

Artificial intelligence in neurosurgery

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Introduction

Recently, artificial intelligence (AI) has experienced a renaissance of sorts, with applications from autonomous vehicles on our roads to digital personal assistants in our homes. But in fleshing out “AI,” it is the second letter of the term that prompts lively debate, for what exactly defines intelligence? Setting aside philosophical ruminations for the moment, AI can be practically thought of as any technology which simulates the cognitive modules of the biological brain, namely: information gathering, processing, learning, and reasoning. In medicine, the exponential growth of peer-reviewed literature and complex datasets in the last half-century has begun to saturate the physician’s ability to stay accurately up-to-date. These increased demands on the modern clinician can exacerbate cognitive biases, which are estimated to contribute to 40,500 patient deaths per year from medical errors.¹ Through the development of reliable, efficient, bias-free AI systems to assist the surgeon, these unacceptable statistics can potentially be reduced.

Among the medical disciplines, neurosurgery has been one of the most to benefit from AI-driven technological innovations. In particular, the subspecialty of stereotactic and functional neurosurgery has seen an explosion of research concerning ways to intelligently automate the diagnosis and treatment of movement-related disorders and epilepsy. Key neurosurgical applications of AI include: robot-assisted surgery, automated preoperative planning, diagnostic brain imaging classification, surgical candidate selection, prediction of postoperative patient outcomes, and localization of epileptic zones within the brain.² Robotic neurosurgery is the first innovation that will be examined in detail here, and deals with the challenges of improving the accuracy, speed, and safety of minimally-invasive targeting of deep brain regions. Second, the role of machine learning (ML) in analyzing the brain’s electrical activity will be presented, with the goal of smarter diagnosis and more individualized therapy for disorders such as Parkinson’s Disease and epilepsy. Finally, the challenges of deploying AI into the operating room will be examined, with a focus on ethical and practical implications.

Robotic Stereotaxy

Functional neurosurgery is fundamentally concerned with minimally-invasive targeting of brain regions for diagnosis or treatment. Since only a small entry burr hole is made in the skull, direct visualization of the target region is impossible. As such,

skull-mounted stereotactic frames have traditionally been used to manually angulate and position the deep brain stimulation (DBS) electrode or brain biopsy cannula.³ A tedious process, the setting of coordinates and calibration of the stereotactic frame is lengthy and prone to human error. Thus, a recent technological innovation was to use software-controlled robotic manipulators to automate the process of localizing and angling the guide cannula at the entry point. Since their debut in the 1960s in automotive factories, robots have proven their suitability in achieving accurate, tremor-free, and complex manipulation at sub-millimeter scales without fatigue.⁴

The first robot to be successfully implemented in the neurosurgical operating room was the Unimation PUMA 200, which was used in 1985 to perform a brain biopsy.⁵ Since then, applications of robotics systems have blossomed to include DBS electrode placement, radiosurgery, placement of stereoelectroencephalographic (SEEG) electrodes for investigations of refractory epilepsy, ventricular catheter placement, and laser ablative procedures.⁶⁻⁹ Though many different systems have been prototyped, only a few have achieved clinical implementation, and a small subset of these have achieved commercial success (Table 1).

Although neurosurgical robotic systems do not automate the entire stereotactic procedure, nor can they learn or adapt to real-time changes in their environment, they critically offload a time-consuming processing step from the surgical workflow, freeing the surgeon’s bandwidth to oversee other aspects of the procedure. State-of-the-art robotic platforms are recording reductions in operative time, especially in repetitive procedures such as multi-electrode SEEG implantation.^{4,8} For instance, one trial using the iSYS1 skull-mounted robot reported a reduction of mean operative time from 148 ± 76 to 93 ± 18 seconds per electrode.⁸

Accurate and precise targeting of deep brain regions is crucial to minimize morbidity to the patient and also to ensure a successful implantation or biopsy on the first pass. As such, a large meta-analysis was recently performed in which the targeting accuracies of automated robotic platforms were compared with surgeon-guided manual electrode insertion using a stereotactic frame.¹⁰ Remarkably, robotically-guided surgery led to lower mean targeting errors (1.71 mm) compared to the conventional manual technique (1.93 mm), demonstrating the potential usefulness of robotic assistance in the operating room.¹⁰ Though a truly intelligent robotic assistant has not yet materialized, automated skull-drilling platforms are currently being prototyped with real-time haptic feedback algorithms to increase their autonomy, precision, and adaptiveness.¹¹

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Table 1. Currently Active Robotic Neurosurgery Systems

System	Developer (debut)	Robot Architecture	Total no. of patients reported in literature ⁴	Estimated Retail Price (USD)
Neuromate	Renishaw (1997)	Portable robotic arm ⁴	215	\$297,000
SurgiScope	ISIS Robotics (2003)	Ceiling-mounted microscope/manipulator ⁴	73	\$400,000
ROSA™	Zimmer Biomet (2012)	Portable robotic arm with integrated navigation ⁷	248	\$700,000
Renaissance	Mazor Robotics (2015)	Small skull-anchored robot ⁴	37	\$650,000
iSYS1	Medizintechnik (2016)	Small skull-anchored robot ⁸	41	\$200,000

Machine Learning

Machine learning (ML) is a subset of AI that allows computers to progressively learn through reinforcement and training, instead of being rigidly programmed to perform a single task. ML algorithms can be classified into supervised, unsupervised, and reinforcement learning.² Supervised algorithms are the most commonly used, where the computer is trained with a set of inputs (e.g. MRI brain scans), and a corresponding set of known outputs (e.g. the correct diagnosis for each scan). With each additional training set, the machine refines a mapping function which relates the input to the output with increasing precision. When the function sufficiently describes the relationship between inputs and outputs, the learning stops, and the machine can apply its training to a novel input dataset (e.g. to diagnose a previously-unseen MRI scan). In contrast, unsupervised learning has no training phase, and the algorithm is left to form its own associations based on inherent groupings in

the data. For instance, an unsupervised algorithm might analyze raw patient demographics found in hospital charts and deduce that female smokers are more likely to develop cerebral aneurysms than the general population. Finally, reinforcement learning algorithms explore an uncharted data territory and attempt to maximize a given reward – this was a key strategy used by Google’s DeepMind supercomputer to best the human grandmaster in the intricately strategic game of GO.¹²

Supervised ML is particularly suited to training on diagnostic datasets, such as those found in neuro-oncologic brain imaging. Typically, MRI brain imaging and clinical features such as age, gender, and symptoms are used as input parameters, and histological tumor classification and grade represent the desired output. A recent review compared the diagnostic performance of ML algorithms with expert neuroradiologists and neurosurgeons.² Surprisingly, after training the ML algorithms with only 33 to 126 known diagnostic sets, the computers performed at least as well as their human counterparts on novel imaging data, and sometimes significantly better.² However, acknowledged limitations of supervised ML applied to complex neuroimaging data include long processing times, as well as poor performance on rare tumors for which large training datasets are not available.^{2,13}

Neurosurgeons and neurologists are often tasked with interpreting electrical recordings from surface EEG, surgically-implanted subdural grids, or intracranial electrodes for the investigation of refractory epilepsy. These recordings can be long and complex, carrying information about dozens of channels of raw electrophysiology data from brain regions interconnected in elaborate ways. Several ML algorithms have been developed and tested in epilepsy patients to automatically detect seizures before they occur.^{2,14} These seizure warning systems can be immensely helpful for the patient, as they prompt administration of anticonvulsive medications or trigger the patient to move to a safer area. For instance, after training an algorithm on publicly-available intracranial EEG recordings, the software was able to automatically select optimal channels for analysis and achieve a 96% sensitivity for seizure prediction, with only 0.12 false detection per hour.¹⁴ Indeed, seizure advisory systems such as NeuroVista are commercially available, though they currently lack a way to optimize their algorithms in real time based on the patient’s individual pattern of electrical activity. Instead, automated seizure detection systems are able to achieve sub-second latencies due to pre-programmed algorithms within the device, which may have previously undergone the ML training process in the development stage. Taken a step further, closed-loop DBS devices are being developed with algorithms that detect patterns highly suggestive of impending seizures, and then automatically deliver electrical stimulation to abort the seizure (Figure 1).^{15,16} Several stimulation

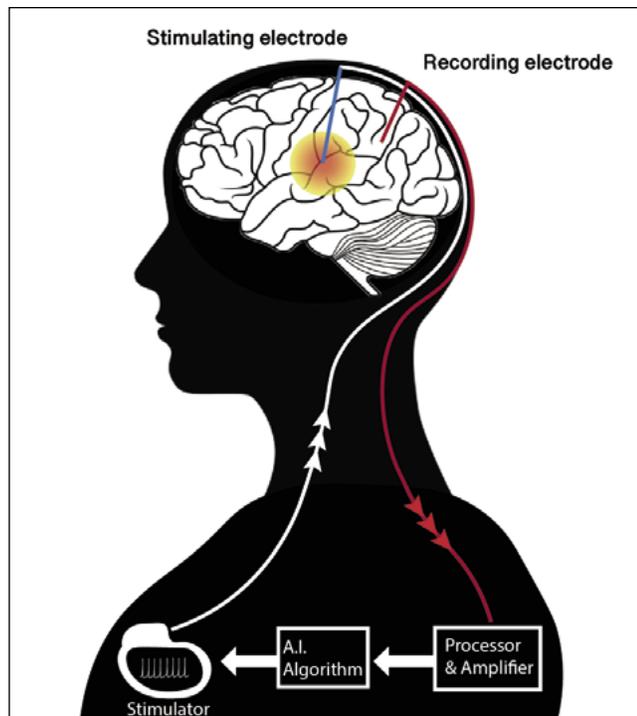


Figure 1. Schematic of a typical closed-loop deep-brain stimulation system with machine learning abilities. Recording electrode(s) first detect a specific pattern of electrical brain activity, such as a seizure or dysfunctional oscillations. Next, an amplifier digitizes and feeds the signal into an AI machine learning algorithm, which has been trained on a previous data set. The algorithm decides when and how to prompt electrical stimulation of target brain region(s) to achieve therapeutic effect (e.g. the anterior thalamic nucleus for seizure suppression).

targets have shown promise in seizure reduction, including the anterior and centromedian thalamic nuclei, and the hippocampus, depending on the epileptic syndrome.

Intelligently-delivered deep brain stimulation is also being developed for neurodegenerative diseases including Parkinson's Disease (PD) and Alzheimer's Disease (AD).¹⁷⁻¹⁹ It is increasingly being recognized that diseases such as PD involve dynamic desynchronization of brain circuitry, which correlates with symptomatic fluctuations. Accordingly, an adaptive algorithm that senses subcortical oscillations, and delivers ramped electrical stimulation to the subthalamic nucleus, has recently been tested in PD patients.²⁰ The study demonstrated safety of the sense-and-deliver paradigm, as well as substantial improvements in patients' clinical symptoms.²⁰ Although promising, DBS strategies for Alzheimer's disease are in their infancy and only open-loop systems have been implemented in patients to date. Looking ahead, the dysregulation in the memory circuits involved in AD may prove an even more suitable task for AI-based closed-loop strategies. Since the formation of memories involve distinct acquisition, encoding, and retrieval phases, the parameters of therapeutic DBS conceivably need to be tailored according to real-time patient behaviour and their brain network activity.¹⁸ Future preclinical and clinical studies are needed to illuminate the sites of pathologic electrical activity in the AD brain, and to discover which ML algorithm strategies are optimal for delivering the most effective stimulation paradigms.

Ethical Issues with Medical AI

As assistive technologies with AI capabilities increase in sophistication and autonomy, a third-party is introduced into the physician-patient relationship, and issues regarding patient welfare naturally arise. At the moment, we must acknowledge that ultimate responsibility for the patient rests with the attending surgeon alone, regardless of the perceived "intelligence" of the technology. Thus, AI-enabled devices must strongly incorporate robust and redundant safety features in their design to mitigate potential complications.

In a recent systematic review, we compared the complication profile of robot-assisted procedures to manual stereotactic procedures.⁴ We found that although the non-diagnostic and mortality rates were comparable between groups, robotic-assisted cranial surgeries were 4% more likely to result in intracranial hemorrhage.⁴ As with any new complex technology, a learning curve exists, which may contribute to patient morbidity if adequate training and familiarization with the equipment are not ensured.

With respect to ML algorithms within closed-loop DBS devices, interrogation and troubleshooting of the system should be easily accessible at all times, and the device should ideally have wireless charging capabilities to allow for quick reprogramming. Looking ahead, it is conceivable that future brain stimulation devices will rely on cloud-based computing, or the ability to update their algorithms using crowdsourced data. Robust encryption and data-sharing guidelines based on the principles of confidentiality and autonomy should be in place to prevent unauthorized or malignant use of a patient's personal data. Finally, an intelligent algorithm should not have the ability to rewrite its own core firmware: "I'm sorry Dave, I'm afraid I can't do that."

Conclusions and Future Directions

Neurosurgical robots and machine learning algorithms have the potential to save surgeons time, streamline complex procedures, and deliver more individualized treatment to the patient. Future study designs should assess the performance of clinical experts alone versus AI-assisted treatments to prospectively determine whether patient outcomes benefit. As with any new technology, graded and cautious incorporation guided by preclinical studies and strong ethical principles is necessary.

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