RESEARCH ARTICLE

Translation and Validation of the Neurologic Assessment in Neuro-Oncology Scale into Indonesian (NANO-Ina)

Michelle Cancera Angelita[1]*, Putri Widya Andini[1], Rini Andriani[2], Henry Riyanto Sofyan[1], Irma Savitri[1], Tiara Aninditha[1]

Abstract

Objective: Assessment of treatment efficacy in neuro-oncology is measured by radiographic criteria. This can be misleading, as imaging findings may not translate into clinical benefit. The NANO scale, constructed by multidisciplinary experts, is an objective and measurable metric of neurological function that can be evaluated during routine examinations in brain tumor patients, so that patients receive an overall assessment of progression, along with radiological findings. This study aims to determine the validity and reliability of the Indonesian version of the NANO scale (NANO-Ina). **Methods:** The study was performed at Cipto Mangunkusumo National Referral Hospital, Jakarta. The validity and reliability process incorporated forward and backward translation to ensure cross-cultural equivalence, and an initial trial was conducted with 10 physicians to identify potential issues and refine item clarity. Subsequently, the 9 domains of the NANO-INA version were tested on 30 pathologically confirmed brain tumor patients by 2 distinct physicians separately. Inter-rater reliability was analyzed using the Kappa statistics. **Result:** A total of 30 subjects were enrolled from January to August 2023, which included subjects mostly diagnosed with brain metastasis (30%), and the rest were equally distributed among meningioma, glioblastoma, and other primary brain tumors (23.3%). Among these, the majority had not received any treatment (77%), and the remaining were on chemoradiation (10%), chemotherapy (10%), and radiation (3.3%). Our inter-observer variability study demonstrated that the NANO-INA scale exhibits substantial to almost perfect agreement (kappa statistic ranging from 0.629-0.935) for all domains ($p<0.05$), with the highest agreement observed in strength, facial strength, and language. **Conclusion:** The NANO-INA scale shows a high level of inter-observer agreement and serves as a reliable tool for assessing neurological function in patients with brain tumors in clinical settings in Indonesia.

Keywords: Brain tumor- Indonesia- neuro-oncology assessment- reliability- translation- validation

Introduction

The global incidence of brain and central nervous system (CNS) tumors has shown a steady upward trend, with more than 300,000 new cases reported in 2020 and projections suggesting an increase of over 90% compared to 1990 [1]. While these tumors represent a smaller proportion of overall cancer diagnoses, they are associated with high morbidity and mortality, often affecting individuals during their most productive years and generating significant social and economic consequences [1–3]. In Indonesia, GLOBOCAN 2018 estimated 5,323 new brain and CNS tumor cases and 4,229 related deaths, accounting for approximately 2% of all cancer mortality in the country [4].

Functional performance has long been recognized as a key prognostic factor in neuro-oncology. The Karnofsky Performance Scale (KPS) is one of the most frequently applied instruments, and together with the Eastern Cooperative Oncology Group (ECOG) scale, it contributes to treatment response assessment within the Response Assessment in Neuro-Oncology (RANO) framework [5–7]. Nevertheless, these scales primarily assess general functional capacity and do not directly measure neurological deficits. Consequently, subtle yet clinically important neurological changes may go undetected, thereby limiting their value in monitoring disease course and prognosis.

To overcome these limitations, the Neurologic Assessment in Neuro-Oncology (NANO) scale was created by an international panel as a structured tool designed to measure nine specific neurological domains through direct clinical observation [8, 9]. In contrast to the KPS and ECOG scales, the NANO scale provides a focused assessment of neurological function, enabling a more accurate evaluation of tumor-related changes.

[1]Department of Neurology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia. [2]Department of Neurology, Dharmais Cancer Hospital, Jakarta, Indonesia. *For Correspondence: michellecanceraa3006@gmail.com

Although its use has been expanding in both clinical practice and research, the NANO scale has not yet been adapted or validated for Indonesian patients with brain tumors. This study, therefore, aimed to translate and validate the Indonesian version of the NANO scale (NANO-Ina), to provide a culturally adapted and reliable instrument for neurological assessment in this population.

Materials and Methods

Study Design

This was a cross-sectional observational study conducted from January to August 2023 at Cipto Mangunksumo Hospital, a tertiary referral center for neuro-oncology in Indonesia. The institutional ethics committee approved the study, and all participants provided written informed consent prior to inclusion.

Translation and Cultural Adaptation

The initial translation of the NANO scale from English to Indonesian was conducted using a standardized forward–backward translation approach. Two independent bilingual translators with medical expertise first carried out the forward translation into Indonesian. These two versions were then harmonized into a single preliminary version by a panel of experts. Following this, a separate pair of bilingual translators, who had no prior knowledge of the original scale, performed a back-translation into English. The resulting back-translated version was then reviewed by the expert committee—comprising neurologists, neuro-oncologists, and linguists—to identify and resolve any inconsistencies, ensuring that the final version maintained semantic, idiomatic, cultural, and conceptual fidelity to the original instrument.

Content Validity

Content validity was evaluated by an expert panel of ten healthcare professionals consisting of neuro-oncology specialists and neurology residents who independently rated each item for relevance, clarity, and cultural appropriateness using a four-point Likert scale. The Content Validity Index (CVI) was calculated at the item level (I-CVI) and the scale level (S-CVI/Ave).

Participants

Patients aged ≥18 years with a histologically confirmed diagnosis of primary or secondary brain tumors (e.g., glioma, meningioma, brain metastasis, or another primary brain tumor) were recruited consecutively from outpatient and inpatient units.

Inter-Rater Reliability Assessment

To assess inter-rater reliability, two independent raters (physicians trained in using the Indonesian version of the NANO scale independently evaluated each participant on the same day without knowledge of each other's assessments. Each domain of the NANO scale was scored, and inter-rater agreement was analyzed using weighted Cohen's kappa (κ) for ordinal items. Kappa values were interpreted as follows: <0.20 (poor), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (substantial), and >0.80 (almost perfect agreement).

Data Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. Inter-rater reliability was evaluated using weighted Cohen's kappa with 95% confidence intervals. Statistical analyses were performed using SPSS version 29.

Results

In the process of translating the NANO scale into Indonesian, no inconsistencies were identified at any stage, including translation, initial revision, back-translation, and finalization (the Indonesian version is presented in Figure 1). Following the translation process, the instrument was evaluated in a sample of 30 patients. The demographic characteristics of the study participants are summarized in Table 1.

Kappa statistics ranged from 0.629 (substantial agreement) for sensation to 0.935 (almost perfect agreement) for facial strength. Our inter-observer variability study demonstrated that the NANO-INA scale exhibits substantial to almost perfect agreement across all domains (p<0.05), with the highest agreement observed in strength, facial strength, and language (Table 2). There were three instances in three patients where certain domains were recorded as "not assessed" or "not evaluable" by only one investigator. These scores were included in the statistical analysis.

Discussion

This study represents the first attempt to translate and culturally adapt the Neurologic Assessment in Neuro-Oncology (NANO) scale into Indonesian. The aim was to provide a validated instrument for assessing neurological function in patients with brain tumors, addressing an unmet need in Indonesian neuro-oncology practice. Globally, brain and CNS tumors impose a growing burden [1–4], and in this context, accurate evaluation of functional outcomes

Table 1. Patient Demographics for NANO-Ina Scale Inter-Observer Variability Study

Patient Characteristics	N=30
Median age, y (range)	48 (18-67)
Sex	
Women	22 (73.3%)
Men	8 (26.7%)
Type of brain tumor	
Glioblastoma	7 (23.3%)
Meningioma	7 (23.3%)
Brain metastases	9 (30%)
Other primary brain tumors	7 (23.3%)
Ongoing treatment at the time of NANO-Ina assessment	
Chemotherapy	3 (10%)
Radiation	1 (3.3%)
Chemoradiation	3 (10%)
None	23 (76.7%)

Domain 1: Gaya berjalan
Sebaiknya dinilai sedikitnya 10 langkah
0 [ ] Normal
1 [ ] Abnormal namun dapat berjalan tanpa bantuan
2 [ ] Abnormal dan membutuhkan bantuan (pendamping pasien, alat bantu jalan, dll.)
3 [ ] Tidak dapat berjalan
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Domain 2: Kekuatan
Lakukan pemeriksaan untuk setiap ekstremitas secara terpisah. Dianjurkan untuk melakukan penilaian kelompok otot mayor proksimal (di atas lutut atau siku) dan distal (di bawah lutut atau siku). Nilai yang dicatat adalah nilai pada area dengan performa terburuk. Pasien dengan penilaian awal 3 pada salah satu kelompok otot ekstremitas, dapat dinilai berdasarkan otot ekstremitas yang lain.
0 [ ] Normal
1 [ ] Terdapat gerakan namun menurun jika diberikan tahanan
2 [ ] Terdapat gerakan namun tidak dapat melawan tahanan
3 [ ] Tidak ada gerakan
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Domain 3: Ataksia (ekstremitas atas)
Tidak dapat dievaluasi jika kekuatan terganggu. Batang tubuh/ekstremitas bawah dinilai melalui domain gaya berjalan. Pemeriksaan ini sangat penting bagi pasien dengan tumor batang otak dan serebelum. Skor didasarkan pada respons terbaik dari setidaknya 3 percobaan.
0 [ ] Dapat melakukan 'tes tunjuk hidung' tanpa kesulitan
1 [ ] Dapat melakukan 'tes tunjuk hidung' namun mengalami kesulitan
2 [ ] Tidak dapat melakukan tes 'tunjuk hidung'
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Domain 4: Sensasi
Dianjurkan untuk mengevaluasi area tubuh utama secara terpisah (wajah, anggota gerak, dan trunkus). Nilai yang dicatat adalah nilai pada area dengan performa terburuk. Modalitas sensorik meliputi raba halus, tusuk, suhu, dan propriosepsi. Pasien dengan nilai awal 2 pada salah satu area tubuh utama, dapat dinilai berdasarkan area-area tubuh utama lainnya.
0 [ ] Normal
1 [ ] Menurun namun masih dapat merasakan modalitas sensorik
2 [ ] Tidak dapat merasakan modalitas sensorik
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Domain 5: Lapang pandang
Pasien yang menggunakan kacamata atau lensa kontak harus dinilai saat memakai alat tersebut. Penilaian dilakukan pada masing-masing mata dengan pencatatan nilai pada mata dengan performa terburuk
0 [ ] Normal
1 [ ] Hemianopsia parsial tidak konsisten atau meragukan (≥ kuadranopia)
2 [ ] Hemianopsia parsial konsisten atau jelas (≥ kuadranopia)
3 [ ] Hemianopsia total
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Figure 1. The Final Version of NANO-Ina Scale

is essential for both clinical management and research. Performance status measures, such as the Karnofsky Performance Scale (KPS) and the Eastern Cooperative Oncology Group (ECOG) score, have long been used as prognostic tools and are incorporated into the Response Assessment in Neuro-Oncology (RANO) criteria [5–7, 10]. However, these instruments primarily capture overall functional ability rather than specific neurological deficits. This limitation may obscure subtle but clinically relevant changes, potentially creating discrepancies between radiological findings and neurological status, particularly in situations such as pseudoprogression or pseudoresponse [8, 9].

To overcome these shortcomings, the NANO scale was developed by an international working group as a structured, standardized tool to evaluate nine domains of neurological function [9]. Unlike the KPS and ECOG scales, the NANO scale is designed to directly assess neurological deficits directly, providing a more accurate reflection of tumor-related changes. The prognostic value of NANO has been demonstrated in various glioma populations, including patients with IDH-wild-type

---

Domain 6: Kekuatan wajah
Penting untuk dinilai pada tumor batang otak. Kelemahan meliputi mendatarnya lipatan nasolabialis, senyum tidak simetris, dan sulit mengangkat alis
0 [ ] Normal
1 [ ] Kelemahan ringan/sedang
2 [ ] Kelemahan wajah berat
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Domain 7: Bahasa
Penilaian berdasarkan ucapan yang disampaikan. Isyarat non-lisan atau tulisan tidak dapat digunakan. Dinyatakan abnormal jika: Level 1: meliputi kesulitan mencari kata-kata; parafasia ringan /neologisme/substitusi kata; namun dapat membentuk kalimat (penuh/terbata-bata). Level 2: tidak mampu membentuk kalimat (<4 kata per frasa/kalimat); luaran kata terbatas, ucapan lancar tidak bermakna
0 [ ] Normal
1 [ ] Abnormal namun dapat menyampaikan maksud kepada pemeriksa dengan mudah
2 [ ] Abnormal dan sulit menyampaikan maksud kepada pemeriksa
3 [ ] Abnormal. Jika verbal, tidak bisa menyampaikan maksud kepada pemeriksa. ATAU non-verbal (bisu/afasia global)
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Domain 8: Tingkat kesadaran
0 [ ] Normal
1 [ ] Mengantuk (mudah dibangunkan)
2 [ ] Somnolen (sulit dibangunkan)
3 [ ] Tidak dapat dibangunkan/koma
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Domain 9: Perilaku
Penting untuk dinilai pada tumor lobus frontalis. Perubahan meliputi apati, disinhibisi, atau bingung. Pertimbangkan kejang subklinis jika terjadi perubahan perilaku yang bermakna
0 [ ] Normal
1 [ ] Perubahan perilaku ringan/sedang
2 [ ] Perubahan perilaku berat
  [ ] Tidak dinilai
  [ ] Tidak dapat dievaluasi

Figure 1. Continued

Table 2. Inter-Rater Reliability (Kappa Statistic*) Per Individual Domain

Domain	Inter-observer agreement (Kappa statistic)	P
Gait	0.722	<0.001
Strength	0.904	<0.001
Ataxia (upper extremity)	0.767	<0.001
Sensation	0.629	<0.001
Visual field	0.862	<0.001
Facial strength	0.935	<0.001
Language	0.926	<0.001
Level of consciousness	0.783	<0.001
Behavior	0.845	<0.001

*<0.00, poor agreement; 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; 0.81–1.0, almost perfect agreement.

glioblastoma [7, 11, 12]. It has been increasingly applied in both clinical trials and observational studies [8, 13, 14]. Translation and validation efforts in other languages, such as Brazilian Portuguese, have further expanded its applicability [15].

The present study demonstrated that the Indonesian version (NANO-Ina) achieved substantial to almost perfect inter-rater reliability, with kappa values ranging from 0.629 to 0.935, comparable to earlier reports [9, 11, 12]. The domains of strength, facial strength, and

language demonstrated the highest levels of agreement, reflecting both their objective nature and familiarity to clinicians in routine practice. In contrast, domains such as gait, ataxia, and visual field assessment were slightly less reliable, likely due to their subjectivity and dependence on clinical context, but still showed substantial agreement. These results indicate that the NANO-Ina can be reliably administered in daily practice, requiring only a short administration time (median, 4 minutes), which is consistent with its feasibility in other studies [9, 11, 12, 15].

The practical value of this study lies in providing a culturally and linguistically adapted instrument for use in Indonesian neuro-oncology. While the methodological design was straightforward, the validation of NANO-Ina offers a clinically relevant contribution. In Indonesia, where KPS and ECOG remain the predominant tools, the availability of NANO-Ina allows clinicians to capture neurological changes more precisely, complementing radiological findings and improving the accuracy of treatment response assessments [10, 16]. Furthermore, the scale may facilitate standardized evaluation in clinical trials, support early prognostic stratification in glioma [5–7, 11, 12], and serve as a valuable outcome measure in studies of treatment interventions, including novel clinical trial designs [8, 13].

Nevertheless, some limitations should be acknowledged. The sample size was relatively small (n = 30), the study was conducted at a single academic center, and only inter-rater reliability was examined. Test–retest reliability, convergent validity, and more advanced psychometric analyses were not performed. In addition, the assessments were conducted by experienced neuro-oncology clinicians, which may not reflect broader practice variability [6, 17]. These limitations restrict the generalizability of the findings, and future multi-center studies with larger cohorts are required to confirm and extend the utility of NANO-Ina in diverse Indonesian settings.

In conclusion, the Indonesian version of the NANO scale (NANO-Ina) demonstrated strong inter-rater reliability and feasibility, supporting its use as a practical and reliable tool for neurological assessment in Indonesian patients with brain tumors. By complementing existing scales such as KPS and ECOG, the NANO-Ina provides a more comprehensive framework for evaluating functional outcomes, aligning Indonesian practice with international standards while addressing local cultural and clinical needs [16, 18].

Study Limitations

This study has several limitations. The sample size was relatively small (n=30), and the research was conducted at a single academic center, which may restrict the generalizability of the findings to other hospitals or community settings. Furthermore, the evaluation was limited to inter-rater reliability; test–retest reliability and more advanced psychometric analyses were not performed. All assessments were carried out by clinicians with prior experience in neuro-oncology, which may not fully reflect the broader variability in clinical practice.

Future studies with larger, multi-center cohorts and more comprehensive statistical approaches are warranted to confirm and extend these findings.

References

1. Huangfu B, Liu X, Wang X, Niu X, Wang C, Cheng R, et al. Global trends and burden of brain and central nervous system cancers in adolescents and young adults: GBD 2021 study. Sci Rep. 2025;15(1):17049. https://doi.org/10.1038/s41598-025-01368-6
2. Ilic I, Ilic M. International patterns and trends in the brain cancer incidence and mortality: An observational study based on the global burden of disease. Heliyon. 2023;9(7):e18222. https://doi.org/10.1016/j.heliyon.2023.e18222
3. Fan Y, Zhang X, Gao C, Jiang S, Wu H, Liu Z, et al. Burden and trends of brain and central nervous system cancer from 1990 to 2019 at the global, regional, and country levels. Arch Public Health. 2022;80:209. https://doi.org/10.1186/s13690-022-00965-5
4. Globocan. The Global Cancer Observatory, Indonesia; 2022.
5. Gunawan PY, Islam A, July J, Patellongi I, Nasrum M, Aninditha T. Karnofsky Performance Scale and Neurological Assessment of Neuro-Oncology Scale as Early Predictor in Glioma. Asia Pac J Cancer Prev. 2020;21(11):3387–92. https://doi.org/10.31557/APJCP.2020.21.11.3387
6. Chow R, Bruera E, Temel JS, Krishnan M, Im J, Lock M. Inter-rater reliability in performance status assessment among healthcare professionals: an updated systematic review and meta-analysis. Support Care Cancer. 2020;28(5):2071–78. https://doi.org/10.1007/s00520-019-05261-7
7. Kasper J, Wende T, Fehrenbach MK, Wilhelmy F, Jähne K,

Frydrychowicz C, et al. The Prognostic Value of NANO Scale Assessment in IDH-Wild-Type Glioblastoma Patients. Front Oncol. 2021;11:790458. https://doi.org/10.3389/fonc.2021.790458

8. Saraf A, Trippa L, Rahman R. Novel Clinical Trial Designs in Neuro-Oncology. Neurotherapeutics. 2022;19(6):1844–54. https://doi.org/10.1007/s13311-022-01284-x

9. Nayak L, DeAngelis LM, Brandes AA, Peereboom DM, Galanis E, Lin NU, et al. The Neurologic Assessment in Neuro-Oncology (NANO) scale: A tool to assess neurologic function for integration into the Response Assessment in Neuro-Oncology (RANO) criteria. Neuro Oncol. 2017;19(5):625–35. https://doi.org/10.1093/neuonc/nox029

10. Wen PY, Chang SM, Van Den Bent MJ, Vogelbaum MA, Macdonald DR, Lee EQ. Response Assessment in Neuro-Oncology Clinical Trials. J Clin Oncol. 2017;35(21):2439–49. https://doi.org/10.1200/JCO.2017.35.21.2439

11. Ung TH, Ney DE, Damek D, Rusthoven CG, Youssef AS, Lillehei KO, et al. The Neurologic Assessment in Neuro-Oncology (NANO) Scale as an Assessment Tool for Survival in Patients With Primary Glioblastoma. Neurosurgery. 2018;0(0);1–9. https://doi.org/10.1093/neuros/nyy098/4957035

12. Lee J, Park SH, Kim YZ. Prognostic Evaluation of Neurological Assessment of the Neuro-Oncology Scale in Glioblastoma Patients. Brain Tumor Res Treat. 2018;6(1):22. https://doi.org/10.14791/btrt.2018.6.e1

13. Bi WL, Nayak L, Meredith DM, Driver J, Du Z, Hoffman S, et al. Activity of PD-1 blockade with nivolumab among patients with recurrent atypical/anaplastic meningioma: phase II trial results. Neuro Oncol. 2022;24(1):101–13. https://doi.org/10.1093/neuonc/noab118

14. Kalasauskas D, Keric N, Ajaj SA, Cube L von, Ringel F, Renovanz M. Psychological burden in meningioma patients under a wait-and-watch strategy and after complete resection is high — results of a prospective single center study. Cancers (Basel). 2020;12(12):1–13. https://doi.org/10.3390/cancers12123503

15. Velho MC, Andrade Gripp D, Pires de Aguiar PH, Nicacio JA, Formentin C, Greggianin GF, et al. Translation and validation of the Neurological Assessment in Neuro-Oncology scale to Brazilian Portuguese. Front Neurol. 2024;15:1369625. https://doi.org/10.3389/fneur.2024.1369625

16. Fitri FI, Lubis ND, Darman WR, Fithrie A. Correlation between Response Assessment in Neuro-Oncology (RANO) criteria and clinical outcome in patients with brain tumor. J Med Health Stud. 2022;1(1):1–5. https://doi.org/10.32996/jmhs

17. Drexler R, Ricklefs FL, Pantel TF, Göttsche J, Westphal M, Dührsen L. The Comprehensive Complication Index (CCI) as a Measure of Postoperative Morbidity and Neurological Outcome after Elective Intracranial Surgery. J Neurol Surg A Cent Eur Neurosurg. 2024. https://doi.org/10.1055/a-1962-0636

18. Angelita MC, Aninditha T, Andriani R, Tandian D, Al Rasyid, Safri AY, et al. Indonesian version of the Neurologic Assessment in Neuro-Oncology Scale (NANO-Ina) and the Karnofsky Performance Scale (KPS) as Instruments for Assessing Postoperative Response to Meningioma and Its Influencing Factors [thesis]. Jakarta: FKUI; 2025.