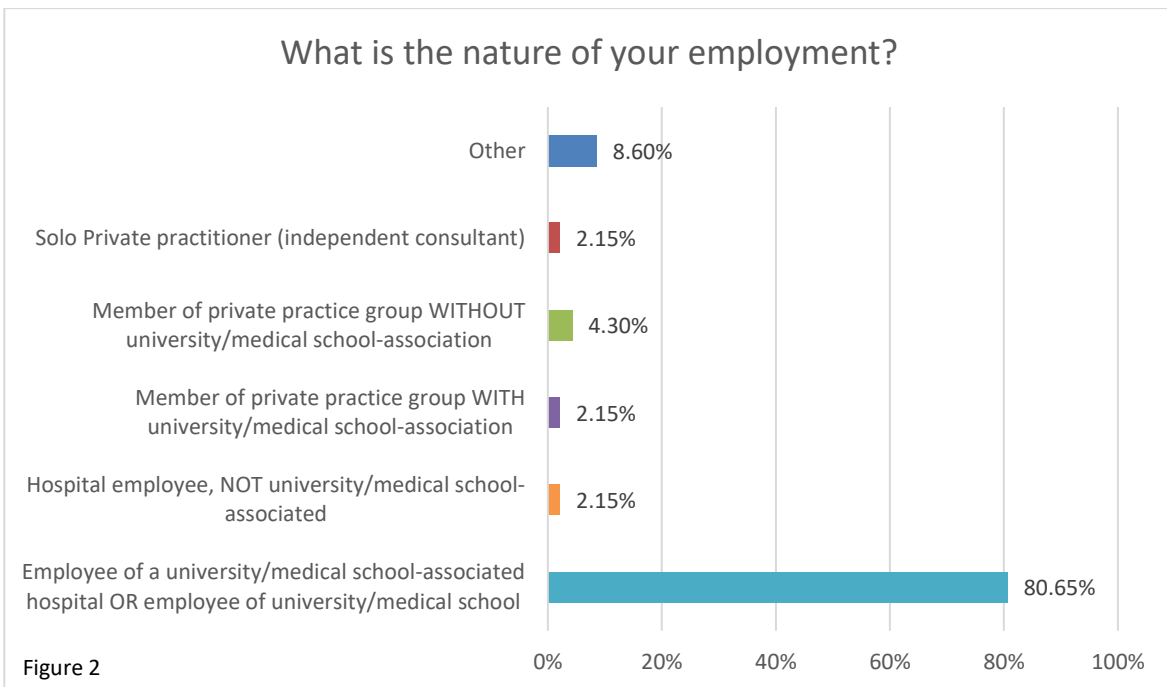
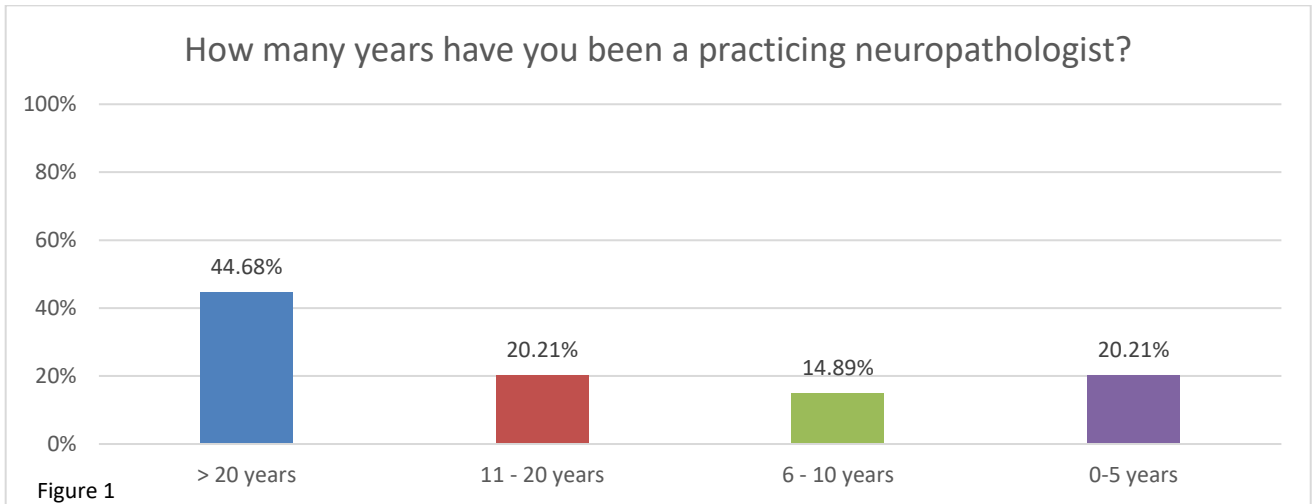


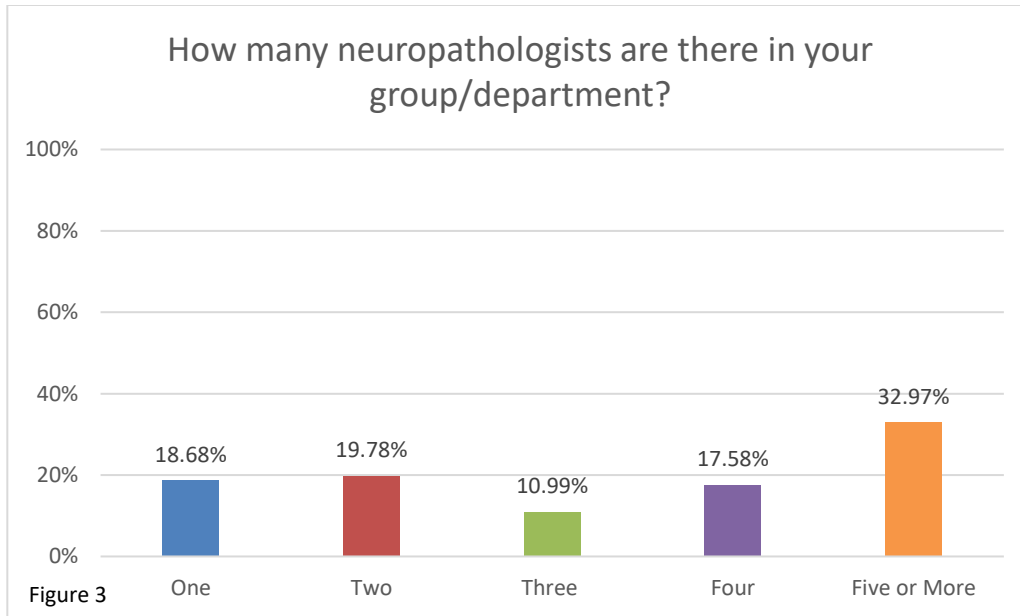
AOE Analysis of AANP’s Fall 2022 Membership Survey

A survey was sent to the membership base of the American Association of Neuropathologists (AANP) in the fall of 2022. This survey is used for planning of future annual meeting topics by providing a better understanding of current neuropathology practice characteristics. A total of 112 members provided responses to the 24 clinical assertion statement questions within the survey and the summary of these results are described below.

The survey asked individuals to provide responses to demographic questions, shown in figures 1-3, to help further contextualize the results.



Other includes: Retired/Semi-Retired (4), Consultant (1), Federal Government Employee (NIH) (1), Industry – not practicing (1), Private Non-Profit Research Institute (1)



Clinical Assertion Statements

The survey asked members to rate 24 different clinical assertion statements using a 5-point Likert-type scale from 1=Disagree Completely to 5=Agree Completely, with a neutral option of 3=Neither Disagree nor Agree. These questions were developed to determine a member's level of knowledge regarding 8 separate topics in neuropathology. Data is presented as mean +/- percent unknown. Percent unknown indicate the number of responses in the incorrect/neutral position of total responses.

Dementia

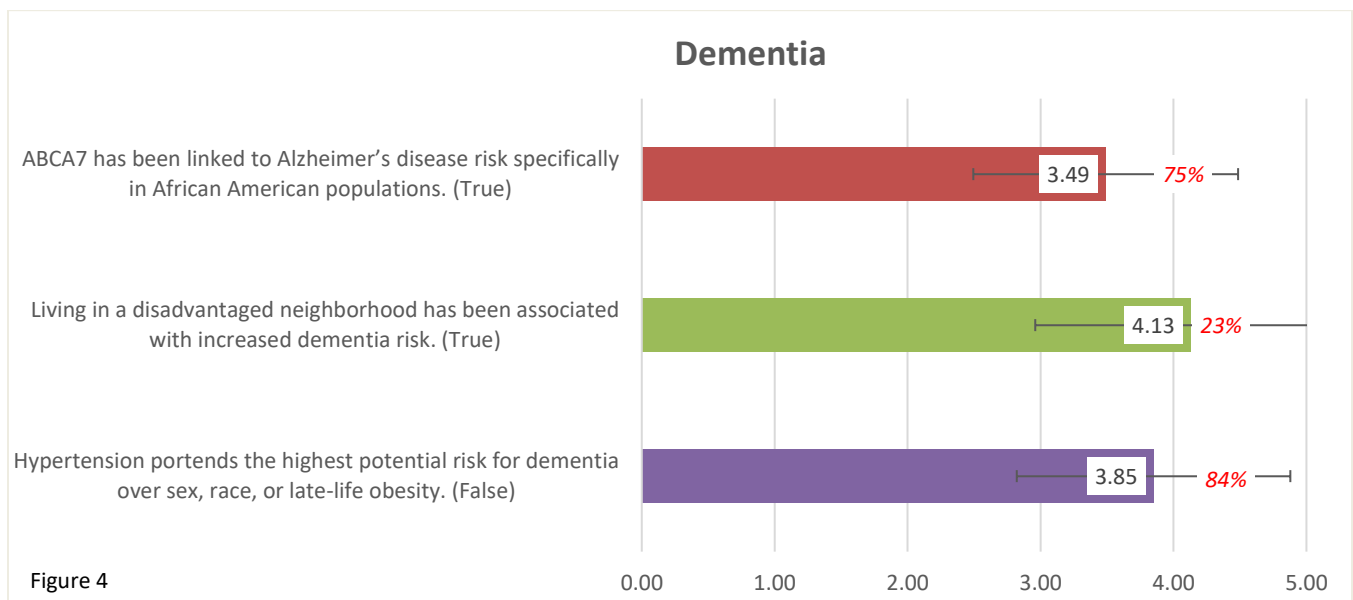


Figure 4 provides the results for the three questions evaluating knowledge in the area of **dementia**. Statements one and two are true, while statement three is false. Statement one and two had mean scores in the desired direction. However, statement one had 75% of the respondents who answered at the neutral/incorrect position which may indicate where additional education is appropriate. Statements three had mean scores in the incorrect direction. In sum, areas of appropriate additional education include:

- Hypertension portends the highest potential risk for dementia over sex, race, or late-life obesity. (False)
- *ABCA7* has been linked to Alzheimer’s disease risk specifically in African American populations. (True)

Neuropathology Practice in the Developing World

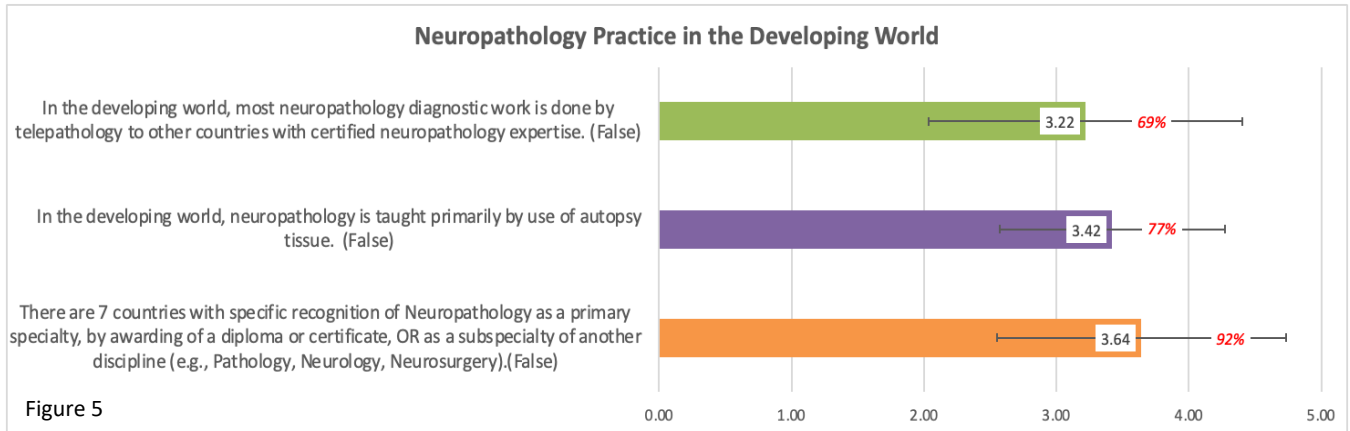


Figure 5 provides the results for the three questions evaluating knowledge in the area of **neuropathology practice in the developing world**. All statements are false. All statements had a mean score on the incorrect side of the scale indicating that additional education is appropriate. In sum, areas of appropriate additional education include:

- There are 7 countries with specific recognition of Neuropathology as a primary specialty, by awarding of a diploma or certificate, OR as a subspecialty of another discipline (e.g., Pathology, Neurology, Neurosurgery). (False)
- In the developing world, neuropathology is taught primarily by use of autopsy tissue. (False)
- In the developing world, most neuropathology diagnostic work is done by telepathology to other countries with certified neuropathology expertise. (False)

Fluid Biomarkers (CSF/blood; tumors/neurodegenerative diseases)

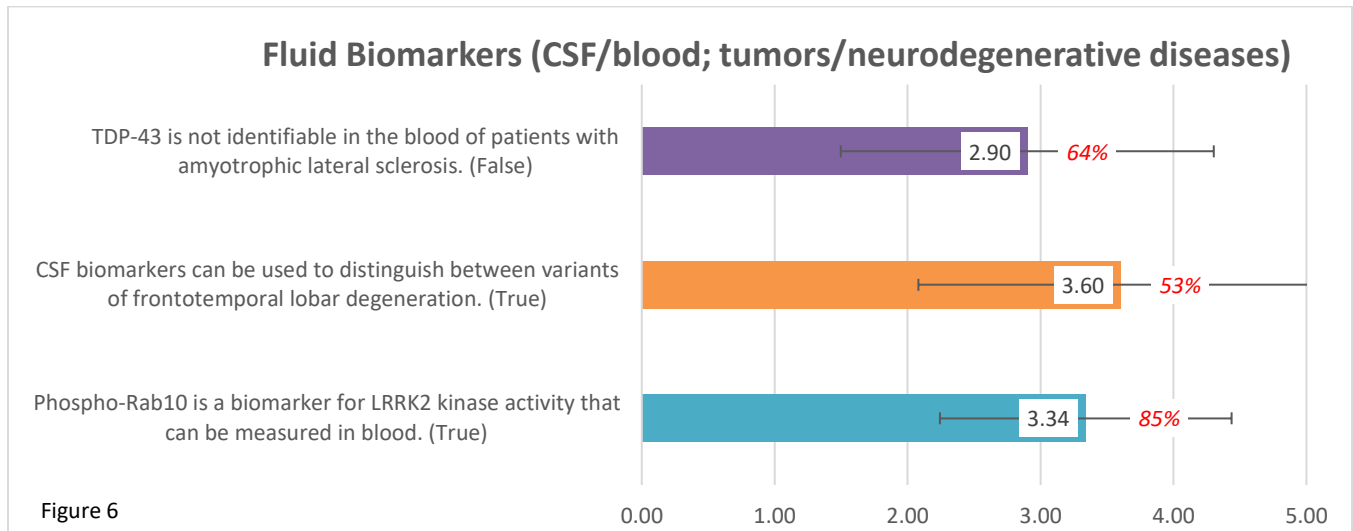


Figure 6 provides the results for the three questions evaluating knowledge regarding **fluid biomarkers (CSF/blood; tumors/neurodegenerative disease)**. Statement one is false, while statements two and three are true. All three statements have a mean close to the neutral position, however, 64%, 53% and 85% of responses, respectively, were incorrect or in the neutral position indicating education is likely appropriate related to these statements. In sum, areas of appropriate additional education include:

- Phospho-Rab10 is a biomarker for LRRK2 kinase activity that can be measured in blood. (True)
- CSF biomarkers can be used to distinguish between variants of frontotemporal lobar degeneration. (True)
- TDP-43 is not identifiable in the blood of patients with amyotrophic lateral sclerosis (False)

Gene Therapy and Neuropathology

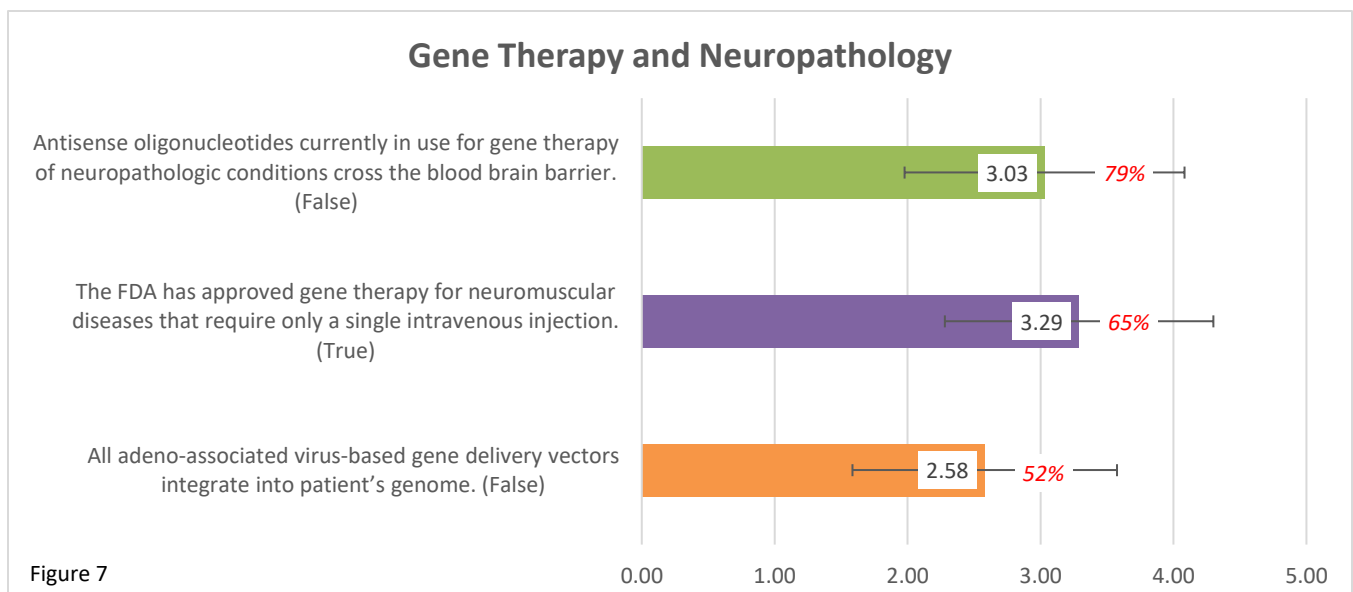


Figure 7 provides the results for the three questions evaluating knowledge in the area of **gene therapy and neuropathology**. Statements one and three are false, while statement two is true. Members selected responses in the desired direction for statement three. Statements one and two had a mean score close to the neutral position and 79% and 65% of responses, respectively, were incorrect or in the neutral position indicating education is appropriate related to these statements. In sum, areas of appropriate additional education include:

- The FDA has approved gene therapy for neuromuscular diseases that require only a single intravenous injection. (True)
- Antisense oligonucleotides currently in use for gene therapy of neuropathologic conditions cross the blood brain barrier. (False)

Eye Pathology

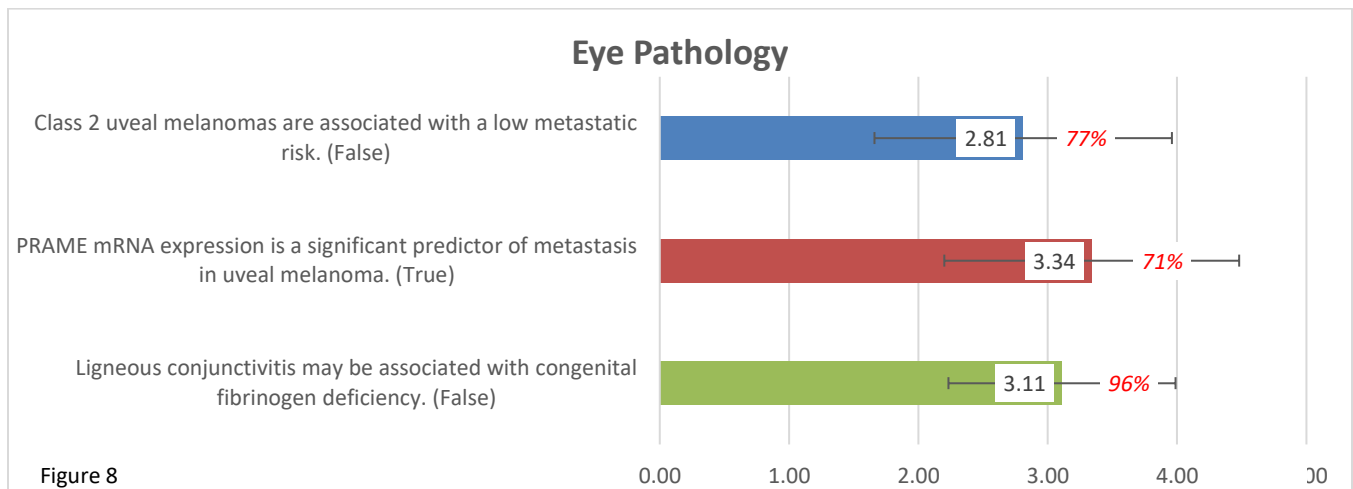


Figure 8 provides the results for the three questions evaluating knowledge in the area of **eye pathology**. Statements one and three are false, while statement two is true. Statement one had mean scores in the desired direction, however 77% of the respondents answered at the neutral/incorrect position which may indicate where additional education is appropriate. Additionally, statements two and three had answers in the incorrect or neutral position, indicating that education may be appropriate. In sum, areas of appropriate additional education include:

- Ligneous conjunctivitis may be associated with congenital fibrinogen deficiency. (False)
- PRAME mRNA expression is a significant predictor of metastasis in uveal melanoma. (True)
- Class 2 uveal melanomas are associated with a low metastatic risk (False)

Neuromuscular Pathology

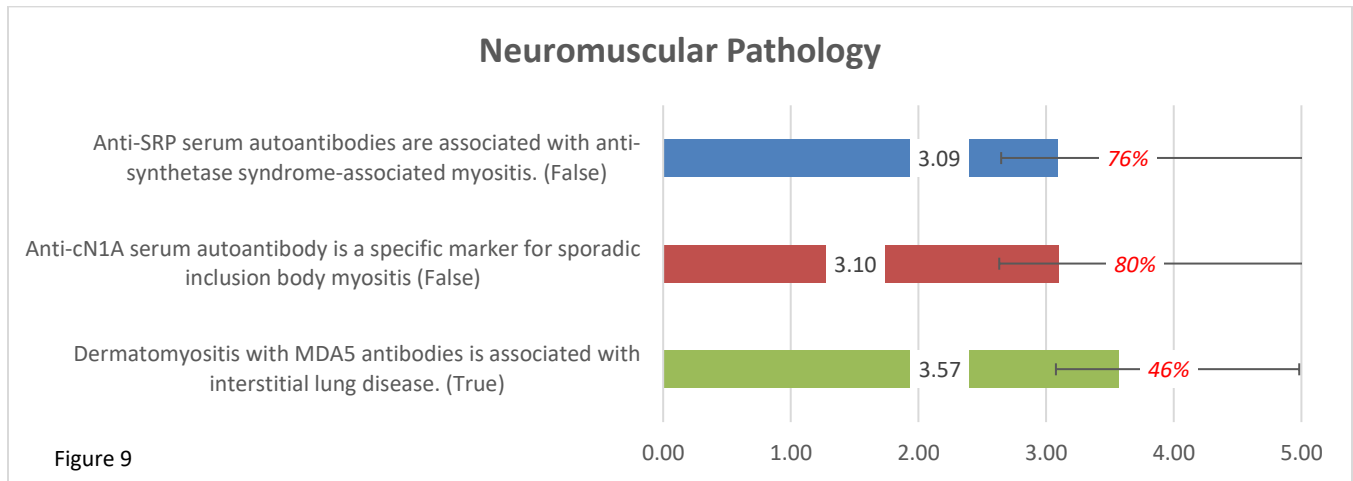


Figure 9 provides the results for the three questions evaluating knowledge in the area of **neuromuscular pathology**. Statement one and two are false and statement three is true. All statements had answers in the incorrect or neutral position, indicating that education may be appropriate. In sum, an area of appropriate additional education include:

- Dermatomyositis with MDA5 antibodies is associated with interstitial lung disease. (True)
- Anti-cN1A serum autoantibody is a specific marker for sporadic inclusion body myositis. (False)
- Anti-SRP serum autoantibodies are associated with anti-synthetase syndrome-associated myositis. (False)

Pediatric Neuropathology

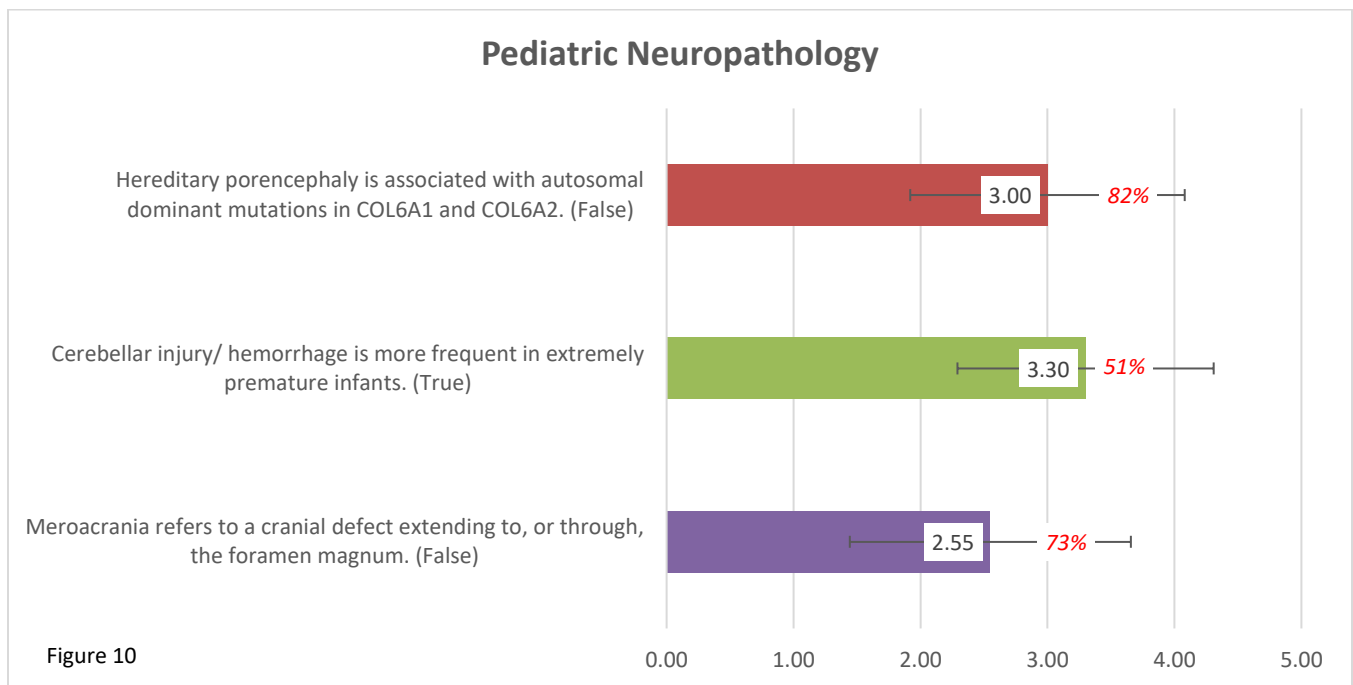


Figure 10 provides the results for the three questions evaluating knowledge in the areas of **pediatric neuropathology**. Statement one and three are false, while statement two is true. Statement three had a mean score in the desired direction, however, 73% of respondents answered in the incorrect or neutral position, indicating additional education may be appropriate. Statement one and two had a mean score in the neutral position, indicating education is appropriate. In sum, areas of appropriate additional education include:

- Meroacrania refers to a cranial defect extending to, or through, the foramen magnum. (False)
- Cerebellar injury/ hemorrhage is more frequent in extremely premature infants. (True)
- Hereditary porencephaly is associated with autosomal dominant mutations in COL6A1 and COL6A2. (False)

New or Provisional CNS5 WHO Entities

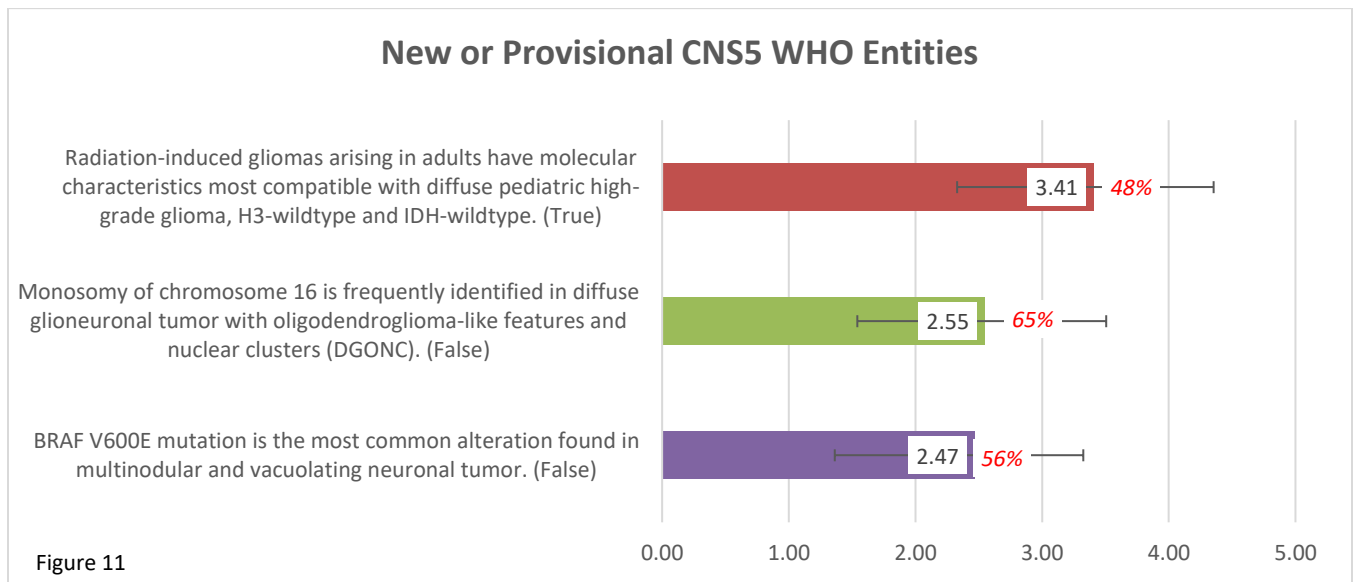


Figure 11 provides the results for the three questions evaluating knowledge in the area of **new or provisional CNS5 WHO entities**. Statement one is true, while statements two and three are false. Statement two and three have a mean score in the desired direction, however, regarding statement two, 65% of respondents answered in the incorrect or neutral position. Statement one had a mean score in the neutral position, indicating education is appropriate. In sum, areas of appropriate additional education include:

- Monosomy of chromosome 16 is frequently identified in diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (DGONC). (False)
- Radiation-induced gliomas arising in adults have molecular characteristics most compatible with diffuse pediatric high-grade glioma, H3-wildtype and IDH-wildtype. (True)

Conclusion:

Based on the analysis of the 2022 Annual Membership Survey, there were some statements where responses were close to neutral and many respondents answered in the neutral position which provides areas where there may be need for additional education. Further, several scores were on the opposite/wrong side of the scale. Both situations indicate that the following are areas of need for additional education:

- **Dementia**
 - Hypertension portends the highest potential risk for dementia over sex, race, or late-life obesity. (False statement; 84% unknown/incorrect responses)

- *ABCA7* has been linked to Alzheimer's disease risk specifically in African American populations. (True statement; 75% unknown/incorrect responses)
- **Neuropathology Practice in the Developing World**
 - There are 7 countries with specific recognition of Neuropathology as a primary specialty, by awarding of a diploma or certificate, OR as a subspecialty of another discipline (e.g., Pathology, Neurology, Neurosurgery). (False statement; 92% unknown/incorrect responses)
 - In the developing world, neuropathology is taught primarily by use of autopsy tissue. (False statement; 77% unknown/incorrect responses)
 - In the developing world, most neuropathology diagnostic work is done by telepathology to other countries with certified neuropathology expertise. (False statement; 69% unknown/incorrect responses)
- **Fluid Biomarkers (CSF/blood; tumors/neurodegenerative diseases)**
 - Phospho-Rab10 is a biomarker for LRRK2 kinase activity that can be measured in blood. (True statement; 85% unknown/incorrect responses)
 - CSF biomarkers can be used to distinguish between variants of frontotemporal lobar degeneration. (True statement; 53% unknown/incorrect responses)
 - TDP-43 is not identifiable in the blood of patients with amyotrophic lateral sclerosis (False statement; 64% unknown/incorrect responses)
- **Gene Therapy and Neuropathology**
 - The FDA has approved gene therapy for neuromuscular diseases that require only a single intravenous injection. (True statement; 65% unknown/incorrect responses)
 - Antisense oligonucleotides currently in use for gene therapy of neuropathologic conditions cross the blood brain barrier. (False statement; 79% unknown/incorrect responses)
- **Eye Pathology**
 - Ligneous conjunctivitis may be associated with congenital fibrinogen deficiency. (False statement; 96% unknown/incorrect responses)
 - PRAME mRNA expression is a significant predictor of metastasis in uveal melanoma. (True statement; 71% unknown/incorrect responses)
 - Class 2 uveal melanomas are associated with a low metastatic risk (False statement; 77% unknown/incorrect responses)
- **Neuromuscular Pathology**
 - Dermatomyositis with MDA5 antibodies is associated with interstitial lung disease. (True statement; 46% unknown/incorrect responses)
 - Anti-cN1A serum autoantibody is a specific marker for sporadic inclusion body myositis. (False statement; 80% unknown/incorrect responses)
 - Anti-SRP serum autoantibodies are associated with anti-synthetase syndrome-associated myositis. (False statement; 76% unknown/incorrect responses)
- **Pediatric Neuropathology**
 - Meroacrania refers to a cranial defect extending to, or through, the foramen magnum. (False statement; 73% unknown/incorrect responses)
 - Cerebellar injury/ hemorrhage is more frequent in extremely premature infants. (True statement; 51% unknown/incorrect responses)
 - Hereditary porencephaly is associated with autosomal dominant mutations in COL6A1 and COL6A2. (False statement; 82% unknown/incorrect responses)
- **New or Provisional CNS WHO Entities**

- Monosomy of chromosome 16 is frequently identified in diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (DGONC). (False statement; 82% unknown/incorrect responses)
- Radiation-induced gliomas arising in adults have molecular characteristics most compatible with diffuse pediatric high-grade glioma, H3-wildtype and IDH-wildtype. (True statement; 48% unknown/incorrect responses)

Additional Survey Questions

The following data regarding CNS tumor testing and reporting and neuropathology resident training were included by the AANP Professional Affairs Committee in order to garner data on these topics.

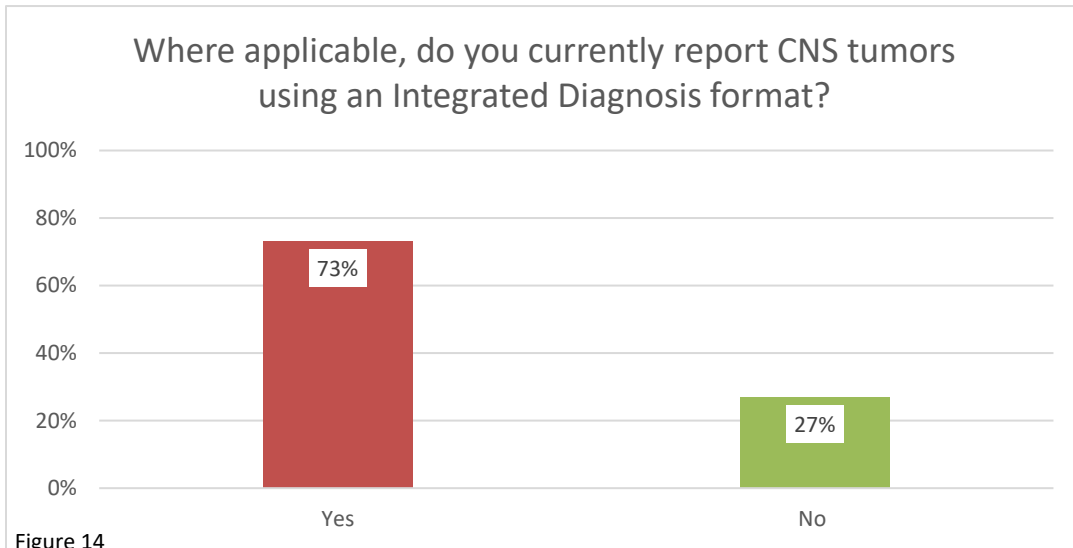


Figure 14 provides the results for the type of format that members use for CNS tumors. Most members, 73%, use an Integrated Diagnosis format to report CNS tumors.

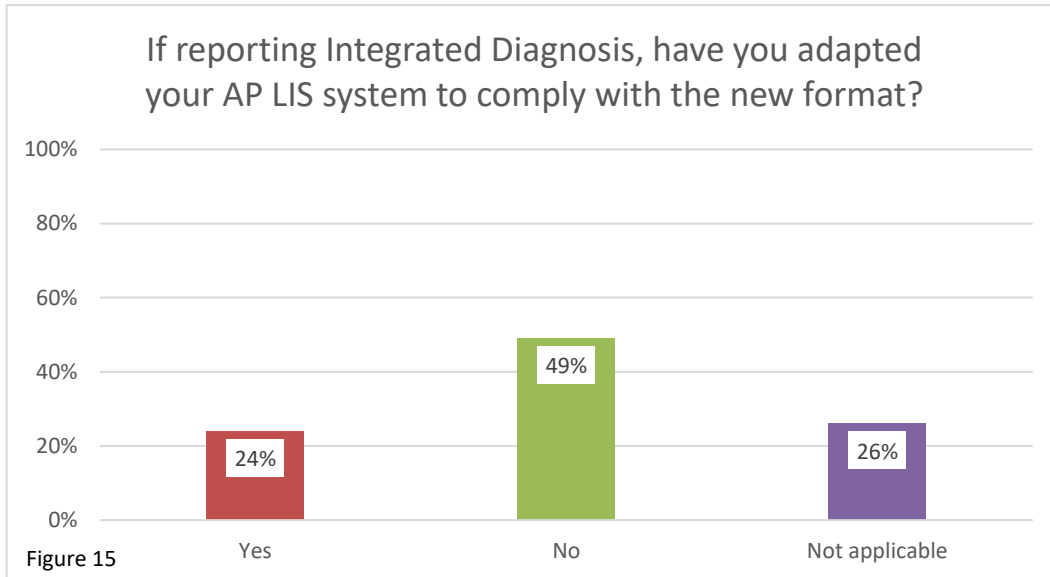


Figure 15 provides the results assessing the formatting of Integrated Diagnosis reporting. (For members who had indicated they do not use an Integrated Diagnosis, were instructed to choose “Not applicable”.) Many members (49%) have adapted their institution’s AP LIS system to comply with the new format.

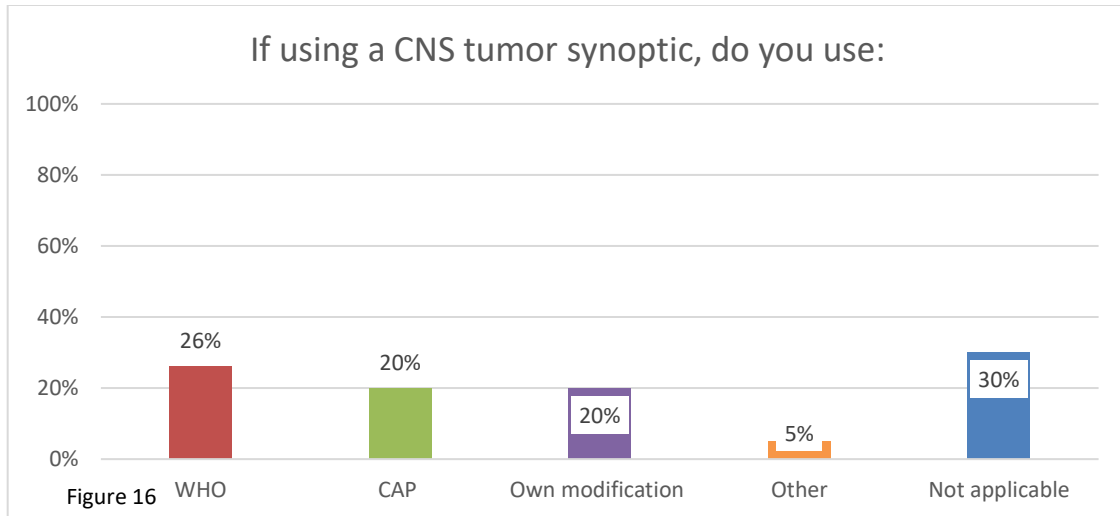


Figure 16 provides the results assessing the frequency of testing if using a CNS tumor synoptic at members’ institutions. (For members who had previously indicated they do not use an Integrated Diagnosis, were instructed to choose “Not applicable”.) Members were split among WHO, CAP and their own modification.

Further, members’ who indicated “Other” were asked to explain more. Answers listed below:

- No synoptic, use micro, comment and topline
- I do not use synoptic for CNS tumors
- Do not use synoptic

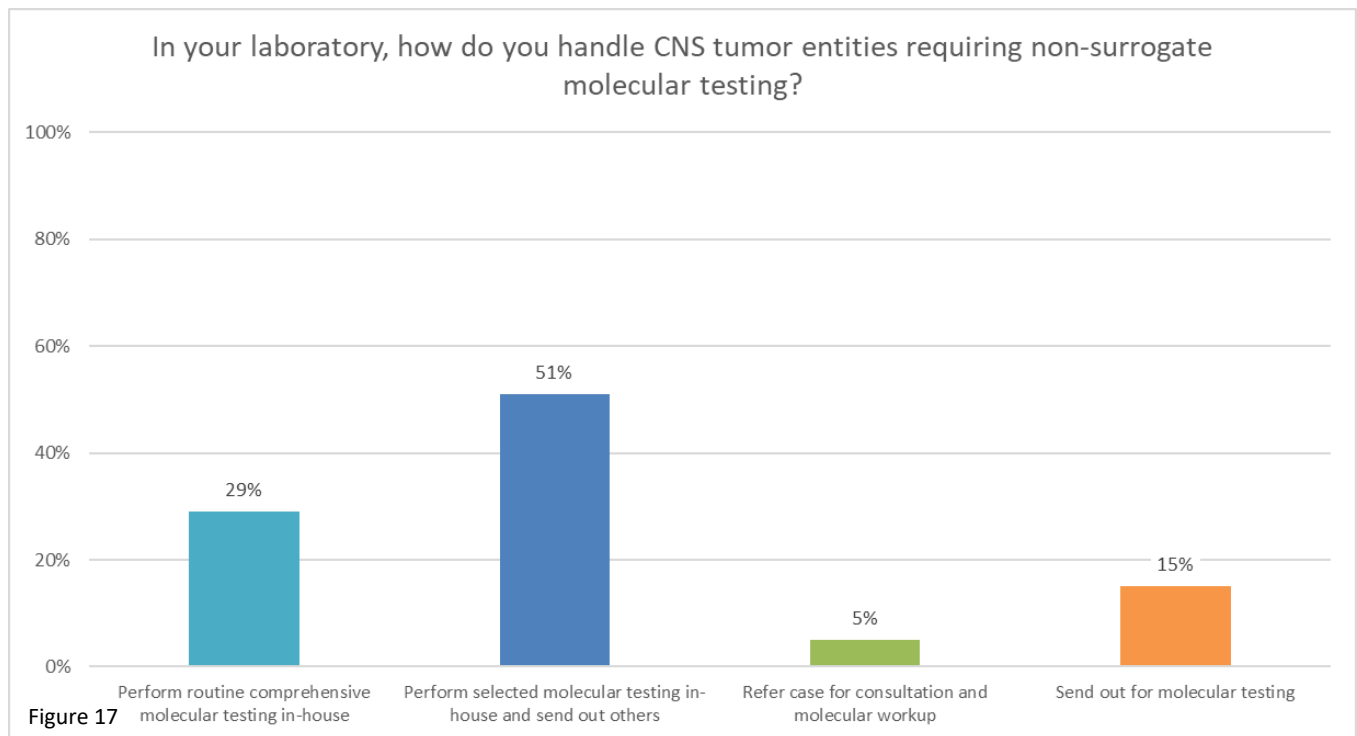


Figure 17

Figure 17 provides the results of how members handle CNS tumors requiring non-surrogate molecular testing. The majority of members (45%) indicated they use a targeted NGS panel at their institution.

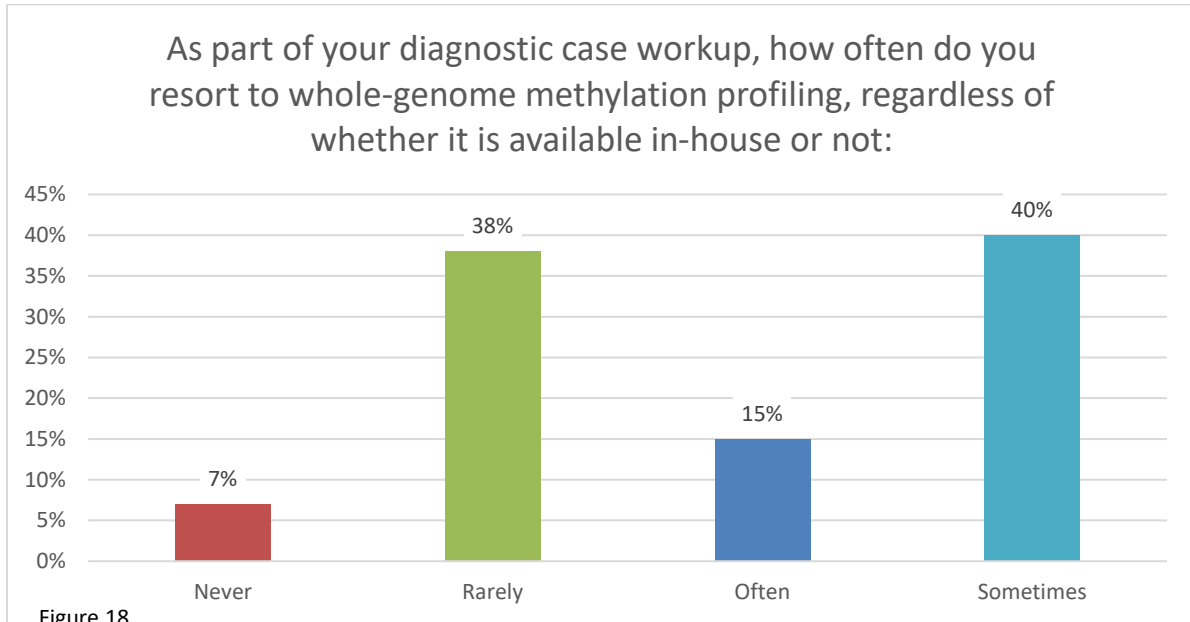


Figure 18 provides the results of how often members use whole-genome methylation profiling. Members were split among the “rarely” and “sometimes,” at 38% and 40%, respectively.

Figure 17

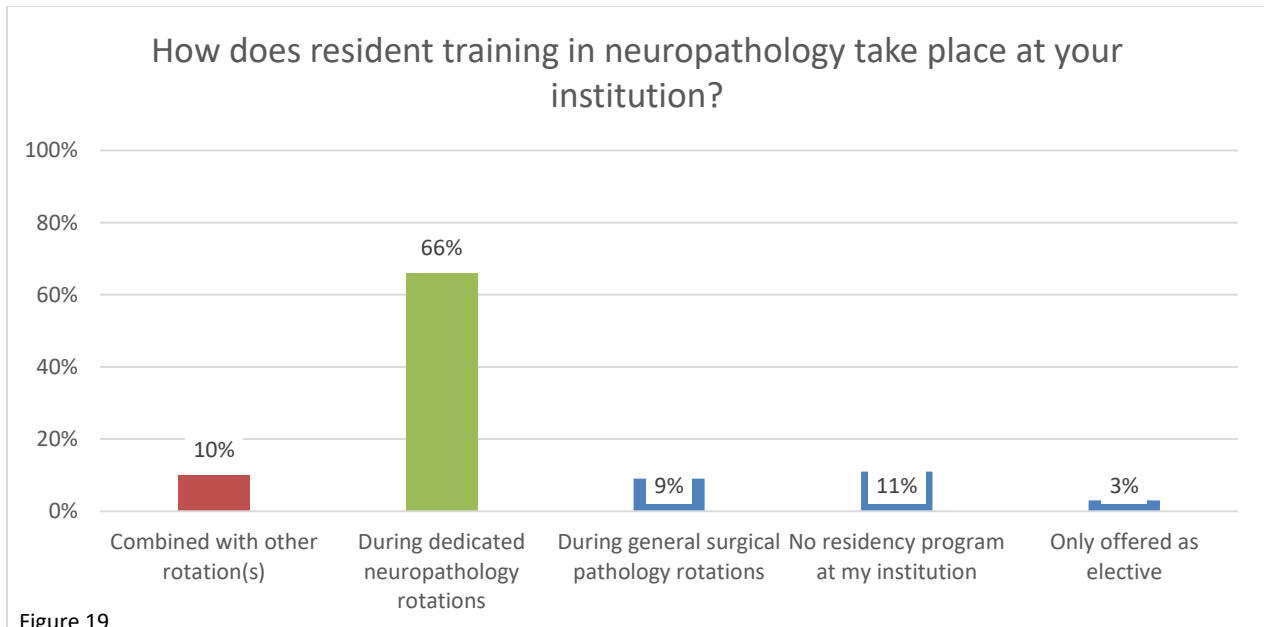


Figure 19 provides the results assessing how resident training in neuropathology occur at the members’ institution. The majority of members (66%) indicated that resident training takes place during dedicated neuropathology rotations.

Members who answered “combined with other rotation(s)” provided the following explanations:

- You do not have the option to select multiple responses. We have dedicated neuropathology rotations, but anatomic pathology residents also partake in everyday surgical neuropathology cases and sign-outs. There is also an elective offered to anatomic pathology residents.
- Our neuropathology elective is now combined with Dermpath, so that our residents only have 2 weeks dedicated NP training. They also see NP surgicals on SP rotation.
- Combined with autopsy (x2)
- With Dermpath
- Combined with head and neck surgical pathology; also offered as stand-alone elective

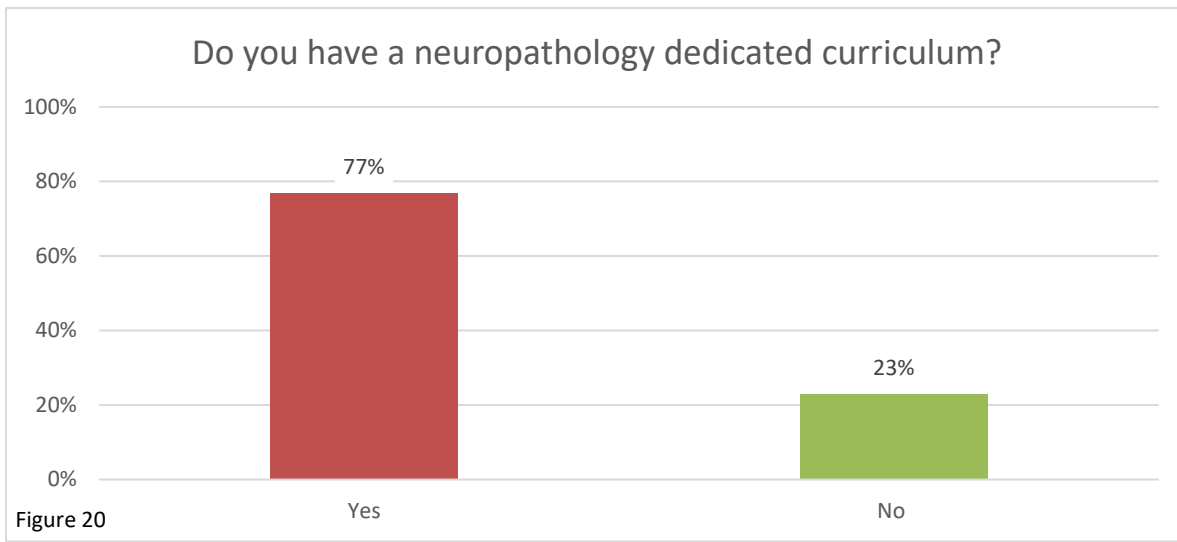


Figure 20 shows if members’ institutions have a dedicated curriculum devoted to neuropathology. The majority of members (77%) indicated that there was a dedicated neuropathology curriculum at their respective institutions.

For those members with a dedicated neuropathology curriculum, they were asked to provide additional detail regarding number of didactics and time period. Answers are listed below:

- 1/week during the year, save for summer break and occasional weeks where academic half day is canceled (eg, cancel for conferences such as AANP, CANP)
- ~ 5 one-hour lectures throughout each year. Some of the topics vary with year (we rotate among ~ 10 or so topics)
- 8 per 2 years
- 22, over 2-year cycle
- As a group we have at least 20 hours of PowerPoint material given either during rotations to pathology/neurology/neurosurgery residents or as part of the pathology residency curriculum
- ~10, over a month
- ~8-10 didactic lectures, ~50 minute each and ~5 slide sessions ~50 minute each over 1.5-month period
- 24 didactic lectures per year
- 10 didactics, 1 hour each, given once every 2 years during a 7-week window
- 4 didactics per each 2-year period
- Variable from year to year and even within year.
- 6 resident didactics over a 2-week period once a year
- 5 years
- 50 per year

- Weekly release – 4-year program
- 8-12, 6 weeks
- Approximately 5-10, 1-hour lectures over the course of a year
- Lecture categories spread out over two years, then repeated
- Around 12 didactic in a period of 8 weeks
- 4 per year to AP residents + 6 per year to neurol/neurosurg residents (we do not have an NP program)
- 6/year (x3)
- 15 per year
- Around half a dozen lectures and 4 unknown slide sessions each year.
- 10-12 didactics over a 2-year period
- About 12. For Pathology residents: over a two-month period. For Neurosurgery residents: Every third Friday of each month. For Neurology residents: NP lectures integrated with Neurology teaching modules throughout the year.
- 6 didactics over a month; but we have online modules too
- 1-2x per month in 2-year cycle
- 6 sessions over two years.
- About 20 lectures over 4-year residency schedule.
- Series of lectures (6-8) as part of curriculum (on a 2-year cycle)
- 23 didactic sessions over a month
- 5 per year
- 1 per month
- It's a two-year program geared toward the fellows with sessions either every month or every other month. One year we go over homemade multiple-choice questions, and the other year we do a textbook review. Rotators and medical students participate.
- 4-week online course with slide boxes and questions'
- Several lectures and slide sessions a year, on a two-year rotation
- 40 lectures in 2 years
- 10 didactics in a two-year rolling cycle (5/year).
- 8-10 didactics, over the course of 2 months
- monthly 24 topics delivered over a 2-year cycle
- 4 - 1-2 months (beginning of resident year)