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A Deep Learning Framework for Deriving Non-Invasive Intracranial Pressure Waveforms from Transcranial Doppler

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Abstract

Increased intracranial pressure (ICP) causes disability and mortality in the neuro-intensive care population. Current methods for monitoring ICP are invasive. We designed a deep learning framework using a domain adversarial neural network to estimate noninvasive ICP, from blood pressure, electrocardiogram, and cerebral blood flow velocity. Our model had a mean of median absolute error (MAE) of 3.88+/−3.26 mmHg for the Domain adversarial neural network and 3.94+/−1.71 mmHg for the Domain Adversarial Transformers. Compared to non-linear approaches such as support vector regression, this was 26.7% and 25.7% lower. Our proposed framework provides more accurate non-invasive ICP estimates than currently available.

GRAPHICAL ABSTRACT:

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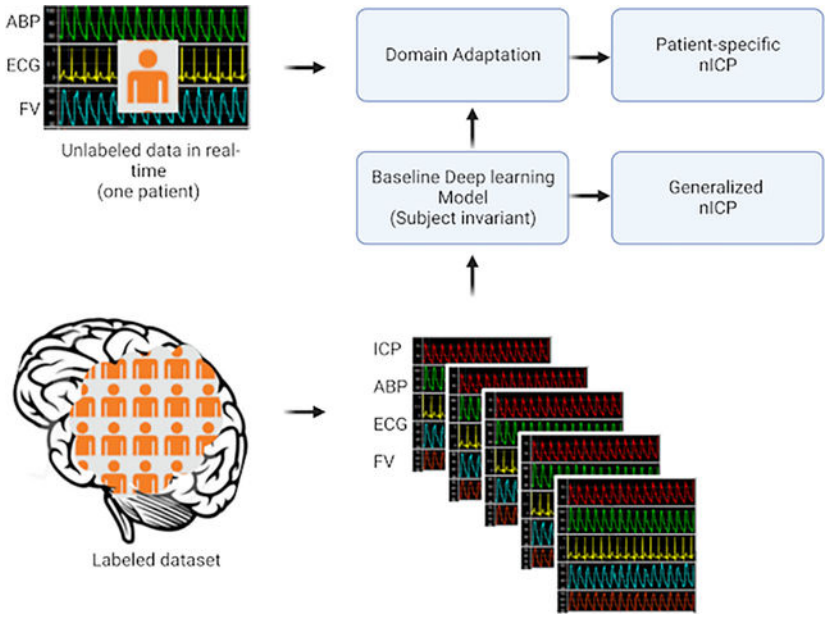
Author Contributions

MM and SP contributed to the conception and design of the study; KT, SP, BW, DN, AV, SG, DR, SA ESC, JC contributed to the acquisition and analysis of the data; MM and SP contributed to drafting the text and preparing the figures.

Potential Conflicts of Interest:

Nothing to report.



Keywords

non-invasive intracranial pressure; Neurocritical care; Deep Learning; Residual Network; Adversarial network; Machine Learning

INTRODUCTION

Increased intracranial pressure (ICP) is one of the leading causes of neurological disability and mortality in neurointensive care population.[1] The current standard for clinical monitoring of ICP requires a hole drilled in the skull to allow a pressure probe or catheter into the parenchyma or ventricular space. Risks associated with invasive monitoring include hemorrhage, dislodgement, blockage, and infection.[2] Some clinical situations would benefit from goal-directed cerebral perfusion but the thresholds to place ICP probes are high (e.g. cardiac arrest, pediatrics, acute liver failure, coagulopathic states, bacterial central nervous system (CNS) infections).

If not for its invasiveness and risks, ICP monitoring could benefit a much larger patient population.[3] There is a need for non-invasive ICP monitoring with clinically acceptable accuracy to provide ICP monitoring for a larger patient population.

Non-invasive intracranial pressure (nICP) estimation[4–7] is an active area of investigation. A detailed review is provided in[5–8]. Of particular interest in the field are techniques that leverage the physiological model of ICP dynamics using noninvasive CNS related measurement inputs (e.g., transcranial doppler (TCD) measurements of cerebral blood flow velocity (CBFV), arterial blood pressure (ABP)). These techniques estimate nICP either using data-driven[9–11] or model-based[3,12] approaches. Model-based approaches have the advantage of relying on the fundamental mechanics of the intracranial compartment,[3] yet lack the ability to provide accurate ICP. Data-driven approaches aim to construct a mapping

between non-invasive CNS signals and ICP using supervised techniques including kernel spectral regression(KSR),[9] support vector machines (SVR, SV-Nu) [10] or neural networks.[11] The limitation of these techniques is the requirement of sufficient training data limiting generalizability.

There are no noninvasive methods that demonstrate sufficient accuracy for continuous monitoring in routine clinical care.[13] According to the Association for the Advancement of Medical Instrumentation, when measuring ICP the margin of error between nICP and real ICP should be less than 10%.[14,15] For ICP measurements between 0 and 20 mmHg, a maximum difference of 2 mmHg is acceptable For data-driven techniques, the mean error varies from +/−5 mmHg to about +/− 20 mmHg with high standard deviation.[13]

We hypothesize that the high errors in data-driven techniques could be due simplistic models that don't capture non-linear temporal dynamics and lack of unseen examples during the training phase. Transfer learning and domain adaptation can adapt to new unseen examples by transferring knowledge from previously seen examples. We developed a domain adaptation approach using TCD and ABP and compared to existing data-driven approaches for nICP estimation.[9,10]

Materials and methods

Patient consent

We studied consecutive subarachnoid hemorrhage patients admitted to the neurocritical care unit at Columbia University Irving Medical Center between 2017–2022 who had external ventricular drainage (EVD).[16] During clamping trials, waveform measurements of flow velocity (FV), electrocardiogram (ECG), arterial blood pressure (ABP), and ICP were digitally acquired. The study was approved by the Institutional Review Board at Columbia University. In all cases, written informed consent was obtained from the patient or surrogate.

Monitoring and Data Acquisition

ICP was monitored using the Integra External Drainage and Monitoring System with Medtronic EVDs (antibiotic impregnated VentriClear II or nonantibiotic impregnated large translucent). EVDs were placed following cefazolin prophylaxis for symptomatic hydrocephalus. Physiologic data for the duration of the intensive care unit stay was acquired using ICM+ software (Cambridge Enterprise, Ltd, UK) from Philips Intellivue MX700 monitors (Netherlands) at 125 samples per second. TCD measurements were acquired by a trained technician or physician using a 2-MHz handheld transducer probe (Delica EMS-9PB; Shenzhen Medical Equipment, China).

Proposed Framework Using Domain Adaptation

Generalizing machine learning models can be challenging due to differences in data acquisition, disease etiologies, and sampling frequency.[17] Transfer learning and domain adaptation can improve generalization. Domain adaptation enhances model training when there are statistical differences in the distribution of data, known as data shift. The goal is to improve the performance of a machine learning model on a target domain

with insufficient data by using/transferring the knowledge from model trained on a labelled source domain. Adversarial networks, a recent domain adaptation technique, have shown promise in estimating blood pressure non-invasively.[18] We propose using domain adversarial networks using convolution neural network(DACNN), residual network(DARN), and Transformer(DAT) for estimating patient-specific nICP by leveraging the nonlinear relationship between ABP and TCD-derived CBFV and compared with other data-driven approaches KSR, SV-R, and SV-Nu.

The Network: The proposed network (Figure 1) has three parts: a) *Domain Classifier* to learn subject-specific ICP dynamics, b) *ICP Estimator,* and c) *Feature Extractor*. Using labelled data (ABP, ECG, FV, and ICP) from a subject in the training set and unlabeled data from subject whose ICP needs to be calculated, the unsupervised domain a adaptation algorithm treats each subject as a separate domain. The Domain Classifier discriminates between source and target domains, while the ICP Estimator maximizes ICP regression accuracy. The Feature Extractor is trained using both losses, but with the gradient reversed for domain classification. This adversarial component ensures that the extracted features are subject-invariant. The model is updated using backpropagation.

Training Phase: During training, the feature extractor is fed with labelled data from source domain and unlabeled data from target. The goal is to find the optimal balance between producing features that are domain invariant and useful for the ICP Estimator. The Feature Extractor parameters are optimized to minimize the ICP Estimator's loss and maximize the domain classifier's loss, which involves the use of a gradient reversal layer.

Estimating ICP: Once the network is trained, then during testing phase the target unlabeled data is passed through Feature Extractor and ICP estimator to derive ICP:

As in linear and non-linear approaches[4,10] we selected our batch size to be spread over 3 cardiac cycles. We used n(=200) points equally spread over one cardiac cycle as our time steps. The optimal learning rate was derived using the grid-search approach. We reported the performance using mean squared error (MSE) +/− standard deviation (SD), Bland-Altman plots for comparing true ICP and non-invasive ICP. We used leave one session out cross-validation technique to report the performance of the models.

We used Python 3.8 with Keras 2.4.3 with Tensorflow 2.4.1 to develop these models.

Results

From 2017 and 2022, data was collected from 13 patients with ICP monitors and TCD. Of 13 patients, 11 were used for analysis, 2 patients were excluded because of data quality issues. Mean age was 51.7±17.3 years and 61.5% were female. We acquired 544,590 data points from 15 sessions (mean: 49508) from these 11 patients (Table 1) with ICP ranging from [0 – 57] mmHg.

Performance of KSR and SVR for nICP

We achieved similar results on our dataset as reported in the literature for SVR with mean +/− SD of 6.82+/−5.03 mmHg. SV Nu performed better with 5.3+/−4.19 mmHg (Figure 2,S1). KSR model did not perform well with 10.11+/−4.99 mmHg.

Performance of the proposed approaches

The performance of the baseline deep learning model (LSTM Resnet, CNN LSTM Resnet, Transformers) without domain adaptation are 4.75+/−4.48, 4.74+/−4.57 mmHg and 4.37+/−4.32. The domain adapted versions DANN, DARN, DACNN and DAT performed better with 3.88+/−3.26 mmHg, 4.57+/−3.32 mmHg 4.43+/−3.15 mmHg and 3.94+/−1.71 mmHg respectively. (Figure 2,S1). All the deep learning models performed better than the existing non-linear approaches.

Statistical Analysis

Figure 3 shows the Bland Altman plots for SV-NU, DANN and DAT approaches. In our proposed approach, 74.45.4% (DAT) and 72.78% (DANN) have ICP error less than 5 mmHg, which is better when compared with 61.8 % (SV Nu) and 39.02 % (SVR) for existing non-linear approaches.

Discussion

We developed a domain adversarial model that performed better than the existing data driven approaches for deriving non-invasive ICP waveforms from TCD. To our knowledge, this is the first study that shows the use of recurrent neural networks, transformers, and the domain adversarial models for deriving patient-specific nICP. We were able to exploit the non-linear relationship between physiologic parameters that translated into a lower error.

Patient-specific nICP estimation techniques with clinically acceptable accuracy would enable or justify monitoring in patients for whom the risk of an invasive procedure is high, allowing for more robust identification of elevated ICP and opportunities for improving patient outcome. This is also the first time a transfer learning using domain adversarial technique is used to derive a patient-specific model, a step towards creating generalizable ML models.

One of the limitations of the proposed technique is the limited number of subjects used to train these models. Second, our proposed models are still not within the acceptable limits of 2 mmHg for ICP<20 mmHg as advised by Association for the Advancement of Medical Instrumentation, but we have achieved a remarkable improvement when compared with existing methods. Deep learning models perform better with more data and our future work is to include more patients to translate these models and achieve an MSE within clinically acceptable limits.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

All relevant data are presented within the article and its supporting information files. Additional information can be obtained upon request to the corresponding author.

Abbreviations:

ABP	Arterial Blood Pressure
CNN	Convolution Neural Network
CSF	cerebrospinal fluid
DANN	Domain adversarial neural network
DACNN	Domain adversarial convolution neural network
DARN	Domain adversarial residual network
DAT	Domain adversarial Transformers
ECG	Electrocardiogram
FV	Flow velocity
ICP	Intracranial pressure
LSTM	Long short term memory
nICP	Non-invasive intracranial pressure
SV nu	Support Vector
SVR	Support Vector Regression

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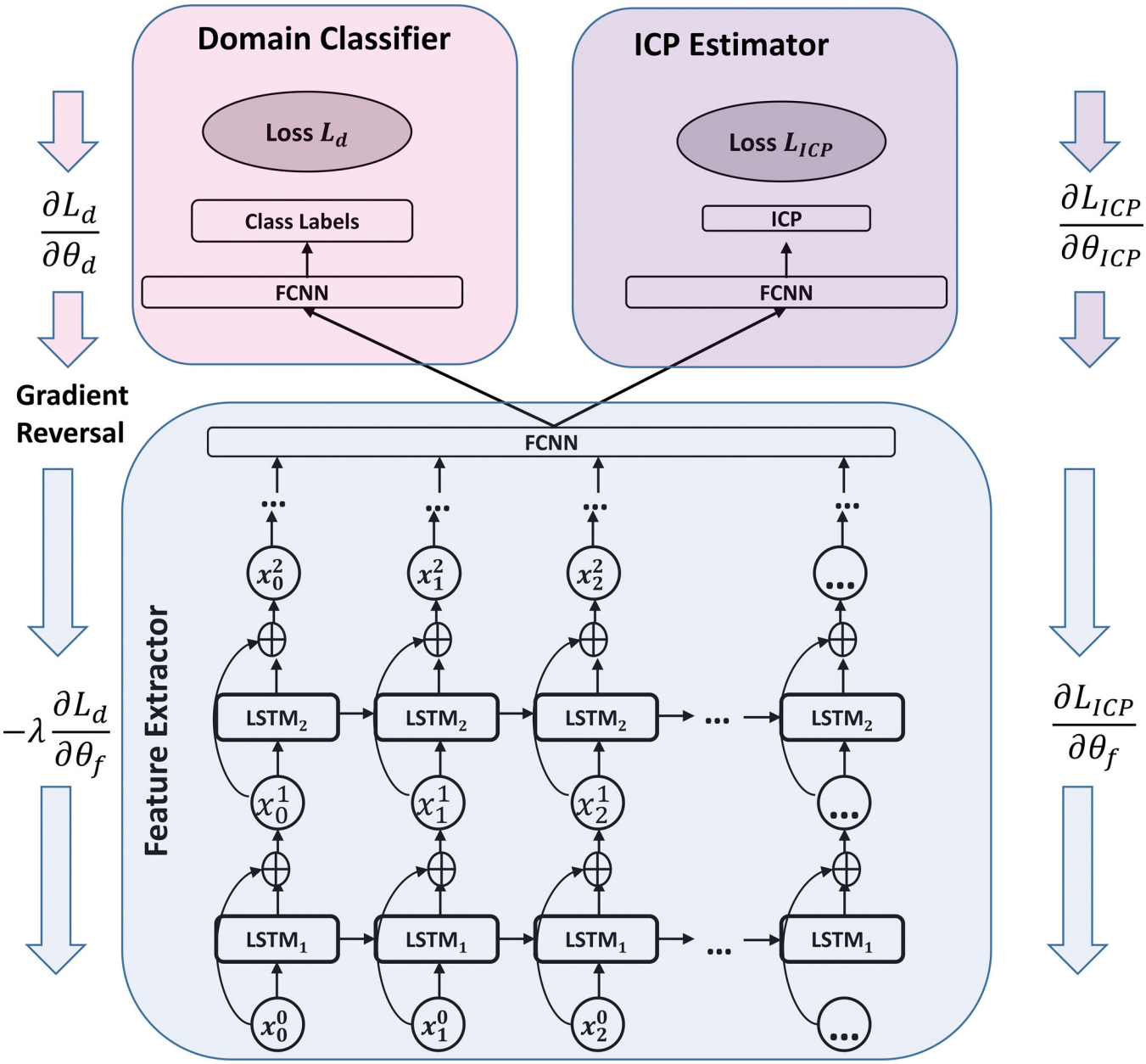

Figure 1:

The proposed Domain Adversarial Residual Network framework, the input x_i^0 to the framework (ABP_i, ECG_i, FV). It consists of three layers: a) Feature extractor, b) ICP Estimator, and c) Domain classifier.

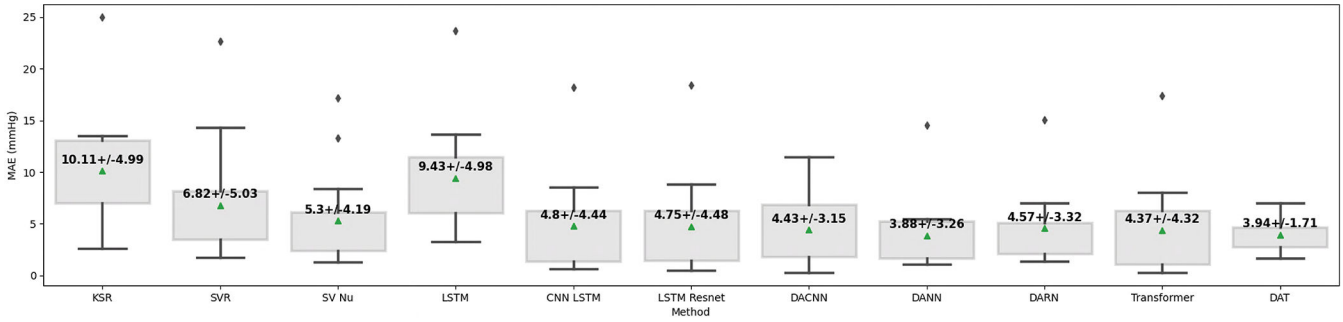

Figure 2: Illustrates the performance of different models for deriving non-invasive intracranial pressure (nICP).

The proposed frameworks DANN and DAT performed best when compared to the current state of the art methods for nICP estimation. Green dot represents the mean.

SV nu: Support Vector, SVR: Support Vector Regression, CNN: Convolutional Neural Network, LSTM: Long short-term memory, DACNN: Domain adversarial convolutional neural network, DANN: Domain adversarial neural network, DARN: Domain adversarial residual network, MAE: Median absolute error, DAT: Domain adversarial transformers.

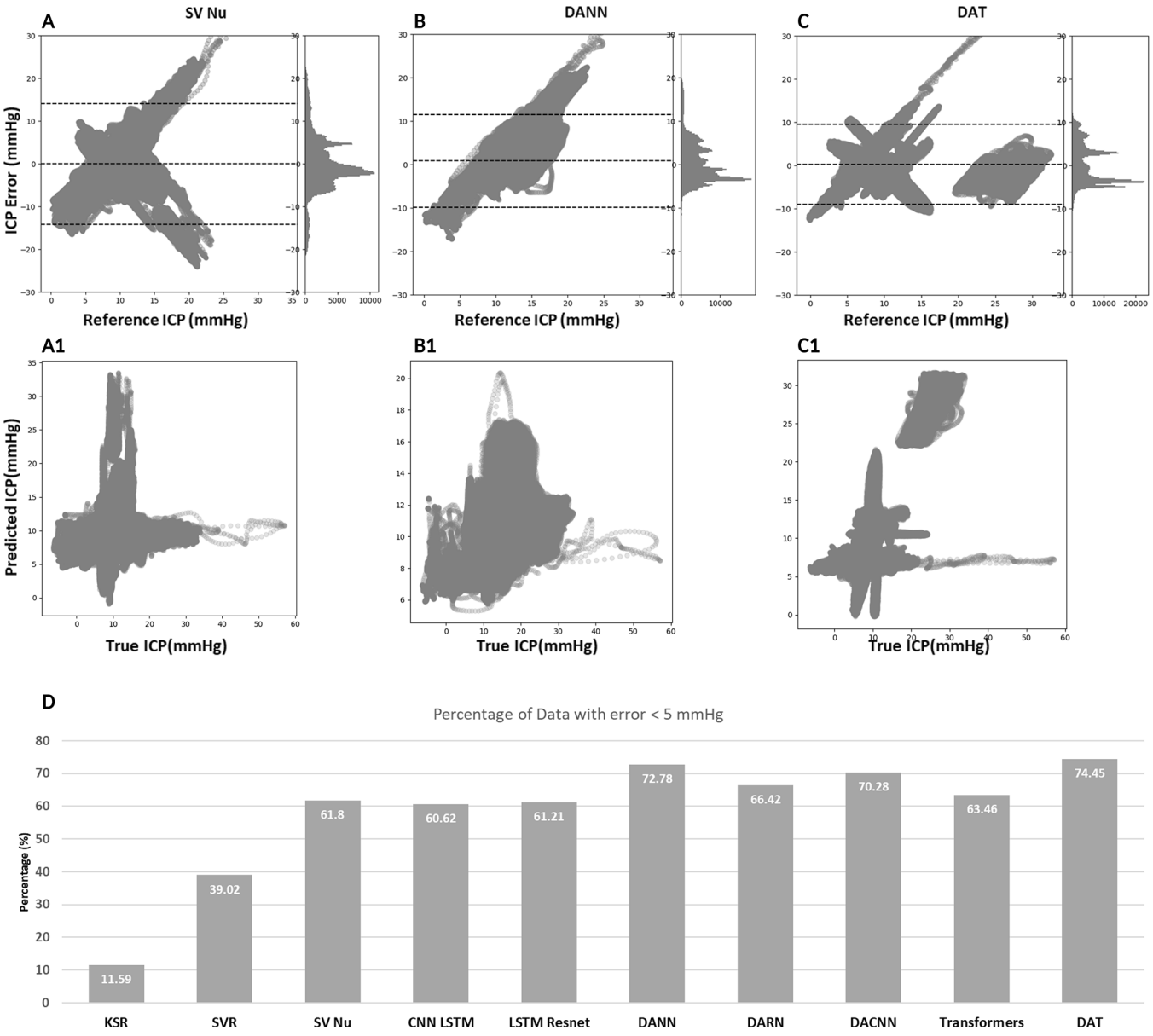

Figure 3: Bland-Altman Plots for comparing true intracranial pressure (ICP) vs non-invasive ICP.

Panels A, B, and C display the reference ICP (mmHg) versus the ICP error (mmHg) for three different methods: SV Nu, DANN, and DAT. Corresponding scatter plots of true ICP versus predicted ICP are shown in panels A1, B1, and C1. Panel D shows the percentage of data with an error of less than 5mmHg for each method. The standard error for the proposed DARN and DANN network is between +/− 10 mmHg, when compared to the current state of the art technique using SV nu. The percentage of ICP error less than 5 mmHg is 74.45% for the proposed framework (DAT), which is better when compared with 61.8% (SV Nu) and 39.02 % (SVR) for current non-linear approaches.

SV nu: Support Vector, SVR: Support Vector Regression, CNN: Convolutional Neural Network, LSTM: Long short-term memory, DACNN: Domain adversarial convolutional

neural network, DANN: Domain adversarial neural network, DARN: Domain adversarial residual network, DAT: Domain adversarial transformers.

Table 1

Demographics of the patients

Identifier	MFS	HH	GCS (admission)	WFNS	Etiology	# TOTAL DATA POINTS	# ARTIFACT FREE Data Points	Data QualitY (G-Good/P-poor)
P1	N/A	N/A	6	5	Left basal ganglia IPH	611252	0	P
P2	3	4	4	5	L MCA aneurysmal SAH	601253	113952	G
P3	N/A	N/A	5	5	CSF leak and pneumocephalus	357500	20836	G
P4	4	4	9	4	SAH/IVH	630002	47042	G
P5	4	4	6	5	aSAH	503750	132963	G
P6	N/A	N/A	15	1	5cm pineal mass with obstructive hydrocephalus	197500	0	P
P7	2	3	15	1	SAH/IVH	153125	33925	G
P8	4	5	4	5	SAH/IVH	66212	46683	G
P9	4	2	14	2	SAH/IVH	165000	35835	G
P10	3	3	6	5	SAH	130176	38693	G
P11	4	2	7	4	SAH/IVH	314375	33068	G
P12	4	5	3	5	SAH	146875	3554	G
P13	N/A	N/A	6	5	Diffuse axonal injury	457502	38039	G

WFNS: World federation of neurosurgical societies scale, MFS: Modified Fisher scale, GCS: Glasgow coma scale, HH: Hunt and Hess scale, aSAH: aneurysmal Subarachnoid Hemorrhage, IVH: Intraventricular Hemorrhage