

1 ***Scoping Review Protocol***

2 ***Title:***

3 **Intracranial compliance concepts and assessment: A scoping review protocol**

4 ***Authors:***

5 Thiago L. Russo¹, PT, Ph.D., Gabriela N. Ocamoto¹, PT, Ph.D., Rafaella M. Zambetta¹,
 6 PT, MSc, Gustavo H. F. Vilela², Ph.D., Cintya Y. Hayashi^{2,3}, R.N., B.S.N, MSc, Sérgio
 7 Brasil³ M.D. Ph.D., Nícollas Nunes Rabelo^{2,3,4}, M.D., Deusdedit L. Spavieri Junior²,
 8 Ph.D.

9 ***Affiliations:***

10 ¹Physical Therapy Department, Federal University of São Carlos, UFSCar, Rodovia
 11 Washington Luís, Km 235, São Carlos, SP, Brazil.

12 TLR: russo@ufscar.br; GNO: gabynagai@gmail.com; RMZ:
 13 rafa.m.zambetta@gmail.com

14 ²Brain4Care Inc. Av. Bruno Ruggiero Filho, 971, Santa Felícia, São Carlos, São Paulo,
 15 Brazil. Zip code: 13562-420.

16 GHFV: gustavo.frigieri@brain4.care; CYH: cintya.hayashi@brain4.care; DLSJ:
 17 deusdedit.spavieri@brain4.care

18 ³Department of Neurology, Medical School, University of São Paulo, Av. Dr. Enéas de
 19 Carvalho Aguiar, 255–5º andar, Cerqueira Cesar, São Paulo, SP, Brazil. Zip
 20 Code: 05403-000.

21 SB: sergio.brasil@brain4.care

⁴Department of Neurosurgery, UniAtenas Center University, Paracatu-MG, Brazil. Rua Euridamas Avelino de Barros, R. Romualda Lemos do Prado, 60 - Lavrado, Paracatu - MG, 38602-018.

NNR: nicollasrabelo@hormail.com

Corresponding author: Thiago Luiz de Russo. Departamento de Fisioterapia. Universidade Federal de São Carlos – UFSCar. São Carlos, São Paulo, Brazil. Zip Code: 13565-905. Phone: +551633066702 / +5516981172023. russo@ufscar.br

Abstract

Background: Monitoring patients with acute brain injury is crucial in neurocritical care. Intracranial compliance (ICC) has been studied to complement the interpretation of intracranial pressure (ICP) and help the neurocritical care team to anticipate brain function deterioration. ICC has been found to be related to compensatory mechanisms that maintain the stability of ICP (e.g., the higher the compensation, the higher the compliance of intracranial content to adapt to changes in volume and pressure). However, ICC has not been properly translated to clinical practice and has remained a critical technology gap in clinical neuroscience. The objective of this study is to establish a protocol for a scoping review to map the key concepts of ICC in the literature. In addition, this study is designed to characterize the relationship between ICC and ICP, as well as systematically describe the outcomes that are used to assess ICC, considering both the invasive and noninvasive methods.

Methods: The scoping review protocol will be conducted according to the Joanna Briggs Institute's recommendation. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews will be followed. Animals and humans

are considered as the population to be investigated. No age criteria or health condition will be considered. ICC, as well as the relationship between ICC and ICP, will be considered as a core concept in this review. Information will be screened based on the context of neurocritical care. Several databases (PubMed, CINAHL, Web of Science, EMBASE, Epistemonikos, Grey Literature Report, clinical trial registries, and Cochrane Clinical Trials) will be searched to identify literature using a combination of keywords and descriptors, and there will be no restriction on the time frame. Data will be extracted systematically by the research team and the results will be summarized.

Discussion: No systematic review has mapped the concepts of ICC and its relationship with ICP. Providing the key concepts of ICC and the methods of assessment might show its possible applications in clinical practice and the gaps in research.

Systematic review registration: Currently, scoping review protocols are not eligible for registration in the International Prospective Register of Systematic Review database.

Keywords: mapping review, brain compliance, intracranial elastance, brain pulsatility

Background

The “consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care” has provided a key rationale for neurocritical care units around the world [1]. The multimodality monitoring of patients with acute neurological disorders is a complementary approach to the frequent bedside examinations and should be considered for the detection of early neurological worsening before irreversible brain damage occurs and to help clinicians guide

individualized therapeutic decisions, which can improve, for example, acute and long-term prognosis [2].

In this sense, the monitoring of intracranial pressure (ICP) has been considered fundamental to the care of patients with acute brain injury. In the literature, there is a strong recommendation with moderate quality of evidence that ICP and cerebral perfusion pressure should be used as a part of protocol-driven care in patients who are at risk of elevated ICP based on clinical and/or imaging features [1]. The fundamental principles of raised ICP are condensed in the Monro-Kellie doctrine, in which the volume of the intracranial cavity is constant under normal conditions and the maintenance of a steady ICP depends on the volume of the intracranial contents (brain tissue, blood, and cerebrospinal fluid) [3,4].

Methods for ICP monitoring include invasive and noninvasive approaches. Regarding invasive methods, the external ventricular drain is considered the gold standard for ICP monitoring [1]. Nevertheless, the efficacy of treatments based on invasive ICP monitoring regarding improving outcomes such as survival time, impaired consciousness, and functional and psychological status after hospital discharge is questionable [5]. According to Chesnut et al. [5], patients diagnosed with severe traumatic brain injury showed no superior gains when guidelines-based management for monitoring mean values of intra-parenchymal ICP was used compared to the protocol in which treatment was based on imaging and clinical examination.

On the other hand, intracranial compliance (ICC) or its inverse—intracranial elastance—has been studied for decades in an attempt to complement ICP interpretation and describe brain homeostasis more precisely, thus helping the neurocritical care team to anticipate brain function deterioration [6,7]. ICC has been found to be related to the compensatory mechanisms used to maintain ICP's stability [4]—for example, the higher the

compensation, the higher the compliance of intracranial content to adapt to changes in volume and pressure. However, ICC has not been properly translated to clinical practice and this has remained a critical technology gap in clinical neuroscience, probably because of the number of factors involved in it.

Czosnyka and Citerio [6] hypothesized that ICC is a nonlinear function from the association of venous, cerebrospinal fluid, and arterial pools, with the influence of other vascular factors such as the regulation of cerebral blood flow, tension of arterial smooth muscles, partial pressure CO₂, endothelial function, brain hydration, metabolism, and so on.

Very good reviews are available about ICP monitoring in neurocritical care [4,7], which are focused on new technological approaches and gaps in research that can be translated into clinical practice. Nevertheless, nowadays, there is no standardization for ICC concepts according to invasive and noninvasive techniques.

The objective of this study is to establish a protocol for a scoping review, which can be used to map the key concepts of ICC used in the literature. As secondary questions, this study is designed to characterize the relationship between ICC and ICP, as well as systematically describe the outcomes that are used to assess ICC, considering both invasive and noninvasive methods. Finally, this study will also provide information about gaps in the body of knowledge to support future studies.

Methods/Design

The scoping review protocol will be conducted according to the Joanna Briggs Institute's recommendation [8,9]. A priori review protocol is important to improve the transparency of the searching strategy and peer review process. Unfortunately, scoping review

protocols are not eligible for registration in the International Prospective Register of Systematic Review database. Therefore, considering that scoping reviews are conducted in an iteratively way to adjust and refine methods throughout the study, this protocol will serve as a basis for documenting possible changes.

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews, which was developed according to guidelines published by the Enhancing the Quality and Transparency of Health Research Network for the development of reporting guidelines, will be followed [10].

Search strategy and data source

A primary but limited search will be performed independently by three investigators (TLR, GNO, and RMZ) on PubMed (via National Library of Medicine) and CINAHL databases to analyze the titles, abstracts, and index terms used. The combination of “intracranial compliance” OR “intracranial elastance” OR “cerebral compliance” OR “brain compliance” OR “compliance monitoring” AND “intracranial pressure” OR “intracranial pulse amplitude” OR “intracranial pulse wave” OR “pressure-volume curve” will be used for this first search. Then the MeSH database will be consulted to identify and confirm appropriate terms obtained in this first search, which will be included in the second search strategy.

Subsequently, in the second search, all the identified keywords and index terms described in the first step will be used across the PubMed (via National Library of Medicine), CINAHL with Full Text (EBSCO), Web of Science (Thomson Scientific/ISI Web Services), and EMBASE databases. Epistemonikos, Grey Literature Report, clinical trial registries, and Cochrane Clinical Trials will also be searched. Afterward, as a third step,

the reference list of identified studies will be examined for additional sources that can be included in this review.

Selection process

According to Peters et al.'s [9] recommendations, 75% (or greater) level of agreement between reviewers is necessary before data selection. Therefore, a random sample of 25 titles and abstracts will be selected for screening using the eligibility criteria and definitions before conducting the second search, and adjustments will be made where necessary. The screening process will start only after the recommended level of agreement has been reached.

To systematize and organize the search and data extraction, the State of the Art through Systematic Review (Available from http://lapes.dc.ufscar.br/tools/start_tool) will be used. Two reviewers will independently perform the selection process based on the eligibility criteria. Initially, duplicates will be excluded using the State of the Art through Systematic Review. Then the potentially eligible articles will be selected based on the titles and the abstracts. Afterward, these articles will be retrieved for full-text reading to verify whether they will meet all the inclusion criteria. In cases of disagreements between the two reviewers, a third reviewer will be consulted to determine the study's eligibility. The authors will be contacted when access to full-text articles is not available.

Eligibility criteria

The main question of this study is based on the population, concept, and context criteria. Animals and humans will be considered as the population to be investigated, and information will be organized in subgroups according to their relevance when possible. No age criteria or health condition will be considered. ICC will be considered as a core concept in this review, as well as the relationship between ICC and ICP. Both invasive

and noninvasive methods for assessment of ICC will be considered. Information collected will be screened based on the context of neurocritical care. Literature from all countries will be included.

Experimental and epidemiological studies, including randomized controlled trials, nonrandomized controlled trials, quasi-experimental, before and after studies, prospective and retrospective cohort studies, case-control studies, and analytical cross-sectional studies will be included in the analysis. In addition, not only literature reviews such as narrative reviews, meta-analysis, and systematic reviews but also gray literature (e.g., governmental reports, theses, etc.) and theoretical and opinion articles will be considered. On the other hand, conference abstracts, personal blogs, and social media will be excluded.

For feasibility reasons, the English, Spanish, Italian, Portuguese, and German languages will be considered. There will be no restriction on the time frame for the collection of data.

Data analysis

Data extraction

A standardized electronic data extraction form will be built in the Microsoft Excel™ spreadsheet to obtain key information about the studies that will be included in this review. The data extracted from each primary study will be as follows: authors, year of publication, origin/country of origin, aims/purpose, type of literature, research design, population and demographic characterization, health condition, sample size, methods used for ICC assessment, and outcomes considered as ICC by authors. Accuracy, sensitivity, specificity, and other possible comparators will also be extracted and presented.

189

190 *Data synthesis*

191 Extracted data will be condensed and displayed according to similarities and differences
192 under the main conceptual categories. Then conclusions will be presented according to
193 the objectives. The results will be presented as a map of the data extracted, using graphs
194 and tables. The results will be presented in narrative form. Graphs and tables will be used
195 for data presentation. Frequency counts of concepts, populations, and methods will be
196 presented as tables.

197

198 *Discussion*

199 Complementary approaches to ICP monitoring can be a relevant guide that will help the
200 neurocritical team to accelerate therapeutic decisions to improve the survival and
201 recovery of patients with acute brain injury. In this sense, ICC monitoring could be
202 considered as a complementary resource to ICP monitoring and clinical exam. Although
203 ICC gained much attention in the neurosurgical literature decades ago, it has been barely
204 used in clinical practice [11]. Nowadays, with the advance of data science and the
205 interface of cardiovascular and central nervous system researches, different methods are
206 being used to assess directly or indirectly the intracranial pressure-volume reserve
207 capacity. However, no systematic review has mapped the concepts of ICC, as well as its
208 relationship with ICP, considering the invasive and new noninvasive methods. Providing
209 key concepts for ICC and the methods of assessment might show possible applications in
210 clinical practice and the gaps in research.

211

Abbreviations

ICC: Intracranial compliance

ICP: Intracranial pressure

Funding: This study was supported by Brain4Care Inc. This funding does not have any role in the design of the protocol.

Availability of data and materials: Not applicable.

Ethics approval and consent to participate: Not applicable.

Competing interests: The authors declare that they have no competing interests.

Acknowledgments: Authors appreciate the contributions of Dr. Sâmia Wayhs who provided technical advice to ensure the success of this study.

Authors' contributions: TLR designed and wrote the initial version of this manuscript. GNO, RMZ, GHFV, CYH, SB, and DLSJ critically reviewed the manuscript and helped to refine it.

References

- 233 1. Le Roux P, Menon DK, Citerio G, Vespa P, Bader MK, Brophy GM, et al. Consensus
 234 summary statement of the International Multidisciplinary Consensus Conference on
 235 Multimodality Monitoring in Neurocritical Care: A statement for healthcare
 236 professionals from the Neurocritical Care Society and the European Society of
 237 Intensive Care Medicine. *Neurocrit Care*. 2014;21(S2):1–26.
- 238 2. Lara LR, Püttgen HA. *Continuum* (Minneapolis, Minn). Multimodality monitoring in the
 239 neurocritical care unit. *Neurocrit Care*. 2018;24(6):1776–1788.
- 240 3. Steiner LA, Andrews PJD. Monitoring the injured brain: ICP and CBF. *Brit J Anaesth*.
 241 2006;97(1):26–38.
- 242 4. Harary M, Dolmans RGF, Gormley W. Intracranial pressure monitoring – Review and
 243 avenues for development. *Sensors*. 2018;18:465. doi:10.3390/s18020465
- 244 5. Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, et al. A trial of
 245 intracranial-pressure monitoring in traumatic brain injury. *N Engl J Med*.
 246 2012;367(26):2471–81.
- 247 6. Czosnyka M, Citerio G. Brain compliance: the old story with a new ‘et cetera’.
 248 *Intensive Care Med*. 2012;38:925–927.
- 249 7. Heldt T, Zoerle T, Teichmann D, Stocchetti N. Intracranial pressure and intracranial
 250 elastance monitoring in neurocritical care. *Ann Rev Biomed Eng*. 2019;21:523–549.
- 251 8. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for
 252 conducting systematic scoping reviews. *Int J Evid Based Healthc*. 2015;13(3):141–
 253 146.
- 254 9. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil, H. Scoping
 255 reviews. In: Aromataris E, Munn Z, editors. *Joanna Briggs Institute Reviewer’s*
 256 *Manual* [Internet]. 2020 version. Joanna Briggs Institute; 2020. Available from:
 257 <https://reviewersmanual.joannabriggs.org/> <https://doi.org/10.46658/JBIMES-20-12>

- 258 10. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA
259 extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Ann Intern*
260 *Med*. 2018;169:467–473. doi: 10.7326/M18-0850
- 261 11. Eide PK. The correlation between pulsatile intracranial pressure and indices of
262 intracranial pressure-volume reserve capacity: results from ventricular infusion
263 testing. *J Neurosurg*. 2016;125(6):1493–503.