Contents lists available at ScienceDirect

Brain and Spine

journal homepage: www.journals.elsevier.com/brain-and-spine

Advanced neuromonitoring powered by ICM+ and its place in the Brand New AI World, reflections at the 20th anniversary boundary

P. Smielewski^{a,*}, E. Beqiri^a, C. Mataczynski^b, M. Placek^a, A. Kazimierska^c, P.J. Hutchinson^{a,b,c,d}, M. Czosnyka^{a,1}, M. Kasprowicz^{c,1}

^a Brain Physics Laboratory, Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK

ABSTRACT

ideas at the bed-side.

^b Department of Computer Engineering, Faculty of Information and Communication Technology, Wroclaw University of Science and Technology, Wroclaw, Poland

^c Department of Biomedical Engineering, Faculty of Fundamental Problems of Technology, Wroclaw University of Science and Technology, Wroclaw, Poland

^d Neurosurgery Department, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

Introduction: Adoption of the ICM+® brain monitoring software by clinical research centres worldwide has been continuously growing over the past 20 years. This has necessitated ongoing updates to accommodate evolving neuromonitoring research needs, including recent explosion of artificial intelligence (AI).

Research question: We sought to provide an update on the current features of the software. In particular, we aimed to highlight the new options of integrating AI models.

Material and methods: We reviewed all currently available ICM+ analytical areas and discussed potential AI based extensions in each. We tested a proof-of-concept integration of an AI model and evaluated its performance for real-time data processing.

Results: ICM+ current analytical tools serve both real-time (bed-side) and offline (file based) analysis, including the calculation engine, Signal Calculator, Custom Statistics, Batch tools, ScriptLab and charting. The ICM+ Python plugin engine allows to execute custom Python scripts and take advantage of complex AI frameworks. For the proof-of-concept, we used a neural network convolutional model with 207,000 trainable parameters that classifies morphology of intracranial pressure (ICP) pulse waveform into 5 pulse categories (normal to pathological plus artefactual). When evaluated within ICM+ plugin script on a Windows 10 laptop the classification of a 5 min ICP waveform segment took only 0.19s with a 2.3s of initial, one-off, model loading time required. *Conclusions*: Modernised ICM+ analytical tools, reviewed in this manuscript, include integration of custom AI models allowing them to be shared and run in real-time, facilitating rapid prototyping and validating of new AI

1. Introduction

ICM+® is a Windows desktop clinical research software for high resolution (i.e., full waveform at maximum available sampling frequency) physiological monitoring data integration and real-time analysis. It was developed in the early 2000s at the Brain Physics Lab, Dept of Clinical Neurosciences, University of Cambridge (https://icmplus.neurosurg.cam.ac.uk) and is managed by Cambridge Enterprise Ltd, the subsidiary of Cambridge University, which has been licensing it to other clinical research centres starting from 2004. Since its first public release, ICM + has been gradually taken up by an increasing number of

centres globally (as of writing this manuscript exceeding 300 sites). Given the continuous expansion of the user base, a plethora of analytical functions have been integrated over time to meet evolving research needs. However, this growth necessitates periodic updates for the community to ensure users can navigate the software effectively and capitalize on its full potential.

Meanwhile, in the recent years, the deep learning-based artificial intelligence (AI) revolution has erupted across all areas of science and industry, including healthcare (Ngiam and Khor, 2019; Mazzanti et al., 2018; Jiang et al., 2017; Ngiam and Khor, 2019; Mazzanti et al., 2018; Jiang et al., 2017). This has been fuelled by many factors, notably the

https://doi.org/10.1016/j.bas.2024.102835

Received 30 June 2023; Received in revised form 6 May 2024; Accepted 17 May 2024 Available online 19 May 2024

2772-5294/© 2024 Published by Elsevier B.V. on behalf of EUROSPINE, the Spine Society of Europe, EANS, the European Association of Neurosurgical Societies. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).



ARTICLE INFO

Handling Editor: Dr W Peul

Advanced neuro-monitoring

Intracranial pressure analysis

ICP pulse wave morphology

Traumatic brain injury

Pulse shape index

Keywords.

ICM+ software





^{*} Corresponding author. Peter Smielewski, Brain Physics Laboratory, Division of Neurosurgery, Dept of Clinical Neurosciences, University of Cambridge, UK. *E-mail address:* ps10011@cam.ac.uk (P. Smielewski).

¹ These authors contributed equally.

emergence of open source, easy to use frameworks for building, training and evaluating neural networks like TensorFlow (2023), Keras (2023) or PyTorch (2023). In parallel, the data science skills proliferated widely, also in the medical research community, with a large volume of manuscripts published across the whole range of healthcare applications, including critical care (Yoon et al., 2022). One hugely attractive quality of the deep learning models is that they can learn the salient features of the data without the necessity of manual engineering (extraction) of those features first. Although this requires large volumes of available data, and the data needs to fulfil the 5 V's big data requirements (Zhou et al., 2017), it is only a matter of time before the critical mass of such data will be met in any area of healthcare. In the neuro-monitoring case, this will be accelerated by the increasing understanding of the importance of full resolution data collection and growing support by the industry. At the same time, new, more powerful network architectures are being developed and made available to individual data scientists, along with pretrained models for a growing number of data types, or foundation models, allowing faster model building and training (Hendrycks et al., 2019; CRFM, 2023). The model training process includes the network weights learning, validation and testing on fresh datasets. Such process requires, in general, powerful hardware, and may take a long time, often great many days (or weeks), to complete (Chollet, 2021). However, once trained, the evaluation of such models can be easily achieved by hardware with moderately advanced specifications, and the prime example here are smart phones running apps powered by AI models, like Google's Magic Eraser App (Google, 2023), or Stable Diffusion on an Android phone (Qualcomm, 2023). Thus, it should be perfectly feasible for a bed-side ICU monitoring data integration tool like ICM+ to take advantage of such an approach in real-time processing, given that appropriate AI environment is provided and interfaced with. This would offer an easily accessible platform for experimentation with AI models, right at the bedside, in order to attempt validation of the usefulness of such new algorithms in clinical practice. Therefore, it has become imperative to raise awareness about such developments in the ICM+ community.

Moreover, the past decade or so has witnessed a strong growth in scripting skills amongst the clinical community. Environments/languages like Matlab (Mathworks Inc), R (R-Project, 2023) and Python (2023) have become familiar to the new generation of neuro-intensivists and neurosurgeons, who are getting well accustomed to simple and often quite complex coding activities. In addition, the advent of AI tools like ChatGPT (OpenAI. ChatGPT, 2023) and similar, which can easily assist in coding (e.g. GitHub Copilot (GitHub, 2023), Amazon CodeWhisperer (Amazon, 2023)), makes it even more likely that the end-user clinical researches will be able to take full advantage of such a plugins capability.

Our objective was to offer a comprehensive update to the ICM + community regarding the ICM+ analytical tools developed over the years, catering to both online and offline analyses. We wanted particularly to emphasize the flexibility in incorporating Python scripts, showcasing how AI integration can seamlessly occur within this widely-used software for real-time applications.

2. Material and methods

We conducted a review of ICM+ and its analytical features, describing its native scripting capabilities and indicating ways of adding custom extensions. To highlight the integration of AI within ICM+, we introduce a proof-of-concept plugin that implements a recently proposed method for calculating an index of cerebral compliance based on ICP pulse shape analysis (Mataczynski et al., 2022).

3. Results

3.1. ICM + as a mature tool for multimodal monitoring clinical research

The ideas incorporated in ICM+ from its birth were in fact a direct continuation of an earlier, MS DOS, version, ICM, developed at Warsaw University of Technology (Czosnyka et al., 1994) and used in the nineties in adult ICU at Addenbrookes Hospital, Cambridge, before being replaced by its modern successor. The ICM+ software originally focused on real-time processing of neuro-monitoring data streamed from bed-side monitors that used analogue output for their data export (Smielewski et al., 2005). Gradually, as the digital protocols of data export started phasing out the analogue output solutions, ICM+ has acquired more and more individual interface modules, whose count has by now reached almost 60. However, the high-resolution data collection and integration feature has always been only a means to an end, an enabling feature, that presented the possibility of processing data streams from bed-side monitors in order to extract derived metrics that could better reflect changing pathophysiological process than the original measurements alone. ICM+ offers a real-time data processing engine that allows the user to put together even complex computation pipelines by decomposing them into individual little steps using the moving calculation window principle (calculations performed on a data buffer/window which is then moved forward by a specified amount), as outlined in Fig. 1. This simple technique allowed to explore many ways of processing of neuro-monitoring data and, in time, produced several derived metrics that have received a lot of attention by the neuro-critical care community: the pressure reactivity index (PRx) (Czosnyka et al., 1997), the mean flow index (Mx) (Czosnyka et al., 1996), the autoregulation index (COx) (Brady et al., 2007), the cerebrospinal compensatory reserve index (RAP) (Kim et al., 2009), the optimal cerebral perfusion pressure (CPPopt) (Aries et al., 2012) and optimal blood pressure (ABPopt) (Silverman et al., 2019), and many more (Zeiler et al., 2017; Varsos et al., 2014). These have been investigated in retrospective or prospective studies for several pathologies like adult (Zeiler et al., 2020) and paediatric (Young et al., 2016) traumatic brain injury, neonatal intensive care (Rhee et al., 2016), spine injury (Phang et al., 2015), subarachnoid haemorrhage (Papaioannou et al., 2021), hydrocephalus (Smielewski et al., 2012), cardiac arrest (Sekhon et al., 2016), stroke (Sykora et al., 2019), sepsis (Steiner et al., 2009), and intraoperatively in cardiac surgery (Brown et al., 2019) and neurosurgery (Begiri et al., 2024). In some cases, such metrics have been implemented in clinical protocols (Menon and Ercole, 2017; Khellaf et al., 2019). The software has also been applied in experimental conditions (Lee et al., 2011), as well as an educational tool (e.g. Applied Neuromonitoring workshops at Neurocritical Care Society annual meetings (Neurocritical Care Society, 2022), Global Neuro workshops (Global Neuro, 2022), ICM + user group meetings, and others).

On the whole, the software has contributed to close to 170 peerreviewed publications in medical journals as of the date of this writing, and has been used as a platform for several big clinical trials/ multicentre data collection projects, including CENTER-TBI (Maas et al., 2015), BONANZA (Leach and Shutter, 2021), STARSHIP (Agrawal et al., 2023), REVERT (Smielewski, 2023a), PANGEA (Pressura Neuro, 2023), BrainVent (Beqiri et al., 2023a) and COGiTATE (Tas et al., 2021).

3.1.1. ICM + calculation engine and the plugins extensions

ICM+ is a fully configurable tool for integrating physiological monitoring data streams, either on-line from the bed-side monitors or off-line using retrospective datasets, and applying signal analysis methods to those data streams. There are several areas that benefit from functional expansions via plugins (Fig. 2) which are briefly summarized here:

a. The real-time calculation engine, fed either from live data streams or recorded data files.



Fig. 1. Schematic diagram of the ICM + data integration and real-time processing engine. The waveforms and numeric data are streamed into the laptop running ICM + via an analogue/digital converter or directly digitally, via a serial or a network connectivity. The data streams are integrated and then processed using moving calculation windows at several layers of the pipeline. Each layer of the pipeline receives data streams from the output of the previous layer. The rate of the data buffer progression defines the sampling rate of the output streams. These are independent for each parameters calculated, except at the final stage where all trends are presented to the visualisation charts at the same final rate, e.g 1 per minute.



Fig. 2. Areas for plugin expansions within ICM+ . The areas within ICM+ that are suitable for plugin expansion are represented, including the real-time calculation engine for processing data streaming from the bed-side monitors (the dialog lists functions available to use in the formulas), the signal calculator (showing an example of intracranial pressure signal detrending), the custom stats tool (where custom formulas or macros could be used to define metrics), the ScriptLab tool (for in depth, interactive, exploration of data), the Custom Charts (showing an example of a multiscale entropy chart) and batch tools (showing configuration of batch summary statistics to be performed on all dataset in the folder).

The main concept of this engine is that it processes the data in stages of progressively reduced granularity of the resulting time trends of calculated parameters, as illustrated in Fig. 1. This general architecture has been previously described (Smielewski et al., 2005). Essentially, the first layer, 'Virtual Signals' allows to apply different signal conditioning/transformation functions to the full data stream. All the subsequent layers require specification of a calculation buffer length, for example 10 s worth of data samples, and the rate at which this calculation window should be advanced (for example 1 s at a time, thus allowing for 90% overlap in this case). These two parameters are independent from each other. Calculations are prescribed by putting together formulae using a battery of signal processing and statistical time series analysis functions.

b. The Signal Calculator, used for off-line data analysis. This tool allows to work on the whole data set in one go. It allows to treat or transform existing data time series or create new ones which can then be saved along with the original data. The calculation configuration includes, as in the real-time calculation engine, specification of formulae but it also allows for more elaborate short scripts to be defined.

- c. The Custom Statistics, used to apply custom summary statistics calculations on user selected sections of the data in trend charts.
- d. The Batch Tools, which allow to repeat the same, user defined, signal analysis on a large volume of patients' datasets, optionally limited to selected time periods defined relative to specific time points, like the date/time of the injury, or specific annotated events.
- e. The ScriptLab, a data exploration workbook, which allows to interrogate interactively data from a selected section of recording. This tool also allows to define, debug, and test macro scripts that can later be used in all the places described above. The macros can also be easily shared with other users.
- f. The charts for visualising the data in the time series datasets. The battery of charts available for the users can also be extended via plugins which can take control over what type of chart to use to visualise the data and add visual annotations with defined shapes such as points, lines, ovals, rectangles, arrows etc.

3.1.2. ICM + Python integration

to restart the software, allowing for speedy experimentation. In order to facilitate development and debugging of the Python code, the terminal output is captured and redirected either into the ScriptLab window in ICM+, if that tool is used for explorations/testing, or into a log window, if the Python function is used in the real-time engine.

3.2. AI integration in ICM+ - The Pulse Shape Index plugin

All the common machine learning (ML) libraries require 64-bit version of Python, and thus it's host software ICM+. Furthermore, given the complexity of ML libraries interdependencies Python scripts are usually run within pre-defined environments managed by tools like for example Anaconda (Anaconda Inc, 2023) or Miniforge (GitHub). To that effect, a chosen Python engine/environment path needs to be configured in the system settings in ICM+. For Anaconda environments (but not for Miniforge), ICM+ needs to be launched from a Windows batch file that activates the environments first, e.g:



Integration of AI within ICM+ is facilitated via the Python plugin interface capable of evaluating trained deep learning AI models in realtime, as well as on retrospective data, in all the extendible areas of ICM+ (Fig. 2). The user interface includes a Python extension definition dialog, which allows the user to specify the description of the function to be added, how many input signals the function should expect, and define additional parameters/options, including their types (Fig. 3). Once the function specification is completed, a function definition file in xml format is created, along with a skeleton Python script template ready for the user to fill in with the action/calculation code (Fig. 4). These two files are automatically stored within the Python plugins folder and get automatically registered at software restart, with the function names getting an automatic prefix 'Py' (Figs. 5 and 6). From then on, modifications to the Python code are picked up immediately without the need

This is equivalent to running the two commands in Command Prompt, one after the other.

The plugin interface has been successfully tested with various versions of Python 3 (up to 3.10), both with Anaconda and Miniforge environments.

The proof of concept plugin presented and evaluated here is a comprehensive implementation example for ICP pulse shapes classifier model developed by Mataczynski et al. (2022).

3.2.1. Compliance classification model

It has long been postulated that the relationship between the three distinct peaks in an ICP pulse reflects cerebral compliance (Germon, 1988). Specifically, the ratio of the first peak, denoted P1, to the second



Fig. 3. ICM + **Python plugin definition user interface**. The interface allows to define a function to be implemented by the Python script, and specify the number of input data variables expected as well as a number of options (additional parameters) that will need to be defined by the user at the time of using the function in the formulae. Once defined, a template python script and its accompanying descriptor file will be created automatically.



Fig. 4. Example of the generated plugin Python files by the ICM+ **plugin definition wizard.** Panel A) shows an example of a plugin definition file, while panel B) shows the accompanying Python scripts template. The user simply needs to fill in the function 'calculate' with custom script (or in general a call to an external script, which may include calls to a machine learning framework, like Keras or PyTorch).



Fig. 5. Using Python functions within the real-time calculation engine.

Panel A) presents a typical configuration editor used to set up a calculation within the calculation engine. In the formula bar, the function created with the python plugin ('PySomeFucntion ()') was called and applied to ICP, and the parameters of the function were defined. Both calculation period and update period were set at 10 s. The variable derived with this calculation was called 'SomeIdx'.

Panel B) presents the visualisation of the time trends resulted from the analysis of the data, and in particular the variable 'SomeIdx' is presented in the bottom chart. ICP: intracranial pressure; ABP: arterial blood pressure; PbtO2: brain oxygenation.

peak, denoted P2, has been quoted as the compliance index (Kazimierska et al., 2021). However, the P1 peak can often be very difficult to detect, particularly in the critical circumstances of increased ICP and markedly decreased compliance. Hence, Mataczynski et al. proposed a deep learning algorithm to assess the overall pulse shape, rather the peaks only, and to assign that shape to one of four classes of progressively decreasing cerebral compliance (plus one class of artefactual/disturbed shape) (Mataczynski et al., 2022). In order to increase the resolution/sensitivity as well as the robustness of this approach, the authors then proceeded to define a combined index named the Pulse Shape Index (PSI) which assesses the proportion of the shapes of each type within the calculation window of several minutes (Fig. 7) (Uryga et al., 2022; Kazimierska et al., 2023). The higher the index, the more likely the compliance is low or disturbed.

The classification model was developed using Python PyTorch machine learning framework (PyTorch, 2023). For the purpose of the current manuscript, no additional work was done to the classification model above and beyond that reported by Mataczynski et al.

The model was trained on high resolution ICP data acquired in 50 patients (39 patients suffered from traumatic brain injury and 11 had confirmed aneurysmal subarachnoid haemorrhage) admitted to the Neurointensive Care Unit (NICU) of University Hospital in Wrocław, Poland, between 2014 and 2019. The study was conducted with approval from the Bioethics committee at the Wroclaw Medical University, Poland (approvals no KB–624/2014 and KB–134/2014). The patients were selected out of all patients admitted to the NICU during this period on the basis of availability and acceptable quality of ICP recordings. Details of this cohort, the model and the pre-processing steps are provided in the original publication (Mataczynski et al., 2022).

3.2.2. The Pulse Shape Index plugin implementation

The compliance index PSI function plugin was written using the



Fig. 6. Using Python functions within the ScriptLab. The python function created with the python plugin ('pysomefunction ()') is available to use in the toolbox in the extended functions tab (Ext Functions). Here it also shows an example of how statements printing messages from within the script show up in the workspace, allowing convenient debugging messages to be incorporated in the script.

PyTorch framework. Details of the model itself are given elsewhere (Mataczynski et al., 2022), but briefly, it is based on convolutional architectures with residual connections, with a total of 207,000 trainable parameters and the input of ICP pulses segmented using a modified Scholkmann algorithm proposed by Bishop and Ercole (2018). The Python code for this plugin is available at the public repository GitHub, including the trained weights (Mataczynski, 2023).

Within the ICM+ python plugin file the main 'Calculate' function (Fig. 5) simply calls an external module that implements the model. At each invocation it is passed the data buffer (length defined by the user, as explained in the section 3.1), the time stamp of that buffer, the variables identifiers, and the data sampling frequency. It returns the PSI index calculated through evaluation of the pretrained model, parameters of which (i.e. the weights of the pre-trained network) are distributed along with the code. Once this function is added to the data analysis configuration profile, and thus loaded with the data acquisition/analysis project, the use of that function is seamless for the user who then sees the PSI trend being generated and integrated with other multimodality time series, like ICP, CPP, Prx, PbtO2 etc. (Fig. 8).

3.2.3. Training vs running hardware and time benchmarks

The hardware used for training of the model in Mataczynski et al. was a Windows 10 workstation with GeForce RTX 3090 GPU, 32 GB memory, and Ryzen 3900XT processor, powered by NVIDIA CUDA drivers. The hardware used to evaluate the model within the ICM+ plugin environment was a Windows 10 laptop, processor Ryzen 9 5900HS, 16 GB memory.

At the time of training the extracted pulses and the annotations were fed into the model 100 times (100 epochs) and the whole training process took 4 min (Mataczynski et al., 2022). On the other hand, its execution within ICM+ for evaluating streams of ICP waveforms in real-time on the test laptop took only 0.19 s when fed 5 min' worth of ICP data at 100 Hz sampling frequency. This could therefore be easily accommodated within the pipeline of real-time calculations with a rate of one value generated every 10s or 1min, as it is performed by default in TBI patients when processing neuro-monitoring data for calculations of indices like PRx. There is an initial penalty of 2.3s needed for the model loading and initialisation, but that is done only once at the start of data acquisition/analysis.

4. Discussion

ICM+, at its 20th anniversary, is well known within the academic neuro-intensive care community, with great many installations world-wide. In this manuscript we provided an updated review of the impact of the software as a clinical research platform, the analytical tools developed over the years for waveform data analysis, and the integration of AI within this platform.

The importance of processing of waveforms of measured modalities in an intensive care scenario has been understood in some areas of monitoring more than others. For example, processing of electroencephalography (EEG) and electrocardiography (ECG) signals has





STEP 3: ICP PULSE CLASS TIME COURSE

STEP 4: PULSE SHAPE INDEX CALCULATION





Fig. 7. The principle of the pulse classifier, which was implemented here as a proof-of-concept plugin for ICM+. The algorithm first extracts individual ICP pulses, then classifies them using pre-trained deep neural network (when plotted against time at long scales variability of pulse shape classification is apparent), then calculates a weighted average class assignment index over an assembly of pulses extracted from a period of 1 min, and plots it against time.

attracted a lot of attention and is generally well appreciated. Other intensive care monitoring modalities, like arterial blood pressure (ABP), intracranial pressure (ICP), brain oxygenation (local tension as per PbtO2, or regional saturation as per near-infrared spectroscopy – NIRS - derived rSO_2) and cerebral blood flow measures (eg. thermodilution, Hemedex, or transcranial Doppler, TCD, derived), have taken perhaps a bit longer to be appreciated for their full waveform complexity. This is likely because the simplest metrics derived from them, such as beat-to-beat mean values, as well as systolic and diastolic values, already provide a certain, and immediately interpretable, clinical information. However, in the clinical research community there has long been understanding that careful analysis of the full waveforms of those modalities, particularly ICP, can provide additional 'windows' into the

cerebral physiology and pathophysiology (Czosnyka et al., 2007). In order for these voices to be heard and appreciated, it has been essential to provide real-time analysis of waveforms and importantly a possibility for those analyses to be freely configured and experimented with right at the bedside (Smielewski et al., 2005). ICM+ offered this kind of framework, which is ultimately pivotal for advancement of neurocritical care monitoring.

ICM+ development is also supported by regular user group meetings, hands on workshops (ICM+ Workshop, 2018) and online lectures (Czosnyka and Smielewski, 2022), allowing dissemination of the knowledge and experience gained in Addenbrooke's Hospital by the Brain Physics Lab over the past three decades (Donnelly et al., 2019). The concepts behind it are such that it allows the more-technically



Fig. 8. Time trend of PSI parameter. The ICM+ layout shows minute-by-minute time trends of ICP (top chart) and PSI over more than 4 h of a patient with subarachnoid haemorrhage. The minute-by-minute time trend of PSI was generated according to the function defined within the calculation engine in ICM+, as shown in the configuration editor window. The python plugin-based function 'PyClassifyWaveforms' was applied to ICP over 300 s of data buffer and updated every 60 s.

minded clinicians to take advantage of its comprehensive calculation engine in order to create, extend or modify data acquisition and analysis configurations initially provided, facilitating clinically and physiologically guided explorations in individual patients or on populations. On the other hand, data scientists tend to work within their own comfortable programming/analytical environments, with Python being the prime candidate when deep learning neural networks are being used. In order to facilitate further advances in the field, active collaborations between clinicians and data scientists are required, and this should be aided by availability of a common platform that is able to provide the analysts with the data they badly need and at the same time allow to test-run promising models directly at the bedside. This is very much in contrast to the natural language or image processing areas of AI development, where there is an abundance of highly varied and often annotated data available to data scientists, and which does not require any additional expertise to interpret.

As exemplified by the successes of the ICM+ provided metrics like PRx, COx, and RAP (Czosnyka et al., 1997; Brady et al., 2007; Kim et al., 2009), much can be achieved by stacking up standard signal/time series analysis functions such as moving average and correlation coefficient. However, often more complex algorithms are necessary that involve calculation loops or conditional statements, and these require custom code to be written for their implementation. For example, the CPPopt algorithm has been implemented in ICM+ as a 'special' extended function, available to the users in their individually configured 'pipeline' of analysis (Smielewski et al., 2005; Beqiri et al., 2023b). Metrics that the function provides can then be used in much the same way as any of the standard statistical functions for further finetuning of the ultimate 'final' derived parameters. However, any addition of such functions, or they subsequent modifications, requires full new software releases. On the other hand, the concept of plugins allows flexible, custom extension of software functionality by third parties. Early on, ICM+ provided a plugin interface that allowed computer scientists to develop extensions using compiled languages like C or C++. Such extensions could offer extra 'special' functions to be added to the battery of functions in the ICM+ calculation engine. One example of such a plugin is the non-invasive ICP plugin originally created and managed by the Chemnitz University of Technology (Schmidt et al., 2018), now distributed freely with ICM+. These solutions provide high performance of computation but are difficult to modify as they require support from the developers. ICM+ innately offers the ability to add simple user scripts or macros to the battery of available functions, and this goes some way towards extending the possibilities of the end user. Nevertheless, the ultimate freedom for the user can only be provided by allowing the plugins to be written in interpreted languages which enable fast prototyping and explorations. The growth of the capabilities of ICM+ reflects the current trends, given it is foremost a tool for all the neuro-monitoring clinical research activities of the Brain Physics Lab (Smielewski, 2023b) and its many collaborators. The possibility of enhancing the ICM+ toolbox with Python scripts has already been possible for some time and there are a few creative examples of its use (Froese et al., 2021; Placek et al., 2021; McNamara et al., 2022). However, new developments in computer science are now placing increased demand on such a plugin system.

The push for integrating AI within ICM+ led to a successful and important extension of its plugin interface, exemplified here with the implementation of the compliance classification plugin. It allowed to create a mechanism whereby AI models created by data scientists working on advanced neuro-monitoring may be shared easily with all the members of the ICM+ clinical research community. This empowers the end-user clinician to take full advantage of the methodologies developed by their local collaborators and by data scientists from other centres. Yet at the same time, such development allows further on-site tweaking of the whole analysis pipeline, from bed-side monitoring data streams to the final visualisation of the derived metrics. The proofof-concept plugin for calculating the compliance index PSI using pretrained deep learning model based on analysis of ICP pulse wave performed well when run inside ICM+, easily allowing to trend this index against other parameters of the multimodal monitoring set up.

Due to ready availability of deep learning frameworks and relevant training materials many AI models are being proposed in the literature, also in the neuro-monitoring field (Liu et al., 2021; Güiza et al., 2017; Deimantavicius et al., 2022; Scalzo et al., 2012; Hüser et al., 2020; Quachtran et al., 2016). However, most do not move beyond the proof-of-concept stage, usually involving rather rudimental testing performed by the authors, and thus remain buried in the sea of publications with no clear pathway forward. Taking advantage of an environment already present in many clinical research centres is a natural option for quick validation/verification of models, driving forward improvements in the 'smart ICU' field (Al-Mufti et al., 2019).

The deep learning models are essentially huge neural networks, often with millions of parameters that need to be tuned based on the training data. This requires vast processing power, possibly with massive parallel processing architectures, and may take a very long time. In contrast, once these parameters are learnt, validated and tested on a fresh data set, ready to be used for processing of new data coming in, it takes surprisingly little time to evaluate these huge networks on a regular, modern laptop computer, not necessarily equipped with any special AI accelerators. This makes it feasible to harness the AI power within bedside solutions like ICM+ in order to integrate AI derived metrics within the whole battery of multimodal monitoring parameters. An even more powerful solution for an integrated ICU clinical decision support system is a scenario where data is continuously streamed across the network to a farm of high-performance servers, which then stream back the results of complex AI models evaluation to the bed-side visualiser. Such an enterprise level solution, with an example already elegantly implemented in Perth, Australia (McNamara et al., 2022) will also allow for continued, near real-time updating/retraining of the AI models finetuning them to individual patients. It is quite likely that similar systems, which are being pursued by others as well (CONNECT, 2023), will eventually become an integral part of the healthcare IT infrastructure, after the legal and ethical frameworks are well established (Moberg et al., 2022). Furthermore, this kind of infrastructure could enable bringing together all the parameters into a 'smart' alarm system alerting the attending physician to development of a detrimental event that warrants careful scrutiny of all the individual measurements, clinical assessments and laboratory tests, leading to appropriate corrective action, if possible (McNamara et al., 2023). Of course, this is also likely to be 'outsourced' eventually to an AI algorithm, as elegantly argued in (Komorowski et al., 2018) to a smaller or larger degree. Eventually, perhaps, but not just yet.

Meanwhile, local bed-side solutions like ICM+ continue to play their important role in pushing the boundaries of advanced neuromonitoring and enabling clinical research in this field at minimal costs.

5. Conclusions

In this work, we provided an overall update on the ICM+ platform analytical tools. We highlighted the most recent developments related to integration of AI within ICM+, via means of a proof-of-concept experiment. This demonstrated the ease with which AI models can be shared and run in real-time in neuro-monitoring platforms such as ICM+, with modest hardware requirements. The addition of Python based extensions, available for all the computational areas of ICM+, gives access to machine learning frameworks from within the ICM+ calculation engine and opens new possibilities for this already versatile, and well proven, tool for high resolution physiological monitoring data integration and real-time analysis. This could facilitate rapid prototyping and validating of new AI ideas, given relatively wide global spread of this software in clinical research centres. It will also ensure fruitful collaborations between the data scientists and clinicians, in particular those working with critically ill patients.

Funding

PS, MP were supported by REVERT project (https://revertproject.or g) funded by the ERDF (European Regional Development Fund) via the Interreg France (Channel) England Programme.

EB was supported by the Medical Research Council (grant no.: MR N013433-1) and by the Gates Cambridge Scholarship.

CM, AK, MK were supported by the National Science Centre, Poland (grant no. UMO-2019/35/B/ST7/00500).

PJH is supported by the National Institute for Health Research (NIHR): research professorship, Biomedical Research Centre and Global Neurotrauma Research group and the Royal College of Surgeons of England.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

Peter Smielewski reports a relationship with Cambridge Enterprise Ltd, Cambridge, U.K. that includes: consulting or advisory. Peter Smielewski has patent with royalties paid to Cambridge Enterprise Ltd, Cambridge, U.K. Marek Czosnyka reports a relationship with Cambridge Enterprise Ltd, Cambridge, U.K. that includes: consulting or advisory. Marek Czosnyka has patent with royalties paid to Cambridge Enterprise Ltd, Cambridge, U.K.

References

- Agrawal, S., Placek, M.M., White, D., Daubney, E., Cabeleira, M., Smielewski, P., et al., 2023. Protocol: studying Trends of Auto-Regulation in Severe Head Injury in Paediatrics (STARSHIP): protocol to study cerebral autoregulation in a prospective multicentre observational research database study [cited 2023 Jun 5] BMJ Open 13 (3), e071800. Available from:/pmc/articles/PMC10008199/.
- Al-Mufti, F., Dodson, V., Lee, J., Wajswol, E., Gandhi, C., Scurlock, C., et al., 2019. Artificial intelligence in neurocritical care [cited 2023 Jun 28] J. Neurol. Sci. 404, 1–4. Available from: http://www.jns-journal.com/article/S0022510X19302849 /fulltext.
- Amazon, 2023. AI Code Generator Amazon CodeWhisperer [Internet] [cited 2023 Jun 21]. https://aws.amazon.com/codewhisperer/.
- Anaconda Inc. Anaconda [Internet], 2023 [cited 2023 Jun 29]. Available from: https://www.anaconda.com.
- Aries, M.J.H.H., Czosnyka, M., Budohoski, K.P., Steiner, L.A., Lavinio, A., Kolias, A.G., et al., 2012. Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury. Crit. Care Med. 40 (8), 2456–2463.
- Beqiri, E., Smielewski, P., Guérin, C., Czosnyka, M., Robba, C., Bjertnæs, L., et al., 2023a. Neurological and respiratory effects of lung protective ventilation in acute brain injury patients without lung injury: brain vent, a single centre randomized interventional study [cited 2024 May 1] Crit. Care 27 (1). Available from: https:// pubmed.ncbi.nlm.nih.gov/36941683/.
- Beqiri, E., Ercole, A., Aries, M.J.H., Placek, M.M., Tas, J., Czosnyka, M., et al., 2023b. Towards autoregulation-oriented management after traumatic brain injury: increasing the reliability and stability of the CPPopt algorithm. J Clin Monit Comput [Internet] 37 (4), 963–976. https://doi.org/10.1007/s10877-023-01009-1 [cited 2023 Jun 5]; Available from: https://pubmed.ncbi.nlm.nih.gov/37119323/.
- Beqiri, E., García-Orellana, M., Politi, A., Zeiler, F.A., Placek, M.M., Fàbregas, N., et al., 2024. Cerebral autoregulation derived blood pressure targets in elective neurosurgery. J Clin Monit Comput [Internet] [cited 2024 Apr 30]; Available from: https://pubmed.ncbi.nlm.nih.gov/38238636/.
- Bishop, S.M., Ercole, A., 2018. Multi-scale peak and trough detection optimised for periodic and quasi-periodic neuroscience data. Acta Neurochir. Suppl. 126, 189–195.
- Brady, K.M., Lee, J.K., Kibler, K.K., Smielewski, P., Czosnyka, M., Easley, R.B., et al., 2007. Continuous time-domain analysis of cerebrovascular autoregulation using near-infrared spectroscopy. Stroke 38 (10), 2818–2825.
- Brown, C.H., Neufeld, K.J., Tian, J., Probert, J., Laflam, A., Max, L., et al., 2019. Effect of targeting mean arterial pressure during cardiopulmonary bypass by monitoring cerebral autoregulation on postsurgical delirium among older patients: a nested randomized clinical trial. JAMA Surg 21287, 1–8.
- Chollet, F., 2021. Deep learning with Python [Internet]. In: Deep Learn with Python, second ed. [cited 2023 Jun 5]; Available from: https://www.oreilly.com/library /view/deep-learning-with/9781617296864/
- Connect moberg analytics [Internet] [cited 2023 Jun 21]. Available from: https://moberganalytics.com/solutions/connect/.
- CRFM, 2023. On the opportunities and risks of foundation models [Internet] [cited 2023 Jun 21]. Available from: https://fsi.stanford.edu/publication/opportunities-and-risk s-foundation-models.
- Czosnyka, M., Smielewski, P., 2022. Brain Physics Lecture Series [Internet] [cited 2023 Jun 29]. Available from: https://icmplus.neurosurg.cam.ac.uk/home/resources/brai n-physics-lectures/.
- Czosnyka, M., Whitehouse, H., Smielewski, P., Kirkpatrick, P., Guazzo, E.P., Pickard, J. D., 1994. Computer supported multimodal bed-side monitoring for neuro intensive care. Int. J. Clin. Monit. Comput. 11 (4), 223–232.
- Czosnyka, M., Smielewski, P., Kirkpatrick, P., Menon, D.K., Pickard, J.D., 1996. Monitoring of cerebral autoregulation in head-injured patients. Stroke 27 (10), 1829–1834.
- Czosnyka, M., Smielewski, P., Kirkpatrick, P., Laing, R.J., Menon, D., Pickard, J.D., 1997. Continuous assessment of the cerebral vasomotor reactivity in head injury. Neurosurgery 41 (1), 11–19.
- Czosnyka, M., Smielewski, P., Timofeev, I., Lavinio, A., Guazzo, E., Hutchinson, P., et al., 2007. Intracranial pressure: more than a number. Neurosurg. Focus 22 (5), 5–11.
- Deimantavicius, M., Chaleckas, E., Boere, K., Putnynaite, V., Tamosuitis, T., Tamasauskas, A., et al., 2022. Feasibility of the optimal cerebral perfusion pressure relies distribution without a class the ister large. Sci Res (Internet) 19 (1): 1, 12
- value identification without a delay that is too long. Sci Rep [Internet] 12 (1), 1–12. https://doi.org/10.1038/s41598-022-22566-6. Donnelly, J., Czosnyka, M., Adams, H., Cardim, D., Kolias, A.G., Zeiler, F.A., et al., 2019.
- Twenty-five years of intracranial pressure monitoring after severe traumatic brain injury: a retrospective, single-center analysis. Clin. Neurosurg. 85 (1).
- Froese, L., Dian, J., Batson, C., Gomez, A., Sainbhi, A.S., Unger, B., et al., 2021. Computer vision for continuous bedside pharmacological data extraction: a novel application of artificial intelligence for clinical data recording and biomedical research. Front Big Data 4, 1–9. August.
- Germon, K., 1988. Interpretation of ICP pulse waves to determine intracerebral compliance. J Neurosci Nurs [Internet] 20 (6). Available from: https://journals.lww. com/jnnonline/Fulltext/1988/12000/Interpretation_of_ICP_Pulse_Waves_to_Dete rmine.4.aspx.
- GitHub conda-forge/miniforge: A conda-forge distribution. [Internet]. [cited 2024 May 1]. Available from: https://github.com/conda-forge/miniforge.
- GitHub, 2023. GitHub Copilot Code Generator [Internet] [cited 2023 Jun 21]. https: //github.com/features/copilot.
- [Internet] Global Neuro, 2022 [cited 2023 Jun 29]. Available from: https://globalneuro. org/EN/home.html.

P. Smielewski et al.

Google, 2023. Magic Eraser App [Internet] [cited 2023 Jun 21]. https://blog.google/pro ducts/photos/magic-eraser-android-ios-google-one/

- Güiza, F., Depreitere, B., Piper, I., Citerio, G., Jorens, P.G., Maas, A., et al., 2017. Early detection of increased intracranial pressure episodes in traumatic brain injury external validation in an adult and in a pediatric cohort. Crit. Care Med. 45 (3), e316–e320.
- Hendrycks, D., Lee, K., Mazeika, M., 2019. Using Pre-training Can Improve Model Robustness and Uncertainty [Internet] [cited 2023 Jun 5]. PMLR, pp. 2712-2721. Available from: https://proceedings.mlr.press/v97/hendrycks19a.html.
- Hüser, M., Kündig, A., Karlen, W., De Luca, V., Jaggi, M., 2020. Forecasting intracranial hypertension using multi-scale waveform metrics. Physiol. Meas. 41 (1).
- ICM+ Workshop, 2018 [cited 2023 Jun 29]. Available from: https://icmplus.neurosurg. cam.ac.uk/workshops/icm-workshop2018/.
- Jiang, F., Jiang, Y., Zhi, H., Dong, Y., Li, H., Ma, S., et al., 2017. Artificial intelligence in healthcare: past, present and future [cited 2023 Jun 5] Stroke Vasc Neurol [Internet] 2 (4), 230-243. Available from: https://svn.bmj.com/content/2/4/230.
- Kazimierska, A., Kasprowicz, M., Czosnyka, M., Placek, M.M., Baledent, O.,
- Smielewski, P., et al., 2021. Compliance of the cerebrospinal space: comparison of three methods. Acta Neurochir. 163 (7), 1979-1989.
- Kazimierska, A., Uryga, A., Mataczyński, C., Czosnyka, M., Lang, E.W., Kasprowicz, M., 2023. Relationship between the shape of intracranial pressure pulse waveform and computed tomography characteristics in patients after traumatic brain injury [cited 2024 May 5] Crit. Care 27 (1), 1-13. Available from: https://ccforum.biomedo entral.com/articles/10.1186/s13054-023-04731-z
- Keras, Keras, 2023. Deep Learning for Humans [Internet] [cited 2023 Jun 21]. Available from: https://keras.io/.
- Khellaf, A., Khan, D.Z., Helmy, A., 2019. Recent advances in traumatic brain injury. J. Neurol. 266, 2878-2889.
- Kim, D.J.D.-J., Czosnyka, Z., Keong, N., Radolovich, D.K., Smielewski, P., Sutcliffe, M.P. F.F., et al., 2009. Index of cerebrospinal compensatory reserve in hydrocephalus. Neurosurgery 64 (3), 494-501.
- Komorowski, M., Celi, L.A., Badawi, O., Gordon, A.C., Faisal, A.A., 2018. The Artificial Intelligence Clinician learns optimal treatment strategies for sepsis in intensive care [Internet] Nat. Med. 24 (11), 1716-1720. https://doi.org/10.1038/s41591-018-0213-5.
- Leach, M.R., Shutter, L.A., 2021. How much oxygen for the injured brain can invasive parenchymal catheters help? [cited 2023 Jun 5] Curr. Opin. Crit. Care 27 (2), 95. Available from:/pmc/articles/PMC7987136/.
- Lee, J.K., Brady, K.M., Mytar, J.O., Kibler, K.K., Carter, E.L., Hirsch, K.G., et al., 2011. Cerebral blood flow and cerebrovascular autoregulation in a swine model of pediatric cardiac arrest and hypothermia [cited 2023 Jun 5] Crit. Care Med. 39 (10), 2337. Available from:/pmc/articles/PMC3178742/.
- Liu, J., Guo, Z.N., Simpson, D., Zhang, P., Liu, C., Song, J.N., et al., 2021. A data-driven approach to transfer function analysis for superior discriminative power: optimized assessment of dynamic cerebral autoregulation. IEEE J Biomed Heal Informatics. 25 (4), 909–921.
- Maas, A.I.R., Menon, D.K., Steyerberg, E.W., Citerio, G., Lecky, F., Manley, G.T., et al., 2015. Collaborative European neurotrauma effectiveness research in traumatic brain injury (CENTER-TBI): a prospective longitudinal observational study [Internet] Neurosurgery 76 (1), 67-80 [cited 2023 Jun 5]. https://pubmed.ncbi.nlm.nih.gov/ 25525693/
- Mataczynski, C., 2023. ICM+ Intracranial Pressure Waveform Classification Plugin [Internet]. Available from: https://github.com/CMataczynski/ICMPWaveformClass ificationPlugin.
- Mataczynski, C., Kazimierska, A., Urvga, A., Burzynska, M., Rusiecki, A., Kasprowicz, M., 2022. End-to-End automatic morphological classification of intracranial pressure pulse waveforms using deep learning. IEEE J Biomed Heal Informatics 26 (2), 494-504
- Mazzanti, M., Shirka, E., Gjergo, H., Hasimi, E., 2018. Imaging, health record, and artificial intelligence: hype or hope? Curr. Cardiol. Rep. 20 (6).
- McNamara, R., Meka, S., Anstey, J., Fatovich, D., Haseler, L., Fitzgerald, M., et al., 2022. The monitoring with advanced sensors, transmission and E-resuscitation in traumatic brain injury (MASTER-TBI) collaborative: bringing data science to the ICU bedside [cited 2023 Jun 3] Crit Care Resusc 24 (1), 39-42. Available from: http //search.informit.org/doi/10.3316/informit.364827909671874.
- McNamara, R., Meka, S., Anstey, J., Fatovich, D., Haseler, L., Jeffcote, T., et al., 2023. Development of traumatic brain injury associated intracranial hypertension prediction algorithms: a narrative review [cited 2023 Jun 5] J. Neurotrauma 40 (5-6), 416-434. Available from: https://www.liebertpub.com/doi/10.1089/neu.20 22 0201
- Menon, D.K., Ercole, A., 2017. Critical care management of traumatic brain injury [Internet] [cited 2021 May 22]. In: Handbook of Clinical Neurology, first ed. Vol. 140. Elsevier B.V., pp. 239-274. https://doi.org/10.1016/B978-0-444-63600-3 00014-3
- Moberg, R., Moyer, E.J., Olson, D.W., Rosenthal, E., Foreman, B., 2022. Harmonization of physiological data in neurocritical care: challenges and a path forward [cited 2023 Jun 21] Neurocritical Care 37 (Suppl. 2), 202-205. Available from: https://pubmed. ncbi.nlm.nih.gov/35641807/
- Neurocritical Care Society, 2022.

Ngiam, K.Y., Khor, I.W., 2019. Big data and machine learning algorithms for health-care delivery. Lancet Oncol. 0 (5), e262-e273.

OpenAI. ChatGPT, 2023. Available from: https://openai.com/.

Papaioannou, V.E., Budohoski, K.P., Placek, M.M., Czosnyka, Z., Smielewski, P., Czosnyka, M., 2021. Association of transcranial Doppler blood flow velocity slow waves with delayed cerebral ischemia in patients suffering from subarachnoid hemorrhage: a retrospective study [cited 2023 Jun 5] Intensive Care Med Exp [Internet] 9 (1). Available from:/pmc/articles/PMC7994457/.

- Phang, I., Werndle, M.C., Saadoun, S., Varsos, G., Czosnyka, M., Zoumprouli, A., et al., 2015. Expansion duroplasty improves intraspinal pressure, spinal cord perfusion pressure, and vascular pressure reactivity index in patients with traumatic spinal cord injury: injured spinal cord pressure evaluation study [cited 2023 Jun 5] J. Neurotrauma 32 (12), 865. Available from:/pmc/articles/PMC4492612/
- Placek, M.M., Khellaf, A., Thiemann, B.L., Cabeleira, M., Smielewski, P., 2021. Pythonembedded plugin implementation in ICM+: novel tools for neuromonitoring time series analysis with examples using CENTER-TBI datasets [cited 2023 Jun 5] Acta Neurochir Suppl [Internet] 131, 255–260. Available from: https://pubmed.ncbi.nlm. nih.gov/33839
- Pressura neuro [Internet] [cited 2023 Jun 21]. Available from: https://pressuraneuro. com
- Python [Internet] [cited 2023 Jun 29]. Available from: https://www.python.org.
- PyTorch [Internet] [cited 2023 Jun 21]. Available from: https://pytorch.org/
- Quachtran, B., Hamilton, R., Scalzo, F., 2016. Detection of intracranial hypertension using deep learning. Proc - Int Conf Pattern Recognit. 0, 2491-2496
- Qualcomm, 2023. Stable Diffusion Android App [Internet] [cited 2023 Jun 21]. Available from: https://www.qualcomm.com/news/ong/2023/02/worlds-first-on -device-demonstration-of-stable-diffusion-on-android.

R-project [Internet] [cited 2023 Jun 29]. Available from: https://www.r-project.org. Rhee, C.J., Fraser, C.D., Kibler, K., Easley, R.B., Andropoulos, D.B., Czosnyka, M., et al., 2016. The ontogeny of cerebrovascular critical closing pressure. Acta Neurochir. 122. Supplementum.

- Scalzo, F., Asgari, S., Kim, S., Bergsneider, M., Hu, X., 2012. Bayesian tracking of intracranial pressure signal morphology. Artif. Intell. Med. 54 (2), 115-123.
- Schmidt, B., Cardim, D., Weinhold, M., Streif, S., McLeod, D.D., Czosnyka, M., et al., 2018. Comparison of different calibration methods in a non-invasive ICP assessment model [cited 2023 Jun 5] Acta Neurochir Suppl [Internet] 126, 79-84. Available from: https://pubmed.ncbi.nlm.nih.gov/29492
- Sekhon, M.S., Smielewski, P., Bhate, T.D., Brasher, P.M., Foster, D., Menon, D.K., et al., 2016. Using the relationship between brain tissue regional saturation of oxygen and mean arterial pressure to determine the optimal mean arterial pressure in patients following cardiac arrest: a pilot proof-of-concept study [Internet] Resuscitation 106, 120-125. https://doi.org/10.1016/j.resuscitation.2016.05.019.
- Silverman, A., Kodali, S., Strander, S., Gilmore, E.J., Kimmel, A., Wang, A., et al., 2019. Deviation from personalized blood pressure targets is associated with worse outcome after subarachnoid hemorrhage [Internet] Stroke 50 (10), 2729-2737 [cited 2023 Jun 5]. https://pubmed.ncbi.nlm.nih.gov/31495332/
- Smielewski, P., 2023a. Interreg reversible dementia project [Internet] [cited 2023 Jun 21]. Available from: https://revertproject.org/.
- Smielewski, P., 2023b. The Brain Physics Laboratory. University of Cambridge.
- Smielewski, P., Czosnyka, M., Steiner, L., Belestri, M., Piechnik, S., Pickard, J.D., 2005. ICM+: software for on-line analysis of bedside monitoring data after severe head trauma. Acta Neurochir. Suppl. (95), 43-49.
- Smielewski, P., Czosnyka, Z., Kasprowicz, M., Pickard, J.D., Czosnyka, M., 2012. ICM+: a versatile software for assessment of CSF dynamics. Acta Neurochir. 114. Supplementum.
- Steiner, L.A., Pfister, D., Strebel, S.P., Radolovich, D., Smielewski, P., Czosnyka, M., 2009. Near-infrared spectroscopy can monitor dynamic cerebral autoregulation in adults. Neurocritical Care 10 (1), 122-128.
- Sykora, M., Siarnik, P., Szabo, J., Turcani, P., Krebs, S., Lang, W., et al., 2019. Baroreflex sensitivity is associated with post-stroke infections. An open, prospective study. J. Neurol. Sci. 406.
- Tas, J., Beqiri, E., Van Kaam, R.C., Czosnyka, M., Donnelly, J., Haeren, R.H., et al., 2021. Targeting autoregulation-guided cerebral perfusion pressure after traumatic brain injury (COGiTATE): a feasibility randomized controlled clinical trial. J. Neurotrauma 38 (20), 2790-2800.
- TensorFlow [Internet] [cited 2023 Jun 21]. Available from: https://www.tensorflow.or
- Uryga, A., Ziółkowski, A., Kazimierska, A., Pudełko, A., Mataczyński, C., Lang, E.W., et al., 2022. Analysis of intracranial pressure pulse waveform in traumatic brain injury patients: a CENTER-TBI study [cited 2023 Jun 21] J Neurosurg [Internet] 1–11. Available from: https://pubmed.ncbi.nlm.nih.gov/36681948/. Varsos, G.V., Kasprowicz, M., Smielewski, P., Czosnyka, M., 2014. Model-based indices
- describing cerebrovascular dynamics. Neurocritical Care 20 (1).
- Yoon, J.H., Pinsky, M.R., Clermont, G., 2022. Artificial intelligence in critical care medicine [cited 2023 Jun 21] [Internet] Crit. Care 26 (1). https://pubmed.ncbi.nlm. nih.gov/35337366/.
- Young, A.M.H.H., Donnelly, J., Czosnyka, M., Jalloh, I., Liu, X., Aries, M.J., et al., 2016. Continuous multimodality monitoring in children after traumatic brain injury preliminary experience. PLoS One 11 (3), 1-11.
- Zeiler, F.A., Donnelly, J., Menon, D.K., Smielewski, P., Zweifel, C., Brady, K., et al., 2017. Continuous autoregulatory indices derived from multi-modal monitoring: each one is not like the other. J. Neurotrauma 34 (22), 3070-3080.
- Zeiler, F.A., Ercole, A., Czosnyka, M., Smielewski, P., Hawryluk, G., Hutchinson, P.J.A., et al., 2020. Continuous cerebrovascular reactivity monitoring in moderate/severe traumatic brain injury: a narrative review of advances in neurocritical care. Br. J. Anaesth. 124 (4).
- Zhou, L., Pan, S., Wang, J., Vasilakos, A.V., 2017. Machine learning on big data: opportunities and challenges. Neurocomputing 237, 350-361.