may be applied in ideal situations. Generalizability of such approaches is a critical question in a highly heterogeneous and complex disorder such as ischemic stroke, where middle cerebral artery occlusion can lead to divergent imaging patterns of ischemia from case to case. The efforts to simplify stroke care with protocols, care pathways, algorithms and even the prospect of robotics may fall short in achieving the expertise of complex medical-decision making often encountered. The prospects of AI are therefore limited by whether we believe there exists a perfect algorithm to treat stroke. Furthermore, the development of machine

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learning requires training, from clinical care models where much of practice is empiric and not-evidenced based. For future AI, we will have to provide incredibly large multi-dimensional datasets and apply many rules of evidence where data are lacking. Clinical decision-making in stroke is often chaotic or erratic, where clinicians rapidly change course as in withdrawal of care after aggressive therapeutic interventions.

Can we mimic the human brain of complex medical decision-making in stroke care with AI? Imaging interpretation and mapping of tissue fate seems to be a good start, if it is faster and just as accurate as the current clinical standard which may be horrifically poor in most scenarios of stroke imaging interpretation. From a clinical perspective, however, stroke care involves far more than imaging and the clinical decision-making may be far beyond a simple logical method. Perhaps the novel approach by Tang et al. is a deeper learning experience than routine, but it yields merely superficial insight relative to the complex challenges we face in delivering stroke care around the world every hour.

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