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Artificial Intelligence and Neurology

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Abstract

Computers and information technology has played a pivotal role in the advancement of healthcare. Artificial Intelligence (AI) in medicine has significantly evolved over the last few decades, now making it possible to initiate its involvement in real world clinical practice. AI can also be incorporated in a personalized, integrated, adaptive and context aware environment creating the so called Ambient Intelligence (AmI). Neurology is a discipline of medicine that deals with the disorders of nervous system. Large amount of literature exist in regards to utilization of AI and AmI in several aspects of neurology. Using AmI, individual's neurological function can be monitored around the clock for early recognition of neurological disorders. Electroencephalography and electromyography data can be interpreted by AI with high accuracy. Treatment responses can be monitored objectively by AmI in many conditions like movement disorders and epilepsy. Large quantity of data produced in the neurocritical care units can be processed by AI for better monitoring, treatment and outcome prediction. AI can reduce the cost of care and may potentially benefit remote parts of the world by playing role of an expert adviser. In this brief article, author has discussed the application and potential of AI and AmI in neurology. Some obstacles in their development are briefly discussed and several speculations about their future are made.

Keywords: Neurology; Artificial Intelligence (AI); Ambient Intelligence (AmI); Pervasive healthcare

Introduction

Medical knowledge has significantly expanded in the era of information technology making it impossible for a single human to keep track of all the knowledge. This has led to heavy utilization of computer and information technology in medicine. While artificial intelligence (AI) in medicine has been around since 1970s, the initial systems (e.g. INTERNIST-1 [1], MYCIN [2], ONCOCIN [3]) had major limitations requiring extensive programming by humans and exhibited little or no self-learning behavior. Since then, the field of artificial intelligence has significantly evolved with introduction of a number of sophisticated algorithms, some of which are capable of self-learning. Rule based fuzzy expert systems [4] and supervised learning algorithms like artificial neural networks [5] and support vector machines [6,7] are the examples of most widely utilized AI techniques in healthcare; but the list is by no means limited to them. Despite of many advances in the AI, some experts believe that its application in healthcare is still far from its true potential and that our efforts are limited [8].

The concept of pervasive health monitoring involves deploying electronic sensors and wireless networks in the individual's surroundings that are ubiquitous and allows real time personalized health monitoring of every individual in the population, irrespective of location and time [9,10]. It includes smart monitoring devices embedded in the living environment (including cell phones, homes, hospitals, work places, automobiles, etc.), wearable intelligent textiles that continuously records a number of physiological parameters, wearable motion sensors, brain computer interface and many more [11-18]. Ambient Intelligence (AmI) incorporates AI and pervasive health monitoring to create a personalized, integrated, intelligent and context aware environment for the individuals [19].

Neurology is a discipline of medicine that deals with the disorders of nervous system. Clinical examination of the nervous system is an integral part of the diagnosis and treatment of neurological disorders. Some aspects of clinical examination, like cognitive and motor function assessment, may readily be performed by AmI with reasonable accuracy over a prolonged period of time. AI may be able to assist humans even in many non-clinical aspects of neurology. In this article, author has discussed the application, impact and potential of AI and AmI in neurology. Some obstacles in their development are briefly discussed and several speculations about their future are made.

Applications in Neurology

Stroke is one of the most common neurological disorders and AmI can potentially have heavy impact on its epidemiological and clinical course. Stroke occurs when there is either an interruption of blood supply to part of brain (known as ischemic stroke) or the rupture of a blood vessel in the brain causing hemorrhage (known as hemorrhagic stroke). Treatments for ischemic as well as hemorrhagic strokes are time sensitive and are most effective when administered within first few hours of onset [20-22]. However, the patients commonly don't recognize the symptoms or they may be rendered disabled to activate emergency medical services. Therefore, these treatments are largely underutilized [23,24] due to delayed hospital presentation [25,26] or unclear time of symptom onset (as in patients waking up with strokes) [27]. Using AmI, individual's neurological function can be monitored around the clock [28-30] and presence of any alarming neurological signs can activate emergency medical services, even without patient's knowledge [19]. AmI in conjunction with tele-stroke networks [31], automated imaging interpretation [32-34] and prehospital thrombolysis [35] can exclude significant sources of delay in the management of acute stroke. Prognosis of stroke can also be predicted, even prior to treatment using the AI [36,37]. AmI can detect cardiac arrhythmias (especially atrial fibrillation) in cryptogenic strokes and can even potentially prevent the first cerebrovascular event by monitoring every individual in the population [38-40]. Stroke recovery can be improved as well using AmI in the neurorehabilitation [18,41,42].

Seizures are defined as transient, synchronous activation of a large number of neurons that results in focal or generalized dysfunction in brain activity and consciousness. Such disturbance in the electrical activity of the brain can sometimes be recorded using a number of recording electrodes on the scalp in form of an electroencephalogram (EEG). Due to transient duration of the event, the abnormality may not be recorded on the EEG and therefore, continuous EEG monitoring with automatic seizure detection could dramatically change the management of these patients. AI algorithm based seizure detection techniques for scalp EEG [43-48] and intracranial EEG [49-53] have evolved significantly and even surpassed human ability in certain aspects [44]. Responsive cortical stimulation involves implantation of seizure detection device that not only detects seizures, but can also suppress the seizure from spreading [54]. Ambulatory/ home EEG and accelerometers as parts of AmI can yield critical information on seizure frequency and semiology in certain patients [55-58]. Algorithms have been developed that can predict risk of recurrent seizures in the future based on several patient risk factors [59]. AmI can ensure better compliance in taking seizure medications [19], as forgetting a single dose may result in a breakthrough seizure. Self-driving cars will be able to provide more mobility and independence to the millions of patients across the world living with seizures or other neurological disabilities [60,61]. Similar to the EEG recordings, electrical potential recordings of the muscle and nerves (electromyography) can also be interpreted by AI [62,63] and then integrated with clinical [64] and imaging [65] data to help with the diagnosis of a number of neuromuscular disorders.

Neurodegenerative disorders (e.g. Alzheimer's disease, Parkinson's disease, Lou Gehrig's disease etc.) result in a very gradual decline in individual's cognitive and/or functional status, and such conditions may be diagnosed earlier with help of AmI that monitors individual's neurological function over a prolonged period of time. AmI can assist with activities of daily living in the cognitively impaired [66,67]. A brain computer interface device has been successfully implanted in a patient of Lou Gehrig's disease, enabling her to communicate better [68]. AI has been extensively studied in the field of movement disorders, especially in Parkinson's disease that often leads to disabling tremors and muscle rigidity. It can differentiate different types and subtypes of movement disorders [69-73] and can even interpret the neuroimaging [74]. Quantification of movement abnormalities can be utilized in the medical and surgical management [75]. Electrical stimulation of certain deep structures in the brain (also known as deep brain stimulation) significantly improves the symptoms of Parkinson's disease. Various stimulation parameters require frequent adjustments to obtain optimal clinical response and certain closed loop systems have been developed that can optimize these parameters automatically for individual patient by feedback information received from the body motion sensors [76,77].

Several catastrophic neurological emergencies like neurotrauma, large strokes, status epilepticus and brain infections require more frequent monitoring of neurological and other bodily functions, which is usually done by nurses and physicians. Neurocritical care units are equipped with a number of patient monitoring systems that generate large quantity of data pertaining to ventilation, hemodynamics, intracranial pressure, body temperature, fluid intake-output, serial neurological examinations and neurophysiologic parameters (e.g. electromyography, continuous EEG). Many of these parameters may require expert supervision around the clock that can potentially be provided by a single intelligent computer system to a large number of patients simultaneously. Closed-loop AI systems can potentially perform real time adjustment of ventilator settings [78-81], antiepileptic drugs, anesthetics/analgesics [82-84], neuromuscular blockade [85,86], glucose management [87], and blood pressure, fluids and electrolytes management [88,89] etc. with little or no human input [90,91]. Intelligent algorithms have been developed that can predict mortality in hemorrhagic stroke [92] and outcome after traumatic brain injury [93,94]. Prediction of intracranial pressure has also been achieved by AI [95,96]. More complex predictive algorithms in the future may take thousands of variables into account in order to predict complications and outcome with fair degree of certainty, well ahead of time. Wealth of data produced in the neurocritical care units makes them an ideal environment to incorporate AI techniques that can efficiently handle such data.

Future Direction and Limitations

AI systems have been developed which can learn from the electronic medical records and develop their own optimal treatment plan [97]. Such selection of optimum path can be individualized for each patient and can dynamically change over time to adapt the changes in clinical scenario. Nowadays, large scale projects are under progress to develop cloud based intelligent computer systems to integrate and analyze enormous amount of patient data and medical literature [98]. These platforms may thrive on the exponentially increasing healthcare data and learn from it. The expected final product might be a capable expert computer system that is always up to date with medical knowledge, contain medical records of every individual, may guide physicians and surgeons around the world and may even learn from its own experience to become better over time. Initial goal would be to incorporate these systems effectively in physician's workflow and then eventually to replace the physician in performing many tasks. Complex medical conditions might be managed with the guidance of these systems at a very little or no cost, even in the remote parts of the world.

Very small number of professionals with both clinical and programming proficiency, lack of international biomedical information sharing network platforms and lack of credible international standards for communication and data exchange has been few of the major obstacles resulting in slow development and underutilization of AI [8]. Furthermore, new ethical, legal and privacy issues may arise [99,100] and dramatic shifts in the role and demand of medical personnel as well as in their reimbursement may occur. Major changes in the education curriculum of medical professionals may have to take place. Thus, the path towards utilizing AI in real world medicine may not always be straightforward. But the rising cost of healthcare [101-104] may prove to be an independent driving force to develop these technologies. We know that the health information technology not only improves the quality of care, but also reduces its cost significantly [105,106]. Many of these observations led to formation of funding programs (e.g. HITECH) by the US federal government to stimulate investment in the electronic health records [107]. Similarly, AI may also potentially reduce the cost of care markedly [97] and in future, this may translate into creation of promotional policies to accelerate investment in AI by rewarding the hospitals and the physicians who incorporates it into their workflow. Initial monetary investments can eventually be paid off by the numerous advantages of AI. Despite of certain limitations, the advantages of these systems are numerous. With the aid of advanced AI and AmI, acute neurological emergencies may be timely managed, chronic neurological diseases may be recognized early, treatments may be individualized and the quality of life with neurological disability may be improved.

References

1. Miller RA, Pople HE Jr, Myers JD (1982) Internist-I, an experimental computer-based diagnostic consultant for general internal medicine. New Engl J Med 307: 468-476.
2. Shortliffe EH, Davis R, Axline SG, Buchanan BG, Green CC, et al. (1975) Computer-based consultations in clinical therapeutics: explanation and rule acquisition capabilities of the MYCIN system. Comput Biomed Res 8: 303-320.
3. Shortliffe EH, Scott AC, Bischoff MB, Campbell AB, Van Melle W, et al. (1984) An expert system for oncology protocol management. In: Buchanan BG and Shortiffe EH (eds.) Rule-Based Expert Systems, pp: 653-665.
4. Torres A, Nieto JJ (2006) Fuzzy logic in medicine and bioinformatics. Bio Med Res Int.
5. Rosenblatt F (1958) The perceptron: a probabilistic model for information storage and organization in the brain. Psychol Rev 65: 386-408.
6. Cortes C, Vapnik V (1995) Support-vector networks. Mach Learn 20: 273-297.
7. Byvatov E, Schneider G (2003) Support vector machine applications in bioinformatics. Appl Bioinformatics 2: 67-77.
8. Patel VL, Shortliffe EH, Stefanelli M, Szolovits P, Berthold MR, et al. (2009) The coming of age of artificial intelligence in medicine. Artif Intell Med 46: 5-17.
9. Varshney U (2003) Pervasive healthcare. Comput 36: 138-140.
10. Varshney U (2007) Pervasive healthcare and wireless health monitoring. Mobile Netw Appl 12: 113-127.
11. Pantelopoulos A, Bourbakis NG (2010) A survey on wearable sensor-based systems for health monitoring and prognosis. IEEE Transactions Systems, Man, and Cybernetics, Part C: Applications and Reviews 40: 1-12.
12. Chen M, Gonzalez S, Vasilakos A, Cao H, Leung VC (2011) Body area networks: A survey. Mobile Netw Appl 16: 171-193.
13. Ding D, Cooper RA, Pasquina PF, Fici-Pasquina L (2011) Sensor technology for smart homes. Maturitas 69: 131-136.
14. Park S, Jayaraman S (2010) Smart textile-based wearable biomedical systems: a transition plan for research to reality. IEEE T Inf Technol B 14: 86-92.
15. Paradiso R, Loriga G, Taccini N (2005) A wearable health care system based on knitted integrated sensors. IEEE T Inf Technol B 9: 337-344.
16. Poh MZ, Swenson NC, Picard RW (2010) A wearable sensor for unobtrusive, long-term assessment of electrodermal activity. IEEE T Bio-Med Eng 57: 1243-1252.
17. Fletcher RR, Poh MZ, Eydgahi H (2010) Wearable sensors: opportunities and challenges for low-cost health care. Engineering in Medicine and Biology Society (EMBC), 2010 Annual International Conference of the IEEE, pp: 1763-1766.
18. Patel S, Park H, Bonato P, Chan L, Rodgers M (2012) A review of wearable sensors and systems with application in rehabilitation. J Neuroeng Rehabil 9: 21.
19. Acampora G, Cook DJ, Rashidi P, Vasilakos AV (2013) A Survey on Ambient Intelligence in Health Care. Proc IEEE Inst Electr Electron Eng 101: 2470-2494.
20. Atlantis T (2004) Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. The Lancet 363: 768-774.
21. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, et al. (2015) Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 372: 1019-1030.
22. Bechtel BF, Nunez TC, Lyon JA, Cotton BA, Barrett TW (2011) Treatments for reversing warfarin anticoagulation in patients with acute intracranial hemorrhage: a structured literature review. Int J Emergen Med 4: 1-8.
23. Prabhakaran S, McNulty M, O'Neill K, Ouyang B (2012) Intravenous thrombolysis for stroke increases over time at primary stroke centers. Stroke 43: 875-877.
24. Moradiya Y, Crystal H, Valsamis H, Levine SR (2013) Thrombolytic utilization for ischemic stroke in US hospitals with neurology residency program. Neurology 81: 1986-1995.
25. Jin H, Zhu S, Wei JW, Wang J, Liu M, et al. (2012) Factors associated with prehospital delays in the presentation of acute stroke in urban China. Stroke 43: 362-370.
26. Lacy CR, Suh DC, Bueno M, Kostis JB (2001) Delay in presentation and evaluation for acute stroke: Stroke Time Registry for Outcomes Knowledge and Epidemiology. Stroke 32: 63-69.
27. Mackey J, Kleindorfer D, Sucharew H, Moomaw CJ, Kissela BM, et al. (2011) Population-based study of wake-up strokes. Neurology 76: 1662-1667.
28. Rai P, Oh S, Shyamkumar P, Ramasamy M, Harbaugh RE, Varadan VK (2014) Nano-bio-textile sensors with mobile wireless platform for wearable health monitoring of neurological and cardiovascular disorders. J Electrochem Soc 161: B3116-B3150.
29. Lorincz K, Kuris B, Ayer SM, Patel S, Bonato P, et al. (2007) Wearable wireless sensor network to assess clinical status in patients with neurological disorders. Proceedings of the 6th international conference on information processing in sensor networks. ACM, pp: 563-564.
30. López G, Custodio V, Moreno JI (2010) LOBIN: E-textile and wireless-sensor-network-based platform for healthcare monitoring in future hospital environments. IEEE T Inf Technol B 14: 1446-1458.
31. Müller-Barna P, Schwamm LH, Haberl RL (2012) Telestroke increases use of acute stroke therapy. Curr Opin Neurol 25: 5-10.
32. Chawla M, Sharma S, Sivaswamy J, Kishore L (2009) A method for automatic detection and classification of stroke from brain CT images. Engineering in Medicine and Biology Society, 2009 EMBC 2009 Annual International Conference of the IEEE, pp: 3581-3584.
33. Cocosco CA, Zijdenbos AP, Evans AC (2003) A fully automatic and robust brain MRI tissue classification method. Med Image Anal 7: 513-527.
34. Bagher Ebadian H, Jafari-Khouzani K, Mitsias PD, Soltanian-Zadeh H, Chopp M, et al. (2009) Predicting final extent of ischemic infarction using an artificial neural network analysis of multiparametric MRI in patients with stroke. Neural Networks, 2009 IJCNN 2009 International Joint Conference IEEE, pp: 229-235.
35. Walter S, Kostopoulos P, Haass A, Keller I, Lesmeister M, et al. (2012) Diagnosis and treatment of patients with stroke in a mobile stroke unit versus in hospital: a randomised controlled trial. Lancet Neurol 11: 397-404.
36. Cheng CA, Lin YC, Chiu HW (2014) Prediction of the prognosis of ischemic stroke patients after intravenous thrombolysis using artificial neural networks. Stud Health Technol Inform 202: 115.
37. Asadi H, Dowling R, Yan B, Mitchell P (2014) Machine learning for outcome prediction of acute ischemic stroke post intra-arterial therapy. PLoS One 9: e88225.
38. Nemati E, Deen MJ, Mondal T (2012) A wireless wearable ECG sensor for long-term applications. Communications Magazine, IEEE 50: 36-43.

39. Rubel P, Fayn J, Nollo G, Assanelli D, Li B, et al. (2005) Toward personal eHealth in cardiology. Results from the EPI-MEDICS telemedicine project. J Electrocardiol 38: 100-106.
40. Choe WC, Passman RS, Brachmann J, Morillo CA, Sanna T, et al. (2015) A comparison of atrial fibrillation monitoring strategies after cryptogenic stroke (from the Cryptogenic Stroke and Underlying AF Trial). Am J Cardiol 116: 889-893.
41. Haeuber E, Shaughnessy M, Forrester LW, Coleman KL, Macko RF (2004) Accelerometer monitoring of home- and community-based ambulatory activity after stroke. Arch Phys Med Rehabil 85: 1997-2001.
42. Horak F, King L, Mancini M (2015) Role of body-worn movement monitor technology for balance and gait rehabilitation. Phys Ther 95: 461-470.
43. Ghosh Dastidar S, Adeli H, Dadmehr N (2007) Mixed-band wavelet-chaos-neural network methodology for epilepsy and epileptic seizure detection. IEEE T Bio Med Eng 54: 1545-1551.
44. Ghosh Dastidar S, Adeli H, Dadmehr N (2008) Principal component analysis-enhanced cosine radial basis function neural network for robust epilepsy and seizure detection. IEEE T Bio-Med Eng 55: 512-518.
45. Song Y, Crowcroft J, Zhang J (2012) Automatic epileptic seizure detection in EEGs based on optimized sample entropy and extreme learning machine. J Neurosci Meth 210: 132-146.
46. Temko A, Thomas E, Marnane W, Lightbody G, Boylan G (2011) EEG-based neonatal seizure detection with support vector machines. Clin Neurophysiol 122: 464-473.
47. Meier R, Dittrich H, Schulze Bonhage A, Aertsen A (2008) Detecting epileptic seizures in long-term human EEG: a new approach to automatic online and real-time detection and classification of polymorphic seizure patterns. J Clin Neurophysiol 25: 119-131.
48. Yang C, Deng Z, Choi KS, Jiang Y, Wang S (2014) Transductive domain adaptive learning for epileptic electroencephalogram recognition. Artif Intell Med 62: 165-177.
49. Feldwisch Drentrup H, Schelter B, Jachan M, Nawrath J, Timmer J, et al. (2010) Joining the benefits: combining epileptic seizure prediction methods. Epilepsia 51: 1598-1606.
50. Aarabi A, Fazel Rezai R, Aghakhani Y (2009) Seizure detection in intracranial EEG using a fuzzy inference system. Engineering in Medicine and Biology Society, 2009 EMBC 2009 Annual International Conference of the IEEE, pp: 1860-1863.
51. Rabbi AF, Fazel Rezai R (2012) A fuzzy logic system for seizure onset detection in intracranial EEG. Comput Intell Neurosci.
52. Liu Y, Zhou W, Yuan Q, Chen S (2012) Automatic seizure detection using wavelet transform and SVM in long-term intracranial EEG. Neural Systems and Rehabilitation Engineering, IEEE Transactions 20: 749-755.
53. Yadav R, Swamy M, Agarwal R (2012) Model-based seizure detection for intracranial EEG recordings. IEEE T Bio Med Eng 59: 1419-1428.
54. Morrell MJ, RNS System in Epilepsy Study Group (2011) Responsive cortical stimulation for the treatment of medically intractable partial epilepsy. Neurology 77: 1295-1304.
55. Patel K, Chua CP, Fau S, Bleakley CJ (2009) Low power real-time seizure detection for ambulatory EEG. Pervasive Computing Technologies for Healthcare, 2009 PervasiveHealth 2009 3rd International Conference on IEEE, pp: 1-7.
56. Chiang J, Ward RK (2014) Energy-efficient data reduction techniques for wireless seizure detection systems. Sensors (Basel) 14: 2036-2051.
57. Poh MZ, Loddenkemper T, Reinsberger C, Swenson NC, Goyal S, et al. (2012) Convulsive seizure detection using a wrist-worn electrodermal activity and accelerometry biosensor. Epilepsia 53: e93-e97.
58. Kramer U, Kipervasser S, Shlitner A, Kuzniecky R (2011) A novel portable seizure detection alarm system: preliminary results. J Clin Neurophysiol 28: 36-38.
59. Aslan K, Bozdemir H, Sahin C, Ogulata SN (2010) Can Neural Network Able to Estimate the Prognosis of Epilepsy Patients Accorrding to Risk Factors? J Med Syst 34: 541-550.
60. http://www.google.com/selfdrivingcar/
61. Krumholz A (2009) Driving issues in epilepsy: past, present, and future. Epilepsy Curr 9: 31-35.
62. Koçer S (2010) Classification of EMG signals using neuro-fuzzy system and diagnosis of neuromuscular diseases. J Med Syst 34: 321-329.
63. Reaz M, Hussain M, Mohd-Yasin F (2006) Techniques of EMG signal analysis: detection, processing, classification and applications. Biol Proced Online 8: 11-35.
64. Pandey B, Mishra R (2009) An integrated intelligent computing model for the interpretation of EMG based neuromuscular diseases. Expert Syst Appl 36: 9201-9213.
65. Srivastava T, Darras BT, Wu JS, Rutkove SB (2012) Machine learning algorithms to classify spinal muscular atrophy subtypes. Neurology 79: 358-364.
66. Aloulou H, Mokhtari M, Tiberghien T, Biswas J, Yap P (2014) An adaptable and flexible framework for assistive living of cognitively impaired people. IEEE J Biomed Health Inform 18: 353-360.
67. Zhang S, McClean SI, Nugent CD (2014) A predictive model for assistive technology adoption for people with dementia. IEEE J Biomed Health Inform 18: 375-383.
68. Vansteensel MJ, Pels EG, Bleichner MG, Branco MP, Denison T, et al. (2016) Fully Implanted Brain-Computer Interface in a Locked-In Patient with ALS. N Engl J Med 375: 2060-2066.
69. Hossen A (2012) A neural network approach for feature extraction and discrimination between Parkinsonian tremor and essential tremor. Technol Health Care 21: 345-356.
70. Rocchi L, Palmerini L, Weiss A, Herman T, Hausdorff JM (2014) Balance testing with inertial sensors in patients with Parkinson's disease: assessment of motor subtypes. Neural Systems and Rehabilitation Engineering, IEEE Transactions 22: 1064-1071.
71. Wile DJ, Ranawaya R, Kiss ZH (2014) Smart watch accelerometry for analysis and diagnosis of tremor. J Neurosci Methods 230: 1-4.
72. Bhidayasiri R, Petchrutchatachart S, Pongthornseri R, Anan C, Dumnin S, et al. (2013) Low-cost, 3-dimension, office-based inertial sensors for automated tremor assessment: technical development and experimental verification. J Parkinson's Dis 4: 273-282.
73. Hossen A, Muthuraman M, Al-Hakim Z, Raethjen J, Deuschl G, et al. (2012) Discrimination of Parkinsonian tremor from essential tremor using statistical signal characterization of the spectrum of accelerometer signal. Bio-Med Mater Eng 23: 513-531.
74. Salvatore C, Cerasa A, Castiglioni I (2014) Machine learning on brain MRI data for differential diagnosis of Parkinson's disease and Progressive Supranuclear Palsy. J Neurosci Meth 222: 230-237.
75. Lieber B, Taylor BE, Appelboom G, McKhann G, Connolly ES Jr (2015) Motion Sensors to Assess and Monitor Medical and Surgical Management of Parkinson Disease. World Neurosurg 84: 561-566.
76. Shukla P, Basu I, Graupe D, Tuninetti D, Slavin KV (2012) A neural network-based design of an on-off adaptive control for Deep Brain Stimulation in movement disorders. Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE, pp: 4140-4143.
77. Shukla P, Basu I, Tuninetti D (2014) Towards closed-loop deep brain stimulation: Decision tree-based Essential Tremor patient's state classifier and tremor reappearance predictor. Engineering in Medicine and Biology Society (EMBC), 2014 36th Annual International Conference of the IEEE, pp: 2605-2608.
78. Tehrani FT (2012) A closed-loop system for control of the fraction of inspired oxygen and the positive end-expiratory pressure in mechanical ventilation. Comput Biol Med 42: 1150-1156.
79. Tehrani F, Rogers M, Lo T, Malinowski T, Afuwape S, et al. (2004) A dual closed-loop control system for mechanical ventilation. J Clin Monit Comput 18: 111-129.
80. Wysocki M, Brunner JX (2007) Closed-loop ventilation: an emerging standard of care? Crit Care Clin 23: 223-240.

81. Lellouche F, Brochard L (2009) Advanced closed loops during mechanical ventilation (PAV, NAVA, ASV, SmartCare). Best Pract Res Clin Anaesthesiol 23: 81-93.
82. Liu N, Chazot T, Hamada S, Landais A, Boichut N, et al. (2011) Closed-loop coadministration of propofol and remifentanil guided by bispectral index: a randomized multicenter study. Anesth Analg 112: 546-557.
83. Liu N, Chazot T, Genty A, Landais A, Restoux A, et al. (2006) Titration of propofol for anesthetic induction and maintenance guided by the bispectral index: closed-loop versus manual control: a prospective, randomized, multicenter study. Anesthesiology 104: 686-695.
84. Puri G, Kumar B, Aveek J (2007) Closed-loop anaesthesia delivery system (CLADS (TM)) using bispectral index: a performance assessment study. Anaesth Intens Care 35: 357.
85. Janda M, Simanski O, Bajorat J, Pohl B, Noeldge-Schomburg G, et al. (2011) Clinical evaluation of a simultaneous closed-loop anaesthesia control system for depth of anaesthesia and neuromuscular blockade*. Anaesthesia 66: 1112-1120.
86. Eleveld DJ, Proost JH, Wierda JM (2005) Evaluation of a closed-loop muscle relaxation control system. Anesth Analg 101: 758-764.
87. Cavalcanti AB, Silva E, Pereira AJ (2009) A randomized controlled trial comparing a computer-assisted insulin infusion protocol with a strict and a conventional protocol for glucose control in critically ill patients. J Crit Care 24: 371-378.
88. Rinehart J, Lee C, Cannesson M, Dumont G (2013) Closed-loop fluid resuscitation: robustness against weight and cardiac contractility variations. Anesth Analg 117: 1110-1118.
89. Kramer GC, Kinsky MP, Prough DS, Salinas J, Sondeen JL, et al. (2008) Closed-loop control of fluid therapy for treatment of hypovolemia. J Trauma 64: S333-S341.
90. Uemura K, Sugimachi M (2013) Automated cardiovascular drug infusion system to control hemodynamics. Adv Biomed Eng 2: 32-37.
91. Rinehart J, Liu N, Alexander B, Cannesson M (2012) Closed-loop systems in anesthesia: is there a potential for closed-loop fluid management and hemodynamic optimization? Anesth Analg 114: 130-143.
92. Edwards DF, Hollingsworth H, Zazulia AR, Diringer MN (1999) Artificial neural networks improve the prediction of mortality in intracerebral hemorrhage. Neurology 53: 351-357.
93. Rughani AI, Dumont TM, Lu Z, Bongard J, Horgan MA, et al. (2010) Use of an artificial neural network to predict head injury outcome. J Neurosurg 113: 585-590.
94. Amin AP, Kulkarni HR (2000) Improvement in the information content of the Glasgow Coma Scale for the prediction of full cognitive recovery after head injury using fuzzy logic. Surgery 127: 245-253.
95. Zhang F, Feng M, Pan SJ (2011) Artificial neural network based intracranial pressure mean forecast algorithm for medical decision support. Engineering in Medicine and Biology Society, EMBC, 2011 Annual International Conference of the IEEE, pp: 7111-7114.
96. Schmidt B, Bocklisch S, Pabler M, Czosnyka M, Schwarze J, et al. (2005) Fuzzy pattern classification of hemodynamic data can be used to determine noninvasive intracranial pressure. Intracranial Pressure and Brain Monitoring XII: Springer, pp: 345-349.
97. Bennett CC, Hauser K (2013) Artificial intelligence framework for simulating clinical decision-making: A Markov decision process approach. Artificial Intelligence in Medicine 57: 9-19.
98. http://www.ibm.com/smarterplanet/us/en/ibmwatson/health
99. Miller RA, Schaffner KF, Meisel A (1985) Ethical and legal issues related to the use of computer programs in clinical medicine. Ann Intern Med 102: 529-536.
100. Kumar P, Lee HJ (2011) Security issues in healthcare applications using wireless medical sensor networks: A survey. Sensors 12: 55-91.
101. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData
102. Brown DL, Boden Albala B, Langa KM, Lisabeth LD, Fair M, et al. (2006) Projected costs of ischemic stroke in the United States. Neurology 67: 1390-1395.
103. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML (2011) Projections of the cost of cancer care in the United States: 2010-2020. J Natl Cancer Inst 103: 117-128.
104. Anderson GF, Hussey PS, Frogner BK, Waters HR (2005) Health spending in the United States and the rest of the industrialized world. Health Aff (Millwood) 24: 903-914.
105. Shekelle PG, Morton SC, Keeler EB (2006) Costs and benefits of health information technology. Evid Rep Technol Assess (Full Rep), pp: 1-71.
106. Buntin MB, Burke MF, Hoaglin MC, Blumenthal D (2011) The benefits of health information technology: a review of the recent literature shows predominantly positive results. Health Aff 30: 464-471.
107. https://www.healthit.gov/policy-researchers-implementers/health-it-adoption-programs