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Understanding Artificial Intelligence and Machine Learning in Anaesthesia

Stephanie Naidoo

Moderator: L Pillay



UNIVERSITY OF
KWAZULU-NATAL

INYUVESI
YAKWAZULU-NATALI

School of Clinical Medicine
Discipline of Anaesthesiology and Critical Care

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ARTIFICIAL INTELLIGENCE IN ANAESTHESIA

INTRODUCTION

Anaesthesiology is an art likened to that of pilots. However, we do not get any credit for the lives saved and the numerous safe landings we perform daily. Time is our most precious resource and using Artificial Intelligence allows us to be more efficient but more importantly...it gives us the time to be creative and innovative.

Surgeons have embraced technology and have progressed to performing robotic surgery on patients while sitting comfortably in the corner of the room....Anaesthesia providers give an anaesthetic but most are simple anaesthetics that are labour intensive. There are various factors that has allowed this to still be acceptable today. We have a high success rate and a low complication rate after anaesthesia and thus we like to keep things simple.

Today in 2020, we find ourselves in the 4th Industrial revolution and in a global pandemic. Change is inevitable. It is time to embrace Artificial Intelligence(AI) and use it to our advantage.

DEFINITION

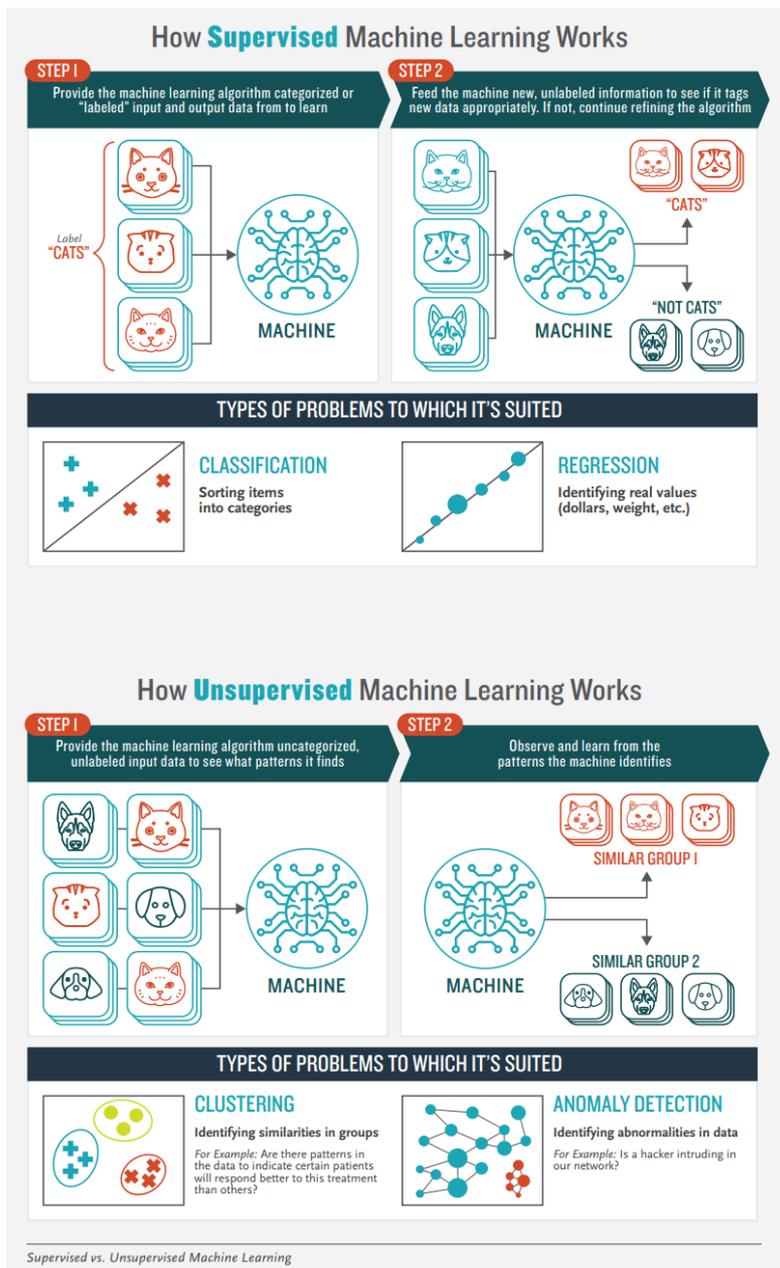
Definition: Artificial intelligence(AI) has been defined as the study of algorithms that give machines the ability to reason and perform functions such as problem-solving, object and word recognition, inference of world states, and decision-making.¹ Simply put, it is getting machines to simulate the ability that humans have, the most important being cognitive tasks.

What is machine learning?

This is the ability of machines to use the information that is being fed into it, to improve the use or experience of the machine as a tool. It uses small and large data sets to compare data to look for patterns. These include numbers, text, images and speech or sounds. These are different from a programme that has a set of rules that is uses to produce outputs from the input received. Common examples are that of your playlist on your cellphone when using Spotify, Youtube music etc. It looks for similarities and common threads to create a new suggested playlist for you. There are 3 broad categories of machine learning namely supervised, unsupervised, and reinforcement learning.

When large amounts of X-rays, which are fed into a computer programme, the computer is able to later identify comparable indications, using labels from X-rays. It will also be able to analyse the diverse labels and compare previous X-rays that were loaded to current X-rays being loaded. This is an example of supervised learning. Supervised learning algorithms try to model relationship and dependencies between the target prediction output and the input features, such that we can predict the output values for new data based on those relationships, which it has learned from previous datasets fed. Essentially this means that there is an answer data set and the model is trained with the correct answer.

Unsupervised learning is a type of learning where no specific outcome is desired. The idea is that the machine will pool similar data and reorganise the data in clusters of similarities.



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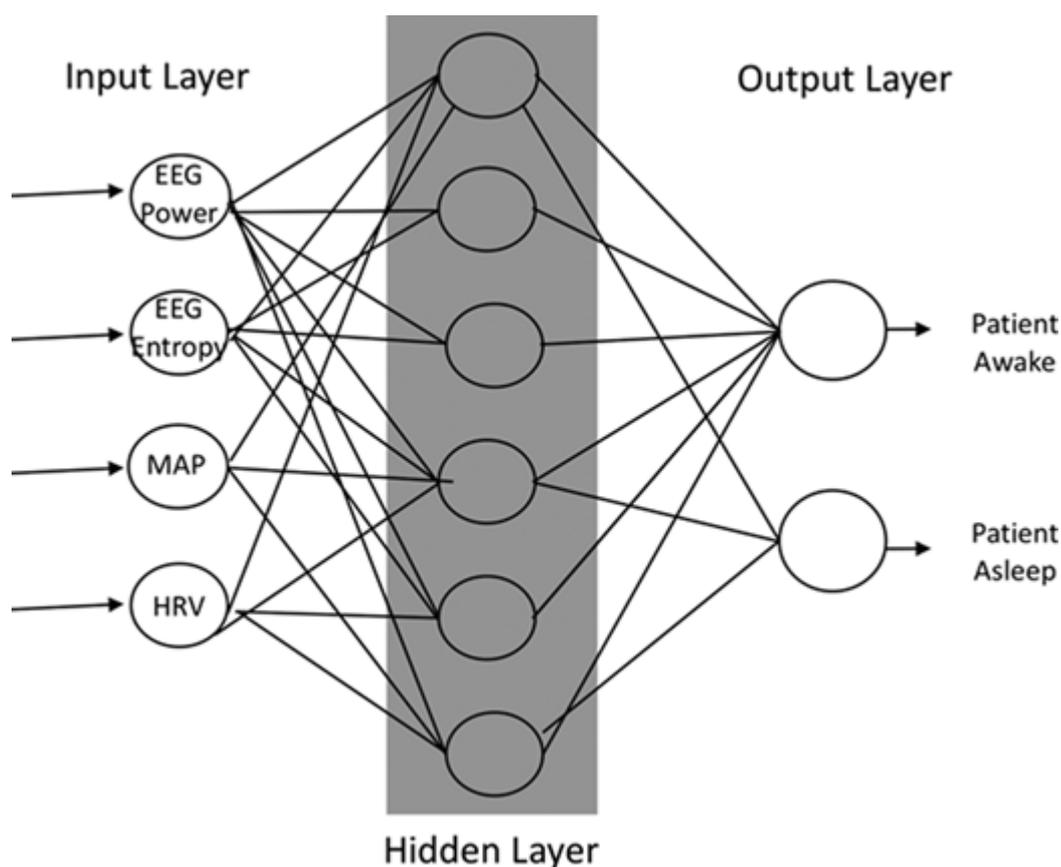
Reinforcement learning

When compared to supervised learning, there is no answer that the machine can be trained with, however there is a goal or reward and the machine will try to achieve it, while avoiding traps or hurdles. It has key areas of functioning:

- Input: The input should be an initial state from which the model will start
- Output: There are many possible output as there are variety of solution to a particular problem
- Training: The training is based upon the input, The model will return a state and the user will decide to reward or punish the model based on its output.
- The model continues to learn.
- The best solution is decided based on the maximum reward.³

Neural Networks and Deep Learning

Neural networks are a popular method responsible for actually doing the work in machine learning today. It copies the physiological idea of the nervous system and processes signals in overlying layers. Each network is made up of an input layer of neurons comprised of features that describe the data, at least one hidden layer of neurons that conducts different mathematical transformations on the input features, and an output layer that yields a result.⁴ Between each layer are multiple connections between neurons that are parameterized to different weights depending on the input-output maps. Thus, neural networks are a framework within which different machine learning algorithms can work to achieve a particular task (eg. image recognition, data classification).⁴



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Classification of different forms of Artificial Intelligence

1. **Narrow or weak:** focused on one single narrow task. It possesses a narrow-range of abilities. Narrow AI is something most of us interact with on a daily basis. Think of Google Assistant, Google Translate, Siri, Cortana, or Alexa. They are all machine intelligence that use Natural Language Processing (NLP). NLP is used in chatbots and other similar applications. By understanding speech and text in natural language they are programmed to interact with humans in a personalized, natural way.⁵
2. **Strong:** about as capable as a human, is still an emerging field.
3. **Superintelligence:** more capable than a human.

Why is AI significant?

IBMs Deep Blue, a computer system beat Garry Kasparov, world champion chess player on 10 February 1996. Why is this significant? Computers can analyse the rules and the legal moves allowed to formulate a plan to get an outcome. This may take thousands of cross referencing, which is what we do too... when playing chess... The ability to do this quickly and repetitively at 2am in the morning may be why I like AI. Fatigue is a problem for humans and this is how AI can be of assistance to us.

“To err is human..to forgive divine” Alexander Pope

The operating room is a hive of activity and we are constantly being bombarded with multiple variables. The main source of human error in anaesthesia is the high number of variables an anesthesiologist has to monitor: up to 100 parameters, whereas the human brain cannot simultaneously process more than four or five parameters⁶. Automation of tasks would enable us to spend less time on doing mundane and simple tasks, thus enabling us to make smarter clinical decisions.

Implications for Anaesthesia

There are 3 types of robots in Anaesthesia currently. The first 2 types, pharmacological and mechanical (or manual) robots, are designed to eliminate the repetitive part of the workload by automating simple tasks and giving support to the clinician, respectively.⁷ The third category of robots, broadly referred to herein as “artificial intelligence” systems, offer updated and pertinent recommendations related to specific clinical scenarios detected automatically⁷. This would allow them to analyse critical events and thereafter make decisions or be able to act on the clinical scenario.

A review performed by Hashimoto et al found six main clinical applications of artificial intelligence research in anesthesiology: (1) depth of anesthesia monitoring, (2) control of anesthesia, (3) event and risk prediction, (4) ultrasound guidance, (5) pain management, and (6) operating room logistics.⁴

From these applications, a summary of the most commonly encountered artificial intelligence sub-fields (e.g., machine learning, computer vision, natural language processing) and methods (classical machine learning, neural networks, fuzzy logic) was presented. Most applications of artificial intelligence for anesthesiology are still in research and development; thus, the current focus of artificial intelligence within anesthesiology is not on replacing clinician judgment or skills but on investigating ways to augment them.⁴

Can a machine beat my Anaesthesia technique?

A machine would not be able to replace the warmth, reassurance and the allaying of an anxious patients fears. However technically, machines will soon be able to deliver the entire anaesthetic. The current challenges are the cumbersome intubating techniques, however this is being addressed currently.

In a study by Joosten et al, automated closed loop systems outperformed manual control and had a significant beneficial impact on postoperative neurocognitive recovery. This was the primary endpoint of the study (automated versus manual control) and the effect was

minimal yet very important. For this study Anaesthesia(hypnosis and analgesia, fluid administration and ventilation were controlled by separate and independently working closed loop systems. Patients were assessed 1 week after anaesthesia.⁸

In the secondary analysis, a decrease in cognitive function corresponded significantly to the percentage of time the Bispectral Index dropped lower than 40. Interestingly the end-tidal carbon dioxide less than 32 mmHg or mean arterial pressure less than 60 mmHg did not correlate with a decrease in neurocognitive function⁷. The reason this is so, is that the algorithms constantly change the rate of administration to achieve the target. Humans do not change the rates frequently.

As a professional Anaesthesiologist, one has many different skills to impart to junior doctors. We multitask a number of administrative tasks and still monitor the patient, surgeon(table up, table down), nurses, recovery room patients as well as overseeing the smooth running of the theatre slate for day.

Once these automated closed loop systems are approved for use... it will standardise the general type of anaesthesia across the world. It would definitely improve the quality of care our patients receive. This no doubt would allow us to perform other tasks that require explicit human skill.

CURRENT MODALITIES IN OPERATING ROOMS

Depth of Anaesthesia monitoring

Bispectral index monitoring used to maintain anaesthesia started in the 1950s when Bickford described this concept of using summated electroencephalography(EEG) to help with the maintenance of anaesthesia. He used the EEG system which was linked to and controlled the plunger of a syringe for ether and thiopentone. It used a closed feed back system with rules to manage certain endpoints which are necessary for the maintenance of general anaesthesia eg. hypnosis. We have evolved now to target a Bispectral index number must be identified and these can be used with intravenous agents. The algorithm will then use the rules to govern its behaviour to achieve the set target. In practical terms it would constantly measure the bispectral index to determine drug administration rates.⁹

Control of Anaesthesia

The Target controlled infusions are well known and used. This is one of the most simple yet effective forms of integrating automation and machine learning. The McSleepy, named after the popular television show Greys Anatomy is the prototype of the automated anaesthesia machine.

It encompasses the 3 key features of hypnosis, analgesia and muscle relaxation. It has infusion pumps attached to the anaesthesia workstation but runs off a software programme called Labview. The attending doctor can watch the patients response on a laptop. The patient needs intravenous access as per the standard and has sensors applied to their muscles. The attending doctor inputs age, weight, height, sex etc and the desired doses and the procedure being performed. The McSleepy runs the data in the algorithms every minute to avoid miscalculations and drug errors.¹⁰

It measures depth of anaesthesia, muscle relaxation with a Train of Four count and uses Analgосcore for pain measurements. Closed loop systems do not have a user interface that tells you the exact amount of drug administered, but the McSleepy does. Thus it is not a black box and the transparency enables surgeons and the anaesthetist to have a clear understanding of what is going on but also to make adjustments. In the event of an error in terms of feedback from sensors it averages out the doses given within 15 minute intervals and administers that to ensure anaesthesia is maintained.

Artificial intelligence is combined with mathematical algorithms in the McSleepy. After approximately 20 surgeries with the same surgeon it learns patterns and times of the procedure. Naturally the data trends are stored at the end of procedures. Furthermore...it learns and stores the surgeons preferences during surgery. So it combines AI with human intervention which in reality creates the safest option for patients. The McSleepy is planned to be deployed as personal digital assistants. This allows control of anaesthesia from a distance. In today's Covid-19 pandemic this would be extremely useful. It allows anaesthesia providers to mitigate the risk of infectious airborne diseases.

In resource limited settings having the McSleepy could allow a doctor to oversee greater number of anaesthetics given to more patients where the disease burden is high.

Event and Risk Prediction

This is an important tool which when applied would help identify patients at risk thus allowing counselling but more importantly real time action. Post induction hypotension is a well known entity and despite knowing physiology, pharmacology and patient profiles this is still an important event that may be improved upon. Simple algorithms may not be able to accurately risk stratify patients. Kendale et al did a study using AI to detect post induction hypotension. They looked at on table blood pressures from induction until 10 minutes post induction. A mean arterial blood pressure less than 65mmHg was used for the definition. They incorporated perioperative data such as age, American Society of Anaesthesiology rating etc together with blood pressures on table to develop a ROC curve that correlates with post induction drops in blood pressure. This is different since it does not use waveform data but can do this with non invasive blood pressure. They suggest the data be populated from health records then have an alert notification that the clinician would see to flag patients at high risk.¹¹

This may be especially important for more junior levels of staff while allowing a decrease in preventable morbidity in the form of Acute kidney injury and Myocardial infarction.

Ultrasound guidance

We love the advent of the ultrasound and yes with many hours our skills as radiology fellows are improving...however sometimes we just want to deliver a good anaesthetic quickly or sometimes we can only offer regional anaesthesia so success is imperative. Despite becoming more skilled in ultrasound, there often times that we require assistance and I for one would appreciate some help or guidance at night especially. The Magellan device offers the use of a joystick to inject the patient with the block needle. It has a high success rate of identifying the nerve 100% of the time.

Artificial intelligence techniques were used to assist in the performance of ultrasound-based procedures, and neural networks were the most commonly employed method of achieving ultrasound image classification.⁴

Neural networks were used to identify the femoral artery or vein while distinguishing it from other potentially similar appearing ultrasound images such as muscle etc. The neural network analysis is approximately 94% accurate since it analyses the horizontal edges with greater priority than the vertical edges. Vertebral interspaces L1-L5 and the sacrum were automatically identified and this was done in real time.

Operating room logistics

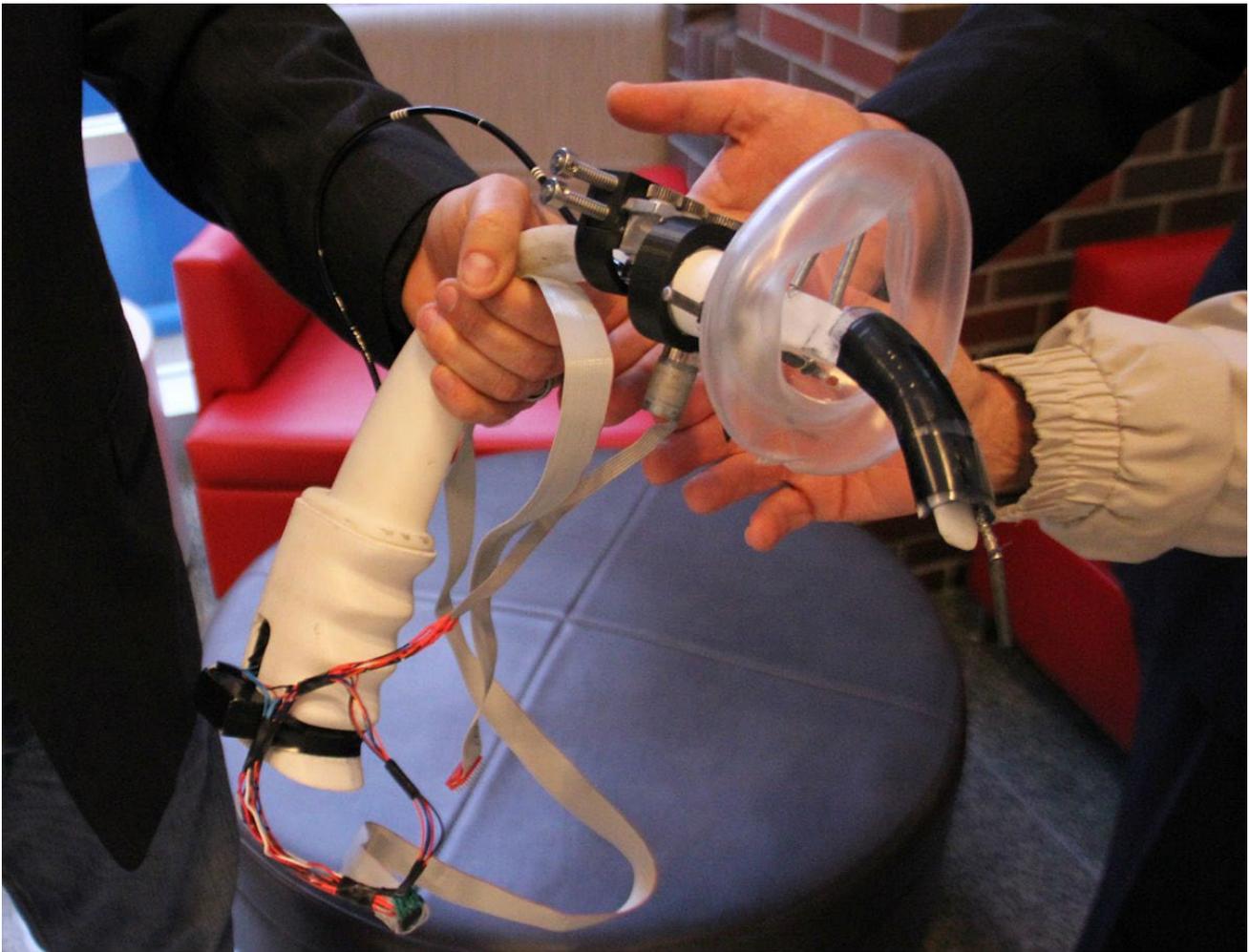
Currently there has been little done to improve logistics in theatre with AI. However the different areas that are being reviewed are theatre work flow, movement of staff in theatre to improve patient safety and scheduling operating room time.

Airway management

The Kepler intubation system was developed in 2012 and was done primarily as a pilot study to check the feasibility of remote intubation techniques (hemmerling end). The system comprised of a videolaryngoscope with the endotracheal tube and this was held by a robotic arm, which was controlled by a joystick. The user manoeuvre's said joystick which would control the robot by a software system. The system can allow remote intubations within 40-60 seconds.

Researchers at The Ohio State University have designed a robot to replace their limited visual guidance. Initially it was designed to assist medical personnel in the field due to the rate of failed intubations. Mechanical Engineering Associate Professor Tony Luscher, and the group teamed up with Anesthesiologist Dr. Hamdy Awad, to develop a prototype of this technology.

The device which is autonomous would secure patients' airways more accurately with increased consistency by propelling a robotic endoscopic device, which "receives three-dimensional information about its anatomical location by means of a small speaker placed on the skin near the patient's laryngeal prominence emitting sound and magnetic waves detected by accelerometers and magnetic fields, respectively."¹³



Robotic intubation device in development at The Ohio State University.¹³

CURRENT MODALITIES IN ICU

Intensive care units are an essential yet expensive niche in any hospital. The increased longevity of populations with advancements in health care will see the number of patients requiring ICU almost doubling in the near future. Streamlining care with the use of automated devices will enable a higher number of ICU beds for 2 reasons. Firstly, nursing personnel, a scarce resource can be freed up to do clinical work for a higher number of patients. Secondly the cost of monitoring patients will be reduced with automation.

Severity Scoring and Mortality prediction

This has always been an interesting topic. There are many scoring systems used in ICUs however the complex nature of patients imply that individuals do not always get the most accurate evaluation since these scores are aimed at population groups.¹⁴

The APACHE II and SAPS II overestimate the mortality for patients. A Super learner ICU algorithm was developed to compare hospital mortality with the SOFA, APACHE-II and SAPS-II. The super learner used 2 sets of variables to compare outcomes. In the first it used 17 variables that were fed into SAPSII. Next the original variables were fed into it. The versions used by super learner gave a probability of mortality of 0.12, SAPSII 0.3 and SOFA 0.12.¹⁵ This study was validated externally in a French hospital.

Sepsis

AI has been used to predict risks in ICU. Sepsis in ICU is an important treatable condition yet it may unclear until late stages. A programme was used to predict sepsis and AI improved the time to diagnosis by 12hrs in 1 study. The authors developed an Artificial Intelligence Sepsis Expert(AISE) to assist with identifying early sepsis. The system used high resolution vital signs and Electronic medical data. Every hour 65 variables were calculated and passed to the AISE used to predict the onset of sepsis. The area under receiver operator curves were compared. While the sequential organ failure assessment(SOFA) and the simplified acute physiology score II(SAPS II) had area under the curves of 0.725 and 0.700 respectively, the AISE had an area under the curve of 0.83 and the detection occurred 12 hours earlier.¹⁶

ICU databases have been used to trial other aspects with the use of machine learning. These include weaning from ventilation, readmission and deterioration of patients.

ROLE OF ANAESTHETISTS

Anaesthesia Information Management Systems(AIMS) and Clinical Decision Support(CDS) Anaesthesia providers record data during the operating room however the data can be harnessed and interpreted to optimise the theatre environment. There are various ways in which the data may be used: improving the quality of patient care, decreasing costs of health care, enhancing reimbursement for cases ,improving documentation and monitoring physiological parameters and getting near real time information and providing intraoperative point of care recommendations.¹⁷

All of the above mentioned information together with near real time alerts and posthoc messages are fall under the umbrella of the term Clinical Decision Support. This extremely helpful to perioperative medicine and the many facets of which can be tailored to assist busy clinicians.

Practical examples are having algorithms that flag certain users who use high Fresh gas flow rates. The outliers are the people who need to be informed, thus a kindly worded email notifies that doctor of his high Fresh gas flow usage and gently reminds him to drop the excessive flow rates. Thus in this way, the entire department who has been adhering to guidelines escapes reprimand and a change is made. Below are examples of emails sent by Epstein for his department.¹⁷

Personalized FGF report for William Morton for Sevoflurane During the last 10 cases you performed with SEV, your average FGF during the interval from Surgery Begin to End was 2.49 L/min Your flow rate was 24.3% higher than our target of 2.00 L/min* Please try to reduce the flow rates during maintenance for your subsequent SEV cases.

* If the provider's FGF was $\leq 101\%$ of the target, this line was replaced with: "Congratulations on reaching the goal line. Keep up the good work!" If the provider's FGF was $\leq 110\%$ of the target the line, this line was replaced with: "You are almost at the goal line. Thank you for your efforts so far." (FGF = fresh gas flow; MAC = minimum alveolar concentration)

Next Blood pressure monitoring is more often than we would like to admit, delayed. In a quality improvement project using AIMS, the 2nd case study that Epstein uses, is the delay in blood pressure monitoring. A pop up is displayed on the workstation in real time, if blood pressure monitoring is not initiated within 10 minutes of entering the operating room or switching on the anaesthesia machine. The provider then has the option to acknowledge this or delete the message.

In a survey in Germany conducted from 2019 to 2020 during the COVID 19 pandemic, staff highlighted key concerns. The high number of false positive alarms and many sensor cables are a significant problem. Many respondents felt that wireless sensors and reducing the number of false positive alarms would make ICU work easier. They agreed that continuous remote patient monitoring would enable fewer practitioners to care for a high number of patients especially in times of pandemics.¹⁸

Fluid responsiveness: automation

In theatre Passive leg raising test is not a practical option. Clinicians require robust and easy to use methods enabling the prediction of fluid responsiveness even when the tidal volume is less than 7 mL/kg. Lung Recruitment Maneuvers are part of protective mechanical ventilation strategies and are susceptible to induce significant changes in hemodynamics. Their quantification could be automatized so that the detection of fluid responsiveness would become part of the functionalities of future anesthesia machines and mechanical ventilators.¹⁹ This would be a great addition to our armamentarium.

ETHICS

Ethics of Artificial Intelligence

Bias

Machine learning does unfortunately lend itself to bias. Machine modelling presents a problem based on design. 23 sources of bias were identified in a paper by Mehrabi.²⁰ One may argue that as clinicians we are biased when we make decisions on a daily, when risk stratifying patients. The main concern is that of racial gender bias and the relationship of risk modelling to informed consent²¹. Doctors may not have time to evaluate the model's development. This may lead to the idea that variables not included are non-significant, whereas it may have not been included previously for other reasons.²¹ Other bias may occur with 'auto machine learning'.

Risk Prediction

The issue with risk prediction is the chain of events that follow when algorithms make incorrect assumptions. Clinicians then present risks to patients and colleagues which then sets off sequential reactions. The American Heart Association's 'Get with the Guidelines' Heart Failure Risk Score assigns 3 additional points to patients who are 'non- Black'. Thus when White patients present with the same symptoms and clinical picture the algorithm predicts a higher risk of mortality for White patients thus doctors are more likely to watch these patients closely but also allocate more resources to them.²² In healthcare, the prognosis is important and especially in resource limited settings this is very important. Doctors and medical personnel might limit the choices offered to patients when certain risks weigh in as high.

Health insurance like all insurance, aim to make profitable economic decisions. Risk calculators may then decide what interventions may be appropriate for patients and bypass autonomy.²¹

Artificial intelligence systems are approved by the US Food and Drug Administration-regulated medical devices to help with clinical decision support. This is different from decision making but this then influences our management of patients. The question arises...who is responsible for the liability when adverse outcomes occur? Machine learning and AI use databases when developing algorithms. It is reassuring to note that the US National Institute of Health's All of Us Research Program has been tasked with addressing the issue of lack of diversity in these.

As we move forward, and embrace the assistance that AI provides, we can evaluate AI based research. Traditionally journals are dominated by case control studies and randomized control studies, yet we can start including the different models as well as examining the datasets to assess bias. The adoption of guidelines by scientific journal bodies will help to improve the quality of work published. See section below for further information regarding guidelines.

Evaluation and Transparency

Machine learning and AI needs to be accurate and thus requires validation for all the reasons mentioned previously. The only way to illustrate the superiority of AI is clinical trials. There was a total of 368 clinical trials in the field of AI or ML registered on ClinicalTrials.gov. in the United States of America as of July 2019²³. The Consolidated Standards of Reporting Trials (CONSORT) and Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statements are used to assess and evaluate studies of predictive models. However, these are not sufficient to evaluate the special needs of AI.

Liu²³ are preparing extensions of the CONSORT and SPIRIT statements, CONSORT-AI and SPIRIT-AI, which will specifically focus on clinical trials in which the intervention includes an ML or other AI component. The transparent reporting of a multivariable prediction model for individual prognosis or diagnosis-ML extension by Collins and Moons looks at the validation stage of predictive AI model.²⁴ All the above standards will help ensure that transparency is maintained, as the ML models are taken from observational studies to prospective clinical trials.

AI IN A RESOURCE LIMITED ENVIRONMENT

AI in a resource limited setting

There are many areas with very little manpower and skill in developing countries. AI once it has been made available commercially would offer patients in these locations access to healthcare and the possibility of having treatments which may cure their disease.

For example, the automated closed loop systems that would deliver an anaesthetic in New York could provide the same or equivalent anaesthetic in rural Africa. It would also enable more theatres to be monitored and operated concurrently which is also very helpful during missions to rural areas.eg Operation Smile. While some argue that the expert skill of an Anaesthetist is not present for the case...if more people would benefit without harm, it's a win. The same concept changed the automation of the car industry.

LIMITATIONS

Machine learning is excellent for high volumes of patients and data and has been shown to make a significant difference in wards. However, it may be argued that the information one receives is only as good as the information entered into the machine. In the theatre environment data that is processed is subject to interference, artifacts and physiological data may be damped. Missing or inaccurate data may lead to an inaccurate endpoint.

Currently there are no machines that are prescriptive. There are predictive algorithms that allow us a warning ahead of the clinical scenario like sniffers detecting that something started to happen.²⁵

COVID19 and AI

The pandemic that started in 2019 has been devastating. We are currently in the 2nd wave and like the Spanish flu that occurred....the 2nd wave is worse than the first wave. There have been many health care workers who have been tirelessly working to help many patients. The result is that they themselves have become infected and have succumbed to the illness. The sequential effect has led to many people questioning their choice of careers.

The ICUs are overflowing and there is simply not enough staff to care for patients. There are great limitations with manpower. The use of personal protective equipment has also led to higher waste and it cannot be recycled due to the biological hazard. There are many things to learn from the pandemic.

The question we need to ask is: Why would one choose to work as a medical professional following the pandemic?

If it was marketed as having a lower biological risk to people, higher remuneration, good working hours and job satisfaction, then many people would sign up.

AI can help achieve this goal. By introducing automated systems that enable limited times around high risk patients, we limit our exposure to the virus. In ICUs, we have a higher bed capacity since we can monitor patients remotely and manage patients with pharmacological

robots that can be topped up. This allows human work to be targeted and reallocated to essential tasks. The reduced costs and wastage translate into efficient ICUs, theatres and hospitals. This in turn allows for higher bed capacities which allow more people to benefit from care, which can translate into lower mortality.

Sadly the pandemic may not be the last. So we need to adapt to take care of ourselves as healthcare workers. This means partnering with automated devices and robots of the future.

CONCLUSION

The limitations noted thus far is that although we know medical personnel require advances in patient monitoring...we have not collaborated with engineers to develop many prototypes.

This how Thomas Hemmerling describes the future in his editorial.

How will we do anesthesia in the future? It is 2030 and I am scheduled to supervise anesthesia for a 40-yr-old patient undergoing laparoscopic cholecystectomy.

In the operating room, I tell my robot—let's call it A-bot—about the surgery, the patient, and the type of anesthesia I would like performed. "Can I get a propofol, remifentanil-based anesthesia? Can we target 45 as a Bispectral Index? A-bot, can you maintain mean arterial pressure around 65? Can you maintain cardiac index during surgery of more than $2.5 \text{ l} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$? A-bot, I would like to use rocuronium, bolus application is good enough, but please keep neuromuscular blockade lower than 25% at all times. Please choose a respiratory rate of 12 and adjust tidal volumes to maintain end-tidal carbon dioxide of 32 mmHg in 50% air! Let's provide preemptive analgesia using morphine and ketorolac—usual dosages, A-bot, you know."

A-bot answers: "Sure will, Tom—you keep me informed about surgical progress?"

"Yep."¹⁰

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