TRAINING AND EDUCATION IN NEUROSURGERY: STRATEGIES AND CHALLENGES FOR THE NEXT TEN YEARS

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PUBLISHED IN: Frontiers in Surgery

frontiers Research Topics

ISSN 1664-8714
ISBN 978-2-83250-059-0
DOI 10.3389/978-2-83250-059-0

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TRAINING AND EDUCATION IN NEUROSURGERY: STRATEGIES AND CHALLENGES FOR THE NEXT TEN YEARS

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Citation: Zoia, C., Chaurasia, B., Bongetta, D., eds. (2022). Training and Education in Neurosurgery: Strategies and Challenges for the Next ten Years. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-83250-059-0

Table of Contents

TYPE Editorial
PUBLISHED 16 August 2022
DOI 10.3389/fsurg.2022.984208

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

RECEIVED 01 July 2022
ACCEPTED 05 July 2022
PUBLISHED 16 August 2022

CITATION
Bongetta D and Zoia C (2022) Editorial: Training and education in neurosurgery: Challenges and strategies for the next ten years.
Front. Surg. 9:984208.
doi: 10.3389/fsurg.2022.984208

Editorial: Training and education in neurosurgery: Challenges and strategies for the next ten years

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Editorial on the Research Topic
Training and education in neurosurgery: Challenges and strategies for the next ten years

by Zoia C, Chaurasia B and Bongetta D. (2022) Front. Surg. 9: 984208. doi: 10.3389/fsurg.2022.984208

Training and education are the foundation of progress in every field of science. Even more so in surgical specialties, in which a sort of craftsmanship component is implied. In this regard, Neurosurgery has always been blessed by a fertile master-apprentice approach since its beginnings with Harvey Cushing being a mentor to Walter Dandy, all the way through the foundation of the most famous residency programs after WWII. In turn, Sir William Osler, the inventor of residency itself, was a mentor to Harvey Cushing (who, among other accolades, won a Pulitzer prize for writing a biography on him!). In his own words, Sir William Osler famously expressed the need for a combined theoretical-practical approach in medical learning: "He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." (1). Even though this predicament is more than 100 years old, we should all agree that it is still true nowadays. But how are we providing notions and practical knowledge to new generations right now, and what are going to be the advances in training and education in the next ten years?

Challenges

Several challenges have emerged in the last few years. First of all, Neurosurgery is expanding at an exponential rate. The advances made in subspecialties (endoscope use, interventional neuroradiology, minimally invasive spinal surgery), all come with the burden of a learning curve to master the technologies and techniques applied. The era of an omnicompetent neurosurgeon is quickly coming to an end as future generations should be ever more sub-specialized. Hence, the need for specialized, accurate, reliable training simulation solutions is emerging (García Feijoo et al.). Strictly related to these issues is the necessity for a trainee to be exposed to a sufficient caseload to become a specialist in a given procedure.For example, in dealing with the well-known debate on vascular neurosurgery, how could future generations learn to operate complex aneurysm surgeries if the number of craniotomies is diminishing each and every year? Moreover, the next generation will be ever more under the judgment of an open-data, quality-driven consumer market. During their training and practice, neurosurgeons will increasingly be asked to prove the quality of both their training and clinical outcomes. Residency programs, too, will undergo such a judgment, hence validation, implementation, reliability, and cost-effectiveness issues of training strategies will also be challenges to address. Dealing with cost issues, in particular, the urgent need for neurosurgeons in several Low-to-Middle-Income Countries (LMIC) clashes with the scarcity of affordable, widespread educational resources. The recent pandemic limitations too, have limited the possibilities to access lectures, courses, and workshops (2). Lastly, on a pedagogical level, newer generations might have different learning abilities that should be accounted for. Albeit poorly debated in scientific literature, attention span might be an issue for late millennials to early gen Z (born between 1990 and 2010). Marketing and new media companies report that due to the constant audiovisual stimulation to which they are exposed since childhood, newer generations are the first to tune out a speaker when the content does not engage them (3). On the contrary, the majority being familiar with video gaming activities, younger students demonstrate faster learning curves in acquiring surgical skills in which hand-eye coordination is more challenged, like robotic surgery and endoscopy (4).

Strategies

How is the neurosurgical community responding to these challenges? Albeit the limitations of such an analysis, querying PubMed database it appears that the number of publications about training and education in neurosurgery has grown steadily in the last two decades meaning an increasing interest (**Figure 1**).

Different approaches have emerged, all linked to increased use of technology which everyday becomes more available, powerful, and affordable (Calloni et al., Hanalioglu et al.).

On the training side, the improvement of computational power and the development of specific devices (eg Oculus and HoloLens) have led to the introduction of augmented or virtual reality (AR or VR) integration in surgical procedures (5, Cannizzaro et al). This not only has allowed the students to experience an unprecedented understanding of both normal and pathological anatomy, but it has also empowered neurosurgeons in rehearsing and simulating the different steps of a specific intervention (Turan Dundar et al.). The availability of 3D printing technology, moreover, has led to the possibility of hands-on training both on "home-made" models or on commercially available ones (6). This may be beneficial also in better preparing the students for well-

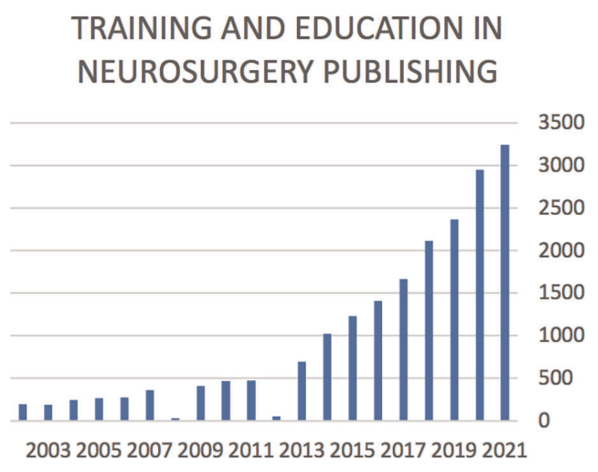

FIGURE 1
Number of publications about training and education in neurosurgery in the last two decades.

established, classic, training tools such as cadaver dissections, whose access is limited by ethical, economic, and logistic constraints. Lastly, both virtual and 3D simulation tools may be soon employed as evaluation tools for residency programs, thus fostering both practical training and objective evaluation (Petrone et al.).

On the educational side, several digital tools have emerged in neurosurgery with free and low-cost mobile content. Nicolosi et al. have already outlined the potential advantages of such information sources (WFNS Young Neurosurgeons Forum Stream, Brainbook, NeuroMind, UpSurgeOn, The Neurosurgical Atlas, Touch surgery, The 100 UCLA Subjects in Neurosurgery, Neurosurgery Survival Guide, EANS Academy, Neurosurgical.TV, 3D Neuroanatomy, The Rhoton Collection, and Hinari) (7). In particular, they stress their optimal usability, with no time, space, device, or country of origin restraints. Indeed, these new digital tools may prove to be an excellent solution, especially for LMIC and considering the need for engaging, interactive, new teaching means for digital native students (Tiefenbach et al., Zoli et al.). The pandemic emergency limitations, furthermore, have boosted the organization of webinars on all topics of Neurosurgery. This has had obvious advantages, as webinars have been proven to be positively associated with achievement in knowledge, behavior, and skills. Nevertheless, the plethora of information provided has already been deemed potentially too overwhelming, calling for their better regulation by national and international scientific committees (8). Eventually, a new teaching trend is emerging in this hyper-technological era in which students have a tremendous wealth of information at their fingertips. Specifically, mentors should shift from the classical top-down teaching to a so-called "facilitating learning" method. The best teachers will be then those who will help students uncover and understand the information they find, with the ultimate goal of making them take ownership of their learning (9).

Conclusions

The aim of this collection has been then to gather an up-to-date collection of high-quality original papers that could potentially inspire present and future masters and apprentices in our beloved craft of Neurosurgery. Moving from the excellent efforts collected, paraphrasing Sir William Osler, we might conclude that in the next ten years: “He who studies medicine without (books) technology sails an uncharted sea (or travels without Google maps!), but he who studies medicine without (patient) simulations firsts should not go to sea at all.”

Author contributions

All authors contributed to the conception and design of the manuscript. DB wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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frontiers in Surgery

ORIGINAL RESEARCH
published: 08 February 2022
doi: 10.3389/fsurg.2022.840523

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Increasing Medical Student Exposure to Neurosurgery: The Educational Value of Special Study Modules, Student Selected Components, and Other Undergraduate Student Projects

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Objectives: Neurosurgery is a tertiary specialty, and exposure to medical students limited. One way to increase engagement and offer experience in neurosurgery is through Student Selected Components (SSC), Special Study Modules (SSM), or independent projects. Our aim was to assess the educational value of such projects and evaluate their effectiveness in exposing students to the field.

Methods: A survey was designed and distributed to Edinburgh University medical students and alumni who completed a neurosurgical project within the last 5 years. The survey was anonymous and collected responses over a fortnight. The results were analyzed in Microsoft Excel 2020 Software.

Results: Twenty-four respondents completed the survey −42% were students and 58% junior doctors. Respondents overwhelmingly enjoyed their project (96%) and reported increased interest in neurosurgery (62%). The project helped improve their knowledge of neurosurgical procedures, pathologies, and/or clinical presentations and allowed connections with the local department. On a Likert scale, 37% felt they gained a good insight into the field. Only 33% felt the project was a good "taster" for the specialty. This is reasonable given that 92% of projects focused on data analysis, and none were designed as clinical attachments. A large number of students had their work published (50%) and presented at conferences (55%).

Conclusion: Lack of exposure to neurosurgery at medical school is a known limitation within a busy curriculum. Selected Components/Special Study Modules/independent projects help students learn about certain aspects of neurosurgery and raise their level of interest. A majority of participants either achieved presentation at conferences or published their work. However, our results suggest neurosurgical projects complement but do not replace traditional clinical attachments in providing insight into the craft of this specialty.

Keywords: SSM (Special Study Module), SSC (Student Selected Component), undergraduate neurosurgery, medical school curriculum, undergraduate student projects, neurosurgical education

OPEN ACCESS

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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: *21 December 2021*
Accepted: *10 January 2022*
Published: *08 February 2022*

Citation:
Tiefenbach J, Kaliaperumal C and Demetriades AK (2022) Increasing Medical Student Exposure to Neurosurgery: The Educational Value of Special Study Modules, Student Selected Components, and Other Undergraduate Student Projects. Front. Surg. 9:840523. doi: 10.3389/fsurg.2022.840523

INTRODUCTION

Neurosurgery is a tertiary medical specialty that has been under-represented in the medical school curriculum. The lack of early exposure in recent years has led to a decreased number of residency applications (1). Repeated calls have been made to allocate more time toward neurosurgical teaching at an undergraduate level and to develop a national curriculum (2–4). To our knowledge no universal actions have been taken to address this important issue for neurosurgery or any other similarly sized surgical specialty.

The benefits of increased neurosurgical teaching are clear—medical students could increase their confidence in dealing with neurosurgical emergencies and get clinical exposure to the field. A study by Skarparis et al. found that as many as one-third of final-year medical students in the United Kingdom (UK) have difficulty identifying the need for a neurosurgical referral (5). This is a concerning finding, considering the importance of early presentation and devasting consequences of common neurosurgical emergencies when left untreated. In another study, medical students rated experimental neurosurgical teaching sessions highly and overwhelmingly recognized the benefits of such sessions in their professional and clinical development (6). Taken together, these papers demonstrate there is a clear need and benefits to be gained from increased neurosurgical teaching at an undergraduate level.

Neurosurgical teaching can be achieved in many different formats, including but not limited to bedside teaching, lectures, tutorials, clinics, theater exposure, on-call shadowing, and student projects. The majority of medical schools in the UK do not provide any formal neurosurgical teaching (2); a common route for an interested medical student to get exposure to the field is by completing a neurosurgical project. The scope of these projects can vary greatly, such as conducting an audit, a literature review, a cohort study, or a meta-analysis under the supervision of a local neurosurgical consultant. Students can organize these projects independently or complete them as part of a structured medical school module frequently known as a Student Selected Components (SSC) or Special Study Module (SSM). These projects allow students the opportunity to also extend beyond the scope of the curriculum and either be presented or published nationally or internationally.

The existing literature does suggest that this type of project facilitates student learning and provides an insight into the field. For instance, the Northern Medical School SSC Consortium identified undergraduate student projects as an effective way to develop research skills, acquire knowledge and skills outside the core curriculum, and facilitate students' personal and professional development (7). Furthermore, a paper by Clark et al. argues undergraduate projects can improve career prospects and be an effective method of developing clinical competencies in neurosurgery (8). However, despite all the benefits students can realize through undergraduate projects, one may still argue that they are not the most suitable format for the delivery of undergraduate neurosurgical teaching as they fail to provide sufficient exposure to patients and clinical scenarios for the entire student cohort.

The aim of this study was to assess the educational value of medical student projects in neurosurgery and evaluate their effectiveness in exposing students to the field by getting a preview of what a neurosurgical career means to a medical student. We hope the results may give an insight into both benefits and drawbacks of such projects, as well as offer medical students' perspective on this important topic. We believe this will provide valuable insight for medical schools and relevant national bodies, and encourage them to re-assess the role of undergraduate projects and neurosurgery within the medical school curriculum.

METHODS

An online survey aiming to assess the educational value of student projects in neurosurgery was designed by a senior medical student and a consultant neurosurgeon (JT, AKD). The survey was composed of 19-items, containing Likert scale, multiple-choice questions, and free texts fields. The survey collected information on respondents' demographics, the structure of their project, and their overall impressions. Specifically, respondents were asked to rank the impact the project had on their interest in the field; the level of insight they had gained into the specialty; the amount and type of knowledge they had acquired; the connections they had made with the local department; the research output achieved throughout the project; the impact the project had on their career trajectory and their interest in the field; if they considered the experience to be a good taster for neurosurgery and if it provided a unique type of exposure which could not have been achieved through traditional clinical placements. The full list of questions included in the survey can be found in **Table 1**.

The survey was distributed via e-mail to medical students and junior doctors who had completed a project in neurosurgery over the last 5 years under the supervision of two Edinburgh-based neurosurgical consultants (AKD, CK). The data were exported in an excel sheet and subsequently analyzed via Microsoft Excel 2020 Software.

Participants were informed that the survey was anonymous and were not required to provide any identifiable information. They were also explicitly told the result may be published and offered to withdraw their response at any stage of the project. As an audit of educational experience, no ethical forms were deemed necessary for the completion of this project.

RESULTS

Out of 38 medical students and junior doctors who received the survey, a total of 24 (63%) filled in their responses. The respondent cohort comprised both medical students (42%) and junior doctors (58%) at varying stages of their careers (i.e., foundation programme doctors, core trainees, and pre-specialty clinical fellows). Both male (71%) and female (29%) respondents were represented in this survey; the mean age was 25, with the youngest respondent being 21 and the oldest 30. The majority of projects (58%) were completed as part of an SSC/SSM module, while the remaining 42%

TABLE 1 | The list of questions included in the online survey.

Question	Format
What is your gender?	Multiple choice
How old are you?	Free text
At what stage of your training are you currently in?	Multiple choice
How much protected time did you have to work on your project?	Multiple choice
When did you complete your project?	Multiple choice
What was the structure of your project?	Multiple choice
What type of project did you do?	Multiple choice
Did the project make you more or less interested in neurosurgery?	Likert scale
Did the project help you gain a better understanding of what a career in neurosurgery might be like?	Likert scale
Did the project help you develop knowledge in one or more neurosurgical procedure, pathology, and/or presentation?	Likert scale
Did you enjoy working on your project?	Likert scale
Would you recommend neurosurgery centered project to your peers?	Likert scale
Do you think that the project was a good "taster" for neurosurgery?	Likert scale
Do you think that the project provided a type of exposure to neurosurgery that could not have been achieved through a traditional clinical placement?	Likert scale
Did the project help you make valuable connections with neurosurgical registrars and consultants?	Likert scale
Have you had work in relation to your project presented at a conference?	Multiple choice
Have you had work in relation to your project published in a medical journal?	Multiple choice
Did the experience help you when applying for a neurosurgical training post?	Multiple choice
Any other comments you would share regarding your neurosurgical project?	Free text

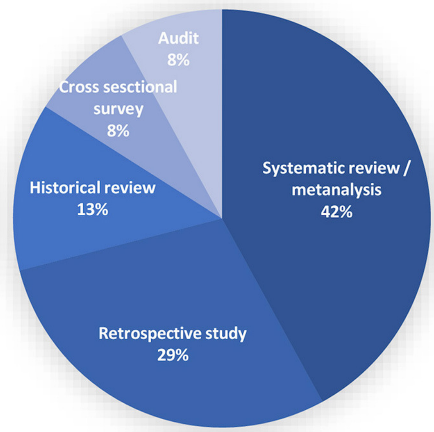

FIGURE 1 | The type of projects undertaken by medical students.

were organized independently outside the medical school curriculum. All projects were completed over the last 5 years, with a majority (37.5%) having been completed in 2019/2020. The students had varying amounts of protected time to work on their projects, ranging from no time at all to more than 12 weeks. The type of projects included systematic reviews/metanalyses (42%), retrospective studies (29%), historical reviews (13%), cross-sectional surveys (8%), and audits (8%) (**Figure 1**).

As many as 62% of respondents reported an increased level of interest in the field after completing their project, while 68% believed the project helped them improve their knowledge in one or more neurosurgical procedures, pathology, and/or presentation. The project benefited students in other ways as well −62% of them published in a medical journal or presented their work at a conference, with another 25% planning to do so in the near future. Students who undertook systematic reviews had the most success in publishing and presenting their work. As many as 79% reported making connections with local neurosurgeons and neurosurgical trainees, which they considered to be of great value in their future careers.

An overwhelming majority enjoyed working on their project (96%) and would recommend a neurosurgical project to their peers (75%). However, only 33% thought this type of exposure to neurosurgery was a good "taster" for this specialty, and only 37% felt the project helped them gain an accurate insight into what a career in neurosurgery would be like (**Figure 2**). Interestingly, retrospective studies were the type of project that was considered the best "taster" for the specialty, as well as the best way to gain an insight into what a career in neurosurgery might be like.

Finally, the junior doctors who had already applied for a neurosurgical training post did not think their undergraduate project was of much influence in their application. As much as 42% believed that the project provided a type of exposure that could not have been achieved through a traditional clinical placement. This was particularly true for audits, cross-sectional surveys, historical, and literature reviews. The free text field inviting students to leave additional comments did not provide any further insight relevant to this study.

DISCUSSION

The Purpose and Benefits of an Undergraduate Project

The purpose of undergraduate student projects has been identified and discussed on multiple occasions. In 2004, the Northern Medical Schools SSC Consortium proposed the purpose of these projects to be: (i) to ensure all students have opportunities to extend their studies beyond the core curriculum, (ii) to develop skills involved in clinical research, (iii) and provide opportunities for personal and professional development (9). The same Consortium revisited the topic in 2005, and produced a list of skills that medical

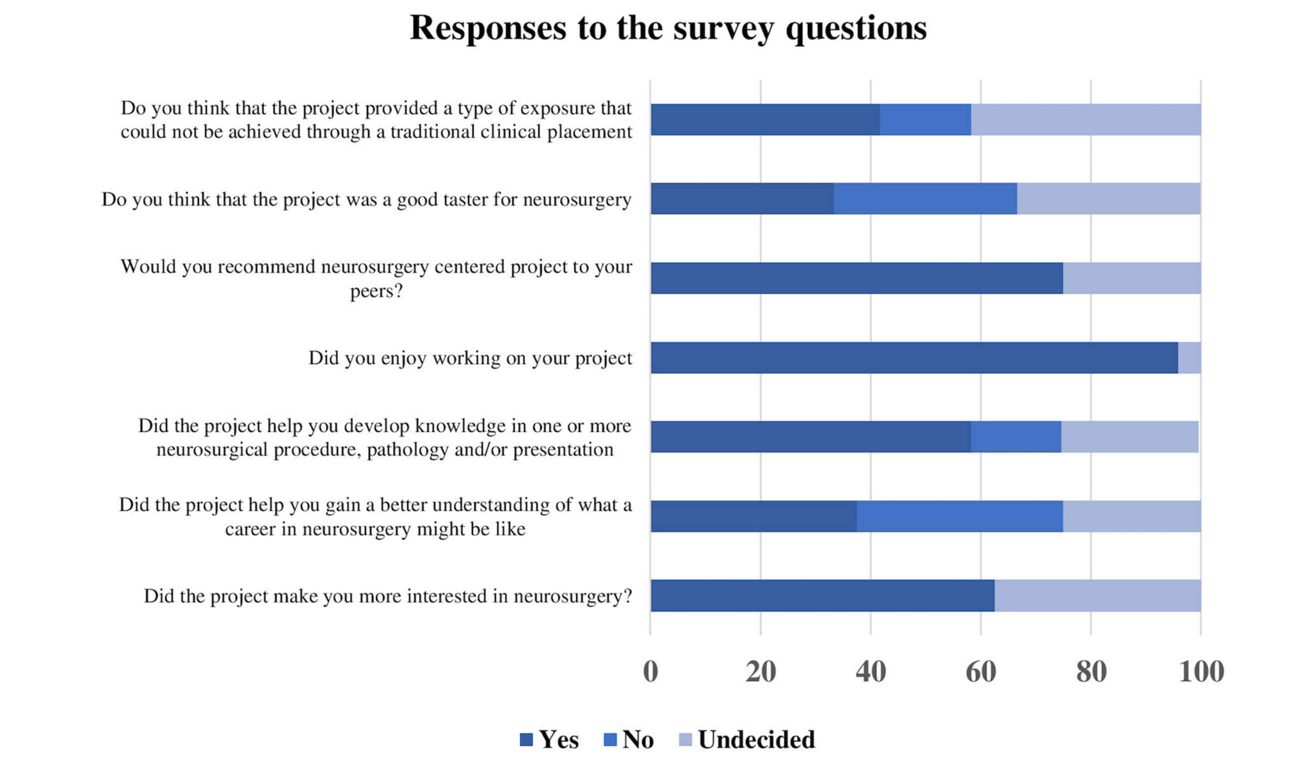

FIGURE 2 | Responses to the survey questions assessing the value of undergraduate projects.

students should be looking to acquire while undertaking undergraduate projects; these included research methods, information gathering, critical analysis and review, data processing, communication skills, self-management, and reflection (7).

The results acquired by our primary survey suggest there are a lot of benefits to these projects, and they do indeed help to develop some of the skills outlined by the Northern Medical School SSC Consortium. Firstly, the projects helped students acquire additional knowledge in neurosurgical procedures, pathologies, and/or clinical presentations which would not have otherwise been covered by their undergraduate curriculum. They have also increased the level of interest in the field and helped them gain more experience in clinical research. A lot of students even published their work in a medical journal or presented at a conference—both of which are very valuable experiences for students' personal and professional development. In addition, projects helped students make connections with local neurosurgical trainees and consultants, which can be incredibly useful for those looking to get further exposure to the field and secure a training post in this competitive specialty.

It is relevant to recognize that the benefits can differ between projects, and largely depend on the assigned supervisor and the type of project the student is attempting to complete. For instance, someone conducting a systematic review will have a very different learning experience from someone running a quality improvement project at the local department. Either way, both students and medical schools should be looking to maximize the value of these projects. A useful starting point to optimize the learning experience of an SSC/SSM comes from a paper published by Riley et al. (10), where 12 highly valuable tips are presented for every participating student to familiarize themselves with.

The Limitations and Shortcomings of Undergraduate Projects

At the same time, our results suggest there are certain educational aspects where undergraduate student projects did not achieve the maximum desired benefits. For instance, only a third of respondents thought that undergraduate projects were a good taster for the specialty or provided an accurate insight into what a career in this specialty would be like. These results may sound at first discouraging, as one of the aims of undergraduate projects is to allow students additional exposure to their field(s) of interest. However, this is hardly surprising, considering the majority of SSCs/SSMs are designed as research projects focused on primary data. It is worth acknowledging that students seemed keener for a research project rather than a clinical attachment, perhaps due to the competitive pressure to publish or present their work in order to progress in their career.

Another potential drawback of undergraduate projects is that they are self-selecting. Only students with a prior interest in neurosurgery will undertake a project and have an opportunity to learn more about this specialty. As a result, the majority of medical students do not get any exposure to neurosurgery, even though some might have found the specialty stimulating and would have chosen it as their future careers.

The Future of Undergraduate Neurosurgical Education

Arguably, the best way to ensure every medical student gets an appropriate exposure to neurosurgery would be through a mandatory clinical placement, which is not the case in every medical school (4). Spending a few days or weeks at the local neurosurgical unit, sitting in clinics, scrubbing in theaters, and joining the daily ward rounds would give students an accurate insight into the specialty and help them grasp what a career in this field might be like. It would also ensure all medical students get some kind of exposure to the field, and in such a way adequately supplement student-selected projects. However, the competing pressures of a busy medical school curriculum are well-recognized (7).

In 1993, Dr. Ralph A.W. Lehman, a neurosurgeon at the University of Pennsylvania, posed an important question—will future medical students be taught neurosurgery? (11). Today, most medical schools in the UK do not have any neurosurgical attachments within their undergraduate curriculum. Furthermore, as many as 28% UK medical school representatives do not think neurosurgery should be taught in medical schools at all (2). With the further accumulation of knowledge and increasing constraints on students' time, it is unlikely we will see medical schools universally introducing neurosurgical clinical attachments in the foreseeable future. This has a significant number of downfalls discussed in the previous paragraph, but yet again one needs to be respectful of the constraints faced by medical schools and the relative importance of other specialties in the medical curriculum. Creating medical student-friendly consortium or interest group run by the junior trainees in neurosurgery and with the oversight of neurosurgeons could be beneficial. Such events had already been piloted by Neurology and Neurosurgery Interest Group (NANSIG) and Society of British Neurosurgeons (SBNS), eliciting great interest among the medical students across the country. However, unless a radical shift is made in the way we approach medical education at the undergraduate level, it is likely that interested medical students will have to continue relying on undergraduate projects as their main gateway into this tertiary specialty. Such projects, as shown, are effective in different domains and are currently a complementary aspect to the curriculum.

Limitations of This Study

While the insights gained from our research are interesting and shed light on this important topic, it is still necessary to address some limitations. Firstly, this was a single center study; thus, our results might not be perfectly generalizable to other universities within and outside the UK. Furthermore, due to the relative size of the specialty, its tertiary level, and limited exposure among medical students, the sample size included only 24 participants. This may have implications for the accuracy and validity of the findings discussed in the paragraphs above. Finally, even though our response rate was satisfactory, this study may have been subjected to non-response bias—it is possible that the students with stronger and more positive feelings toward their project were more inclined to respond and complete the survey.

CONCLUSION

Undergraduate student projects, such as SSMs and SSCs, present an excellent learning opportunity for interested students to explore their specialty of interest. This is particularly true if their specialty of interest is neurosurgery, which is peripheral to the modern medical school curriculum due to understandable constraints. However, our primary survey and existing literature suggest these types of projects, while very beneficial in many ways, do not provide sufficient insight into the specialty and are not an adequate replacement for a traditional clinical placement. It is hoped that medical schools and national bodies responsible for the development of undergraduate medical school curricula will consider these findings and their implications in adapting medical student exposure to a tertiary specialty such as neurosurgery.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

AD: contributed to the study concept. JT and AD: contributed to the design. All authors contributed to the data analysis and manuscript.

ACKNOWLEDGMENTS

We would like to acknowledge the help received by administrative staff at the University of Edinburgh, namely Mr. Jason Andreas, who advised us on how to contact study participants in an effective and General Data Protection and Regulation (GDPR) compliant manner.

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frontiers in Surgery

SYSTEMATIC REVIEW
published: 11 March 2022
doi: 10.3389/fsurg.2022.864792

Augmented Reality in Neurosurgery, State of Art and Future Projections. A Systematic Review

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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: *28 January 2022*
Accepted: *11 February 2022*
Published: *11 March 2022*

Citation:
Cannizzaro D, Zaed I, Safa A, Jelmoni AJM, Composto A, Bisoglio A, Schmeizer K, Becker AC, Pizzi A, Cardia A and Servadei F (2022) Augmented Reality in Neurosurgery, State of Art and Future Projections. A Systematic Review. Front. Surg. 9:864792. doi: 10.3389/fsurg.2022.864792

Background: The use of augmented reality (AR) is growing in medical education, in particular, in radiology and surgery. AR has the potential to become a strategic component of neurosurgical training courses. In fact, over the years, there has been a progressive increase in the application of AR in the various fields of neurosurgery. In this study, the authors aim to define the diffusion of these augmented reality systems in recent years. This study describes future trends in augmented reality for neurosurgeons.

Methods: A systematic review of the literature was conducted to identify research published from December 1st, 2011 to November 30th, 2021. Electronic databases (PubMed, PubMed Central, and Scopus) were screened. The methodological quality of studies and extracted data were assessed for "augmented reality" and "neurosurgery". The data analysis focused on the geographical distribution, temporal evolution, and topic of augmented reality in neurosurgery.

Results: A total of 198 studies have been included. The number of augmented reality applications in the neurosurgical field has increased during the last 10 years. The main topics on which it is mostly applied are spine surgery, neuronavigation, and education. The geographical distribution shows extensive use of augmented reality in the USA, Germany, China, and Canada. North America is the continent that uses augmented reality the most in the training and education of medical students, residents, and surgeons, besides giving the greatest research contribution in spine surgery, brain oncology, and surgical planning. AR is also extensively used in Asia for intraoperative navigation. Nevertheless, augmented reality is still far from reaching Africa and other countries with limited facilities, as no publications could be retrieved from our search.

Conclusions: The use of AR is significantly increased in the last 10 years. Nowadays it is mainly used in spine surgery and for neurosurgical education, especially in North America, Europe and China. A continuous growth, also in other aspects of the specialty, is expected in the next future.

Keywords: augmented reality, neurosurgery, education, training, cranial surgery, spine surgery

INTRODUCTION

Augmented reality (AR) is a general terminology used to define a set of different technologies, all aiming to project virtual content into the real environment (1). In the past years, AR allowed for expanding the limits posed by two-dimensional imaging technologies, providing an unprecedented user experience in widespread fields, ranging from education, simulation, and medical specialties such as surgery and radiology (2). Concerning the medical field, AR has been widely used in different specialties, such as anesthesia, orthopedic surgery, neurosurgery, ophthalmology, urology, general surgery, and oral and maxillofacial surgery (3). Neurosurgery has always been at the forefront of this technology from the beginning, and still gives the greatest contribution to the literature (4). Conventional navigation and imaging technologies have tremendously advanced the field of neurosurgery in the past decades, providing crucial two-dimensional (2D) images, that have educated and guided neurosurgeons all over the world. However, when the surgeon must meet the three-dimensional (3D) extension of matter, these technologies may cause a cumbersome surgical workflow. In AR, computer-generated information is superimposed onto the real environment (the surgical field) to give a 3D semi-immersive experience, and a more integrated vision of the patient's status. The injection of multimodal preoperative and/or intraoperative images into the AR environment (such as MRI, CT, tractography, angiography, or ultrasound) enriches the surgeon's ability to simultaneously process data of different categories, nonetheless of crucial importance. Furthermore, this interactive surgical manipulation and anatomy visualization, integrated with haptic feedback, can significantly strengthen the resident's procedural memory and confidence during the procedure, also reducing the operation time (1, 2). These motivations clearly explain why AR has such great potential to become an essential part of neurosurgical training courses, starting from the earliest stages of a medical student's education to the training of an experienced neurosurgeon. Particularly in neurosurgery, where surgical corridors are often narrow and the margins of error are extremely low, AR has participated in revolutionary applications and brought major advances in all its sub specialties, ranging from the reduction in radiation exposure (5) and revision surgeries (6) to the safety and precision of neuro-oncologic resections (7).

With this systematic review, the authors aim to define the diffusion of AR in the world, highlighting some of the most critical challenges that should be addressed to introduce AR in routine clinical practice (8, 9). The analysis will be based on three layers: we will describe the geographical distribution of AR, the temporal evolution of the related publications in the past 10 years, and finally, we will analyze the relative trends in terms of research content, clinical applications, and education, which can provide crucial cues to predict the future of augmented reality.

MATERIALS AND METHODS

Search Strategy

A systematic review has been conducted to achieve the aim of the study. A systemic broad search was done on PubMed using the search terms "augmented reality" and "neurosurgery" for the last 10 years, from December 1st, 2011 to December 31st, 2021. A broad search of 2 different medical databases (Pubmed and Scopus) has been conducted in order to identify articles that describe the use of AR in neurosurgery. In order to retrieve all the possible articles of interest, several keywords have been included: "augmented reality," "neurosurgery." These were combined with Boolean characters "AND" as well as "OR." References from included articles were manually checked for proper additional studies.

Study Selection

Several inclusion and exclusion criteria have been adopted. The authors only included studies published between December 1st, 2011 and December 31st, 2021. The studies included should also contain a recipient of the proposed augmented reality in neurosurgery. All the studies that did not examine any form of AR that reported technique and outcome were excluded. The authors also excluded all studies not written in English. All the reviews and meta-analyses have been widely searched for other possible inclusions. A qualitative analysis of the articles was performed by three authors (A.C., A.C.B, A.J.M J.). Any uncertainty in study selection was resolved by consensus among all authors.

Data Extraction and Quality Assessment

For all included papers, three reviewers (AP) extracted and categorized data into structured tables. Extracted data included bibliographic information, type of paper, stated methodology, description of topic of application, and any formal research methods used. Data from the articles that were selected for screening was collected and applied to a database that included author, title, year of publication, country, and topic. The included articles were organized into categories based on country of publication, year of publication, and their topic. Once the articles were organized, a correlation between the topic and year of publication along with the topic and country of publication was made.

RESULTS

From 1 December 2011 to 30 November 2021, a total of 267 reports were identified by two authors (A.C., A.C.B.) using the above-mentioned methodology. After title screening, 14 articles were excluded. Of the 253 remaining, 55 articles were excluded after abstract screening, and 198 were included in the final analysis (**Figure 1**).

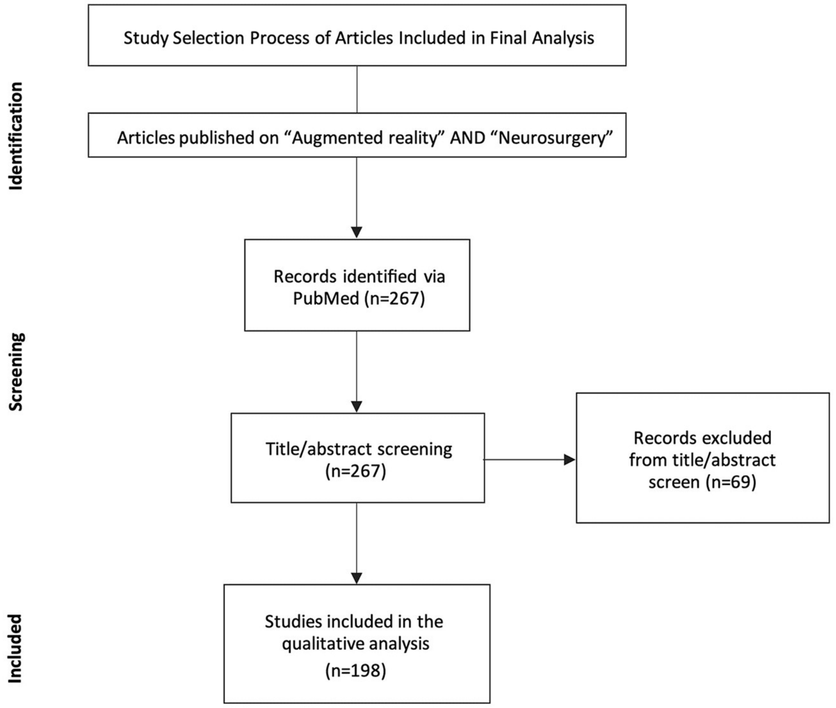

FIGURE 1 | Prisma flow diagram of the literature search.

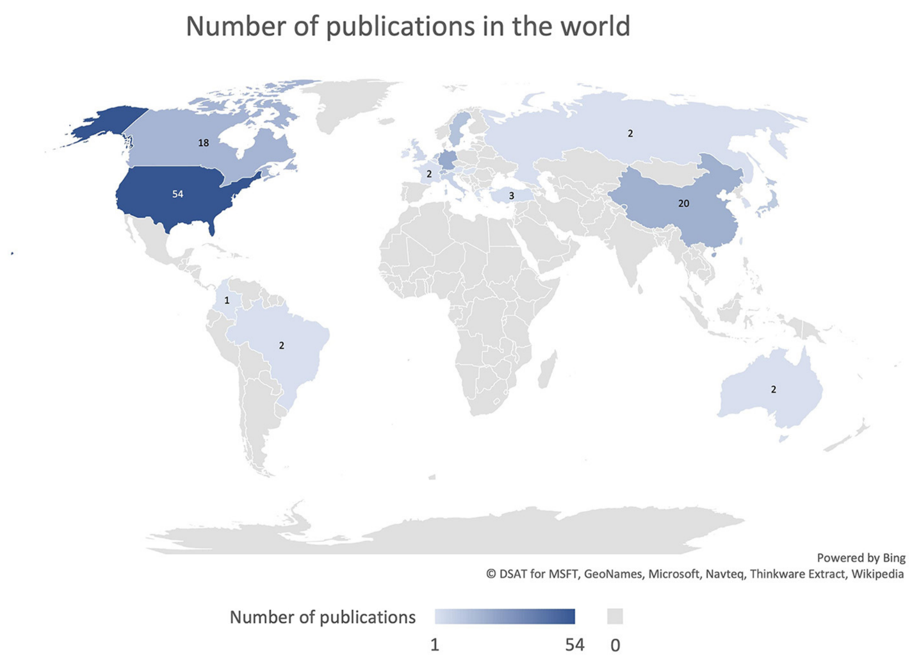

FIGURE 2 | Diagram representing the number of publications per year.

Augmented Reality From 2011 to 2021

The last 10 years have been characterized by a significant increase in the number of publications. The summary of the literature search has been shown in **Figure 2** and reported in **Table 1**. Only 1 articles was published in 2012 about the use of AR in neurosurgery. As well shown in the table, in the first years, up to 2015 there has been a small interest on the topic, consisting in total publication of 24 articles. From 2016, there has been a consistent growing trend on the topic, which has gone from the 13 articles of 2016 up to the 34 studies in 2020, that has further exploded in 2021, resulting in 71 publications.

TABLE 1 | Number of publications that could be retrieved from the search as grouped by the year of publication.

Year	Number of publications
2012	1
2013	6
2014	9
2015	8
2016	13
2017	19
2018	13
2019	24
2020	34
2021	71
Grand total	198

Augmented Reality in Different Countries

The leading countries, in terms of contribution, were the United States, accounting for 27.3% ($n = 54$) of publications, Germany with 11.1% ($n = 22$), China with 10.1% ($n = 20$) and Canada with 9.1% ($n = 18$) (**Figure 3**). The contribution from the different countries is presented in **Figure 4** and **Table 2**.

Augmented Reality and Topic

Of the 198 studies, 19 different topics have been detected. The most discussed topics and objects of our analysis are: education, with 36 articles (18.2%), spine surgery, with 36 articles (18.2%), neuronavigation, with 29 articles (14.6%), vascular, with 20 articles (10.1%), brain tumors, with 20 articles (10.1%), and surgical planning, with 11 articles (5.55%) (**Figure 5**). A correlation was made with each of the included articles ($n = 198$) on the basis of the country of publication and the specific topic (**Figure 6**). There are a total of 19 different topics. Germany and the USA published articles on 11 different topics, the largest variation among the other countries. The USA published 18 articles concerning education. Spine surgery is the most common topic of publication in Germany ($n = 7$) (**Table 3**). China focused on 9 different topics, with 5 of those being related to education and another 5 being related to neuronavigation. Canada reported 8 different topics, of which vascular surgery was the most common topic, with 5 articles, followed by surgical planning and neuronavigation with 3 articles.

Thirty-six articles out of the total were related to the education model. The United States published 18 books, followed by China (5 books), the United Kingdom (4), the Netherlands (3), Canada

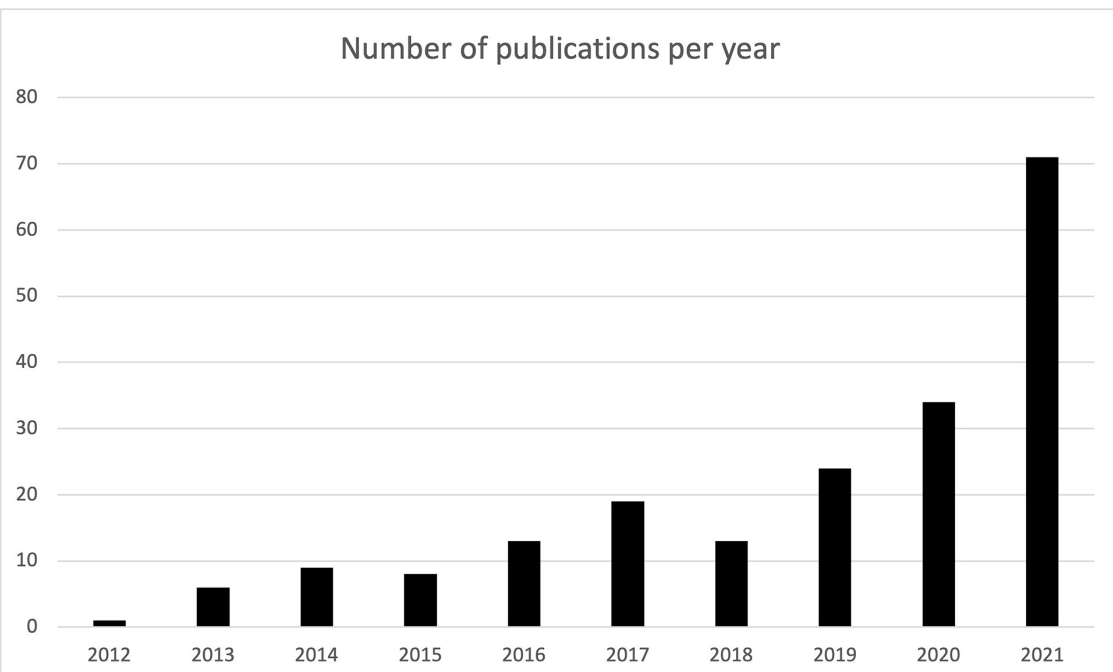

FIGURE 3 | Representation of the number of publication per country.

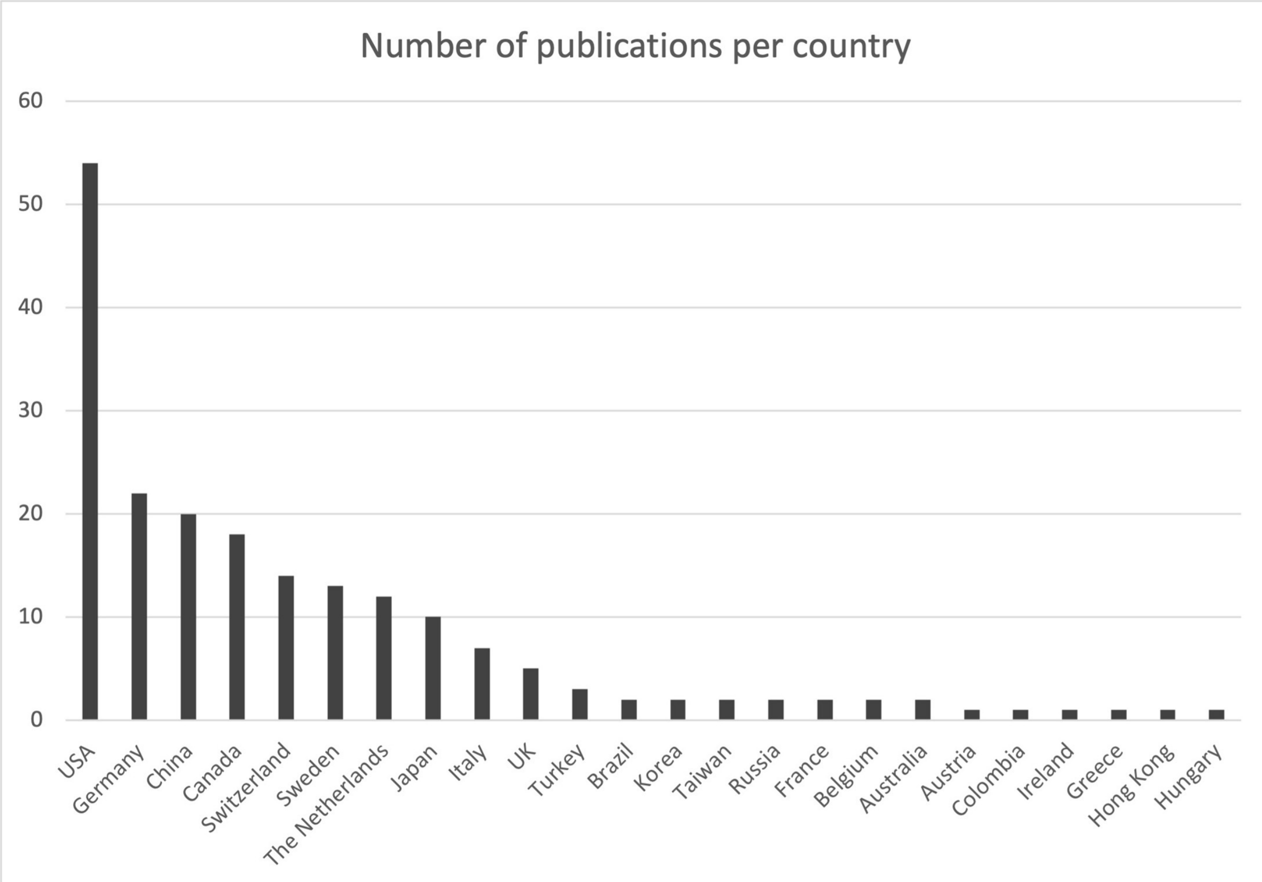

FIGURE 4 | Diagram representing the number of publications per country.

(2), Australia (1), Germany (1), Hungary (1), and Turkey (1). Twenty nine of the total articles (n = 198) that were related to spine surgery were published by the USA (n = 12), Sweden (n = 10), and Germany (n = 7). China (n = 5) published five articles related to neuronavigation, Japan (n = 5), the United States (n = 4), Canada (n = 3), and Switzerland (n = 3) (**Table 4**).

Eleven articles were published that were related to surgical planning in Canada (n = 3), the USA (n = 2), and China (n = 2). Twenty articles related to vascular were published by Switzerland (n = 6), Canada (n = 5), and the USA (n = 4). Twenty articles that were related to brain tumors were published by the USA (n = 3), Germany (n = 3), Switzerland (n = 2), The Netherlands (n = 2), Canada (n = 2), and Japan (n = 2). The correlation between the number of articles per topic is presented in **Figure 6**.

Trends in Neurosurgery

We also investigated the most meaningful trends in neurosurgery applications of AR during the years 2011–2021 (**Figure 7**). The most remarkable growth was accounted for by spine surgery, which was the most popular topic in 2021 publications, accounting for a total of 15 papers. Spine surgery routinely performs augmented reality-assisted pedicle screw insertion, which is probably the most common intervention nowadays that implements this technology. Neuronavigation is also a growing field in AR-assisted neurosurgery, whose frequency oscillated during the period of study, but it has increased steeply in the last year (2021) with a total of 11 publications (**Table 5**).

Surprisingly, despite contributing to a significant portion of publications, AR education research did not increase significantly during the period of study, not even during the first year of the COVID-19 pandemic (2020), when remote learning and alternative technologies were a primary necessity. Only a slight increase was observed in 2021, with a total of 9 publications related to education. We believe it is still not up to the potential of AR. An interesting trend was that of AR-assisted brain tumor surgery, whose number of publications increased in 2021 by more than twice the previous years of study. The non-discussed applications included a small number of articles to make meaningful evaluations, and their trends were generally constant over time, except for vascular surgery, which showed a slight increase in 2020 (5) and 2021 (6). Surprisingly, despite

TABLE 2 | Number of publications that could be retrieved from the search as grouped by the country of publication.

Country	Number of publications
USA	54
Germany	22
China	20
Canada	18
Switzerland	14
Sweden	13
The Netherlands	12
Japan	10
Italy	7
UK	5
Turkey	3
Brazil	2
Korea	2
Taiwan	2
Russia	2
France	2
Belgium	2
Australia	2
Austria	1
Colombia	1
Ireland	1
Greece	1
Hong Kong	1
Hungary	1
Grand total	198

contributing to a significant portion of publications, AR education research did not increase significantly during the period of study, not even during the COVID-19 pandemic (2020–2021), when remote learning and alternative technologies were a primary necessity.

DISCUSSION

Observation and practice have been the basis of learning in all surgical specialties. Surgery requires a deep knowledge of human anatomy and its variants (10–13). In addition, in surgical practice, it is essential to study the anatomical boundaries, structures, and relationship in three-dimensional arrangement (14–16). For this reason, cadaveric models and expert teaching have been considered the gold standard of medical and surgical education. However, in the last 10 years, surgical simulations and augmented reality tools have appeared on the market and have been implemented in order to try to shorten the learning curve and increase the exposure of trainees to practical training (3). AR is currently being used and tested in a variety of medical specialties and settings throughout the healthcare system. Neurosurgery was among the first medical specialties to implement augmented reality technology into practice (3). For what concerns clinical applications, some fields of neurosurgery are particularly relevant. In fact, imaging modalities such as computed tomography and magnetic resonance are indeed crucial in current practice for optimal pre-operative planning in order to determine the optimal approach for the surgery, especially in complex skull base approaches (17–23). AR is used for guidance of screw insertion in pedicles during minimally invasive spinal surgery. Additionally, AR finds application in vascular neurosurgery: some software has been developed for the treatment of cerebral aneurysms and also in the endovascular field for the correct selection of intracranial stents in the most complex conditions or for the practice of young interventionalists (24–27).

In view of the increasingly widespread applicability of AR in neurosurgery, the results of our analysis are not surprising. The number of publications concerning AR has increased steadily in the last 10 years, especially in the last 3 years. This reflects the fact that technologies are more and more included and upgraded in surgical and clinical practice nowadays. The technologies at the base of AR are more easily shared among various neurosurgeons, allowing easy diffusion of the use of these techniques and a consequent increase in scientific production.

The geographic distribution of the implementation of augmented reality technologies in neurosurgery shows a prominence in the USA, Canada, China, and Germany. The USA not only has the highest number of publications on augmented reality but is also characterized by a greater selection of topics than Germany. Furthermore, a constant geographical distribution is observed among the various topics, with the exception of augmented reality in the field of education. The USA has the most extensive adaptation of augmented reality in the training of medical students, residents, and surgeons. Asia deserves a special mention for the use of AR for intraoperative navigation. Despite only 12.6% of the total publication comes from Asian countries, especially China, it should be stated that the large majority of them has been published in the most recent years, showing an important increase in interest that will likely to continue in the next years.

Spine surgery, with the increased use of minimally invasive techniques and the use of intraoperative neuronavigation, has led to a significant increase in the application of AR, especially in the USA, Germany, and Sweden. Finally, Canada offers a major contribution in AR applied to the surgical plans.

AR offers a magnitude of potential advantages to the training of neurosurgeons as it sets up good short processing times and allows training and practice of major neurosurgical procedures outside the operation room (21–23). AR offers a training method with a practical framework by providing a protected training environment (28). This is important as it integrates training and further development of the surgery curriculum that will ultimately lead to a significant reduction in the cost of training.

Current standard training processes will outline areas of further development and improvement by augmented

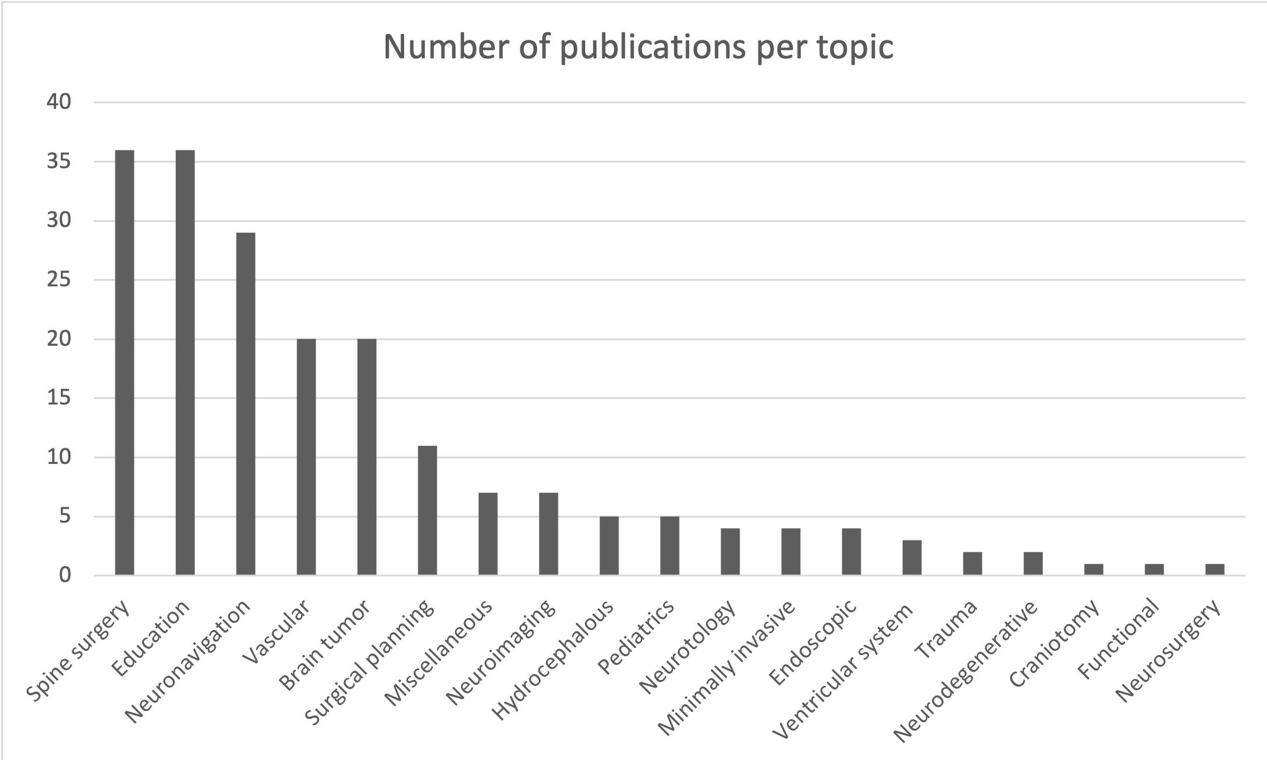

FIGURE 5 | Diagram representing the number of publications per topic.

reality technologies. Furthermore, AR technologies represent an innovative learning medium that enables trainees to have a flexible, on- demand training directive that will enhance their curriculum (3, 8, 28). Different teaching and learning objectives can be achieved through the use of this technology in training, with a special focus on practical learning scenarios in a medical or surgical environment. Direct measures to optimize education and training are needed to meet the requirements of digitalization in neurosurgery and be more successful (22). Conversely, it is recommended that the adapting department have a transparent goal before considering the implementation of augmented reality in training. Moreover, when implementing augmented reality devices in training, the objective and the expectations of the application in training must first be defined. This is imperative because not every augmented reality device can meet the requirements of the planned neurosurgical training curriculum. Furthermore, the requirements in a surgical setting are based on robustness and usability, which enhances technological possibilities such as 3D imaging in a clinical scenario. Therefore, recommending the technology to training departments to determine areas in which specific processes need to be achieved by the device is imperative. Lastly, the framework of implementing such devices in the training and work of surgeons needs to be stratified on an outgoing successful outcome basis for the predetermined goals of training (28).

Furthermore, the adaptation of AR applications in neurosurgery benefits training and simulation due to the creation of a no-risk virtual environment where surgeons can develop and refine skills through harmless repetition since neurosurgery carries a very small margin of error during surgery (21, 22, 29). Conversely, the use of AR in neurosurgery carries some limitations. Primarily, AR applications may result in a delay in the display or projection of the images in AR neuronavigation. This is problematic as it provides inaccurate localization to the user. Secondarily, a major challenge in the use of AR applications is image alignment due to inaccurate calibration and optical distortions that alter the image. It is also important to highlight that tissue movement is a challenge in all AR applications as the movement of tissue during surgery increases the error in image alignment intra-operatively (22, 23), there are also other points to consider. It is likely that AR will have an important role in image-based augmentation of the surgical environment. This will require increasingly powerful microcomputers to drive AR, which is currently limited but will improve with time. For the device to be a natural extension of the surgeon's senses, it has to be light, mobile, comfortable and functional for potentially long

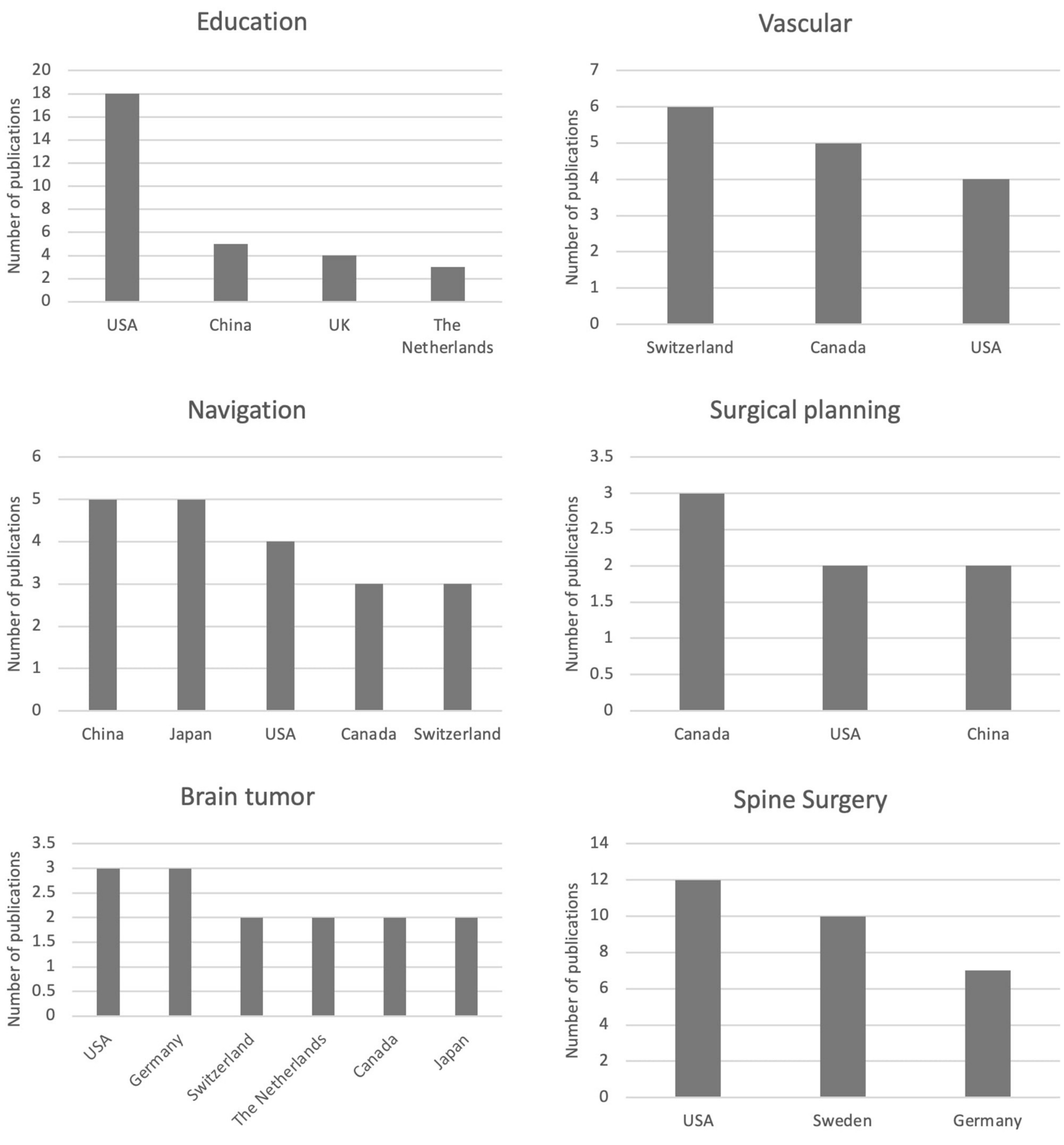

FIGURE 6 | Diagram showing the number of publications per topic per country.

periods of time. Therein lies the limitations of the technology at present, where the battery life is limited, devices are large and the cables can be cumbersome. Such technology has to progress at present and eventually after several generations of development these tools will become as common as surgical loupes (30).

Although augmented reality promises to become an essential part of the future of neurosurgical practice, major challenges have yet to be solved. The two most serious have been registration errors and system delays, which have hampered the use of AR in the most delicate procedures, such as skull base surgery

TABLE 3 | Number of publications that could be retrieved from the search as grouped by the field of application.

Topic	Number of publications
Spine surgery	36
Education	36
Neuronavigation	29
Vascular	20
Brain tumor	20
Surgical planning	11
Miscellaneous	7
Neuroimaging	7
Hydrocephalous	5
Pediatrics	5
Neurotology	4
Minimally invasive	4
Endoscopic	4
Ventricular system	3
Trauma	2
Neurodegenerative	2
Craniotomy	1
Functional	1
Neurosurgery	1
Grand total	198

and any other operation requiring sub-millimetric precision There has been a great effort from the scientific community in trying to address each of these challenges, and in many cases, very promising solutions have been proposed. However, even though it is true that these problems will be partially solved by the ever-evolving progress of technologies, from our investigation of the reviewed articles, we hypothesized that greater synchronization among the most active centers can significantly accelerate this process. Most of the current AR hardware is custom-made and difficult to distribute (31). This not only renders the technology hardly accessible, but it also implies that the research and strategies to solve the above-mentioned challenges are specifically oriented to the customized device that is being developed by the laboratory of interest. Such a lack of synchronization among institutions has limited the impact of individual findings and occasionally led to some confusion. It was, however, possible to find a promising solution for each of the mentioned challenges by investigating more deeply. This means that a more dynamic collaboration among the countries can truly benefit from these advancements, as was also suggested by some authors (32). Furthermore, enhancing the agreement among different centers can also help clarify the evaluation criteria of these technologies. One of the major pillars of our study was not only to investigate how AR will advance neurosurgical

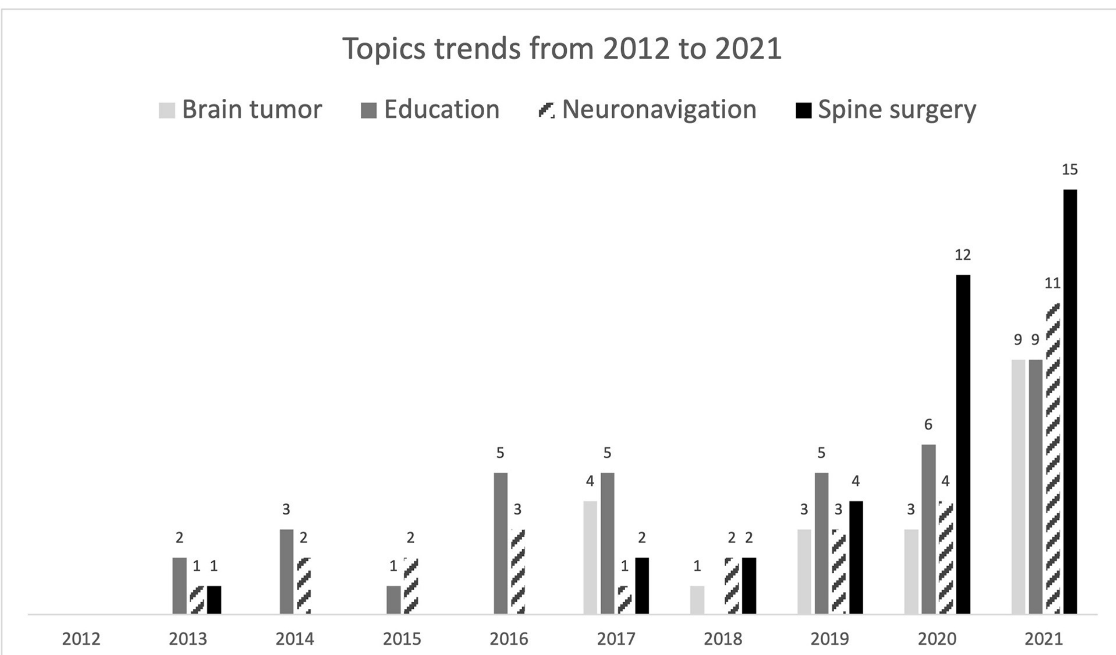

FIGURE 7 | Diagram representing the topics trends per year.

TABLE 4 | Number of publications that could be retrieved from the search as stratified by the country of publication and field of application.

Country	Brain tumor	Craniotomy	Education	Endoscopic	Functional	Hydrocephalous	Minimally Invasive	Miscellaneous	Neurodegenerative	Neuroimaging	Neuronavigation	Neurosurgery	Neurotology	Pediatrics	Spine surgery	Surgical planning	Trauma	Vascular	Ventricular system	Grand total
Australia			1			1														2
Austria											1									1
Belgium						2														2
Brazil																1				1
Brazil																1				1
Canada	2		2							1	3			1	1	3		5		18
China			5	2			1			1	5		1			2	1	1		20
Colombia																1				1
France							1						1							2
Germany	3		1		1				1	2	2			1	7	1		2	1	22
Greece										1										1
Hong Kong	1																			1
Hungary			1																	1
Ireland															1					1
Italy	1	1						1			1				1			2		7
Japan	2								1		5			1	1					10
Korea	1									1										2
Russia	1																1			2
Sweden						1	1				1				10					13
Switzerland	2						1				3				1			6	1	14
Taiwan	2										1									2
The Netherlands	2		3	1				1		1	2				1				1	12
Turkey			1								1				1					3
UK			4	1																5
USA	3		18			1		5			4	1	2	2	12	2		4		54
Grand total	20	1	36	4	1	5	4	7	2	7	29	1	4	5	36	11	2	20	3	198

TABLE 5 | Number of publications that could be retrieved from the search as stratified by the year of publication and field of application.

Year	Brain tumor	Craniotomy	Education	Endoscopic	Functional	Hydrocephalus	Minimally Invasive	Miscellaneous	Neurodegenerative	Neuroimaging	Neuronavigation	Neurosurgery	Neurotology	Pediatrics	Spine surgery	Surgical planning	Trauma	Vascular	Ventricular system	Grand total
2012																		1		1
2013			2							1	1				1			1		6
2014			3	1							2							3		9
2015			1				1			1	2					1		2		8
2016			5	1		1				1	3					2				13
2017	4		5	1		1	1	1		1	1				2	2				19
2018	1							2		1	2		1	2	2			2		13
2019	3		5				2	1	2	1	3		2		4	1				24
2020	3		6	1							4			1	12	2		5		34
2021	9	1	9		1	3		3		1	11	1	1	2	15	3	2	6	3	69
Grand total	20	1	36	4	1	5	4	7	2	7	29	1	4	5	36	11	2	20	3	198

care in the developed world, but also how it could impact the underdeveloped world, where these technologies are unimaginable. No publications could indeed be retrieved from Africa and other developing areas. Addressing how AR could improve the local healthcare system in these countries is an extremely delicate topic, since many such communities are not yet ready to sustain the complementary technologies that go along with AR implementations. However, AR could be a superb tool that the developed world can offer to underdeveloped areas to accelerate and refine the learning and training of simple and large-scale lifesaving procedures, even in the limited time duration of global neurosurgery missions. AR has been repeatedly shown to reduce the learning curves and bridge the expertise gap between students and senior neurosurgeons (33–35). AR could similarly make a difference, even in developing countries.

Study Limitations

Despite the authors' best efforts, the present study exhibits some limitations. Publication limitations may have been present due to the inclusion of studies published only in English. In addition, the included studies were extremely heterogeneous by including multiple augmented reality systems.

CONCLUSION

Augmented reality is still mostly used for education, surgical planning, and neuronavigation. This technology has also been implemented in clinical practice; in the last 10 years, we have observed an exponential increase in the application of augmented reality, especially in spinal surgery. Given the continuous advancement of augmented reality techniques and their increasing popularity, it may be possible to develop a unified education plan for future neurosurgeons. Countries with limited facilities could possibly benefit only if it's coupled with a specific target in this education model.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

DC, IZ, and FS: concept and design. AS, AJ, ACo, ABi, KS, ACB, and AP: acquisition of data. DC, AS, AJ, ACo, AB, KS, ACB, and AP: analysis and interpretation of data. All authors: drafting the article and critically revising the article. All authors contributed to the article and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Surgery

HYPOTHESIS AND THEORY
published: 25 March 2022
doi: 10.3389/fsurg.2022.875111

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Radiosurgery: Teenage Sex or Midlife Crisis?

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Martin Luther King, in his famous speech, mentioned that "Blood alone moves the wheels of history. Stereotactic radiosurgery (SRS) moved the wheel of neurosurgery in the absence of bloodshed. Over the last five decades, SRS has made a phenomenal stride in the pursuit of being minimally invasive but equally effective. Though literature testifies for its effectiveness, feasibility, and applicability, the traditional mindset of a neurosurgeon feels it difficult to accept it open heartedly. Radiosurgery is essentially a neurosurgeon's tool with more partial, conservative, and pragmatic approach with sole intention to maintain lesion control while preserving the quality of life of the patient. It demands a thorough knowledge to be impregnated into young neurosurgeon's mind at the time of their training, else it would fascinate or frighten with biased opinions.

Keywords: radiosurgery (SRS), gamma knife ®, quality of life, minimally invasive, CyberKnife

OPEN ACCESS

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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: _13 February 2022_
Accepted: _24 February 2022_
Published: _25 March 2022_

Citation:
Tripathi M (2022) Radiosurgery: Teenage Sex or Midlife Crisis? Front. Surg. 9:875111. doi: 10.3389/fsurg.2022.875111

> "In my early fifties, I was going through a phase where few things felt right, and I was trying to figure out those that did. It was not uncommon. In your twenties, you pursue your dreams. By your late thirties and early forties, you hit a certain stride. Then you hit your fifties, you get your first annoying thoughts of mortality, you begin more serious questioning of not just the meaning of your life but of what's working, what's not working, and what you still want, and all of a sudden you don't know which way is up. You thought you knew but don't. You just want to get to where life feels okay again."
>
> — Dick Van Dyke, "My Lucky Life in and Out of Show Business"

Munching on the history of Neurosurgery, I realized that neurosurgery took a sharp turn in the 1980s. The introduction and development of micro neurosurgery by Gazi Yasargil made a sea change in the philosophy of neurosurgery. Suddenly, alpha neurosurgeons started considering themselves invincible. They attacked each nook and corner of the human brain, and anything deemed alien to the brain was considered worthy of being taken out. The arachnoid web transformed from a sinewy trap to a guiding pathway that drained CSF, allowing fissures to open-up, and guide surgeons as they slid seamlessly into the depths of the brain. Everything looked promising, too promising to be true. Much water has passed under the bridge from the enucleation of vestibular schwannoma to intraoperative neuronavigation and planned partial resection. However, we are still far from being invincible. Bearing the same frustration, Lars Leksell took a quick walk-in solitude during the matinee session of a conference. His thinking mind was perplexed with the miseries of neurosurgical endeavors, and he came up with the idea of stereotactic radiosurgery (SRS) (1).

Neurosurgeons love the drama inside the "operation theatre" and the persona of a neurosurgeon (2). Most centers have terrific, pragmatic, fast, and smart neurosurgeons. They are confident and tough guys. But, we occasionally find patients marginally improved or even worse than their preoperative status. Neurosurgeons looked down on SRS as a radiation tool and were hostile to neurosurgical philosophy up to three decades earlier. How could some radiation treat a benign or vascular pathology? It seemed a dull and overzealous attempt by those neurosurgeons who had little interest in surgery. But somehow, it maintained its stand and increased its reach to most of the neurosurgical ailments.

For a beginner, radiosurgery seems as fascinating as teenage sex. It has all the ingredients of adolescent attraction. An early career neurosurgeon feels pretty excited and loves to try it. Looking at the limited radio surgical centers in teaching institutes, radiosurgery appears to be a mystical and novel first experience with the radiation tool in the realm of a neurosurgeon. However, without proper guidance, the initial attempts do not feel that enjoyable as there is no immediate result, no blood bath, and the surgeon needs to wait for a longer time for the lesion to disappear or primarily reduce by some quarters at its best. Until you understand the philosophy of radiosurgery, you are bombarded with conflicting messages from traditional neurosurgical practitioners and competing radiation oncologists. As you no more battle with blood and flesh, you remain concerned about what peers think about you. Neurosurgeons interested in radiosurgery feel threatened to be labeled "chicken hearted" or non-operative neurosurgeons; however, once you understand it and learn the science and craft of radiosurgery, you want to perform much better every time you do it.

On the other hand, SRS proved to be a distracting force for some seasoned neurosurgeons. SRS especially made a paradigm shift in managing two intracranial disorders; vestibular schwannoma and arteriovenous malformation (3, 4). It is not uncommon to hear a debate in current neurosurgical conferences on micro neurosurgery vs. radiosurgery for many intracranial diseases. This changed the surgical practice of many traditional skull base and vascular neurosurgeons. With this sweeping change, a hostile environment emerged, mainly because of neurosurgeons trained before the popularity of radiosurgery. They perceived the gamma knife as a threat to the surgical knife and an unwanted encroachment in their field. With growing literature supporting the effectiveness of this new blade, a state of midlife crisis has started to settle in the neurosurgical mindset, where the surgeon is married to the operating room but is having an affair with the radiosurgery station.

Neurosurgery seems far more dynamic in present times (5, 6). In the current era, radiosurgery is an integral aspect of the neurosurgical armamentarium. It is an established field of neurosurgical practice flourishing and prospering with great participation of neurosurgeons themselves. Radiosurgery remains a viable alternative for many neurosurgical patients, and statistics show that patients are happy with the radio surgical experience. With the ever and rapidly growing literature in support of SRS, the stakes have significantly changed. The focus is now on maintaining a good quality of life with long-term lesion control. Once you start understanding operative neurosurgery's limitations and safety profile, you start thinking of radiosurgery as a helpful adjunct or sometimes stand-alone therapy. As you gain practice and experience, coming out of this midlife crisis, you tend to look at the art behind the science. When you are a Picasso or a Rembrandt, the difference is no longer of skill but one of artistic choice. An expert neurosurgeon has to choose between cure and control for their patient, and the question of which knife to use and how remains a philosophical question and Sophie's choice.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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Conflict of Interest: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers | Frontiers in Surgery

REVIEW
published: 18 April 2022
doi: 10.3389/fsurg.2022.884675

Beyond Classic Anastomoses Training Models: Overview of Aneurysm Creation in Rodent Vessel Model

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OPEN ACCESS

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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: 26 February 2022
Accepted: 14 March 2022
Published: 18 April 2022

Citation:
García Feijoo P, Carceller F, Isla Guerrero A, Sáez-Alegre M and Gandía González ML (2022) Beyond Classic Anastomoses Training Models: Overview of Aneurysm Creation in Rodent Vessel Model. Front. Surg. 9:884675. doi: 10.3389/fsurg.2022.884675

Nowadays, due to the decline in the number of microsurgical clippings for cerebral aneurysms and revascularization procedures, young neurosurgeons have fewer opportunities to participate and train on this type of surgery. Vascular neurosurgery is a demanding subspecialty that requires skills that can only be acquired with technical experience. This background pushes the new generations to be ready for such challenging cases by training hard on different available models, such as synthetic tubes, chicken wings, or placenta vessels. Although many training models for vascular neurosurgery have been described worldwide, one of the best is the rodent vessels model. It offers pulsation, coagulation, and real blood flow conditions in a physiologic atmosphere that mimics perfectly the intracranial human vessels environment, especially in terms of size. However, the current differences in governmental different regulations about the use of living animals in medical experimentation and the social awareness, as well as the lack of financial support, cause more difficulties for neurosurgeons to start with that kind of training. In this review, we describe the tools and techniques as basic steps for vascular microsurgery training by using rodent models, that provide an accurate copy of brain vessels environment under stable conditions. The initial three classical known microanastomoses for neurosurgeons are end-to-end, end-to-side, and side-to-side, but in literature, there have been described other more complex exercises for training and investigation, such as aneurysm models. Although there is still little data available, we aim to summarize and discuss aneurysm's training models and reviewed the current literature on the subject and its applications, including a detailed description of the techniques.

Keywords: microsurgery, anastomoses, model, neurosurgery, vascular, training, rodent

INTRODUCTION

Since the endovascular era breakout, a global trend of decreased number of clipping and by-pass procedures can be appreciated worldwide (1, 2). On the one hand, there is a higher proportion of giant and complex aneurysm cases that are not suitable for training (3). On the other hand, many of the neurosurgeons who belong to the new generations have neither participate nor witnessed a complex clipping or a by-pass procedure, although these techniques may be necessary sometime during their career. Furthermore, due to the decline of microsurgical-related procedures, and under these hard conditions, the development of models that mimic intracranial human vessels (4) becomes the best way to be prepared. The time spent on that kind of training could be perceived by the trainee as a waste of time, taking into account the current varied range of techniques which they must master. Considering this situation, is it is a question of whether it is then worth investing time in neurovascular procedures training?

Surgical learning was long based on experimental models, which are fundamental for acquiring the necessary skills to perform safe surgical procedures in the real world. Probably, training on vascular models is one of the most complete trainings for neurosurgeons. These models not only ameliorate vascular skills, but they help to improve microsurgical dissection skills, tiny vessels manipulation micro-technique, and fine suturing (5, 6). Moreover, microsurgical training differs from other macroscopic models on the use of proper instruments, the average size of the treated structures, and the indirect field of view, highlighting the value of hand-eye coordination (or better said: "hand-brain"), a standard of microsurgery.

On this basis, the previous question has an obvious answer, yes. This training constitutes an extra instruction to carry on safely both the common and unusual complex procedures in which the use of microsurgical technique may be necessary.

Progressive learning in microsurgery connotes practicing on different types of models until mastering the technique that allows the trainee to comfortably reproduce similar procedures *in vivo*. Classically, in the beginning, *ex vivo* models, such as plastic tubes, human placenta (7), pig coronaries, or chicken wings have been recommended (8), and recently, thanks to virtual reality some novel simulated models are being explored, promising to bring shortly big advances in the field (9–12).

Despite the latest progress, one of the most accepted and complete models to train on vascular procedures are still the living models (4–6, 13), which offer a real blood flow environment accompanied by pressure, pulsatility, hemostasis, and an angioarchitecture that resemble the human intracranial conditions, being nowadays considered quite superior to the other available non-living models.

In that sense, the living rodent vessels is an optimal model that meets several requirements for high-quality training, and that has been historically widely used by neurosurgeons (4, 5, 14).

The recent recommendations of the European Society for Surgical Research (ESSR) and the International Society for Experimental Microsurgery (ISEM) (15) concerning the animal use for microsurgical training bet for the reduction and the rational use of the number of animals, however, there is a lack of international standardization in the matter, being this issue one of the main worries. To overcome these concerns, some basic experimental microsurgery principles have been developed: 3Rs [Replacement, Reduction, and Refinement, proposed by Russell and Burch in 1959 (16)], 3Cs [Curriculum, Competence, and Clinical Performance, proposed by Kobayashi and Lefor (17)], and GLP (Good Laboratory Practice).

At present, the aforementioned principles are essential for the justified and rational use of animals, more than ever before, taking into account the moral and legal considerations surrounding animal welfare in experimentation. The microsurgery trainees must be enrolled in a training program in which they can acquire the knowledge, aptitudes, and skills for the safe practice of animal experimentation.

The next question to be done is regarding the goal of using these models: whether we want to use them purely for training, or if we can also use them for basic investigation in aneurysm subject. In this sense there is a wide range of techniques described throughout history, most of them explained on macroscopic models or big animals (6, 18). Fortunately, the main basic principles can be exported and adapted to other microsurgical models. Our aim is not only to summarize the different aneurysm models, but also to perform a critical review and compare the different techniques, focusing on rodent vessels model, in which we have a great experience to share from our institution.

EXPERIMENTAL *IN VIVO* ANEURYSM DEVELOPMENT

Many animals' intracranial aneurysm (IA) models have been tested since the first animal experiments were carried on in the early 60s (19). Throughout history, there have been attempts for improving the available IA models by using different strategies, technologies, and animal species. Currently, there are two different classes for experimental development, considering the mechanism of production (20):

- Aneurysm induction models: the aneurysm is obtained by generating the different risks factors that favor its endogenous formation.
- Aneurysm creation models: the aneurysm is crafted by direct microsurgical anastomoses.

Aneurysm models can also be classified according to their anatomical location (18):

- Intracranial models: more suitable to evaluate IA pathobiology.
- Extracranial models: ideal to test endovascular novel therapies and to train microsurgical skills.

Figure 1 summarizes the main strategies for the development of experimental *in vivo* aneurysms, considering the aforementioned issues.

The sections below provide a wide summary of both conceptions, also offering a critical review of their technical aspects and limitations, focusing on the microsurgical performances' tenets.

Aneurysm Induction Models

Due to the several implications of IA rupture, there is a growing interest in their pathogenesis, many times focused on the identification of potential therapeutic targets or an early

Abbreviations: IA, Intracranial aneurysm; SAH, Subarachnoid hemorrhage; CCA, Common carotid artery; MCA, Middle cerebral artery; AIB, Aorto-iliac bifurcation.

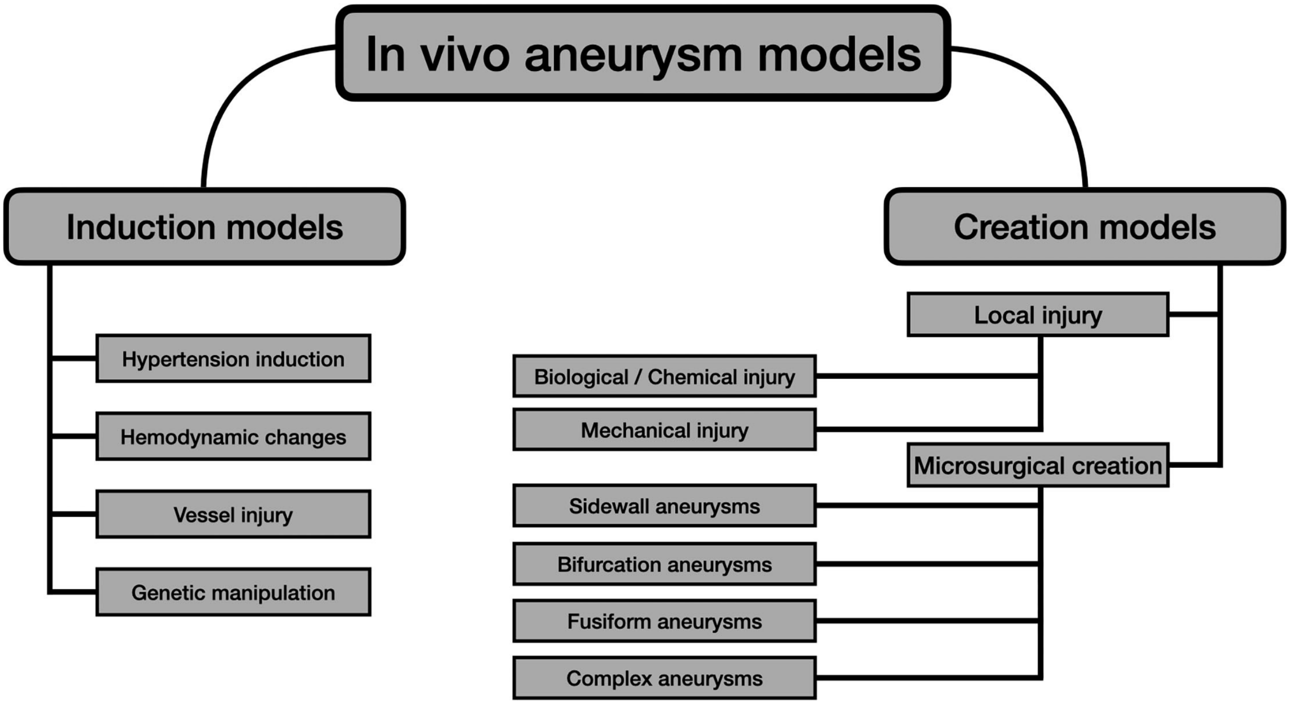

FIGURE 1 | Diagram showing the most common experimental *in vivo* models for IAs.

diagnosis that could avoid the potential devastating consequences following a subarachnoid hemorrhage (SAH) (10, 21).

A historical preference for the use of rodents can be observed, and this trend answers to some reasons such as the similarities between mice and humans in terms of aneurysm location and pathology, including degradation of the internal elastic lamina and thinning of the tunica media. The lower costs and the quick production rate of the animal cohort also make them ideal for these purposes (18, 22).

Despite the high degree of histological similarities, the incidence of natural SAH in mammals other than man is ultra-low (22), being only described in chimpanzees (*Pan Troglodytes*). Consequently, a true aneurysmatic SAH is also a rare entity to find in controlled murine cohorts, where even the presence of induced IAs makes this rupture difficult to predict or synchronize (23). Hence the preference of the direct blood injection into the subarachnoid space or the endovascular perforation of a cerebral vessel as a model for SAH.

On these grounds, nowadays, the precise mechanisms underlying IAintracranial aneurysm formation and rupture remain unclear, although most of the induction models are based on three main principles which can also be found in humans acting as risk factors: hypertension, hemodynamic changes, and vessel injury. Moreover, estrogen deficiency and genetic manipulation are increasing impact on all recent reviews (20, 24). The combination of at least 2 or 3 of these methods is often described in the literature to improve the success rate, however, there is no international consensus about which is the best association.

One of the earliest experiences to induce IAs was reported in 1961 by White JC, by sodium chloride hypertonic (28%) solution injections in the internal carotid artery wall of mongrel canines (19). New agents are lately being explored, oriented to the weakness or degradation of the intracranial arteries connective tissue layers, especially the internal elastic lamina.

One example is elastase, which can be administered stereotactically into the basal cisterns. This enzyme is often combined with an angiotensine-II subcutaneous infusion through an implanted osmotic pump to increase hypertension, augmenting the anterior circulation IA incidence to 70% of the specimens (25).

In most of the surgical hypertension-induced based models, branches of the renal arteries are surgical ligated (26, 27), the rat is nephrectomized or its kidney is wrapped (20). According to this strategy, high-salt diet has been widely used. Deoxycorticosterone acetate-salt administration may have a dose-dependent effect, influencing both aneurysm formation and rupture (23, 28). Despite being one of the favorite methods, by itself, the hypertension induction model is not enough to get an acceptable IA incidence rate (20).

In 1978, the Hashimoto model for experimentally induced IA was described (29). This model aimed for the loading hemodynamic stress to damage arterial walls; a conception that persists to this day with slight modifications as one of the most important milestones in the field. Originally, Hashimoto (29, 30) fed the rats with beta-aminopropionitrile to weak the cerebral arterial wall, and through a unilateral common carotid artery (CCA) ligation, in addition to deoxycorticosterone infusion and salt-diet, the saccular IA incidence rate was increased, showing validity as a model for saccular cerebral aneurysms in humans afterward (31, 32), and exporting the model to other species such as monkeys (33).

Then, in the late 80s, Roda and Alvarez (26, 27) detailed better the influence of the hemodynamic stress on the IA incidence rate in rats, succeeding almost three times more in those animals which developed a higher carotid artery flow, thanks to the combination of unilateral CCA ligation and an end-to-side anastomosis between carotids, in comparison to those which underwent only unilateral CCA ligation (**Figure 2**). Further, they demonstrated how this combination increased the blood flow through the parent carotid artery up to 89% in 5 months, inducing intracranial vessels damage (34). Other modifications from the original model describe the ligation of the external carotid artery and/or pterygopalatine artery (which, in rats, arises more proximal than in humans) to rise the hemodynamic stress through the internal carotid artery (33, 35).

Recently, genetic modification is a promising emerging strategy to improve the IA incidence rate, often based on some human conectivopathies features and hypertensive mechanisms (20). Transgenic mice with altered specific proteins which are supposed to play an important role in IA formation, such as eNOS and SOX17, can be purchased (36). However, as in humans, genetic predisposition by itself is not enough to guarantee IAs obtention, so the knock-out individuals must be further subjected to a combination of some of the previously detailed methods (20).

The size and characteristics of the obtained aneurysms differentiated them from the real ones found in humans, being quite common to observe smaller aneurysms with shallow/wide necks and aneurysmal bulges with a less rounded shape (20).

In spite of all this, at present, the most common technique employed to induce IAs in rodents is still the surgical ligation of CCA and/or renal artery (uni or bilateral) with concomitant induction of hypertension (37).

The principal described induction models for IAs are neither efficient nor useful for training microsurgical skills due to their average volumes and long induction time. Notwithstanding the foregoing shortcomings, some parts of these models require microsurgical skills (end-to-side anastomosis between CCAs or the renal arteries ligation) that can be valuable for training purposes.

Aneurysm Creation Models

After the provided brief summary of the induction models, the pure microsurgical models, which are the main objective of the present review, will be detailed in the sections below. The diagram shown in **Figure 1** divides the creation models into two groups: local injury and microsurgical models.

Unlike the induction models, the microsurgical creation models are preferentially located on extracranial vessels (36) due to their bigger diameter and easier approach. This fact becomes even more relevant considering that the rodent extracranial vessels caliber is very similar to many segments of human intracranial vessels from both anterior and posterior circulation (14).

A recent systematic review (18) on preclinical extracranial aneurysm models, found more than 68 described models/techniques in five different species and confirmed that the most widely used animals for the microsurgical aneurysm creation are mice, rats, dogs, swine, and rabbits, being these models less frequently described on sheep and monkey species.

It is also important to understand the rodent's internal anatomy and vessel approaches, that many times differs from human (5). The vascular anatomy of the rat, in terms of vascular training, can be divided into three main compartments: Cervical, abdominal, and femoral (**Figure 3**). Each compartment exhibits different characteristics related to its anatomical location. For instance, the cervical compartment is more related to the trachea and head structures, in the abdominal compartment the main vessels are surrounded by many organs and fatty tissue, and the femoral compartment offers two tiny parallel vessels accompanied by the femoral nerve lying on a muscle background.

There are three basic concepts that the surgeon needs to bear in mind before starting the exercises: the size of the vessels, the nearby vessels, and the local anatomy of the vessel. The nearby vessels matter when a side-to-side or end-to-side anastomosis is needed (a large donor artery may be helpful for this exercises). Some special configurations of the local anatomy of the vessels are also useful when an anastomosis on a bifurcation or a terminal branch aneurysm are being planned.

There are four types of human IAs attending to their shape and walls: saccular, fusiform, dissecting, and mycotic. However, the most common type found in humans by far, which represents up to 90% in all reviews, is the saccular type (21, 38). For this reason, they are also the most reproduced worldwide as a model for training. Normal saccular IAs growing implies a degradation of the internal elastic lamina and thinning of tunica media, resulting in a sac formation that arises on the arterial wall, covered only by the tunica intima and adventitia (21). Several different techniques and constructions for mimicking the most frequent type of aneurysm have been described, however, it is still not well-established which is the gold standard.

Marbacher et al. (18) described and classified the preclinical models for IAs according to the main anastomosis combination or vessel occlusion employed and its similitude to human IAs into the following types: sidewall aneurysms, stump aneurysms, terminal aneurysms, bifurcation, and other complex aneurysms. The original descriptions in the literature include some endovascular-based models and were made on different animal species, therefore, not all these performances can be adapted to the present model. For academic reasons, and aiming to explore and describe the rodent models for IAs, attending to pure microvascular training objectives, we find it simpler to classify them into four major classes as follow:

1. Sidewall aneurysms
2. Bifurcation aneurysms
3. Fusiform aneurysms
4. Other complex aneurysms.

This proposed classification emphasizes the location of the aneurysm relative to the parent artery and the named subclasses provide a quick conceptual explanation about the technique.

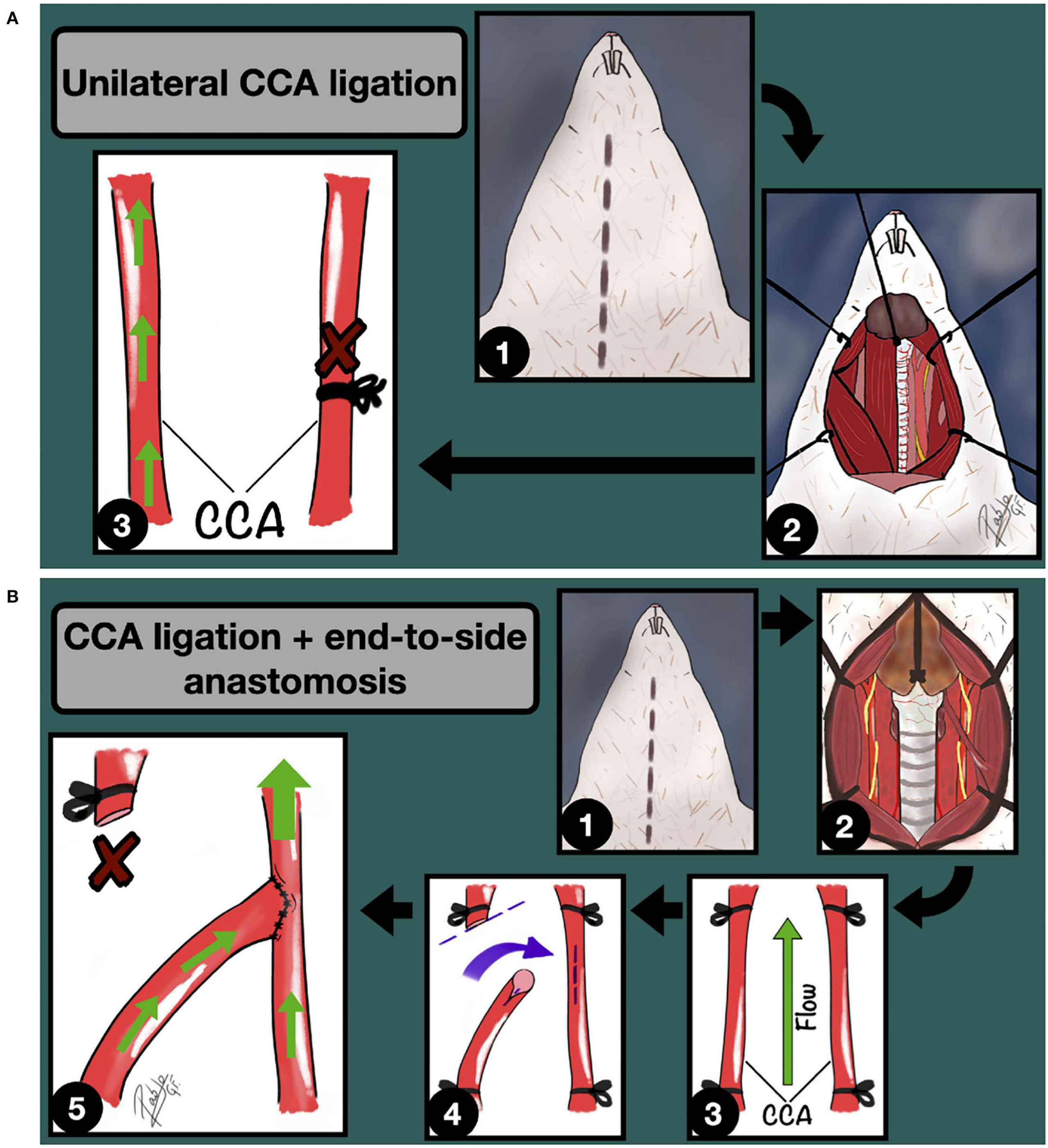

FIGURE 2 | (A) Unilateral CCA ligation model for IA induction through hemodynamic stress increase. 1: Midline cervical incision; 2: Cervical vessels approach and unilateral CCA exposure; 3: Unilateral CCA ligation. The green arrows indicate the blood flow direction. **(B)** Unilateral CCA ligation + Contralateral End-to-side anastomosis model for IA induction through hemodynamic stress increase. 1: Midline cervical incision; 2: Cervical vessels approach, focusing on the left CCA; 3: CCA clamping; 4: Longitudinal arteriotomy of the parent artery and fish-mouth arteriotomy of the donor vessel; 5: End-to-side anastomosis is completed. The green arrows indicate the blood flow direction.

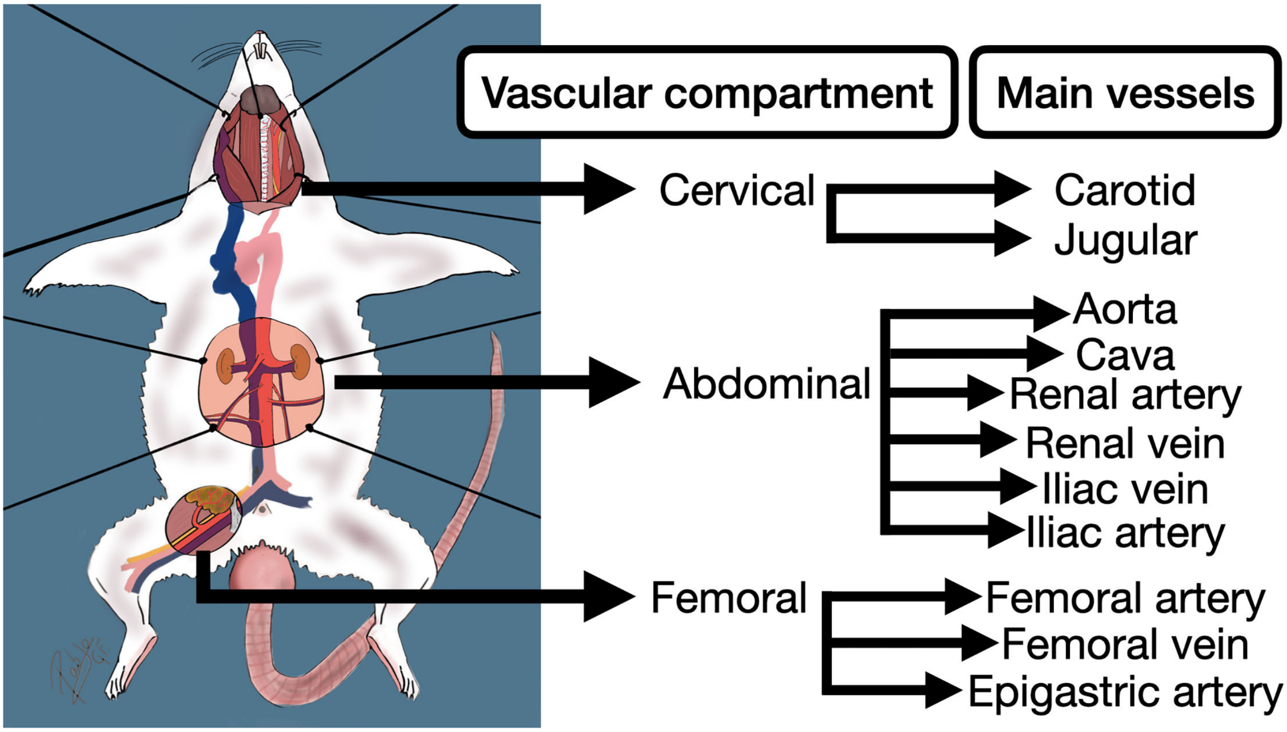

FIGURE 3 | Principal vascular compartments and vessels of the rodent for the practice of anastomoses in extracranial models for aneurysms.

On the other hand, some reported creation models for IAs are not exclusively microsurgery-based, although they suggest some surgical steps different from anastomosis to induce a local injury. This is the case of the fusiform aneurysms created by a CCA isolation followed by local application of elastase (4, 39).

All the exercises must be done under the legal qualification, taking into account animal welfare. In that sense, all the procedures included in the present review, to illustrate the following techniques, were performed at idiPAZ microsurgery laboratory, at our institution, by accredited trainees, under the European directive EU 63/2010 and were approved by an Animal Ethics Committee under PROEX 160/17 according to RD 53/2013 (Spain).

Sidewall Aneurysms

Sidewall aneurysms are considered the most feasible model to be performed, being the first recommended exercise for vascular training within aneurysms. The concept comprises the obtention of a rounded or tubular aneurysm arising from the lateral wall of the parent vessel, which provides a blood inflow into this outpouching portion. The resulting constructions can be easily identified as aneurysms, resembling those that can be found in human intracranial vessels. However, the surrounding tissue differences in comparison to the real IAs, which are located into the deep subarachnoid space (between brain parenchyma), is one of the obvious limitations of all the extracranial models.

The four designed strategies listed below are considered easy to reproduce, considering that only one functional vessel is involved in the performance and that the graft, when needed, is obtained from another expendable vessel, which allows the practitioner to keep undamaged the rest of the circulatory apparatus. Furthermore, the sidewall class can be practiced on the three mentioned vascular compartments of the rat.

End-to-Side Graft Placement

Most of these vascular performances imply an end-to-side anastomosis between a parent artery and a vascular graft, venous or arterial, that can even be artificial. The obtained performance is a rounded vascular formation, that arises from the lateral wall. Depending on the graft material, different variations in terms of final size can be achieved. In our experience, the venous grafts can undergo significant growth that starts some minutes after the declamping and may get a huge size after some days. For this reason, arterial grafts are preferred when standardization is needed (18, 40), since the aneurysm final size is better kept and controlled. According to the Helsinki model (40), this modality is most of the times described for the abdominal aorta or the carotid (6), following these common steps (**Figure 4**):

1. Aorta dissection and subsequent distal and proximal clamping
2. Excisional arteriotomy on the lateral wall, inner arterial flushing with saline, and edges dying
3. Preparation of the graft and placement of the first two anchoring knots of an end-to-side anastomosis
4. End-to-side anastomosis is completed by the rest of the knots
5. The free lumen of the graft is occluded
6. The normal circulation is restored by clamping releasing.

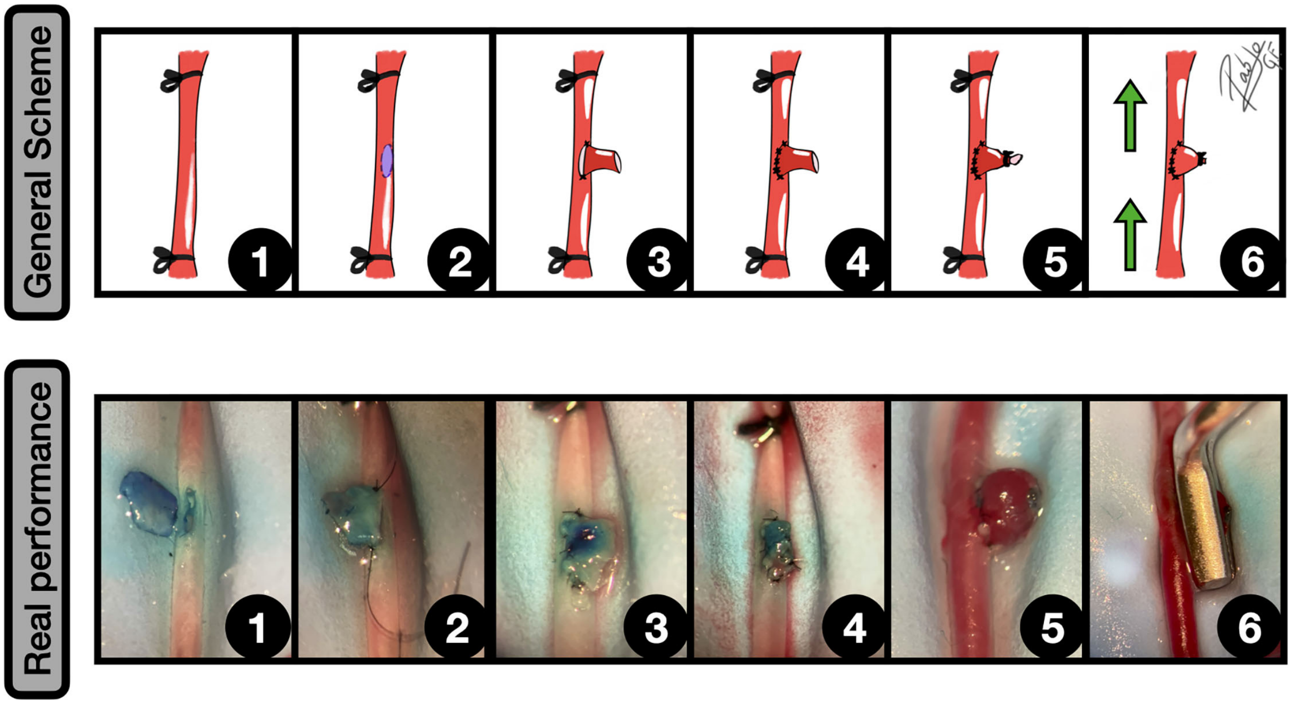

FIGURE 4 | End-to-side graft placement. General scheme: **1:** CCA exposure and proximal and distal clamping; **2:** Lateral wall excisional arteriotomy of the CCA; **3:** The vein graft is placed against the arteriotomy edges, and the two first anchoring knots are made; **4:** End-to-side anastomosis between the graft and CCA is completed; **5:** The free lumen of the graft is occluded; **6:** After clamping releasing an inflow can be observed into the aneurysm. The green arrows indicate the blood flow direction.
Real performance: **1:** Excisional arteriotomy on the *antero-lateral* wall of the CCA. A blue-dried venous graft harvested from a jugular vein is on the left; **2:** The graft is fixed to the arteriotomy by a couple of anchoring knots; **3:** The arteriotomy is fully anastomosed to the graft in an end-to-side fashion; **4:** The free lumen of the graft is occluded by an uninterrupted suture; **5:** After releasing the clamps an inflow is observed into the venous graft, simulating a sidewall aneurysm; **6:** The aneurysm is clipped, preserving the parent vessel circulation.

The previous availability of the graft shortens the surgical time, however, to attempt a most challenging training it is recommended to harvest the graft microsurgically from nearby structures, such as renal vessels or cava (in the abdomen) and the CCA and jugular vein (in the cervical compartment) (6, 40).

The infrarenal segment of the aorta is preferred by many authors because of the fewer number of branches, however, there is a disturbing bilateral major branch called the iliolumbar artery, easy to confuse with the renal arteries and that must be often ligated (5, 40).

Side-to-Side AVF

In principle, this model is more challenging than the previous, since the proposed anastomosis is a side-to-side which involves two parent vessels. They cannot be as comfortably handled as a free graft and are often from different natures (artery and vein is a common combination). After the anastomosis is performed, the vessel that will recreate the aneurysm must be sacrificed by distal and proximal ligation (6, 18). Planning is essential to achieve the best results because the nearby vessels' location must be prior recognized for further considerations about their transposition. Besides the vessels' proximity in the femoral compartment facilitating the exercise, the mistakes in this area do not usually result in fatal hemorrhage (41). The recommendations for the cervical compartment suggest a jugular vein transposition, although, despite the name, this model can be executed by a side-to-side anastomosis between two arteries, such as CCAs. The basic steps are (5, 6, 18) (**Figure 5**):

1. Parallel vessels dissection and clamping
2. Incisional arteriotomy on the anterolateral wall of both vessels, inner arterial flushing with saline, and edges dying
3. Anchoring knots must be placed on the arteriotomy cranial and caudal edges
4. Side-to-side anastomosis by suturing the two resulting walls in a stepwise manner
5. Delayed proximal and distal ligation and section of the recipient artery
6. The sidewall aneurysm is obtained when the blood flow is restored through the parent vessel.

Terminal Branch Occlusion Model

The terminal branch model was originally described to investigate and test endovascular techniques (42), being the most feasible and simple to reproduce in the laboratory. It consists of a surgical arterial occlusion, which is not technically demanding for the trainee. The obtained aneurysm can be a sidewall or a stump aneurysm depending on the parent vessel location and flow direction, and thereby, it constitutes a good

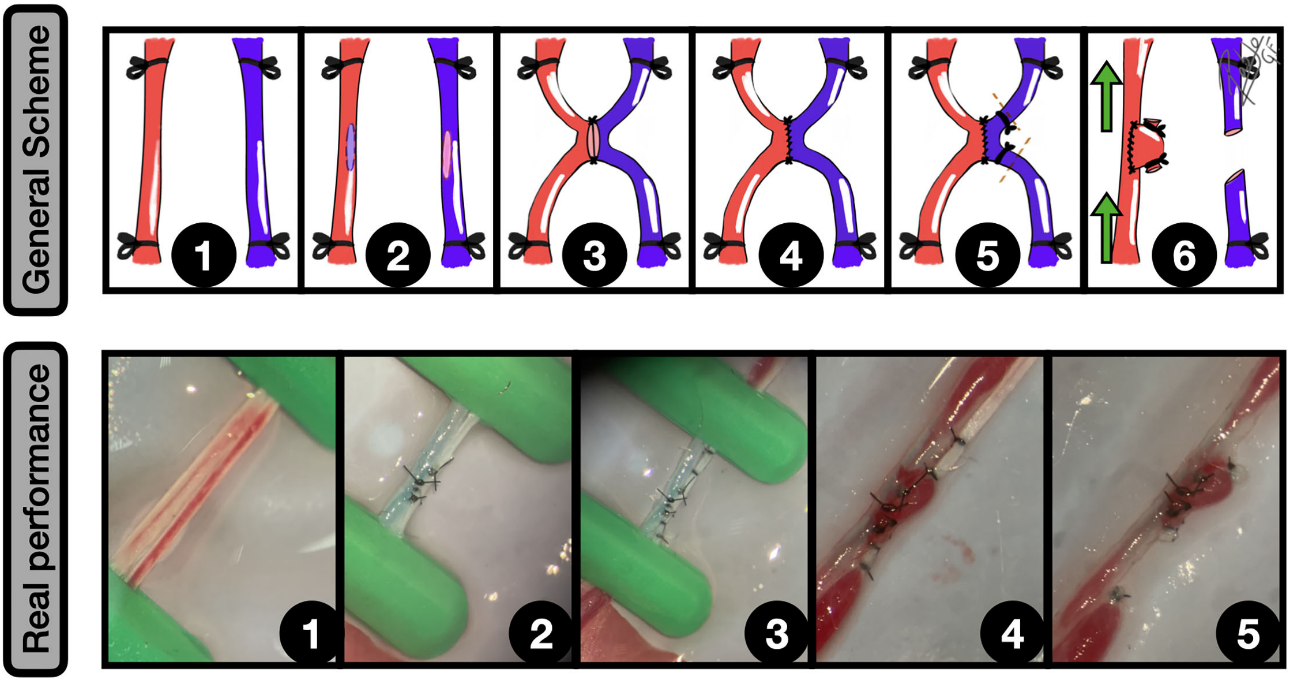

FIGURE 5 | Side-to-side arteriovenous fistula (AVF). General scheme: **1:** Femoral artery and vein are widely exposed and proximal and distal clamped; **2:** Lateral wall longitudinal arteriotomies of both vessels are performed; **3:** The two first anchoring knots are made, bringing both vessels together; **4:** Side-to-side anastomosis between artery and vein is completed; **5:** A double ligature of the vein, near to the anastomotic zone is made, and a subsequent section is performed to create the dome of the aneurysm from this vessel; **6:** After clamping releasing an inflow can be observed into the aneurysm. The green arrows indicate the blood flow direction.
Real performance: **1:** Femoral artery and vein exposure and clamping; **2:** Side-to-side anastomosis; **3:** Distal and proximal femoral vein ligatures, to ensure a proper segment length for the aneurysm; **4:** The clamps are released and the isolated venous segment receives an inflow from the femoral artery, which remains between the ligature limits; **5:** The distal and proximal ligated segments of the femoral vein are sectioned, obtaining a sidewall aneurysm that arises from the femoral artery. Mild vasospasm can be noticed.

model for terminal aneurysms too. The best locations, when a sidewall aneurysm is planned by this method, are closed to natural bifurcations, where the occlusion of one branch, some millimeters far from the divergence, allows to keep the other one patent, simulating a sidewall aneurysm. The few steps needed are listed below (**Figure 6**):

1. Natural bifurcation exposure and dissection of the sacrificed vessel
2. Ligation of one of the vessels near to bifurcation
3. After a distal section of the vessel, the aneurysm is obtained.

No-Neck Sidewall Aneurysms Model

This model is a variation from the end-to-side model that was related before. It is a simple design where a plain vein graft is sutured against a longitudinal incision in the arterial wall, obtaining a lateral wall aneurysm with no neck (43). It differs from the previously described models in the characteristics of the dome, which offers a more realistic, natural, and smooth surface since it does not need any suture or occlusion for its creation, as it is shown in **Figure 7** following the next steps:

1. A plain vein graft is harvested from the jugular vein and a longitudinal arteriotomy in the CCA lateral wall is made
2. The vein graft is fixed to the arteriotomy by a couple of anchoring knots
3. The arteriotomy edges are totally sutured to the vein graft in an end-to-side fashion
4. The blood flow is restored, obtaining a saccular formation with no neck arising from the lateral wall.

Bifurcation Aneurysms

The second type of aneurysms existing in previously published literature refers to those which arise from an arterial bifurcation, which in real-world are often found in the middle cerebral artery (MCA), anterior cerebral artery, anterior and posterior communicating arteries. They represent one of the most common MCA IAs, accounting for up to 85–93% of cases (44) and up to 100% of the anterior communicating artery aneurysms (45), making the difference with their sidewall counterparts, which are more frequently located in the internal carotid artery (75.6%). This configuration is an independent risk factor for rupture (45), being preferred the surgical clipping rather than endovascular treatment by most of the reported case series (44, 45). However, both treatments in such vascular anatomic confluence can be hazardous when proper training is not at first carry on (46). The bifurcation models of IAs provide not only a realistic associated vascular circuit, but an aneurysm neck arising

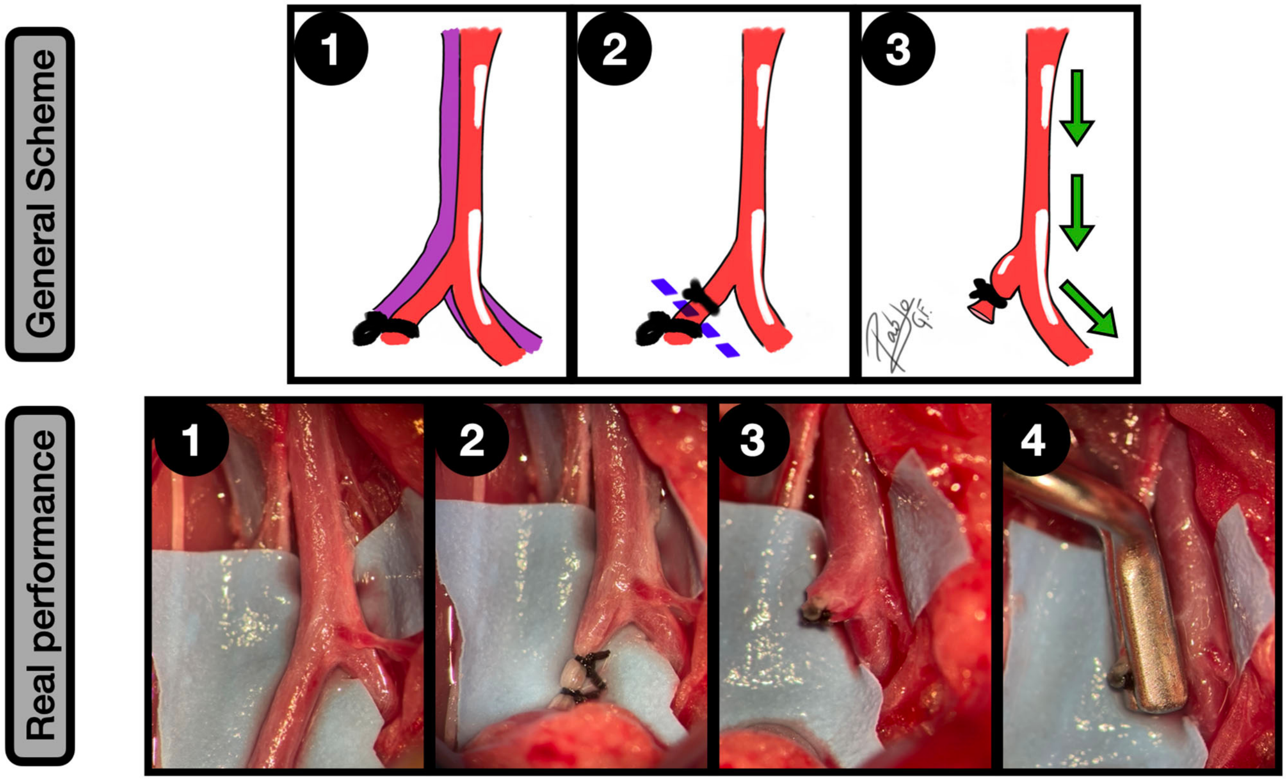

FIGURE 6 | Terminal branch occlusion model. General scheme: **1:** AIB is dissected from the cava and one of the common iliac arteries is ligated; **2:** The common iliac artery is sectioned between the two ligatures, closed to the bifurcation; **3:** The remaining branch of the common iliac artery simulates a sidewall aneurysm while the aorta and contralateral common iliac artery become the parent vessel. The green arrows indicate the blood flow direction.
Real performance: AIB and right common iliac dissection and exposure; **2:** Left common iliac artery ligation in 2 points, with 6/0 silk. The proximal ligature must be placed close to the aortoiliac bifurcation AIB as is shown; **3:** Common iliac artery section. A sidewall aneurism is obtained, acting the aorta and the contralateral common iliac artery as a parent vessel; **4:** The aneurysm is clipped.

directly from the arterial flow divergence. One of the advantages of this model lies in its favorable hemodynamic, preventing thrombosis better than sidewall aneurysms, a characteristic that may be useful when long-term further analyses are needed (18, 46).

Most of these exercises were described on a swine (47), canine (46), or a rabbit model (48, 49), especially on the bifurcation between CCA and external carotid artery. Unfortunately, in rodents, this is not a feasible location for our purposes, although the basic principles can be tailored (6). The recommended vascular compartments depend on the nature of the bifurcation, dividing the currently published models into two major subgroups: natural bifurcation and neobifurcation aneurysms.

Natural Bifurcation Aneurysms

Natural bifurcation aneurysms need the suitable anatomy that a main arterial ramification offers. The abdominal compartment (**Figure 3**) contains the aorto-iliac segment, a major division of the aorta located below the ilio-lumbar vessels and followed by size by the renal arteries (5). The right ilio-lumbar artery normally arises closer (9.7 mm of distance) to the aorto-iliac bifurcation (AIB), being the distal aorta average caliber lower than proximal (1.2 vs. 2.4 mm), but similar to common iliac arteries as it is described in Sprague-Dawley specimen (14). This landmark is a critical structure whose manipulations may compromise seriously the posterior limb's blood flow, unlike the femoral artery. The complete occlusion of this last vessel preserves the flow thanks to an extra-abdominal anastomotic circle between the internal and external iliac arteries (6, 50).

The steps for its performance on rat AIB are (**Figure 8**):

1. Graft harvesting (CCA is highly recommended)
2. AIB dissection from the cava and common iliac arteries exposure
3. Longitudinal arteriotomy on the aorta anterior wall near the bifurcation
4. End-to-side anastomosis between the graft and the aorta
5. The free lumen of the graft is occluded by a ligature (alternatively by an additional graft) and the normal circulation is restored by the clamping releasing, obtaining the aneurysm.

Mücke (13) described this model by using 20 Wistar adult rats, highlighting a mean average volume similar to human IAs, the absence of thrombosis in the zone of central blood inflow into the

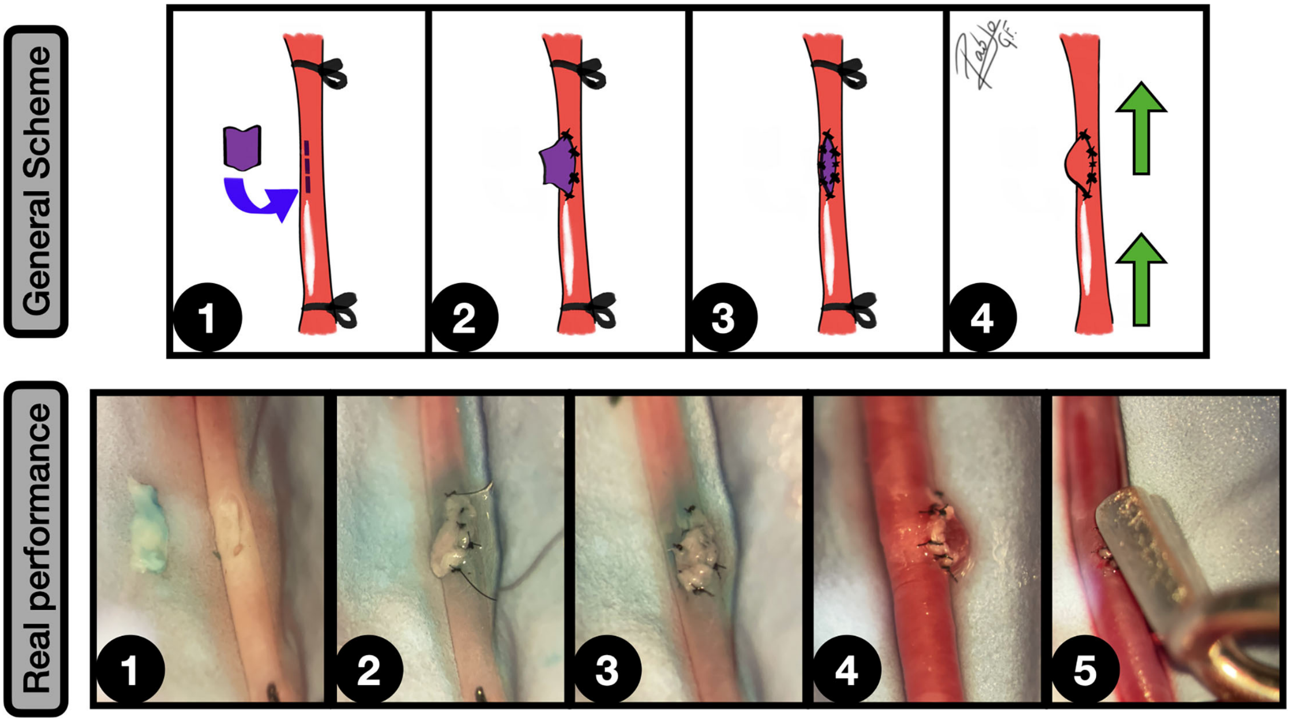

FIGURE 7 | No neck sidewall aneurysms model. General scheme: **1:** CCA is exposed and proximal and distal ligated. A longitudinal arteriotomy in the lateral wall is performed and a plain venous graft from a jugular vein is harvested; **2:** The graft is fixed to the arteriotomy edges by a couple of key anchoring knots; **3:** The arteriotomy is totally covered by the venous graft in an end-to-side fashion; **4:** After clamping releasing an inflow can be observed into the aneurysm. The green arrows indicate the blood flow direction.
Real performance: **1:** A longitudinal arteriotomy on the CCA anterior wall is performed. A plain venous graft, obtained from a jugular vein is shown on the left; **2:** The graft is placed on the arteriotomy and fixed by some anchoring knots; **3:** The graft is fully anastomosed on the arteriotomy, using interrupted stitches; **4:** Clamps are released, appreciating a blood inflow into the graft, which simulates a no-neck sidewall aneurysm; **5:** The aneurysm is clipped, preserving the parent vessel circulation.

aneurysm, and the control of the final dome dimensions thanks to a slight modification provided by a second graft to close the free lumen, instead of direct tighten by a ligature.

Care must be specially taken when the posterior wall of the AIB is dissected from the cava because the artery covers partially the view of the structures behind, where some posterior wall branches may be accidentally injured. To solve this challenge step, this posterior branch must be early identified by mild anterior and lateral transposition of the bifurcation. Secondly, a gentle dissection must be done before proceeding to its ligature.

Additionally, at this level more major arteries and veins than in other locations are present, making riskier the procedures in this area (51). This is the reason why this exercise is one of the most complete microsurgical trainings, combining dissection of an arteriovenous capital confluence, the transference of a free graft harvested from a distant vascular compartment, and the performance of an end-to-side anastomosis on an arterial confluence.

Neobifurcation Aneurysms

This term means the microsurgical performance of an aneurysm model placed on an artificially created vascular bifurcation. Considering that the bifurcation can be created by an end-to-side anastomosis between two nearby vessels, neobifurcation aneurysms can be either located on abdominal or cervical compartments. The steps are described for the CCAs (4, 6, 36, 46, 49).

In fact, this model conceptually consists of a modification of a simple end-to-side anastomosis as it is detailed (**Figure 9**):

1. Wide exposure of both CCA and graft harvesting from a jugular vein
2. Excisional arteriotomy on the anterolateral wall of the parent artery and oblique arteriotomy of the recipient artery
3. End-to-side anastomosis between both carotids, leaving an orifice in the corner which will provide blood a blood inflow into the future aneurysm
4. Suture of the previously obtained venous graft on the orifice
5. The free lumen of the graft is tightened by a ligature
6. The normal circulation is restored by clamping releasing.

It is important to ensure that a proper length of the involved arteries is taken with the aim of avoiding excessive tension in the anastomosis area. The jugular vein is probably the nearest and more suitable vessel to harvest in terms of size, and it must be mentioned that this venous pouch will lead to bigger aneurysm final average volumes in comparison to arterial grafts (36, 49, 52). This model is technically more challenging because the end-to-side anastomosis technique must be mastered, and the graft must be meticulously placed to avoid blood leakages. On the other hand, one of its main advantages is that the angle

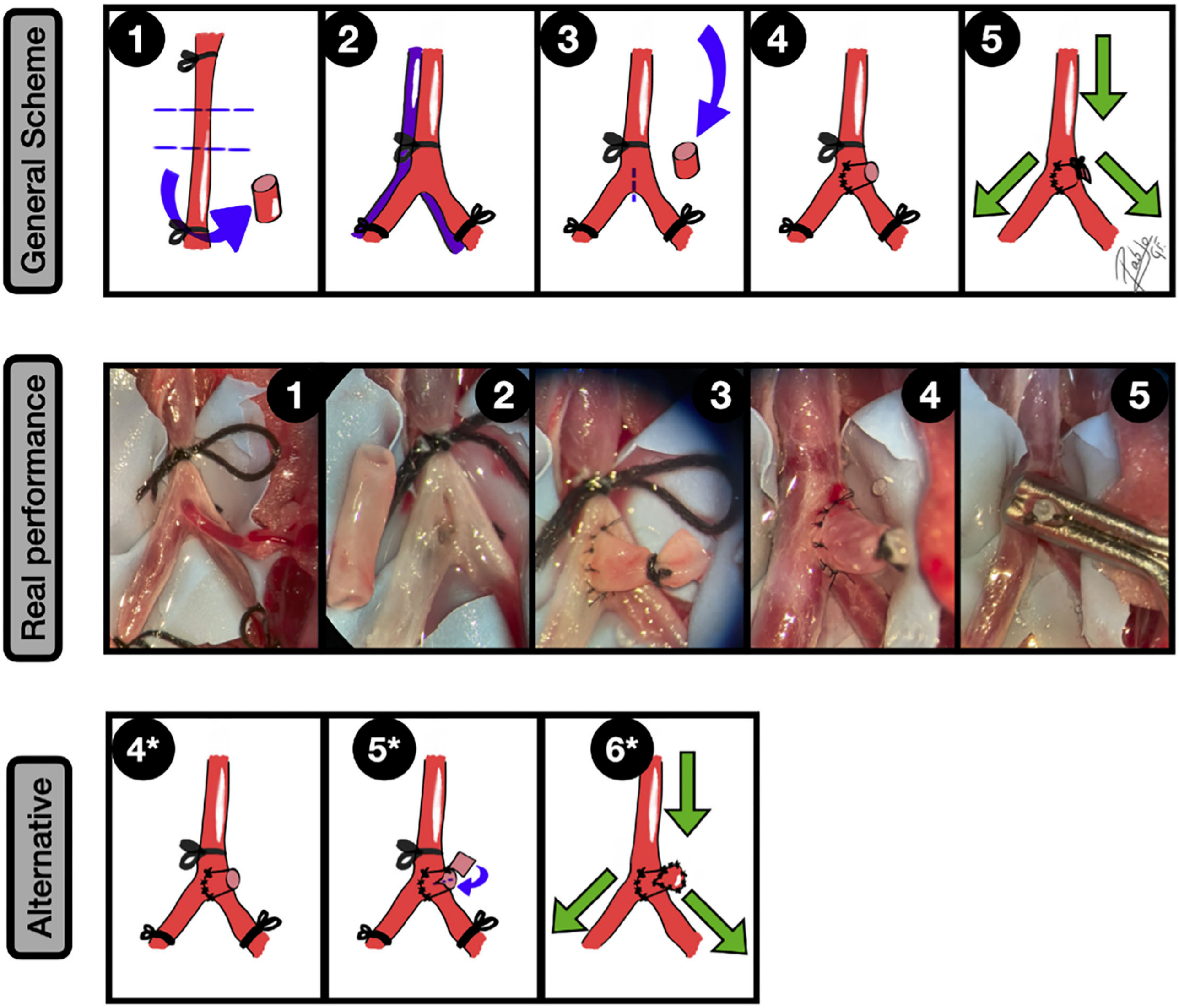

FIGURE 8 | Natural bifurcation aneurysms. General scheme: **1:** A free CCA graft is harvested; **2:** The AIB is gently dissected from the cava vein and common iliac arteries, paying special attention to the posterior branches and subsequent ligation of the aorta and iliac veins is performed; **3:** A longitudinal arteriotomy is made in the anterior arterial wall, near to the bifurcation. After that, the CCA arterial graft is transferred to the abdominal compartment; **4:** An end-to-side anastomosis between the graft and the aorta is made; **5:** The free lumen of the graft is occluded and the clamps are released, leading to an aneurysm formation in the bifurcation. The green arrows indicate the blood flow direction.
Real performance: **1:** Exposure of AIB over the blue contrast background. A posterior branch was ligated; The AIB is gently dissected from the cava vein and iliac arteries, paying special attention to the posterior branches, and subsequent ligation of the aorta and common iliac arteries is performed. In the picture, a third aortic caudal branch is observed; **2:** A longitudinal arteriotomy is made in the anterior arterial wall, near to the bifurcation, removing the tiny arterial branch. The CCA arterial graft is transferred to the abdominal compartment (left); **3:** An end-to-side anastomosis, by interrupted suture, between the graft and the aorta is made. A 6/0 silk ligature is performed to occlude the free lumen of the CCA graft; **4:** The clamps are released, leading to an aneurysm formation in the bifurcation; **5:** The aneurysm is further clipped. Alternative: **4*:** End-to-side anastomosis between the CCA graft and the AIB; **5*:** A fish-mouth arteriotomy is performed in the main CCA graft-free lumen, where a second plain arterial graft is fixed by an anchoring knot. **6*:** The free lumen is fully covered by this plain graft and the clamps are released, obtaining thus a larger aneurysm. The green arrows indicate the blood flow direction.

of bifurcation can be fashioned (47). There is even a model that mimics the human basilar tip aneurysms (6), where the bifurcation is artificially created by a side-to-side anastomosis between both CCAs and then the graft is sutured to an orifice on the top of the construction to simulate the dome.

In this category, another type of aneurysms must be named, due to the similarities in terms of the technical sequence: the confluence aneurysms. This model creates an aneurysm by a venous pouch placed on an end-to-side anastomosis, however, the graft must be located on a confluent blood flow construction instead of a divergence flow. For the CCAs, the conceptual change resides in the arteriotomy and the artery selection, where now the recipient artery becomes a donor (**Figure 9**). This means that the final construction offers two inflow vessels,

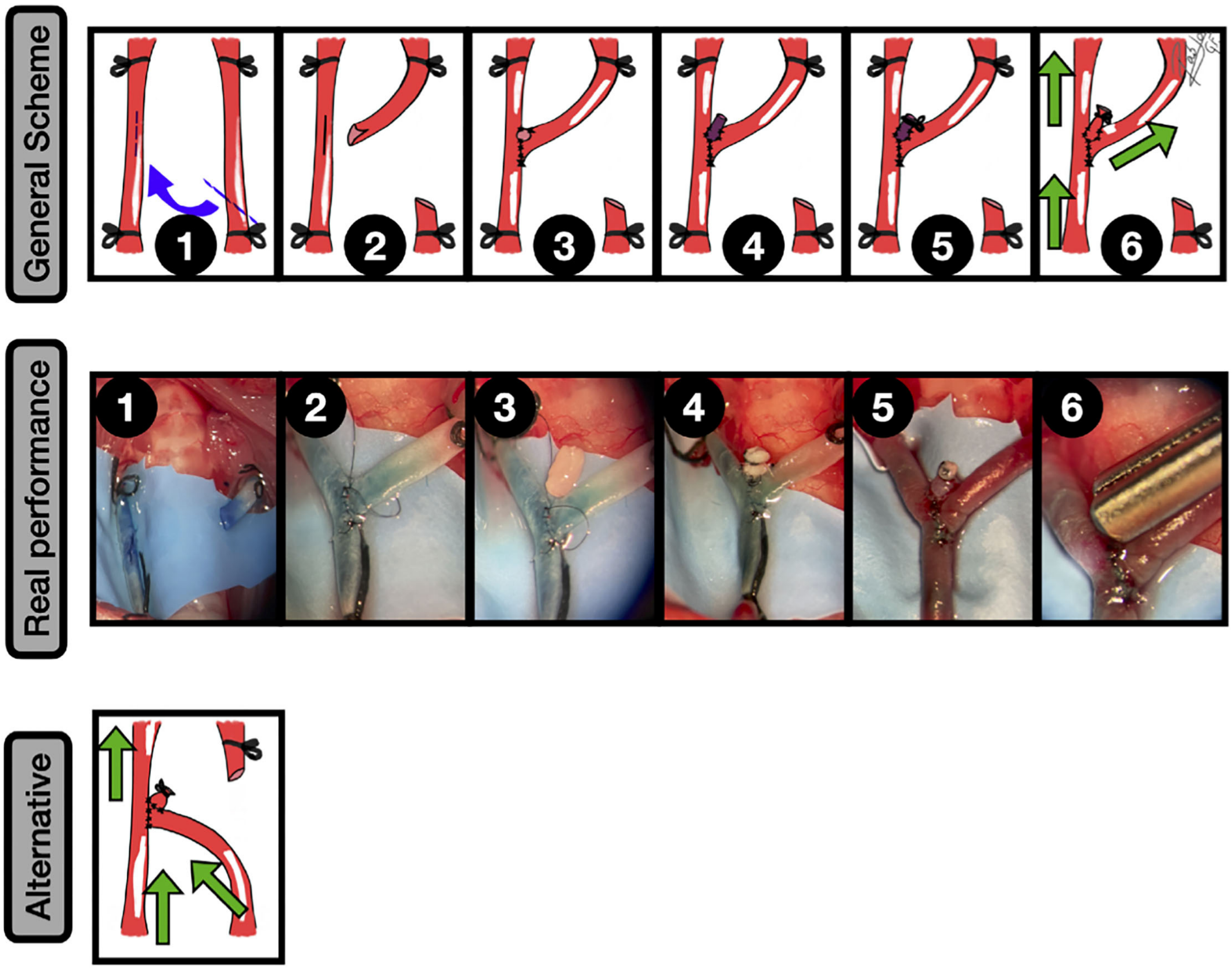

FIGURE 9 | Neobifurcation aneurysms. General scheme: **1:** Bilateral CCAs exposure and proximal and distal ligation. A longitudinal arteriotomy in the anterolateral wall of the left CCA is done and an oblique arteriotomy facing the contralateral artery in the second CCA is performed; **2:** The picture shows the anastomosis construction and the fish-mouth arteriotomy in the recipient artery; **3:** An end-to-side anastomosis between both CCAs leaving a hole on the top is performed; **4:** A free venous graft from a jugular vein is placed on the top of the construction and anchored by a couple of knots; **5:** The anastomosis between the graft and the hole is completed and the free lumen of the graft occluded; **6:** The clamps are released, leading to an aneurysm formation in the bifurcation. The green arrows indicate the blood flow direction.
Real performance: **1:** Exposure of both CCAs and subsequent arteriotomies in an end-to-side fashion, including a fish-mouth arteriotomy of the recipient artery (right). The vessels are dyed by methylene blue; **2:** The end-to-side anastomosis between both CCAs is performed, leaving a hole in the top that will be the neck of the aneurysm; **3:** A free venous graft from a jugular vein is harvested and transferred to the anastomotic area in the showed place; **4:** A second end-to-side anastomosis between the free graft and the hole is performed, and a 6/0 silk ligature is utilized to occlude the free lumen of the venous graft; **5:** The clamps are released, leading to an aneurysm formation in the bifurcation; **6:** The aneurysm is further clipped. Alternative: Confluence aneurysm by an end-to-side anastomosis between the CCAs + venous graft to recreate the aneurysm. The blood flow has a different direction from the aforementioned example. The green arrows indicate the blood flow direction.

remaining only one outflow vessel distal to the aneurysm. In general, high blood flow through the anastomosis is a positive factor for its patency (53). The confluence model mimics, for instance, the real-world hemodynamic conditions presented in human vertebrobasilar junction, where complex cases for both endovascular and clipping techniques are a challenge (46).

Fusiform Aneurysms

The non-saccular aneurysms (fusiform, dolichoectatic, and dissecting) are, by far, less common than saccular among human IAs (38), and the available data revealed internal elastic lamina fragmentation, thinning of the tunica media and tunica intima hyperplasia as was shown in their saccular counterparts (4), although their exact pathogenesis remains unclear. The potentially tortuous arterial pathway makes this translational model more suitable to train endovascular skills than microsurgical clipping. Most of the fusiform models of IAs are described on bifurcation aneurysm (4, 36, 38, 39, 54), adding some modifications to the graft harvesting to enlarge the saccular dilatation longitudinally. The previously described

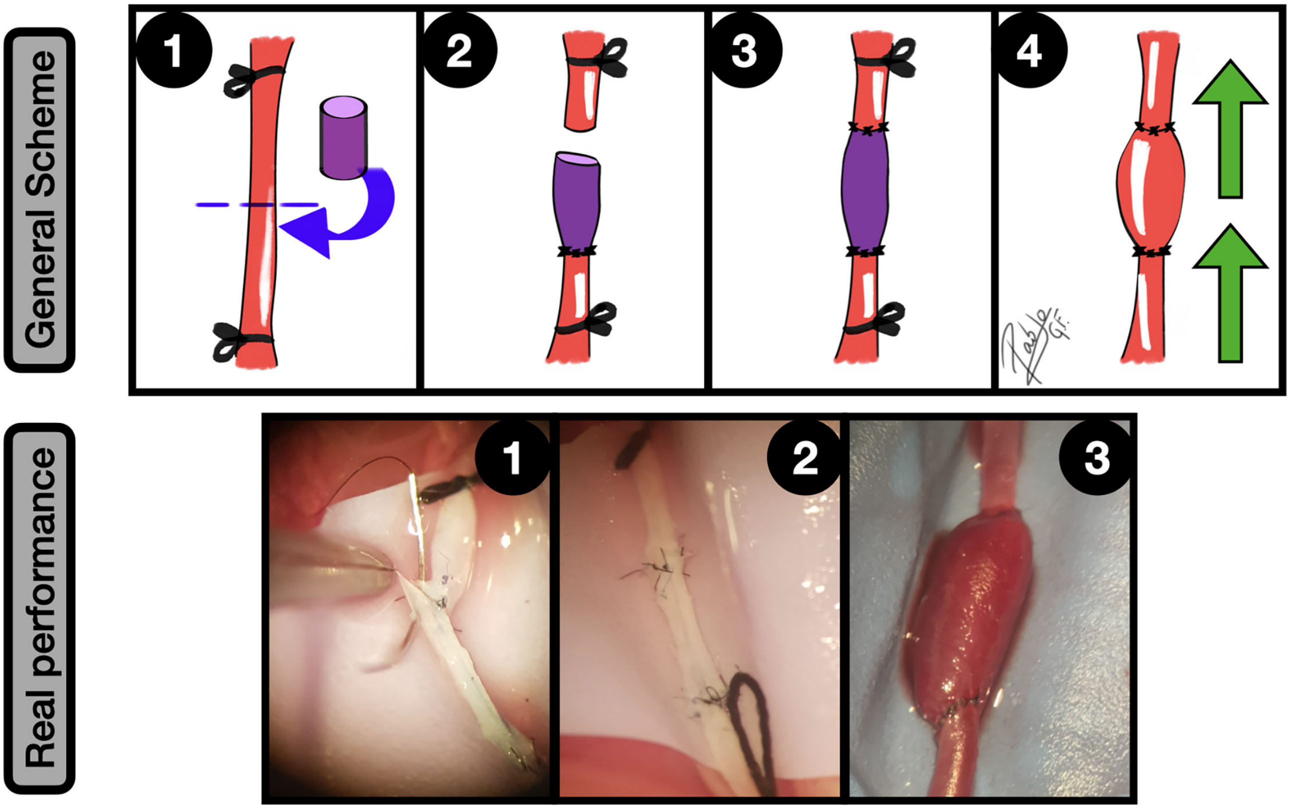

FIGURE 10 | Fusiform aneurysms. General scheme: **1:** Unilateral CCA exposure and proximal and distal ligation. A straight arteriotomy in the middle of the artery is done and a free venous graft from a jugular vein is harvested; **2:** One of the free lumens is sutured to the caudal CCA segment in an end-to-end fashion; **3:** A second end-to-end anastomosis is made between the graft and the proximal CCA, acting as an interpositional venous graft; **4:** The clamps are released and the flow inflates the venous segment of the construction, obtaining a fusiform aneurysm. The green arrows indicate the blood flow direction.
Real performance: 1: Suturing between CCA proximal segment and the free venous graft; **2:** The second end-to-side anastomosis is completed, observing the interpositional venous graft; **3:** After releasing the clamps the blood flow enlarges the venous segment of the construction, simulating a fusiform aneurysm.

tenets are valid for the creation of such exercise, in which often a venous graft is preferred over an arterial (4, 52). However, there is a chance to create by microsurgery a pure fusiform aneurysm on a straight continuous segment of a vessel (6, 55), which may resemble those found, for instance, in human intracranial vertebral arteries. The fusiform aneurysm is obtained immediately or in a short period, in part due to the graft properties, which allows obviating a long time to develop a defective elastic lamina and muscular layers observed in human fusiform IAs (56). While the description is made for CCA as follows, this model can be performed in any of the three vascular compartments of the rat (**Figure 10**):

1. Jugular vein patch harvesting, CCA exposure, clamping, and straight arteriotomy
2. Interpositional venous graft placement on CCA and distal suture in an end-to-end fashion
3. A double end-to-end anastomosis is completed by a second proximal end-to-end anastomosis
4. After the clamping is released, the venous pouch enlarges progressively whilst the blood flows through the lumen, resembling a fusiform aneurysm.

Fukui et al. (56) described this model on the rat CCA, by using an interpositional femoral vein graft, achieving a dramatic fusiform enlargement in 75% and a formation of a giant aneurysm in 53% of the grafts.

Other described modifications of this simple fusiform model include an additional branch (6) emerging from the aneurysm that can contribute to improve the outflow and potentially avoid thrombosis.

Other Complex Aneurysms

The aforementioned types of extracranial models for IAs in rats do not include all the possibilities in terms of anastomoses combination, but they are by far the most common types reported in the literature. Other simulated aneurysms are classified into this group under the name "other complex aneurysms" by some authors (18), attending to unusual shapes resembling several types of human IA, such as dolichoectatic, giant-sized, fusiform, bisaccular (57), or confluence artery aneurysm. The obtained creations are mostly oriented to endovascular therapy training and new device testing rather than microsurgery training, and for this reason, these publications are preferentially found in

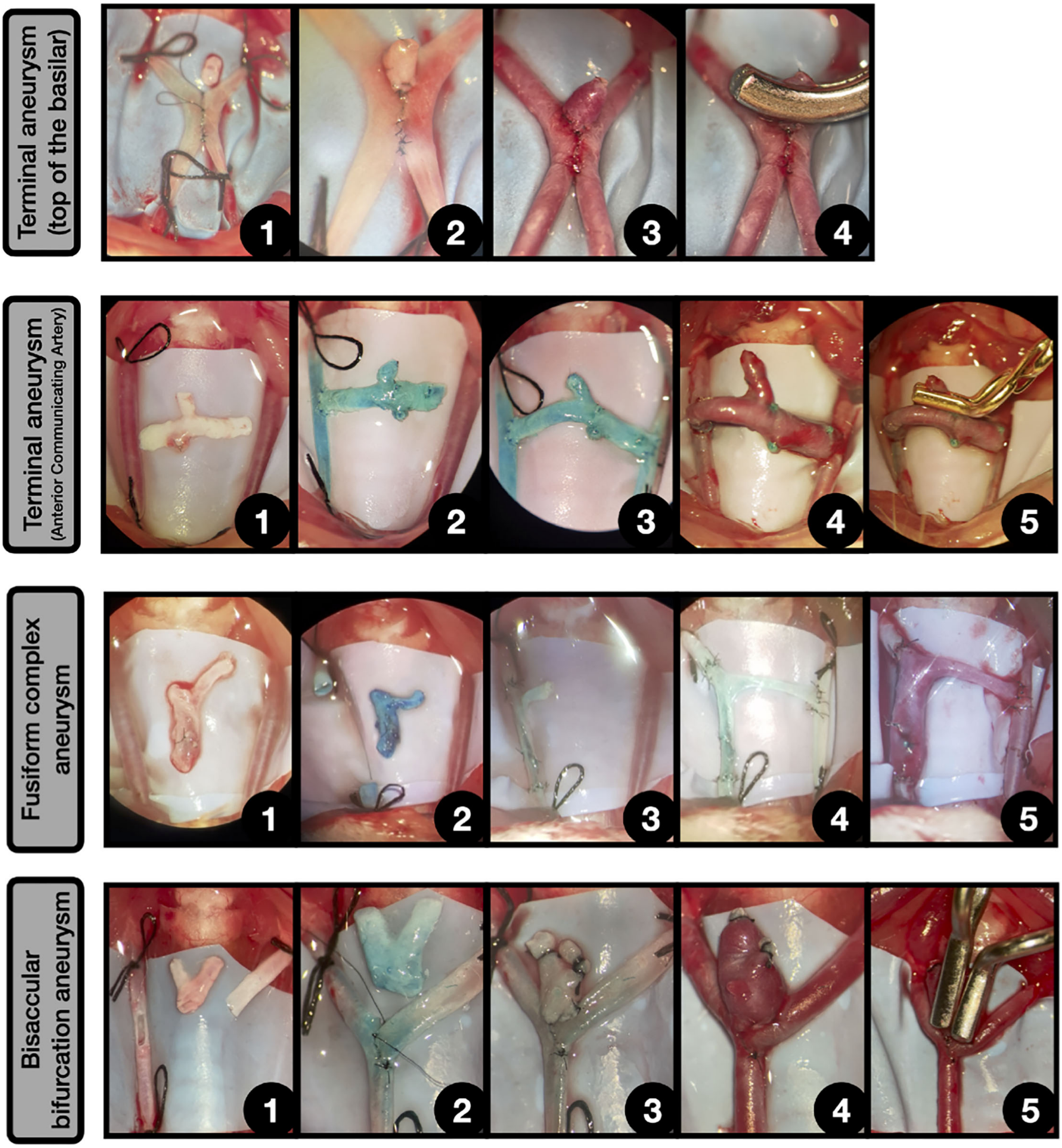

FIGURE 11 | Other complex aneurysms. Terminal aneurysm (Top of the basilar) [4]: **1:** Side-to-side anastomosis between both CCAs, leaving a hole in the top. Above lies a free venous graft; **2:** The graft is sutured to the hole and the free edge is occluded; **3:** After declamping the aneurysm enlarged on the top of the anastomosis, simulating a terminal aneurysm placed on the top of the construction; **4:** The aneurysm is clipped.
Terminal aneurysm (Anterior communicating artery) [4]: **1:** Both CCAs are exposed and ligated and a free graft from jugular vein bifurcation is obtained; **2:** The graft is anastomosed in an end-to-side fashion to the right CCA; **3:** Another end-to-side anastomosis between the graft and the contralateral CCA is performed, obtaining a connection between both CCAs. The remaining above free lumen is occluded by suture; **4:** After releasing the ligatures a terminal aneurysm that arises from the venous graft is obtained, simulating the circuitry of an anterior communicating artery; **5:** The aneurysm is clipped.
Fusiform complex aneurysm [4]: **1:** Both CCAs are exposed and ligated and a free graft from jugular vein bifurcation is obtained; **2:** A straight arteriotomy is made in right CCA and the free venous graft is dyed in blue; **3:** The graft is anastomosed in an end-to-end fashion to both CCAs free lumens, leaving a branch oriented to the contralateral CCA; **4:** The branch is anastomosed to the contralateral CCA in an end-to-side fashion; **5:** After the declamping, the venous segment enlarges, obtaining a complex fusiform aneurysm.

(Continued)

FIGURE 11 | Bisaccular bifurcation aneurysm [77]: **1:** Longitudinal arteriotomy in the parent vessel and oblique fish-mouth arteriotomy in the second vessel for an end-to-side anastomosis. A bifurcation venous graft, obtained from the jugular vein is placed on the surgical field; **2:** Incomplete end-to-side anastomosis between both vessels, leaving a hole on the top; **3:** The venous graft is anastomosed to the top of the construction and the two free lumens are occluded; **4:** After the declamping, the venous graft enlarges, obtaining a complex bifurcation bisaccular aneurysm; **5:** The aneurysm is clipped by using two aneurysm clips.

journals focused on interventional neuroradiology (47, 57). Due to the number of involved vessels and resulting size, these models are unpopular to be practiced in rodents, being more frequently described in bigger animals, such as rabbits or pigs (18).

They are not well-characterized and there are many variations between models, being the design many times ultra-specific (47) with regards to the bifurcation angle, size and complex vessels flow circuitry that allows the trainee to practice sequential temporal clipping to decrease, for instance, the inflow into the aneurysm or to assess the enlargement of the dome when the outflow is clamped.

The giant aneurysm model provides a good example of this class, where enlargement of a huge formation that sometimes needs a week to be appreciated, and that may also be performed at one stage.

Some of the simulations recreate the vessels circuitry found in the human vertebrobasilar system, where the two vertebral arteries bring a blood inflow into a common basilar trunk that later divides into another two vessels: the posterior cerebral arteries. Thanks to these complex models, some specific portions and flow conditions of human intracranial vessels can be simulated, offering a simplified model to understand and assess the clipping practice.

Here is provided a brief summary of some other complex aneurysms which can be crafted on rodents' vessels model (**Figure 11**).

DISCUSSION

Historic Perspective of the Microsurgical Training in Neurosurgery

Surgical training was long based on experimental models, being the animals' involvement in medicine a constant throughout history. The refinement of the microscopes and the advances in the vascular neurosurgery discipline have followed parallel tracks, being impossible to understand both mentioned areas without the presence of each other. A century ago, in 1922, the Swedish otologist Gunnar Holmgren introduced the first binocular surgical microscope in operating theater (58), setting the beginning of a new era for surgery that will take more than 30 years to arrive at Neurosurgery, when, in 1957 the first reported microsurgery attempt in the field took place, by Theodore Kurze, who removed a neurilemoma of the seventh nerve in a child. At the same time, in Vermont, in 1958, R. Donaghy (59) established the world's first microsurgery research and training laboratory for neurosurgeons, after the series production of the Zeiss OpMi 1 started, in the early 50s. His growing interest in the field pushes him and his colleague Jacobson, to report their translational accomplishments in neurovascular surgery, describing in detail the instrumentation and technique for microsurgical reconstruction of small intracranial arteries in a case series (60), which is considered the first human reported microvascular experience in neurosurgery. Prior to this date, in 1939, German and Taffel had documented the first experimental encephalomyosynangiosis in dogs and primates, followed by Kredel in 1942, who did the first attempt in humans (61). However, these revascularization procedures are indirect techniques that were performed without the use of the microscope, essentially because its use was not yet standardized. By 1965, Dr. Donaghy's laboratory had attained global renown, receiving many physicians from all over the world who wanted to learn the microsurgery standards and take part in his annual 2-weeks course (62). One of the most remarkable surgeons among these trainees was G. Yaçargil, whose restless dedication to microneurosurgery will bring huge advances and contributions to the field. He highlighted the need for reproducible animal models to develop microvascular techniques (63), by transferring and adapting the original one described by Alexis Carrel (64) (Nobel Prize 1912), and by introducing specific novel instruments for microsurgery, including the aneurysm clips and appliers or the Malis bipolar coagulation, which was a turning point in his career, as he recognized further. In this sense, his first steps were made on the rabbit femoral artery and dog carotid artery, where he achieved a 66% anastomosis patency rate (61) during his training period at R. Donaghy's laboratory until they purchased a microscope for his department. Nowadays, the best outcomes are achieved by an accepted patency rate of over 95% for extracranial-intracranial bypass procedures, bringing to focus the indispensable resource of microvascular training (61).

In the 1960s and 1970s, thanks to the efforts of many pioneers in the field, the refinement of the techniques was possible, and many new techniques were born, allowing to improve the odds against several craniospinal diseases that were previously considered untreatable. This was the case of Woringen and Kunlin, who performed the first extracranial-intracranial bypass in a real patient by 1963 (65).

The weight of the historical evidence indicates that the major advances in the field of vascular neurosurgery came from the technical improvement and application of microsurgery principles, being further applied to other sub-disciplines such as oncological surgery or spine surgery. Furthermore, it is well-known the association between microvascular training in living models and the development of the most subtle surgeries among the greatest neurosurgeons, who encourage the young generations to follow their steps by routinely practicing on these models (1).

Learning in Microsurgery

Microsurgery is known as a high-demanding discipline where routinely training is indispensable to achieve the best results in the real world, a fact that in modern practice becomes more important than ever due to extremely high expectations toward surgeons (15). Many of the best neurosurgeons of the second half of twentieth century have hypothesized about the importance of cadaveric and animal model training. Contrary to what some people may think, microsurgery training is not about the anastomosis final result, but the essence of microsurgery, and therefore, of bypass surgery too, are the micromovements (1). These maneuvers are mainly based on the hand-eye coordination (or better said: "hand-brain") needed to carry on the finest vascular suturing.

At present, a varied range of training publications takes the quality and number of movements into account, moving the exercise results into the background. This fact is reflected, for instance, in the increasing need to quantify microsurgery training by using scales that attempt to measure these subjective parameters. Despite of the fact that there is still a lack of standardization, some of the main scales compile the following issues (5, 11): self-confidence, theoretical knowledge [Global Rating Scale (GRS) and Northwestern Objective Microanastomosis Assessment Tool (NOMAT)], subjective self-assessment or by a third party [Objective Structured Assessment of Technical Skills (OSATS), University of Western Ontario microsurgical skills acquisition/assessment (UWOMSA), GRS, and NOMAT] (66), objective motion control (The Stanford Microsurgery and Resident Training (SMaRT)) (67), analysis of the final result of the anastomosis (UWOMSA, GRS, and NOMAT), time to complete anastomosis (UWOMSA , GRS) and transferability.

The ideal scale must probably include all these issues (5), however, the high heterogeneity among the available scales in terms of measuring tools, makes it difficult to compare prospective results.

It is also critical a suitable training model selection, adapted to the level and skills of the trainee, who must begin on non-living dry models during the practice of the most basic steps (11) until enough expertise to try on more realistic and living models had been gained. Likewise, the complexity of exercises to be performed in microsurgery varies with the practitioner skills, being recommended a sequential learning program, which means performing and solidifying the knowledge of the most basic steps and anastomoses at the beginning. Then the trainee can advance (5) to other training stages where it is imperative to dominate different types of anastomoses, vessels, and exercises that culminate in complex combinations such as aneurysms performances.

A high-level surgeon does not obtain only a good result, but he looks for good stable results. There are some studies (68) that emphasize the importance of ongoing training for mastering the technique, and compile all these questions, setting over 50 the number of anastomoses as a threshold to master the microsurgery technique.

The proposed stepwise training route (**Figure 12**) for learning in microsurgery is based on the current published recommendations, highlighting the value of the three classical anastomoses technical execution handicap (end-to-end, end-to-side, and side-to-side), which are the basis of experimental microsurgery (1, 5, 11, 68), so as to make possible the further development of the aneurysm creation models, where these techniques are mandatory to be mastered.

A Realistic Model With Limitations

Although the described aneurysm models are technically more demanding, they enable vascular clipping practice, inflow and outflow evaluation, growing patterns assessment, and, in some cases, the flow can be regulated.

The rodent vessels model for IAs is more predictable with regard to size and volume (13, 46) in comparison to induction models, being the neck, angle, and orientation potentially fashioned. The final average volumes are similar to those found in human IAs (35.19 ± 5.64 mm^3) (13), especially to those found in the posterior communicating artery or the postero-inferior cerebellar artery, being useful these trained skills, to our knowledge, during a tumor resection involving posterior circulation vessels, like in medulloblastoma surgery. However, some human aneurysms arising from anterior circulation can achieve a large size that cannot be obtained easily by the mentioned training exercise.

They are not good models for rupture, presenting most of them the increases in size by means of maturation rather than ongoing degradation of the aneurysm wall and true growth that finally results in aneurysm rupture (69). Despite these differences, they are quite good models to train on suturing of an injured aneurysm neck and microsurgical reparation of vessels (69).

In rodents, the surrounding tissue differs from the human arachnoid layers, typically seen during cranial approaches, being the aneurysms located on the three vascular compartments of the rodent, between fatty tissue and abdominal organs. Furthermore, neither induction nor creation models can accurately replicate the real pathophysiology observed in IAs in terms of, for example, atheromatosis (20), timing, or rupture trends.

Unfortunately, none of the available models offer all the ideal features of a good aneurysm model, which should include the following: tissue responses, stability without spontaneous thrombosis when untreated, perianeurysmal environment, physical dimensions, minimal surgical, and endovascular morbidity; similarity to human aneurysm shear stresses, hemodynamic forces, and physical dimensions (70).

It is known that the three classical anastomoses are the pillars of microsurgery training (5, 68), that have been extensively utilized in real patients during by-pass surgery, however, some differences in several aspects from aneurysm creation models are noticed:

- The absence of a direct application for real cases since the creation of an artificial intracranial aneurysm in a human has no sense.
- Sometimes, the artificial connection created between the vessels causes an arteriovenous fistula, a condition of unclear utility in human intracranial vessels.
- A longer ischemia time in comparison to a simple anastomosis exercise.

The last point is of considerable interest, understood as the time required for the aneurysm creation, which is related to

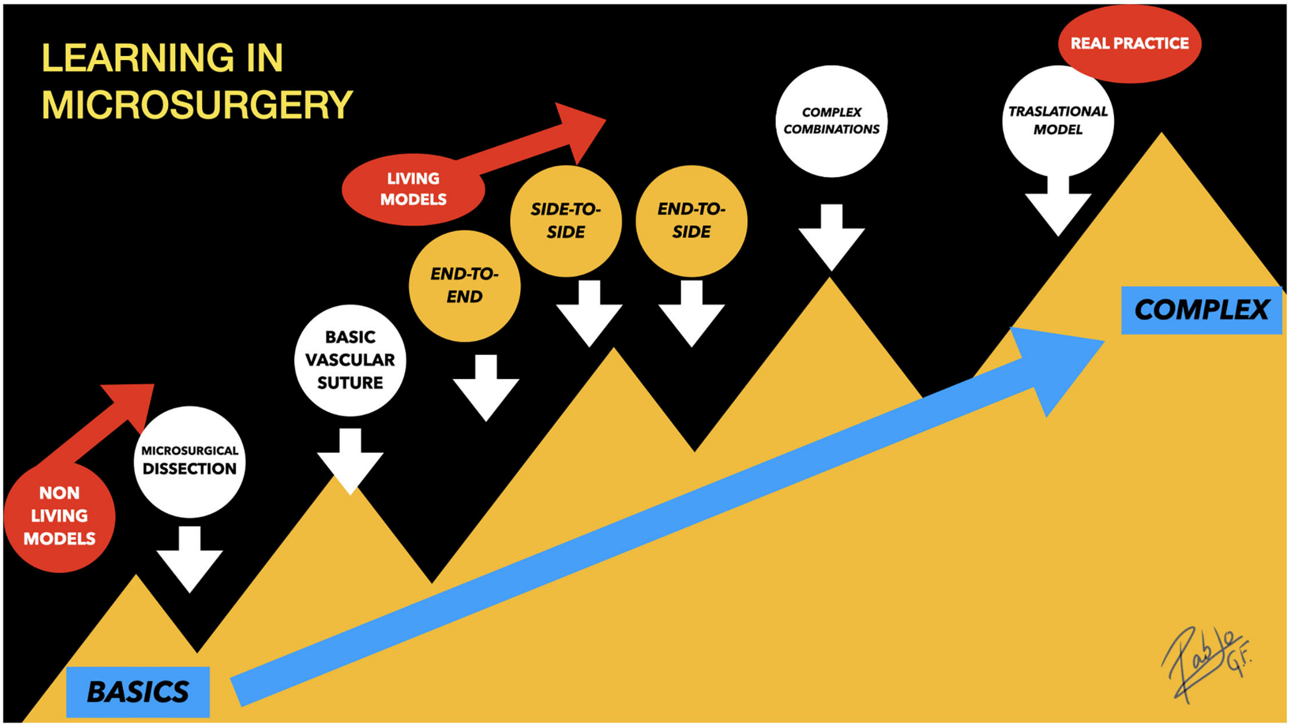

FIGURE 12 | Learning in microsurgery: Stepwise training route for learning in microsurgery. The end-to-side and side-to-side anastomoses are a little harder to be performed than end-to-end, which is considered the simplest anastomosis. The aneurysm performances are located on the top of the complexity, under the name "Complex Combinations," that refers to their underlying microarchitecture that includes portions of the classic three anastomoses.

the time without blood flow. Some authors reported shorter creation times for the simplest models (sidewall, bifurcation stump, and natural bifurcation), which can take around 30–60 min (18). Some publications (13) have even reported 15–20 min of ischemia for the natural bifurcation aneurysm model. However, the full invested time, considering all the steps, such as the graft harvesting and preparation of the parent vessels, is frequently longer than the time for a simple anastomosis, being often necessary 3 h of surgery to performed artificial bifurcation aneurysms (13, 18).

There remains considerable controversy regarding human arterial occlusion time, as it is described in one of the most powerful conducted studies about cerebral Occlusion Surgery Study) (71). This study reports a mean duration of MCA occlusion, among the 78 patients who did not experience a stroke, within 2 days after by-pass surgery of 45.4 ± 24.2 min, ranging from 15 to 123 min. Surprisingly, this study revealed no statistical significance ($p = 0.182$) in terms of MCA occlusion time compared to the stroke cohort. Despite the results, neurosurgeons worldwide still recommend the shortest possible ischemia time during bypass procedures. We believe that this time is essential too, and we encourage the reader to practice on the described models to shorten their by-pass/aneurysm creation time as much as possible.

The rodent model is not ideal for endovascular training (simpler aneurysm creations, shorter vessels caliber, and smaller size), since more realistic aneurysms can be performed in swine or rabbit model, which both offer bigger vessels.

Comparison Between Aneurysm Models

The described aneurysm models are suitable for several research and training-related uses, however, there are many differences between induction and creation models, besides its mechanism of production, that becomes a matter of ongoing interest for the present review. Most of the mentioned induction models in rodents consist of an addition of different risk factors, that are also observed in humans, and that lead to IA incidence (20).

It is known that the costs of rodents are cheaper than the swine, canine o rabbit models, where, additionally, general anesthesia and the presence of a veterinary must be required (18). Furthermore, the costs of the induction models are normally higher, due to the requirement for several drugs administration, the use of knock-out cohorts, or the time needed for an acceptable IA incidence rate, which in some cases can last up to 6 (20) or 13 months (37). Via the creation model, the aneurysm is obtained in a moment. Moreover, in terms of aneurysm shape, the most common IAs induced in rodents are non-rounded or bulges consisting of small outpouchings arising from the animal intracranial vessels (20), normally located in the anterior circulation, that are not suitable to be surgically manipulated due to their size. Whilst in induction models neither the incidence rate nor the aneurysm shape can be predicted, creation models offer several fashionable characteristics such as size, location, type, longitudinal axis length, neck width, aneurysm projection, bifurcation angle, dome-to-neck ratio, and other dome peculiarities (13). All these designable properties make them ideal for training since more similar aneurysms in comparison to human IAs can be achieved, despite being placed on extracranial rodent vessels (18). The hemodynamic circuitry can be also designed, becoming important, for instance, for the bifurcation aneurysms understanding, where the blood flow direction determinates whether a bifurcation whether a confluence aneurysm (46) is created, a subtle distinction that provides a vertebrobasilar junction or an MCA bifurcation aneurysm prototype.

Only two of the described non-pure creation models provide a training opportunity for microsurgical purposes: the Hashimoto induction model (29) and the fusiform aneurysm induction model on CCA (38). The first suggests an end-to-side anastomosis between both CCAs (to secondarily induce IAs), which must be meticulously performed in order to ensure the animal can survive the procedure for several weeks (29–31). The second one implies a gentle dissection of the CCA and its microsurgical isolation before a local high dose administration of elastase (38).

Sidewall aneurysms are the quickest to be performed and they normally imply fewer vessels manipulation. For instance, the terminal branch occlusion model just requires microsurgical dissection and ligation of the main vessel, avoiding a microvascular anastomosis. The complex models are not very popular in rodents, and their angioarchitecture is very variable with poor reproducibility, being more suitable for bigger animals, where the caliber of the vessels allows for novel endovascular devices testing (18).

Probably the most complete models to train on vascular skills are the ones that include several types of vessels (both venous and arterial), where a modified anastomosis is demanded.

More than one creation model exercise can be tried on the same animal, leading to the reduction of the number of employed animals, agreeing with the 3Rs principles proposed by Russell and Burch (16).

New Horizons in Vascular Training

Several milestones have been reached since the introduction of the microscope in the surgical routine one century ago (58), evolving from the macroscopic era into the microneurosurgical era. Despite these accomplishments, since the beginning of the twenty-first century, there is a sustained declining trend of the number of microsurgical clipping and by-pass procedures, motivated by some big trials results such as ISAT (International subarachnoid aneurysm trial) (72) which included a huge cohort of randomized patients suffering aneurysmatic SAH, suggesting lower short-term mortality in the endovascular treatment arm (23.5 vs. 30.9%; 95% CI 3.6–11.2; $p = 0.0001$) when compared to surgical clipping arm. However, a *post hoc* analysis issued eighteen years after (73) invalidated these results, showing no differences between both arms. Finally, in 2012, BRAT (The Barrow Ruptured Aneurysm Trial) (3) was published, highlighting the importance of high-quality surgical clippings when the endovascular treatment has failed and enhancing the need of both surgical and endovascular provisioned centers to achieve the best outcomes. These investigations encouraged new generations to be ready for neurovascular surgery procedures, however, the current fewer vascular surgical cases, which many times are more complex, makes essential the training on different models.

The classic living models continue to be the gold standard for training among senior vascular surgeons, however, the scientific society claims for the refinement of the technique and the avoidance of living animals for training purposes, so new devices are increasingly emerging as alternatives to supply these "old-school" models. Some authors have tried to develop virtual surgery simulation (4), a promising method that presents the main inconvenience of the lack of haptic feedback, typically seen during the *in vivo* models surgical clipping. This handicap has motivated the development of several prototypes of haptic devices for medical use that calculate the required force, returning a calculated proportional response to the user in real-time, as is the case of *Bimanual Haptic Simulator for Medical Training*, *PalpSim*, or *ImmersiveTouch* (12). This field of research is now more active than ever, promising major advances in the coming decades that will further reduce the human-machine interface so that virtual simulations are more realistic. An example is the recent *NeuroVR*^{TM} *Platform*, which integrates a 3D rendering system with binocular output, emulating a surgical microscope, with a bimanual haptic rendering (12).

MicroSure (74) is one of the robots in which the practice of microvascular anastomoses has been evaluated in a live rodent model, by successfully performing end-to-end anastomoses in the aorta and femoral arteries, but still obtaining a suboptimal aesthetic aspect of construction. The use of robots in microsurgical practice requires a certain degree of prior training, in which the typical haptic feedback of conventional microsurgery is dropped. At present, concerning neurosurgery (74), the brachial plexus repair and the sympathetic chain repair to treat Horner's syndrome have been documented, but not any vascular intracranial procedure.

Silicone aneurysm models offer an excellent alternative to animals in both endovascular and clipping training; however, it does not fully replicate the natural arterial biology (36). 3D-printed technologies allow the presurgical accurate recreation of the patient-specific vessels, which can be further processed to form a hollow, silicone-walled artificial vasculature for training and serve as an assessment tool for vascular cases, including even, some of them, a device that induce a simulated blood flow (75, 76).

CONCLUSION

Among twenty-first century neurosurgeons, the lowest complications rate and the perfect refinement of the vascular technique are pointed (15), so a hard training program is mandatory to be completed before starting vascular procedures in real patients.

A stepwise training program with regards to the trainee skills and exercises complexity must be taken into account before starting experimental surgery training involving living models.

The presented aneurysm models suggest new training exercises, different from the classic anastomoses, that can be reproduced following the explained steps and that allowed further realistic clipping due to many similarities to those IAs found in humans.

The present review summarizes the present state-of-the-art microsurgical techniques for the development of both intracranial and extracranial aneurysms in rodents, which are still valid, representing the best training for the vascular by-pass skills reinforcement as a translational model useful for neurovascular surgeons, that can also help to improve the underlying mechanism of the pathophysiology of human IAs. By training on these models, several microsurgical skills are improved, allowing safer practice for neurosurgeons in all stages of their career.

AUTHOR CONTRIBUTIONS

FC and AI provided substantial contributions to the conception and analysis of the work by their experience. MS-A provided a critical analysis of some portions of the review. MG helped during redaction and provided a critical analysis of the review. All authors contributed to the article and approved the submitted version.

FUNDING

This article submission was supported by the grant PI17/00361 by instituto Carlos III of Spanish Ministry of Health and MULTITARGET & VIEW by Community of Madrid (FEDER).

ACKNOWLEDGMENTS

Finally, we would like to thank everyone who helped and motivated us to work on this project, with an especial mention to all the idiPAZ staff for their ongoing support.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflictof interest.

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MINI REVIEW
published: 26 April 2022
doi: 10.3389/fsurg.2022.878293

Exoscope as a Teaching Tool: A Narrative Review of the Literature

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Recently, the emergence of the three-dimensional (3D) exoscope has proven to be a viable alternative to the operative microscope (OM) as a novel workhorse of microneurosurgical procedures. Through its current iteration, the 3D exoscope has been demonstrated to be at least equivalent to the operative microscope in terms of surgical outcomes in many settings. With its superior ergonomics and simplicity of use, the 3D exoscope has been shown in multiple studies to be a powerful visualizing tool during surgical procedures. Moreover, the exoscopic systems, through their current iterations and by means of a high-resolution 3D monitor and 3D glasses, have allowed all participants present in the operative room to attain an unprecedented level of intraoperative visualization of anatomical structures and surgical maneuvers which are traditionally available only to the first operator. Although long-term data are still lacking regarding its future as a replacement of the OM, the 3D exoscope has revealed itself as an intense subject of discussion in neurosurgery regarding its implication for surgical education, especially for residents and junior neurosurgeons. This article is a review of the current state of the literature on the role of the exoscope in surgical education, underlining its strength as a learning tool and its potential future implications in terms of surgical education.

Keywords: exoscope 3D, exoscope, education, training, resident, students, neurosurgery

OPEN ACCESS

Edited by:
Bipin Chaurasia, Neurosurgery Clinic, Nepal

Reviewed by:
Mario Ganau, Oxford University Hospitals NHS Trust, United Kingdom

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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: *17 February 2022*
Accepted: *14 March 2022*
Published: *26 April 2022*

Citation:
Calloni T, Roumy LG, Cinalli MA, Rocca A, Held A, Trezza A, Carrabba GG and Giussani CG (2022) Exoscope as a Teaching Tool: A Narrative Review of the Literature. Front. Surg. 9:878293. doi: 10.3389/fsurg.2022.878293

MATERIALS AND METHODS

We reviewed the English-language literature available on the use of the exoscope as a learning tool, focusing on its involvement in neurosurgical education. Moreover, we used the experience of our center and its use of the three-dimensional (3D) exoscope to guide our review.

The Benefits of the Exoscope as an Alternative to the OM

The key advantages of the 3D exoscope as an intraoperative visualization tool during neurosurgical interventions are enhanced visualization of the operative field and ergonomics. Its use as an educational tool is another promising feature of the 3D exoscope.

Traditionally, the operative microscope (OM) has been the gold standard for most microneurosurgical procedures. Limitations in magnification and positioning (physical limitations deriving from the lens and the system), poor ergonomics, and the limitation of the surgical view of the first surgeon and the assistant are well-established shortcomings of the OM.

In recent years, a flurry of newer generations of 3D exoscope platforms appeared (ORBEYE, VITOM, MODUS V, KINEVO, and AESCULAP Aeos), each of them with different features and pricing (1, 2).

The exoscope is considered to have excellent vision and ergonomics (3). In contrast to the OM where the surgical assistant is put in an uncomfortable posture, limiting their ability to observe and assist the lead surgeon (4), the exoscope allows for a more relaxed position and greater participation of the surgeon assistant. Besides ergonomic benefits, the ability to generate videos and online views with anatomical detail usually available only to operating surgeons and improved educational value and immersion compared to the OM, to the benefit of non-scrubbed personnel are consistently reported to be the strengths of the exoscope over the OM (5–12).

The exoscope furthermore allows for the execution of variation of traditional approaches and could make less frequent approaches more common, such as the retro-sigmoid approach in the supine position, which the exoscope allows to be carried out in an ergonomically comfortable position (13). This could make learning complex procedures more approachable by reducing physical strain on the surgeon.

The exoscope appears to be well-suited to be integrated with the use of intraoperative ultrasound, a technology that has proved useful in settings, such as adult (14) and pediatric (15) brains and spine (16) surgery. Bulky operative microscope heads often need to be removed from the operative field to apply the ultrasound probe to the tissue, while smaller exoscope cameras, which can sit further away from the operative field, allow for use of ultrasound probe without their removal and, indeed, even with picture-in-picture visualization of the ultrasound images on the exoscope screen (7).

Numerous studies have already pointed out the viability of the exoscope as a visualization device in a multitude of neurosurgical settings, including glioblastoma surgery (17), nerve sheath surgery (18), anterior (5) cervical approaches, anterior lumbar approaches (3), pediatric neurosurgery (although the authors report an instance of switching to the OM over illumination concerns, possibly due to the model of exoscope used) (19), skull base procedures (4), transsphenoidal pituitary procedures (9), as well as many other procedures (20–29).

Concerning vascular surgery, while some authors consider the OM to be preferable namely for aneurysm clipping (28), this is not the case for other authors (30–32).

Disadvantages in the Use of the 3D Exoscope

The 3D exoscope has only been recently introduced in neurosurgery as a viable alternative tool to the OM. Like its predecessor the OM, it appears to require extensive training and usage to master as enhanced visualization is not synonymous with ease of use.

However, some authors have expressed reserves about the adoption of the exoscope citing resolution, angled view, and costs among the chief concerns (33).

Various studies point out, in particular, an increase in the average duration of neurosurgical intervention with respect to the same intervention conducted with an OM, although the difference in average duration often proves to be not statistically significant (34). Some authors hypothesize that this difference in operative durations can be explained due to a shallower depth of field and constant need for repositioning and refocusing, at least in experimental settings, which might be variable across different brands of exoscopes (8), while others complain the lack of a mouthpiece (30).

It is intuitive a learning curve exists and the exoscope appears to be rated higher by surgeons who are at least somewhat familiar with it: in a study involving both neurosurgeons and otologic surgeons examining the use of the 3D Robotic Digital Exoscope, the exoscope is rated significantly higher by surgeons more familiar with the device (at least 3 procedures) (10). Of note, this is also the case for overall more experienced surgeons (at least 10 years of surgical experience) (10).

Regarding the steepness of the learning curve, diverging opinions exist in the literature, in which a steep learning curve in microvascular anastomosis with the 3D exoscope has been described which is not as fluid as under OM (35). However, other authors describe relatively short learning curves for exoscope adoption by expert vascular surgeons in an experimental setting with 20–30 reported attempts before proficiency with the exoscope was attained by experienced surgeons (36). Moreover, some authors speculate that extensive experience with endoscopic surgery allows for a quicker learning curve with the exoscope in a variety of settings (3, 19).

The actual duration of training to attain surgical proficiency remains to be more definitely investigated, and it remains a question whether the mastery of the exoscope is simpler or harder to attain than that of the microscope for completely inexperienced trainees.

While the exoscope camera is less bulky than a traditional OM and does not require lining up the eyes of the surgeon and assistant to the eyepieces, a further one or 2 high-resolution monitors, up to 55 inches diagonal, need to be set up in the OR. A complete rethinking of the OR set-up to attain an unobstructed view of the monitors (30) is thus often required and another skill to be acquired by the entire team. On the other hand, neurosurgeons appreciate the use of space afforded by the exoscope more than otologic surgeons, an effect the authors speculate to be due to the bulk of neurosurgical OMs compared to nimbler microscopes used in otologic surgery (37).

Visualization angles for the assistant surgeon have drawn some concern, but this can be significantly reduced by the positioning of the exoscope between the surgeon and the surgical assistant and the screen directly in front of the exoscope (38) or through the use of a second screen matching the assistant's point of view with rotated images, especially in spine surgery (2).

Another dubious drawback of the use of exoscopes, which happens to be the other side of the improved ergonomics, is the uncoupling of the surgeon's line of vision from the surgical approach orientation (39), while some authors consider this to be a problem (33), particularly for more experienced surgeons with more consolidated motor schemes (27) this happens to be the very reason for the improved ergonomics and the possibility to achieve very steep angles of vision (27). In the authors' experience, while being unable to rely on core, shoulder, and neck proprioception to help in surgical orientation is a striking difference to the OM, this is overcome quickly.

The Exoscope as a Potent Tool in Surgical Education

Various studies underline the potency of the exoscope as a surgical learning tool in both simulated and real-life surgical cases.

Since the inception of operating theaters, the importance of watching surgery being performed for trainees has been accepted in the medical community.

It has been reported that one of the main strengths of the exoscope with respect to the standard OM is that it allows all participating staff members present in the operative room to visualize microanatomical details of the surgical field, a level of visualization usually only experienced by the first and second surgeons on operative microscope (5, 10, 25). This tends to be one of the most valued aspects of exoscope use, especially for non-scrubbed-in personnel.

This improved visualization has the potential to revolutionize the way surgical information is conveyed as minute details of the surgical procedure and of the dissection techniques by promoting higher participation of residents, fellows, and as well as scrub nurses (19); this has been apparent since the introduction of the exoscope into the operative setting.

It is furthermore to be noted that the exoscope does not obstruct the view of the lead surgeon's hands, which allows a clear dual perception of the surgical field by the assisting surgeon, and consequently a better orientation on the surgical field. This is particularly true in spinal surgery, which is widely viewed by residents as challenging due to shallow surgical corridors and visualization impediments; in that setting the exoscope solves this issue by allowing high-quality visualization of the operative field and an unobstructed view of the surgeon's hands, instruments, and working angles (25).

However, surgical education is not limited to young neurosurgeons and residents as watching high-resolution surgeries from the first surgeon perspective can prove to be extremely valuable for experienced surgeons as well when it comes to learning about rarer procedures, such as bypass surgery (30).

On the other hand, some authors failed to find a statistically significant difference in self-reported educational usefulness between OM and exoscope. The authors speculate this could be an effect of the highly advanced OM used (Kinevo 900) (40).

Hands-On Training

Mastery of basic skills was shown to be improved regardless of surgical experience in a study involving 20 neurosurgeons training on a 3D printed model simulating both endoscopic and exoscopic intracerebral hematoma (ICH) evacuation. The training program consisted of the aspiration of a gelatin-like substance simulating a hematoma using the exoscope and the endoscope five times. In this simulated setting, surgery duration and weight of hematoma removed were not significantly different between exoscope and endoscope across the groups of neurosurgeons with different degrees of experience (41).

Indeed, in a laboratory training of sutures, when students and residents were trained on both the exoscope and the microscope, the majority of the trainees (6 out of 8) reported higher ease of use with the exoscope. The authors suggest that seeing the results of one's action on the screen resembles the action of playing video games, underlining that one of the users who preferred the microscope reported not playing video games (12). As more digital natives enter the surgical profession, these seem to be a consideration worthy of further investigation.

Concerning hands-on training, the value of exoscope as a teaching tool for residents was underlined also by cadaver dissection studies (42), providing a safe setting for exploring eye-hand coordination on anatomical structures.

The value of exoscope as a tool for young neurosurgical trainees has been explored in a study investigating carrying out the evacuation of an ICH conducted under the supervision of a more experienced surgeon (43). This neurosurgical procedure was selected being the more accessible of neurosurgical intervention requiring the use of magnification. Due to its ergonomics, the exoscope was noted to afford the possibility to perform a four-handed procedure, with the supervisor managing the exoscope to ensure correct placement of the lens to optimize the surgical field of view. This study concluded the feasibility of conducting ICH evacuation by young neurosurgical using the exoscope; comfortable positioning and that shared field of view are definitely advantages favoring the use of the exoscope as a learning surgical tool. Moreover, it seems to us that another added advantage is the possibility for the teaching surgeon to comfortably step in at any time of the procedure to help the resident without needing to operate from an uncomfortable position or to lose time moving around the microscope should a problem requiring the expert surgeon to step in occur, thus possibly increasing the confidence in allowing inexperienced trainees to start carrying out surgical procedures. All of this could incentivize a greater and earlier resident involvement in microneurosurgical procedures without impact on patient safety.

CONCLUSION

Ergonomics and an unobstructed surgical field are the main advantages over the OM. Due to the high-resolution monitors conveying minute anatomical details and unobstructed view of the field and surgeon's hands, high participation levels from residents are expected.

While the exoscope appears to be a promising tool for both neurosurgical practice and neurosurgical education, the overall educational benefits remain to be explored and quantified through future studies, as is the learning curve of the exoscope and the viability of exoscope training independently (i.e., in parallel, or even before) OM training.

Steep adoption costs and the alternative use of the OM might prevent or at least delay widespread adoption of this technology. As of the writing of this article, industry sources for the ORBEYE described fewer than 40 units in use throughout Europe, and the available literature when the first author institution was considered were overwhelmingly from high-income countries.

AUTHOR CONTRIBUTIONS

TC and LR: study conception, literature review, and manuscript drafting and revision. MC, AR, and AH: literature review and manuscript drafting. AT: literature review and manuscript drafting and revision. GC: manuscript revision and scientific oversight. CG: study conception, manuscript revision and study oversight. All authors approved the final version of the manuscript.

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frontiers | Frontiers in Surgery

ORIGINAL RESEARCH
published: 29 April 2022
doi: 10.3389/fsurg.2022.863633

Machine Learning-Based Surgical Planning for Neurosurgery: Artificial Intelligent Approaches to the Cranium

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Objectives: Artificial intelligence (AI) applications in neurosurgery have an increasing momentum as well as the growing number of implementations in the medical literature. In recent years, AI research define a link between neuroscience and AI. It is a connection between knowing and understanding the brain and how to simulate the brain. The machine learning algorithms, as a subset of AI, are able to learn with experiences, perform big data analysis, and fulfill human-like tasks. Intracranial surgical approaches that have been defined, disciplined, and developed in the last century have become more effective with technological developments. We aimed to define individual-safe, intracranial approaches by introducing functional anatomical structures and pathological areas to artificial intelligence.

Methods: Preoperative MR images of patients with deeply located brain tumors were used for planning. Intracranial arteries, veins, and neural tracts are listed and numbered. Voxel values of these selected regions in cranial MR sequences were extracted and labeled. Tumor tissue was segmented as the target. Q-learning algorithm which is a model-free reinforcement learning algorithm was run on labeled voxel values (on optimal paths extracted from the new heuristic-based path planning algorithm), then the algorithm was assigned to list the cortico-tumoral pathways that aim to remove the maximum tumor tissue and in the meantime that functional anatomical tissues will be least affected.

Results: The most suitable cranial entry areas were found with the artificial intelligence algorithm. Cortico-tumoral pathways were revealed using Q-learning from these optimal points.

Conclusions: AI will make a significant contribution to the positive outcomes as its use in both preoperative surgical planning and intraoperative technique equipment assisted neurosurgery, its use increased.

Keywords: approaches, neurosurgery, neurosurgical planning, machine learning, cranial approaches, artificial intelligence (AI), brain tumor

Edited by:
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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: *27 January 2022*
Accepted: *28 March 2022*
Published: *29 April 2022*

Citation:
Dundar TT, Yurtsever I, Pehlivanoglu MK, Yildiz U, Eker A, Demir MA, Mutluer AS, Tektaş R, Kazan MS, Kitis S, Gokoglu A, Dogan I and Duru N (2022) Machine Learning-Based Surgical Planning for Neurosurgery: Artificial Intelligent Approaches to the Cranium. Front. Surg. 9:863633. doi: 10.3389/fsurg.2022.863633

INTRODUCTION

The gold standard surgical strategy for the majority of intra-axial tumors is maximum tumor resection with minimal loss of neurological function (1). The tumoral mass effect on the brain tissue was eliminated while reaching the histological diagnosis with surgical resection. Aggressive surgery also increases radiotherapy and chemotherapy effectiveness in patients who require them by reducing the tumor burden. Subcutaneous tissue incision, craniotomy size, and dura are standardized. However, surgical access to intraparenchymal tumors may vary according to the surgeon's experience and dexterity, technical possibilities, tumor location, and size. Arachnoid dissection, sulcal, and gyral dissection are generally used in direct transcortical approaches while reaching the tumoral tissue. Identification and preservation of anatomical land marks such as fiber tracts, arterial and venous vessels, and basal ganglia are the basis of the surgical strategy for preserving brain functions [(1–3)].

The developments in neuroanatomy, neurophysiology, and pathology, which started with the use of anesthesia and antisepsis in the early 1900s and continued with the use of radiography and new operating instruments, have developed modern neurosurgery (1). Today, a safe postoperative clinical outcome is provided by the analysis of preoperative imaging modalities, the evaluation of data obtained from intraoperative neurophysiological monitoring or imaging modalities (e.g., USG or MRI), and also postoperative ICP, EEG, and biochemical examinations (4, 5). Decision-making mechanisms for the approach to be used for brain tumors of different localizations and sizes are based on clinical guidelines, analyses, and statistics of previous cases.

Artificial intelligence (AI) has risen to prominence in the medical literature in recent years, and its usage is expanding beyond diagnosis to treatment on a daily basis. AI is the name given to machine systems, particularly computer systems, that can replicate human brain cognitive abilities such as learning, reasoning, and self-correction. In the simplest terms AI refers to systems or robots that resemble human intelligence to execute tasks and can improve themselves iteratively based on the data they collect. AI is working just like a simulation of the human brain intelligence and the goal of AI inspired by brain science is to develop systems that have features such as decision-making, lifelong learning, learning by association, long and short-term memory, recognition, classification of learned abilities, and interacting with the environment. In general, AI systems function by processing huge amounts of data, producing correlations and patterns, and using these outcomes to make predictions for future situations. In addition, AI has abilities such as creating and transferring knowledge and self-learning (6–8). Machine learning focuses on how to construct intelligent computer programs (or computational models) that automatically learn and understand the massive amounts of data and turn it into knowledge and action with experience (9).

There are two basic approaches based on the availability of labels in machine learning: supervised learning (labeled data) and unsupervised learning (unlabeled data). In supervised learning algorithms, the model tries to learn the relationship between the desired output and the input features (6). It can be used in daily practice for risk prediction (10) and reveals the effect of clinical prognosis by evaluating different factors (demographic or social changes) on treatment (6).

Unsupervised learning algorithms are mainly used to identify and investigate the unknown patternsin the input data. The model mines for rules, identify patterns, and summarizes meaningful findings (6, 7). On the other hand, unsupervised learning does not require prior knowledge of the output values and the data are unlabeled. When compared to supervised learning algorithms, these algorithms ensure more complex processing tasks. It can be used for diagnostics, patient selection, identifying symptom clusters associated with specific diseases, selecting optimal treatment strategies based on demographic or genetic features, pattern identification or recognition in radiological or photographic images, and other data in daily practice (6, 8).

Reinforcement learning is an interactive machine learning system (or framework) that detects how an AI agent takes action and interacts with the environment to make some sequence of decisions (6, 8, 9). It aims to achieve maximum reward from the rightful actions of the AI agent. AI agent takes action for reaching the goal by maximizing the total reward, and the RL model keeps continues to learn until finding the best solution. When the AI agent acts, it rewards the system for the correct output and punishes it for the incorrect output. RL can be used as a control algorithm to optimize the use of scarce resources in specific situations, such as the selection of patients to be discharged based on clinical logistics requirements and surgical aids or robots.

The classical neurosurgical techniques that reduce patient discomfort and the risk of neurological morbidity, provide shorter hospital stays, and the use of technological developments that support these techniques have been at the center of neurosurgery for decades (11–13). The cranial neurosurgical approaches and their modifications have been standardized for about the last 150 years (1, 11). This study aims to define a machine-learning algorithm to estimate optimal surgical pathways. By using a reinforcement learning approach to solve the path planning problem, the suggested method saves computational time by skipping unrelated cranial areas that were present in screenings while also boosting planned trajectory accuracy.

Q-learning is the most known and frequently used RL algorithm. In Q-learning, agent and environment are two important variables. The agent is an algorithm that takes actions based on the environment. The environment is the system in which the agent makes decisions and learns from its actions. The agent learns by interacting with its environment as a human would. The achievement of the agent's set goal is defined as the reward. Areas that should not go or touch are defined as penalty areas. Actions are defined as such activities performed by the agent. The reward is a measure of the success or failure of the agent. It follows by creating a reward table (14, 15). The agent begins searching for the target at random locations throughout the defined environment, analyzes its future steps, and records its successes and failures. This is the case until the agent discovers the first reward. As soon as the agent gets to a target location, it recalls its position before arriving at the target and records this value in the Q-Table where it has accumulated its own experiences (15–17). The agent develops policy, which is a decision-making strategy.

This article proposes a new heuristic-based surgical path planning algorithm for neurosurgery. The new heuristic estimates accurate optimal surgical paths avoiding critical structures in the brain. It computes the proper entry points on the scalp and then searches for different paths that reach the beginning location of the tumor and finds the optimal linear surgical paths. Then the extracted optimal linear paths from the new heuristic are used as an entry point or an environment [depending on the path width (dimension)] of the Q-learning algorithm for finding nonlinear access paths. Especially while finding nonlinear trajectories, usage of the new proposed heuristic's output can save computational time by skipping unrelated cranial areas that were present in screenings while also boosting planned trajectory accuracy. Moreover, the extracted nonlinear trajectories can

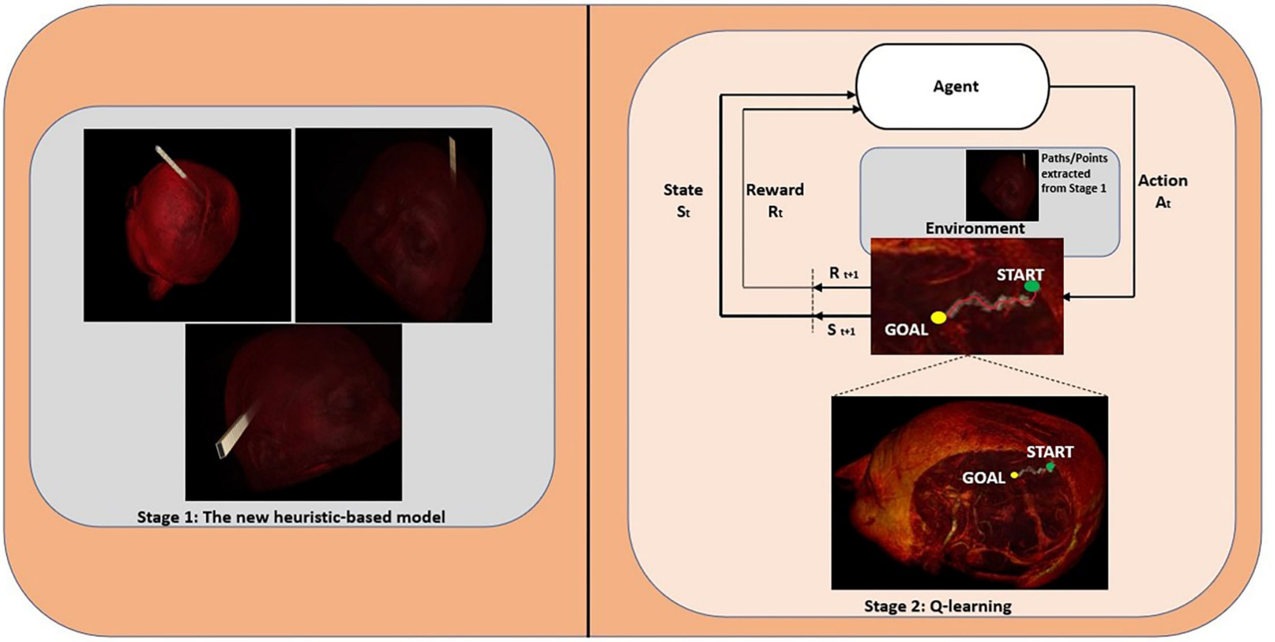

FIGURE 1 | The proposed system architecture for finding linear and nonlinear access paths for neurosurgery.

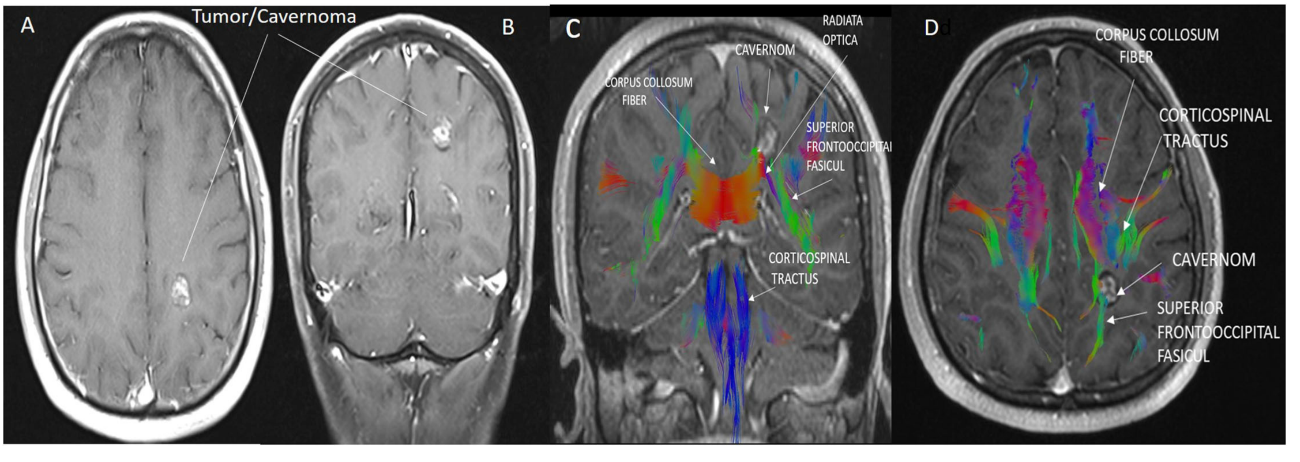

FIGURE 2 | (A,B) Cavernoma appearance on axial **(A)** and coronal **(B)** contrast-enhanced T1 cranial MRI images. **(C,D)** The anatomical relationship of the corticospinal tract, superior fronto occipital fasciculus, and corpus callosum transverse fibers with the cavernoma is shown in sagittal and axial MRI tractography images. Due to the mass effect of the cavernoma, displacement of the superior fronto occipital fasciculus was observed.

improve clinical outcomes because they ensure minimally invasive approaches.

METHODS

The study involved a retrospective MRI analysis with no risk to the patients. This study was approved by the Institutional Clinical Non-Interventional Research Ethics Board (E-54022451-050.05.04-41353). These authors reviewed the cases together and reached a consensus in any disputed case. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. For this type of study, formal consent was not required.

Radiologic Imaging

MRI Technique and MR Tractography

MRI was performed with a 1.5-T system (Magnetom Avanto; Siemens, Erlangen, Germany). First, routine brain MRI protocol included T1-weighted (T1W; TR/TE = 460/14 ms) and T2-weighted (T2W; TR/TE = 2,500/80 ms) sequences in the axial and coronal planes, and fluid-attenuated inversion recovery (FLAIR) images (TR/TE = 8,000/90 ms) in the axial plane with 5-mm-thick sections. The DTI protocol consisted of a single-shot, spin-echo, echo-planar sequence with the fat suppression technique: TR/TE = 2,700/89 ms; matrix, 128 × 128; field of view, 230 mm; and slice thickness, 5 mm. DTI was acquired before the administration of contrast media and 30 diffusion-encoding directions were used at b = 1,000 s/mm^2. After that, T1W 3D magnetization-prepared rapid gradient echo (TR/TE/TI = 12.5/5/450 ms) volumetric sequences with and without contrast medium (gadolinium-diethylenetriamine pentaacetic acid, 0.1 mmol/kg body weight, intravenously) was applied. The Syngo.*via* console (software version VB30A_HF06; Siemens) was used for the postprocessing of DTI data sets, after which the ADC and color-coded FA maps were reconstructed. Sending 30-way DTI images (30 diffusion-encoding directions) to Syngo.*via* console and performing tractography with MR Neuro 3D function. The DTI data sets and 3D MR images were analyzed using freeware for diffusion tensor analysis and fiber tracking (Syngo.*via* console). To depict the motor tracts, the seed area was placed on the cerebral peduncle where the corticospinal tract (CST) is known to run while observing the color-encoded fiber orientation map. Cortical target regions were carefully placed in the suspected primary motor area. We used the two-regions-of-interest method (i.e., seed and target regions) to demonstrate on—well the descending fibers from the primary motor area to the cerebral peduncle.

In MR tractography, the blue coding shows the corticospinal tract with a top-down (craniocaudal) course, the red coding for the transverse course in the corpus callosum and subcortical areas, and the green coding for the anteroposterior front-occipital tracts.

Algorithms

By using all the new heuristic and Q-learning algorithms together, we extract not only linear but also nonlinear access paths. Our model works in two stages, in the first stage the new heuristic is used to find linear paths and in the second stage the Q-learning algorithm is used to find nonlinear paths. We also handle different path dimensions (i.e., each cell contains *nxn* points) such as 16 × 16, 32 × 32, 40 × 40, and 64 × 64 to prove the accuracy of our method. Especially for 16 × 16 and 32 × 32 dimensions, the pathways are so narrow, whence the entry points of these paths are taken as reference entry points for the Q-learning algorithm. For larger dimensions, the extracted paths are used as an environment of the Q-learning algorithm, and then the AI agent takes action and finds the best possible nonlinear

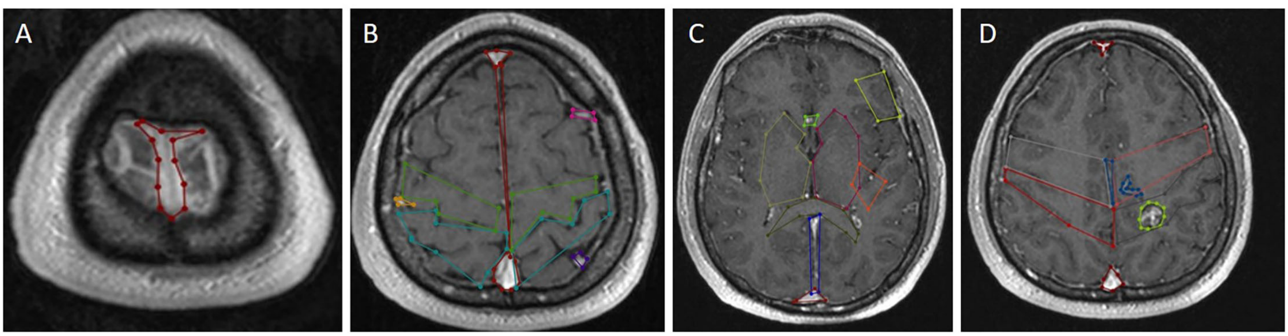

FIGURE 3 | Labeling using contrast-enhanced T1 axial image of cranial MRI. **(A)** Superior sagittal sinus marked in red at the vertex's midline. **(B)** Superior sagittal sinus marked with red in the midline in the supraventricular area, precentral gyrus marked with green, postcentral gyrus marked with turquoise, superficial cortical veins marked with pink on the left and dark yellow on the right adjacent to the bilateral frontal lobes. **(C)** Right basal ganglia and thalamus marked with yellow in the right cerebral hemisphere at the ventricular level; left basal ganglia and thalamus marked with light red in the left cerebral hemisphere at the ventricular level, Broca's area in the left frontal lobe with light yellow, Wernicke's area posterior to Sylvian fissure marked with orange; The anterior cerebral arteries are marked in light green anteriorly in the midline, the corpus callosum splenium in green and the sinus rectus in blue in the midline posteriorly. **(D)** Right postcentral gyrus marked red, cavernom/tumor marked yellow-green, pericallosal artery marked blue on the midline and posterior inferior frontal artery marked blue.

surgical access paths. **Figure 1** illustrates the proposed system architecture for finding linear and nonlinear access paths for neurosurgery.

In the first stage (Stage 1), the proposed heuristic-based algorithm, first, the three dimensions (x, y, z) of given MRI images in DICOM format are extracted. The first two dimensions denote the matrix rows and matrix columns in pixels, respectively and the third dimension denotes the number of axial T1-weighted MR images of the patient with brain tumors. After that, all the surfaces (top, bottom, right-side, left-side, front, and back) of the axial T1-weighted MR images are divided into cells (e.g., each cell contains 16×16 points), and then it is calculated how many cells can take place in these DICOM files. For each dimension of the given MR images, different processes are utilized to calculate all points over each cell, i.e., the x-axis, y-axis, and z-axis do not change for the top and bottom surfaces, the left-side, and right-side surfaces, and front and back surfaces, respectively. The number of total cells gives all the possible starting entry points. Later, the proposed algorithm searches for all paths that reach the beginning location of the tumor (the coordinate points for the tumor and eloquent areas are labeled with Labelme [(18); https://github.com/wkentaro/labelme] which is an image annotation tool) (**Algorithm 1** in **Supplementary Material**), and then the coordinate points in each path are extracted (**Algorithm 3** in **Supplementary Material**). Because of the huge search space and the computation time cost, while calculating the optimum paths the number of all the possible starting entry points has been reduced in four stages. In every stage, the coordinate points over the calculated paths are compared with the labeled critical structures one by one, if these points intersect with these structures the penalty score of the related path is increased. At the end of the comparison, all penalty scores are sorted in ascending order. Finally, at the end of the fourth stage, the top 20 (this number of paths is optional and can be changed) paths are extracted (**Algorithm 5** in **Supplementary Material**).

The new heuristic-based surgical path planning algorithm finds the best optimal n-paths which include all the path points (coordinates), then these paths are used in the second stage (Stage 2–Q-learning algorithm) for finding nonlinear paths. The Q-learning algorithm seeks to find the best action in the given current state. The Q-table is utilized to select the best action based on the q-value, and after each episode, it is updated with the new q-values. While updating q-values, they are adjusted based on the difference between the new q-value and old q-value by using "learning rate" and "discount factor" parameters. The learning rate is defined as the weight of how much we consider the new value, and the gamma is a discount factor and balances the immediate and future reward. With the "np.max" function, the maximum of the future reward is taken, and this value is applied to the reward for the current state (Eq. 1).

NewQ[state, action] = Q[state, action] + learning rate * (reward + gamma * np.max(Q[new_state,:]) — Q[state, action]) (Eq.1)

The agent interacts with the environment (is extracted in **Algorithm 6** in **Supplementary Material**) in two ways exploiting (selecting action with the highest value by referencing the Q-table) and exploring (random action selection). Before starting the Q-learning algorithm, all the points (coordinates) on the paths are classified by using the corresponding labeled structures. Thus, the points of all structures belonging to the same class (label value) in different layers are gathered under an array. All the points are considered as a node, and then the reward and penalty scores are assigned to nodes in each class by considering the penalty score of the critical structures, and "1" penalty score is assigned to all

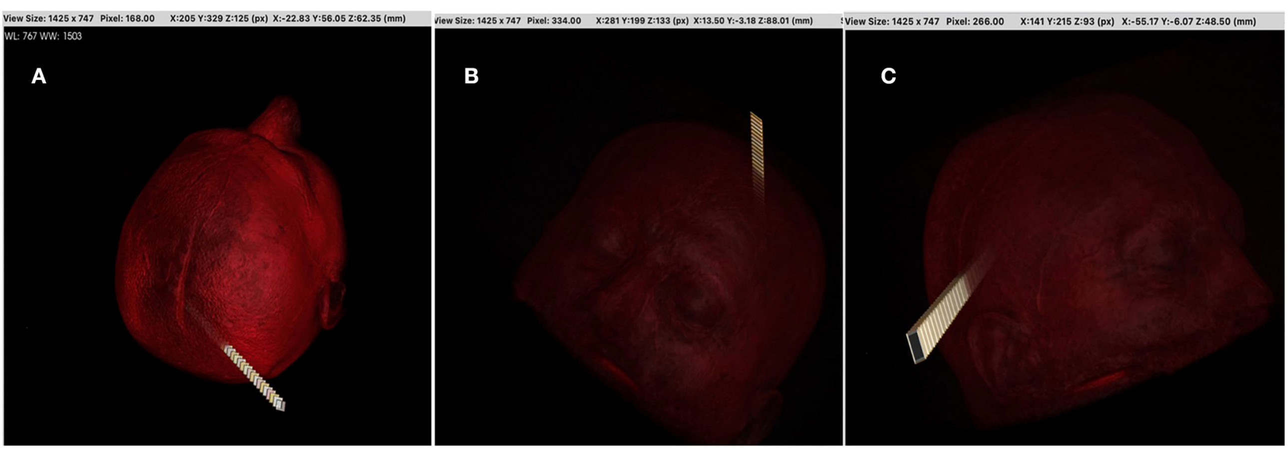

FIGURE 4 | The research algorithm was created for time efficiency compared with the time-consuming RL algorithm. The goal is to find the most ideal cranial entry points. Machine learning was not used in this method. Cranial entry points were scored using the equivalent areas and tumor location in **Table 1** and compared with each other. With this algorithm, it was possible to sort by five most ideal entry points, 10 entry points, or worst entry points. In addition, this algorithm provided a linear access path to tumor tissue in the shape of a rectangular prism or cylinder. The entrance area in the images was determined as 1.5 cm^2. The algorithm has been adjusted to allow this area to be increased or decreased. This algorithm can be useful in tubular operative systems or rigid endoscopic systems. In this study, we took these points (the most ideal 4,900 points) as the starting points of RL. Image **(A,B)** are the ideal best rated and image **(C)** the worst-rated sample entry points.

TABLE 1 | Some major surgical landmarks and their functions for transcortical approaches.

Approach		
Frontal	Gyrus Rectus, Distal AntComA	
	Caudate nucleus	Bottom up attention (goal directed), memory, learning, sleep, emotion, language
	Fornix	Memory
	Inferior Frontal Gyrus (pars opercularisandriangularis)	Langage (lf), theory of mind (bilat), visuospatial cognition (rt)
	Anterior perforate substance Optic tract Precentral gyrus Broadman 44	Corticospinal tract vascular supply
Temporal	Crus cerebri, pca, uncus	
	Lateral sulcus	
	Optic radiation Hippocampus	Optic pathwayMemory pathway
	Visual word form area	Identifying words
	Arcuate fasciculus	Language (lt), visuospatial cognition (rt)
	IFOF cuneus	Language (lt), visuospatial (rt)
Parietal superior	Superior anastomotic vein (trolard)	
	Postcentral gyrus	Sensitive patnway
	Parietal operculum	Sensitive pathway
	Heschl's gyrus	Connection speech
	Superior longitudinal fasciculus III	Language (lt), visuospatial (rt)
	Arcuate fasciculus Language	Language (lt), visuospatial (rt)
Insula	Periinsular sulcus	
	Lenticular nucleus	
	Arcuate fasciculus (lat to claustrum)	Language (lf), visuospatial (rt)
	IFOF (btw claustrum and putamen)	Language (lf), visuospatial (rt)
Veins	Vein of Labbé (inferior anastomotic vein)	Temporoparietal drainage
	Basal vein of Rosenthal	
	Superficial sylvian vein	
	Superior sagittal sinus and another main sinuses	main venous drainage
Arteries	ICA and main branches	
	Basiler arter and main branches	

TABLE 2 | Gives the details in the intermediate steps of the proposed heuristic for the case study.

	Cell Dimension			
	16 × 16	**32 × 32**	**40 × 40**	**64 × 64**
The number of all possible paths	745,984	675,840	641,920	544,768
The *n*-optimal paths in the "SECOND_PATHS_INDEX" sequence	80	80	80	80
The number of checked points in "SECOND_PATHS_INDEX" sequence	46,727,360	83,222,240	112,560,000	76,212,160
The *m*-optimal paths in the "THIRD_PATHS_INDEX" sequence	40	40	40	40
The number of checked points in "THIRD _PATHS_INDEX" sequence	58,339,960	146,084,080	137,648,480	85,084,960
The *l*-optimal paths in the "FOURTH_PATHS_INDEX" sequence	20	20	20	20

Number of MRI slice.

other nodes where the agent can interact in. Each node has a neighboring node. If a node is not on the edge or corner, it has eight neighboring nodes (right, left, up, down, bottom-right, bottom-left, top-right, and top-left) over the same layer. The same node has 18 different neighboring nodes over the one upper layer (9 neighboring nodes) and one lower layer (9 neighboring nodes) (**Figure 5**). The penalty scores of all these 27 different nodes are assigned by considering the penalty score of each class. Then Q-learning algorithm is executed over these nodes to find the best possible nonlinear surgical access paths (**Algorithm 7** in **Supplementary Material**).

Experimental Results

To find the best possible linear and nonlinear surgical paths, the proposed new heuristic and Q-learning algorithms were executed, respectively. As a case study, we used (512 × 512 × 144) axial T1-weighted MRI images of one patient with a brain tumor in DICOM format, then 16 × 16, 32 × 32, 40 × 40, and 64 × 64 path dimensions were evaluated for the new heuristic algorithm. These dimensions correspond to the cell parameter (*n* is equal to 16, 32, 40, and 64, respectively in each case) given in **Algorithm 5** in **Supplementary Material**. For each case, we extracted 20 optimal linear paths, and the extracted linear paths for 16 × 16 and 32 × 32 dimensions were so narrow for executing the Q-learning algorithm. So, we used the entry points of these paths as reference starting (entry) points of the second stage. For the 40 × 40 and 64 × 64 dimensions, each 20 extracted linear path composed the environment of Stage 2. While finding linear paths, the heuristic checked millions of coordinate points. All steps given in **Algorithm 5** in **Supplementary Material** were applied one by one to 16, 32, 40, and 64 cell dimensions. We picked 80, 40, and 20 optimal paths for the second, third, and fourth path index sequences, respectively. The findings in the intermediate steps are given in **Table 2**. The first column in the table gives information about the intermediate steps in **Algorithm 5** in **Supplementary Material**: the number of all possible paths, the number of checked points in the sequence, and the chosen parameters to indicate the number of optimal paths. The second column in the table gives more details for each cell dimension (**Table 2**).

While the total of 40 linear paths extracted from the 16 × 16 and 32 × 32 dimensions was used as reference starting points in Stage 2, the total of 40 linear paths extracted from the 40 × 40 and 64 × 64 dimensions was also used as an environment. Then the extracted nonlinear paths were observed by neurosurgeons. The best path was obtained from the 16 × 16 dimension and are given in **Figure 4**.

DISCUSSION

In this study, we proposed new system architecture which includes two stages to find linear and nonlinear access paths for neurosurgery. In the first stage of the model, linear paths were found, then these paths/or entry points were utilized for finding nonlinear paths in the second stage. We proposed a new heuristic-based surgical path planning algorithm for finding linear paths. Moreover, the Q-learning algorithm was used to find the nonlinear access paths by using the extracted linear paths from the new heuristic. We performed a Q-learning algorithm over cranial MRI scans to learn which steps ensure reaching the beginning location of the tumor with maximum rewards. Touching the critical structures is assigned as a penalty while reaching the tumor tissue is defined as a reward. As an environment, the entire head is taken into account, so the possibility of nontraditional surgical methods was not ignored (different access routes that may be suitable for open face or endoscopic procedures). Some neural fiber routes, arteries, veins, and dural sinuses have been identified as structures that should be avoided (**Table 2**). The algorithm aims to reach the tumor while avoiding these critical locations (evaluated as penalty scores), and uses Q-Table helps to find the best action for each state in the brain. The state that expresses the current status (position) of the AI agent in the environment is the *x*, *y*, *z* coordinated location in cranial MRI (14–17).

The borders of the preoperative brain tumor lesion (reward) were determined as the contrast-enhancing area in T1 contrast MRI imaging (19). Tracts with diffusion tensor imaging (DTI), arterial anatomy with contrast-enhanced MRI angiography (CE-MRA), and those with tumor tissue (20) superficial cortical vessels and dural sinuses are used in surgical planning with MRI venography (21) (**Figure 2**). DICOM images in the respective sequences were imported into the labeling program (labelme 4.6.0, https://github.com/wkentaro/labelme). Functional anatomical areas were marked and labeled by the radiology and neurosurgeon specialist (**Figure 3**). The pixel and voxel values of the anatomical point and the anatomical structure of the point were listed by labeling (22, 23). This gave us the advantage of trading in a cubic system with matrixes.

We used (512 × 512 × 144) axial T1-weighted MRI images of one patient with a brain tumor in DICOM format as a case study. We utilized 16 × 16, 32 × 32, 40 × 40, and 64 × 64 path dimensions to evaluate the success of the proposed system architecture. In the first stage, 20 optimal linear paths were extracted for each dimension by using the new heuristic-based algorithm. The optimal nonlinear path was extracted by using the starting points found in the 16 × 16 path dimension. For the 16 × 16 path dimension, the proposed heuristic found 745,984 possible entry points. The areas in **Table 2** and the target tumor tissue were accepted as reference points. This algorithm gave input fields of desired diameter and size. These 745,984 linear paths were compared according to the reward and penalty points. By using the intermediate steps, the 20-optimal linear paths were chosen. Then the starting points of these paths were used as reference entry points of the Q-learning algorithm (**Figure 4**) in the second stage. Then, a matrix size of 78,030 × 78,030 was created and worked on 50 × 25 × 78,030 points for Q-learning. Extracranial areas were excluded. It was enough to find 500,000 epoch paths in a 16 × 16 × 35 environment, and it almost took 70 min. The Q-learning algorithm returns as the best way "node" (**Figure 5**). Then, the positions of these node values in the matrix were found and the *x*, *y*, and *z* coordinate values were reached. Thus, the coordinates representing the best path were extracted from the DICOM images. The most ideal transcortical tumoral pathway was revealed in **Figure 6**.

On the other hand, all the paths have been shown in DICOM format, thus the usage of MR images in DICOM format has provided data protection while also allowing us to use it in postprocessing systems (OsiriX MD v12.5.0–SNRTech Workstation). One of the achievements of this study is that all the extracted linear and nonlinear paths in DICOM format can be seen in any neuronavigation software. The neuronavigation device utilized in the operating room has been evaluated for availability, but the proposed system is not yet used on a patient during surgery (neuronavigation system). Following the requisite assessment and approval, future work would be used as an intraoperative guide.

The number of studies on artificial intelligence and neurosurgery has risen considerably in recent years (24, 25). In this article, the proposed artificial intelligence-based system architecture was utilized to find the most optimal surgical paths for preoperative patient images that were labeled on the 3-dimensional coordinate plane with cranial MRI voxel values. The results (linear and nonlinear paths) obtained with this basic system architecture (framework) can be used with intraoperative neuronavigation as well as road maps in tubular, endoscopic, robotic, and augmented reality.

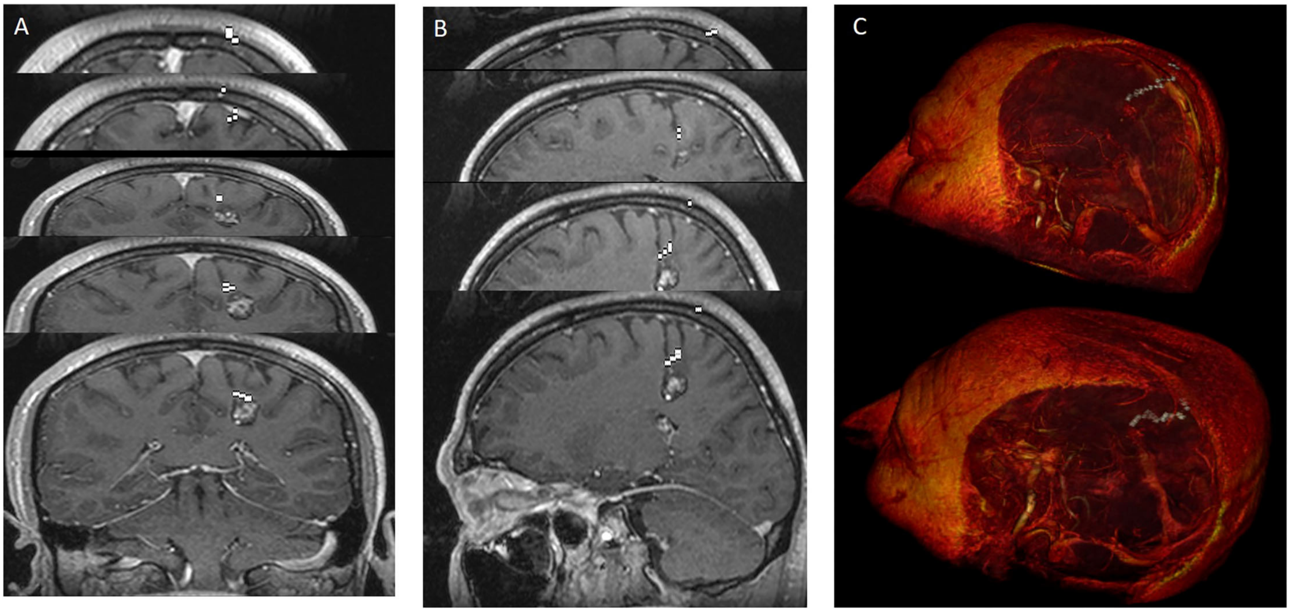

FIGURE 5 | The most ideal cortico-tumoral approach is recommended by RL. Images were added one after another to show the nonlinear pathway. RL extracted the most optimal pathway by performing a random-onset point analysis of the entire intracranial area. Demonstration of the approach reaching the tumor from the base of the postcentral sulcus**. (A)** howing the pathway in coronal sections. **(B)** Showing the pathway in sagittal sections. **(C)** Showing the 3-dimensional pathway with image processing.

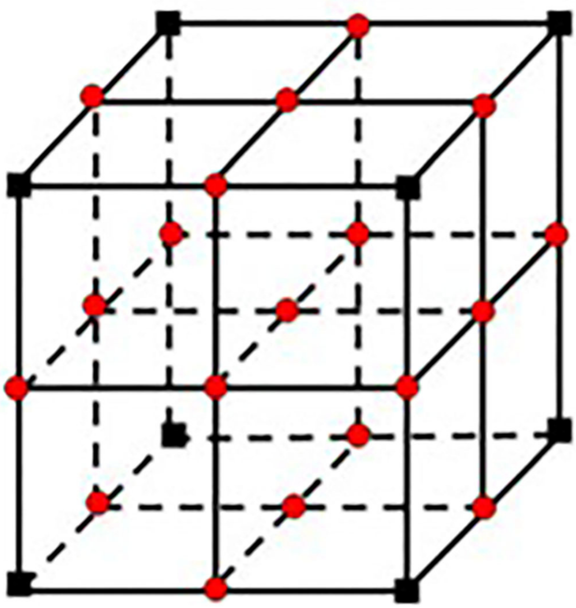

FIGURE 6 | The figure illustrates the proposed system architecture for finding linear and nonlinear access paths for brain surgery.

The mathematical equation of any case provides the advantage of measure and control tools to use in. Many current technical types of equipment and treatment algorithms have evolved through the mathematical equations defined in the past centuries. Introducing Preoperative neuroanatomical points and functions as data to artificial intelligence will highlight patient-specific surgical approaches. The near future will be based on artificial intelligence, which will employ an excessive amount of data, and the relationship between these data will allow surgery to be performed with greater accuracy.

Perioperative monitoring and use of cranial anatomy and functions contribute to a positive outcome. In future work, new methods based on artificial intelligence would be used to analyze data for each stage of neurosurgical interventions, and these initiatives would be maximized. Simultaneously, that will allow patients to benefit from the experience of an unlimited number of clinics and surgeons in personal treatment planning.

Limitation of Study

The first limitation is the manual segmentation of anatomical points. This took a lot of time for both the surgeon and the radiologist. Points were marked in 144 axial images. The second limitation was that we could not create fusion MRI images. We aimed to make a single fusion MRI sequence of T1 contrast axial, DTI, TOF, and venography sequences and use it. However, we could not use the fusion images we obtained as DICOM data. Fusion sequence MRI would enable us to use anatomical accuracy at a single point level. This caused the third limitation of the study, the necessity of specifying four points in the labeling. It made the processing points coarser and larger. Our fourth limitation is the total processing time. We think that when the first three limitations are resolved and the computer processor speeds increase, the processing time will be shortened.

To reduce the computational cost, we did not handle all of the linear paths extracted from the heuristic, and we eliminated most of these paths. In our experiments, we have used a 10-core CPU with eight performance cores and two efficiency cores, 16-core GPU, 16-core Neural Engine, 200 GB/s memory bandwidth, and OS X. We think that by using the more powerful computers all these linear paths can be used and then the found all possible linear paths can be used reference points/environments based on the cell dimension for Stage 2. We also gave a case study to observe the achievement of our system. We used (512 × 512 × 144) axial T1-weighted MRI images of one patient with a brain tumor in DICOM format, then 16 × 16, 32 × 32, 40 × 40, and 64 × 64 path dimensions were evaluated for the new system. The best optimal nonlinear surgical path was found from the 16 × 16 dimension. There are some studies (Liedlgruber et al.) (26) in the literature that use automatic segmentation, but vascular structures are not taken into consideration in these segmentations. Tomasi et al. (27) combined the cerebral cortex anatomy and vascular structures in their studies. In future work, we plan to use automatic segmentation by taking into consideration vascular structures in the brain.

RESULTS

In this article, a new system architecture based on a two-stage is proposed to find linear and nonlinear access paths for neurosurgery. In the first stage, the proposed new heuristic estimates accurate optimal surgical paths avoiding critical structures in the brain. It computes the proper entry points on the scalp and then searches for different paths that reach the beginning location of the tumor and finds the optimal linear surgical paths. In Stage 2, the extracted optimal linear paths from the new heuristic are used as an entry point or an environment for the Q-learning algorithm to find nonlinear optimal paths. Artificial intelligence has the potential to reduce medical errors while also reducing healthcare costs. It will be based on artificial intelligence in the near future, where big data will be used, the relationship between these algorithms and neuroanatomical functions are determined more precisely and neurosurgery can be performed with them.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Materials**, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

This study was approved by the Institutional Cinical Non-Interventional Research Ethics Board (E-54022451-050.05.04-41353). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. For this type of study, formal consent was not required.

AUTHOR CONTRIBUTIONS

TD and ND conceived and designed the analysis. TD, MP, and AM wrote the article. SK, ID, AG, TD, and UY performed the analysis. TD, MD, MK, RT, and ND collected the data. AE, UY, MK, RT, MD, and ND created the algorithms. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2022.863633/full#supplementary-material

Algorithm 1. Algorithm 1 gives the pseudocode for finding the number of all paths that reach the beginning location of the tumor (defined as goalPoint). The given MR images handle as a square prism, then all possible paths have been calculated by using the cell dimensions for six surfaces of the prism.

Algorithms 2 and 3. Algorithm 3 gives the pseudocode for finding all the coordinate points inside each path. The input of Algorithm 3 is the output sequence of Algorithm 1. The algorithm also uses Algorithm 2 which finds the area of the selected part.

Algorithms 4 and 5. Algorithm 5 defines the steps of our new heuristic and gives the pseudocode for finding the optimal n-paths. It also uses the given other algorithms. The output of the heuristic is the n-paths with minimum penalty scores which have been calculated by using Algorithm 4.

Algorithms 6 and 7. Algorithm 6 gives the steps of how optimal linear paths (extracted from Algorithm 5) are converted to an environment. Algorithm 7 (simply Q-learning algorithm) gives the steps of finding the best optimal paths by interacting with the found environment (Algorithm 6).

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
published: 06 May 2022
doi: 10.3389/fsurg.2022.916228

Efficacy of a Mindfulness-Based Intervention in Ameliorating Inattentional Blindness Amongst Young Neurosurgeons: A Prospective, Controlled Pilot Study

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OPEN ACCESS

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Speciality section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: 08 April 2022
Accepted: 22 April 2022
Published: 06 May 2022

Citation:
Pandit AS, de Gouveia M, Horsfall HL, Reka A and Marcus HJ (2022) Efficacy of a Mindfulness-Based Intervention in Ameliorating Inattentional Blindness Amongst Young Neurosurgeons: A Prospective, Controlled Pilot Study. Front. Surg. 9:916228. doi: 10.3389/fsurg.2022.916228

Background: Human factors are increasingly being recognised as vital components of safe surgical care. One such human cognitive factor: inattention blindness (IB), describes the inability to perceive objects despite being visible, typically when one's attention is focused on another task. This may contribute toward operative 'never-events' such as retained foreign objects and wrong-site surgery.

Methods: An 8-week, mindfulness-based intervention (MBI) programme, adapted for surgeons, was delivered virtually. Neurosurgical trainees and recent staff-appointees who completed the MBI were compared against a control group, matched in age, sex and grade. Attention and IB were tested using two operative videos. In each, participants were first instructed to focus on a specific part of the procedure and assessed (attention), then questioned on a separate but easily visible aspect within the operative field (inattention). If a participant were 'inattentionally blind' they would miss significant events occurring outside of their main focus. Median absolute error (MAE) scores were calculated for both attention and inattention. A generalised linear model was fitted for each, to determine the independent effect of mindfulness intervention on MAE.

Results: Thirteen neurosurgeons completed the mindfulness training (age, 30 years [range 27–35]; female:male, 5:8), compared to 15 neurosurgeons in the control group (age, 30 years [27–42]; female:male, 6:9). There were no significant demographic differences between groups. MBI participants demonstrated no significant differences on attention tasks as compared to controls ($t = -1.50$, $p = 0.14$). For inattention tasks, neurosurgeons who completed the MBI had significantly less errors ($t = -2.47$, $p = 0.02$), after adjusting for participant level and video differences versus controls. We found that both groups significantly improved their inattention error rate between videos ($t = -11.37$, $p < 0.0001$). In spite of this, MBI participants still significantly outperformed controls in inattention MAE in the second video following post-hoc analysis (MWU = 137.5, $p = 0.05$).

Discussion: Neurosurgeons who underwent an eight-week MBI had significantly reduced inattention blindness errors as compared to controls, suggesting mindfulness as a potential tool to increase vigilance and prevent operative mistakes. Our findings cautiously support further mindfulness evaluation and the implementation of these techniques within the neurosurgical training curriculum.

Keywords: inattention blindness, cognitive load, safety, surgical training, education, cognitive bias

INTRODUCTION

Patient safety has been at the centre of healthcare for millennia, summarised by Hippocrates' (470–360 BC) as "first, do no harm". This remains a fundamental mantra for modern medicine. Errors in neurosurgery, compared with other surgical settings, can be particularly catastrophic and can result in significant events for the patient, surgeon, and institution (1, 2). Much work has focused on improving patient safety across all surgical specialities, and international initiatives like the WHO Surgical Safety Checklist, have driven a paradigm shift in protocol and culture. Despite this increased awareness of safety, errors continue to routinely occur in surgical care (3). This heralds a systems-approach to surgical safety and the need to consider human factors in the delivery of surgical services.

One example of a human factor in surgery is inattention blindness (IB) – the inability to perceive objects that are visible, when one's attention is focused on another task (4, 5). Failure to recognise and act upon events during surgery can lead to serious clinical incidents, including so-called "never-events", such as retained foreign objects and wrong site surgery (3). These preventable incidents can lead to significant, patient harm, particularly in neurosurgery (2) and often have no relation to other features of safety (6). Contributing to inattention blindness is the difficulty in sustaining a vigilant state for long periods of time, which itself is highly cognitively demanding (7).

Mindfulness is the capacity to monitor sensory and perceptual stimuli and experiences, moment-by-moment in a non-judgmental manner (8). By packaging this construct within a group-based intervention, it has been successfully implemented for patients (9) and has since been trialled as a technique that can reduce burnout among residents, in particular, surgeons (10, 11). Even brief formats of this intervention have recently been shown to improve performance-related factors among surgeons and peri-operative staff in the operating theatre (12). It is likely, at least in part, that the benefits associated with mindfulness in functional performance are linked to improvements in attention, emotional regulation and decision-making which the technique specifically entrains (13). Further, it is postulated that directed mindfulness training can foster greater attention to, and awareness toward ongoing sensory and perceptual stimuli and experiences (13). Indeed, the situational alertness established as a result of mindfulness training may aid in ameliorating inattention blindness.

To that end, we aimed to determine if a mindfulness-based intervention (MBI) reduced inattention blindness among young neurosurgeons, namely, those in training or who had recently been appointed as staff. That this particular group tend to incur more operative complications (14), adopt differing learning mindsets (15) and use different training resources (16) as compared to experienced consultants marks their unique characteristics and potential for improvement with mindfulness training.

Our primary hypothesis was that participants who completed the MBI would demonstrate reduced inattention blindness in a situational operative task as compared to matched controls. We also tested the hypothesis that attention would improve among participants in the interventional group.

METHODS

The study was designed and reported in accordance with STROBE (17) and CONSORT guidelines (18) with adaptation for non-randomised pilot studies (19).

Ethical Approval

The use of data obtained from the course was approved by our academic Institutional Review Board (17019/001) and all subjects gave informed consent.

Participants

Participants were recruited through newsletters from U.K. and European neurosurgical societies, social media groups, and word of mouth. All participants self-referred, and after expressing interest, they were given more information about the study before giving written consent. Surgeons were not obliged to participate in the research study in order to receive mindfulness training. A matched cohort of control participants were recruited from our institution based on surgical grade, age and gender. Individuals who had previously completed a formal mindfulness training programme were excluded from the study. Also excluded were participants not presently working in neurosurgery or attendings who had been in post for more than a year.

Mindfulness Intervention

From October to December 2020, an 8-week virtual MBI programme was delivered by a mindfulness instructor (a physician with 5 years of teaching experience and approximately 5000 h of personal practice time). Weekly 90-minute sessions had specific themes and exercises (see **Supplementary Methods**). Participants were invited to voluntarily practice in their own time and utilise the online learning platform provided. The intervention was based on a course tailored specifically for healthcare professionals that incorporated core concepts of mindfulness and (self-)compassion training (20). The intervention was designed to promote emotional intelligence competencies in clinical environments including self-awareness, self-management, and social awareness. Practical and conceptual differences between our course and traditional mindfulness therapies (9) such as mindfulness-based stress reduction (MBSR) are outlined in the **Supplementary Material**, however the course was similar in concept and design to established, evidence-based surgically directed courses such as enhanced stress resilience training (ESRT) (21–23).

Attention and Inattention Tasks

Within two weeks of completing the MBI, both intervention and control groups were assessed virtually using a task designed to recruit attention and provoke inattention, in an environment and time convenient to each participant. This was adapted from previous work done by Dixon et al. (24), and follows a similar format to the seminal 'Gorilla' study by Simons and Chabris which examined inattentional blindness for complex objects and events in dynamic scenes via a video medium (25). The tasks were calibrated using a seperate, interventional-naive group of neurosurgeons (ranging from intern to attending). This was to ensure content and face validity, an appropriate difficulty level and that the tasks were clinically-relevant, specifically clarifying situations in which inattention blindness may contribute to significant patient harm (e.g. where a swab may be retained).

Each group was shown two 90 s operative videos: the first procedure familiar to neurosurgeons (spinal surgery) and the second unfamiliar and more cognitively demanding (splenectomy). In each video, participants were asked to focus on a part of the procedure (e.g., counting the number of times an instrument was used, i.e. *attention*) and assessed, then questioned on an aspect thought to be out of the scope of the scenario but present in the operative field (e.g., counting the number of swabs left in the surgical site i.e. *inattention*) [**Figure 1**]. Participants were intentionally not informed in advance that the task was designed to test inattention blindness nor revealed that factors other than the area of focus would be assessed. A median absolute error (MAE) score was calculated for both attention and inattention aspects of the video corresponding to the difference between perceived and actual counts. If a participant were

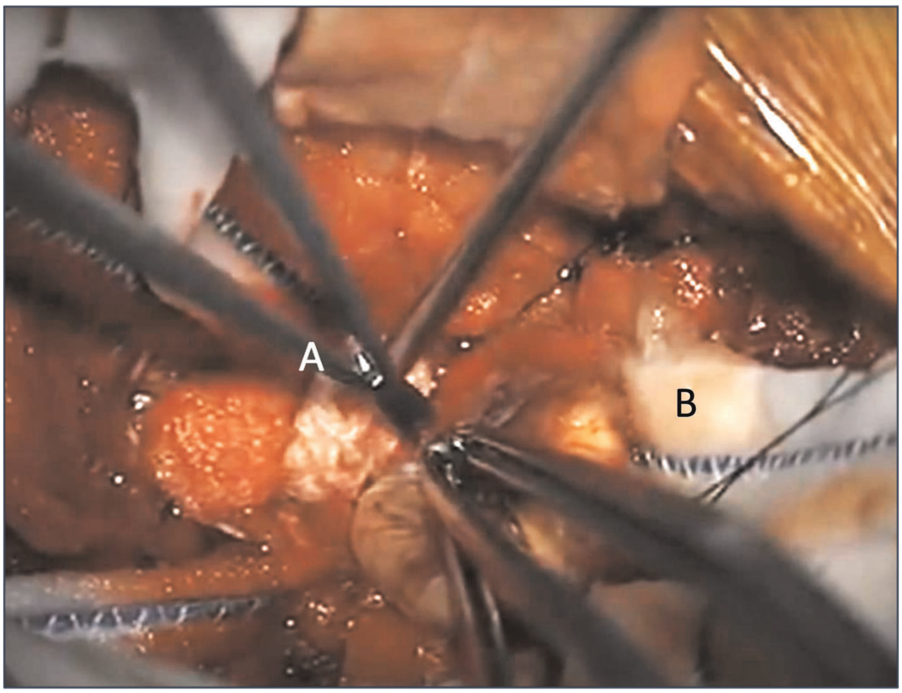

FIGURE 1 | Example screenshot from a spinal surgery operative video, where a nerve sheath tumour is being excised. Participants in the study were asked to focus on and count how many times the scissors (**A**) were used to cut in the attention task. They were then asked to identify the number of cottonoid patties (**B**), outside of their focus, left in the surgical site at the end of the video in the inattention task. Absolute error scores were calculated by taking the difference between the stated and actual count. (Full video available at https://www.youtube.com/watch?v=dGeSd5hU1tw, Prof. Ali Bydon, Johns Hopkins Medicine, uploaded 18th July, 2012. Image reproduced here with permission from the author)

'inattentionally blind' they would miss significant events occurring outside of their main focus and have a higher error score.

Data Analysis

Given the nature of this pilot study, an upper sample threshold of $n = 25$ was derived following consultation with the mindfulness instructor regarding the typical class size limit. The minimum sample size was based on a practical limit of participant recruitment. Participants who failed to complete a minimum of five sessions to receive course certification were excluded from further statistical analysis.

All statistical tests and data visualisation were performed using Python (3.8.6) and RStudio (1.2.1335). Tests for normality were conducted using the Kolmogorov-Smirnov test, and by visually inspecting the distribution and q-q plots of the data and residuals respectively. Given that the procedure video, participant differences and intervention may each have an effect on a surgeon's error score, a generalised linear model was fitted with these predictors and the scaled MAE as the dependent variable for attention and inattention seperately. Interactions between other variables and designation of 'random' or 'fixed' effects were permuted to find the model and distribution with the best fit, namely that one with the lowest Akaike Information Criterion (**Supplementary Results**).

A p-value of <0.05 was considered significant throughout. If the omnibus test was significant, a post-hoc independent t-test or Mann-Whitney U test was employed to assess for specific differences between intervention and control groups. If differences were found between first and second operative videos, a paired t-test or Wilcoxon-Signed-Rank test was then performed.

RESULTS

Demographics

Twenty-one neurosurgeons were recruited to undertake the mindfulness course. Five were ineligible for further analysis due to insufficient sessions being attended and 3 did not complete the post-interventional attention assessment. Thirteen neurosurgeons completed the mindfulness training (median = 7 out of 8 sessions completed) and were eligible for further analysis (age, 30 years [range 27–35]; female:male, 5:8), compared to 15 neurosurgeons in the control group (age, 30 years [27–42]; female:male, 6:9). There were no significant demographic differences between intervention and control groups demonstrating adequate matching (**Table 1**).

TABLE 1 | Demographic characteristics of participants.

	MBI	Controls	p
n	13	15	–
Median age (range)	30 (27–35)	30 (27–42)	0.87 (MWU)
Sex (F)	5	6	0.92 (χ^2)
Grade (SHO/SpR/Consultant)	8/5/0	11/3/1	0.40 (FE)

SHO: senior house officer - equivalent to junior resident; SpR: specialist registrar - equivalent to senior resident; MBI: mindfulness-based intervention; MWU: Mann-Whitney U test; FE: Fisher-Exact test.

Attention

MBI participants demonstrated no differences on attention tasks, compared to controls ($t = -1.50$, $p = 0.14$), although a trending difference was found for the first video (MWU, $p = 0.08$) with controls having higher error scores.

Both groups did demonstrate significant differences between operative videos ($t = 3.84$, $p < 0.0001$). Here, across all participants accounting for their differences and intervention status, error scores increased by 0.92 in the second operative video as compared to the first. On post-hoc analysis, the mindfulness group deteriorated between the first operative video (MAE = 0, range = 0–2) and second (MAE = 2, range = 0–3, Wilcoxon-Rank-Sum = 2.5, $p = 0.02$). Similarly, the control group's attention errors significantly increased between the first (MAE = 0, range = 0–2) and second operative videos (MAE = 1, range = 0–3, Wilcoxon-Rank-Sum = 2.5, $p = 0.03$) [**Figure 2**].

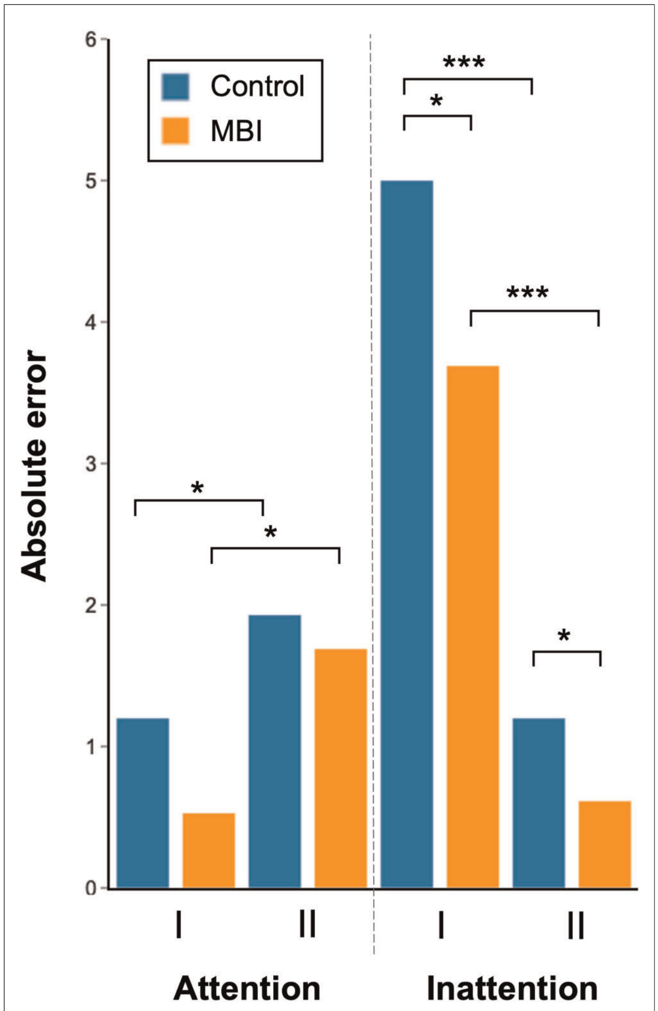

FIGURE 2 | Absolute error scores for attention and inattention tasks for the first (I) and second (II) operative videos. For visualisation purposes the mean absolute error for each group is demonstrated as the height of each bar. (*$p \le 0.05$, ***$p < 0.001$).

Inattention

Inattention scores significantly differed between the MBI group and controls ($t = -2.47$, $p = 0.02$). Here, after accounting both for differences between individuals and videos, by completing the MBI, a participant's error score improved by 0.36. Accordingly, there was a significant difference in error metrics between the MBI group (video 1, MAE = 4, range = 0–6; video 2, MAE = 0, range = 0–3) and controls (video 1, MAE = 5, range = 1–6, MWU = 147.5, $p = 0.02$; video 2, MAE = 1, range = 0–3, MWU = 137.5, $p = 0.05$). Inattention scores also differed significantly between the first and second operative videos for both groups ($t = -11.37$, $p < 0.0001$), where inattention errors were reduced by −1.64 when watching the second video [**Figure 2**].

A repeat analysis was also performed, excluding the single consultant from the control group. This resulted in no changes to the significance or direction of the aforementioned results.

DISCUSSION

In this brief prospective, proof-of-principle study, young neurosurgeons undertaking formal mindfulness training had significantly greater recognition of an unexpected distractor and reduced inattention-related error scores. After the first video was completed, both groups were now aware of the experiment's motive and likely to be more vigilant for other unexpected distractors. Although control participants significantly improved their inattention error rate in the second video procedure, they were still outperformed by MBI participants who had significantly less inattention-related errors. This would suggest that mindfulness exerts an additional effect over the cognitive conspicuity (26) of previously unperceived factors in the operative field in the first video. Using a multivariate model, we found that amelioration of inattention blindness was found to be independently associated with mindfulness training after adjusting for individual and task-related differences.

In contrast, error-metrics related to attention were not significantly different between MBIs and controls in either operative video, although a trend existed for the first procedure. Both groups performed worse during the second procedure as compared to the first, likely, at least in part, because of the added complexity associated with an operation unfamiliar to most neurosurgeons. It is unclear why greater group-wise differences in attention were not observed, since attentional regulation forms a core component of mindfulness training (27). This may be due to high baseline levels of attention, already entrained in this actively working group.

Recent iteratively adapted and tailored MBIs have demonstrated improvements in psychomotor performance, executive function, and attenuated negative psychological states among clinicians (28), and specifically, surgical trainees (22). None, however, have examined the role of mindfulness in reducing harmful cognitive factors within the operating room.

Our findings are aligned with previous work suggesting that mindfulness increases awareness of unexpected stimuli (13). This may be mediated by a number of mechanisms including reductions in stress and cognitive load (10, 29) and increases of working memory (30), all of which may help ameliorate inattention blindness (31). Mindfulness training represents a versatile, low-cost solution to foster operative vigilance and reduce technical errors (32). Certainly, if a pragmatic solution to reduce intraoperative technical errors were available it would have dramatic societal impact. Gawande et al found that 66% of all in-hospital adverse events were found to be surgical in nature (33), most of which occurred in the operating theatre, and that 54% were found to be preventable. Furthermore, a lack of vigilance represents one of the main cognitive factors leading to surgical errors and patient complications (34, 35). While it is accepted that surgery is not-error free, surgical excellence represents the ability to anticipate and manage errors and problematic events during surgery (36). Thus, surgeons engaging in mindfulness practice might be better prepared to deal with intraoperative events and reduce harm to patients, through enhanced awareness of the surgical field.

It has been suggested that mindfulness cannot be taught explicitly, rather modelled by mentors and cultivated in learners (32) and that such learning occurs during observation and practice, and over time. Surgeons who undertook the brief, targeted virtual mindfulness intervention in this study demonstrated a greater recognition of unexpected distractors compared with controls. This suggests that if appropriately directed, surgeons can develop mindfulness as a procedurally-relevant tool in a relatively short time span. These findings lend support toward the integration of mindfulness training within institutional teaching programs, and more widely within the neurosurgical speciality curriculum (37) albeit from an angle of improving patient safety rather than personal resilience. Alongside their personal and professional benefits, it has been shown that mindfulness interventions are both acceptable and feasible in surgical departments where they are used, with no negative effect on surgical training (38). This makes a compelling case for including this intervention in the residency curricula, which are mandated by national accreditation organisations (39, 40).

The limitations of this study include the small, matched but not randomised, sample. We also acknowledge that ameliorating inattention blindness via mindfulness techniques in the heavily constrained, virtual environment may not directly or immediately translate to improved patient outcomes. All sessions and assessments were performed virtually due to the COVID-19 pandemic, potentially resulting in heterogeneous conditions for participants. For the MBI group, attending the weekly sessions were mandatory, whereas "offline" practice was voluntary and therefore difficult to quantify. The control group for comparison was not a waitlist or dummy group and therefore there may have been a selection bias owing to the endogenous differences in motivation amongst the mindfulness participants versus controls (22). The attention and inattention tasks used in this study were somewhat novel, and although some measures were taken to validate each scale, assessments of reliability would have been challenging.

Although a test/retest reliability assessment would be an appropriate method for single outcome instruments (41), in this case the 'trick' of a hidden distractor would be apparent to participants taking the second test, meaning that scores would be poorly correlated.

CONCLUSION

Neurosurgeons who underwent an eight-week MBI had significantly reduced inattention blindness errors as compared to controls, suggesting mindfulness as a potential tool to increase vigilance and prevent operative mistakes. In spite of the aforementioned limitations, we emphasise that this is the first study, to the best of our knowledge, which specifically evaluates the use of mindfulness in attenuating a procedural bias among clinicians, and represents one of few techniques available to improve surgical vigilance in the operating environment. Our findings cautiously support further mindfulness evaluation with larger, randomised cohorts of surgeons, and, if proven, the implementation of these techniques within the neurosurgical training curriculum.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available upon reasonable request.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by UCL Minimal Risk Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AP and HJM conceptualised the study. MG, AR, HLH and AP performed data collection, HLH and AP performed data analysis, HLH, AP and HJM drafted the manuscript. HJM supervised the study. All authors contributed to the article and approved the submitted version.

ACKNOWLEDGMENTS

We would like to acknowledge Dr Reena Kotecha for her expertise and support and the Mindful Medics program. The project was supported by the National Brain Appeal's Small Acorns Fund. AP is supported by a Royal College of Surgeons (England) Surgical Research Fellowship. HLH and HJM are supported by the Wellcome Trust [203145Z/16/Z]. For the purpose of Open Access, the author has applied a CC BY public copyright licence to any Author Accepted Manuscript version arising from this submission. HJM is also funded by the NIHR Biomedical Research Centre at University College London.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/article/10.3389/fsurg.2022.916228/full#supplementary-material.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
published: 16 May 2022
doi: 10.3389/fsurg.2022.878378

Development and Validation of a Novel Methodological Pipeline to Integrate Neuroimaging and Photogrammetry for Immersive 3D Cadaveric Neurosurgical Simulation

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OPEN ACCESS

Edited by:
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Neurosurgery Clinic, Nepal*

Reviewed by:
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Paracelsus Medical University, Austria
Nicola Montemurro,
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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: 17 February 2022
Accepted: 25 April 2022
Published: 16 May 2022

Citation:
Hanalioglu S, Romo NG, Mignucci-Jiménez G, Tunc O, Gurses ME, Abramov I, Xu Y, Sahin B, Isikay I, Tatar I, Berker M, Lawton MT and Preul MC (2022) Development and Validation of a Novel Methodological Pipeline to Integrate Neuroimaging and Photogrammetry for Immersive 3D Cadaveric Neurosurgical Simulation. Front. Surg. 9:878378. doi: 10.3389/fsurg.2022.878378

Background: Visualizing and comprehending 3-dimensional (3D) neuroanatomy is challenging. Cadaver dissection is limited by low availability, high cost, and the need for specialized facilities. New technologies, including 3D rendering of neuroimaging, 3D pictures, and 3D videos, are filling this gap and facilitating learning, but they also have limitations. This proof-of-concept study explored the feasibility of combining the spatial accuracy of 3D reconstructed neuroimaging data with realistic texture and fine anatomical details from 3D photogrammetry to create high-fidelity cadaveric neurosurgical simulations.

Methods: Four fixed and injected cadaver heads underwent neuroimaging. To create 3D virtual models, surfaces were rendered using magnetic resonance imaging (MRI) and computed tomography (CT) scans, and segmented anatomical structures were created. A stepwise pterional craniotomy procedure was performed with synchronous neuronavigation and photogrammetry data collection. All points acquired in 3D navigational space were imported and registered in a 3D virtual model space. A novel machine learning-assisted monocular-depth estimation tool was used to create 3D reconstructions of 2-dimensional (2D) photographs. Depth maps were converted into 3D mesh geometry, which was merged with the 3D virtual model's brain surface anatomy to test its accuracy. Quantitative measurements were used to validate the spatial accuracy of 3D reconstructions of different techniques.

Results: Successful multilayered 3D virtual models were created using volumetric neuroimaging data. The monocular-depth estimation technique created qualitatively accurate 3D representations of photographs. When 2 models were merged, 63% of

Abbreviations: 2D, 2-dimensional; 3D, 3-dimensional; AI, artificial intelligence; CSF, cerebrospinal fluid; CT, computed tomography; HU, Hounsfield unit; MRI, magnetic resonance imaging.

surface maps were perfectly matched (mean [SD] deviation 0.7 ± 1.9 mm; range −7 to 7 mm). Maximal distortions were observed at the epicenter and toward the edges of the imaged surfaces. Virtual 3D models provided accurate virtual measurements (margin of error <1.5 mm) as validated by cross-measurements performed in a real-world setting.

Conclusion: The novel technique of co-registering neuroimaging and photogrammetry-based 3D models can (1) substantially supplement anatomical knowledge by adding detail and texture to 3D virtual models, (2) meaningfully improve the spatial accuracy of 3D photogrammetry, (3) allow for accurate quantitative measurements without the need for actual dissection, (4) digitalize the complete surface anatomy of a cadaver, and (5) be used in realistic surgical simulations to improve neurosurgical education.

Keywords: 3D rendering, depth estimation, neuroanatomy, neuroimaging, neurosurgical training, photogrammetry, virtual model

INTRODUCTION

One of the most challenging aspects of neurosurgery is visualizing and comprehending 3-dimensional (3D) neuroanatomy. The acquisition of this knowledge and its successful clinical application require years of practice in the operating room and anatomical dissection laboratory. However, both of these training resources may be limited by institutional resources. Furthermore, residents' work-hour restrictions, decreases in cadaver availability, and the interruption of hands-on training courses as a result of the COVID-19 pandemic have increased the difficulty of acquiring appropriate anatomical training for neurosurgeons. However, the advent of new technology that enables 3D rendering of neuroimaging has allowed the development of 3D virtual models that can be used to augment neurosurgical education. Such tools have been shown to improve performance and have become a complementary part of neurosurgical education when access to cadaveric specimens is restricted and will likely achieve more integration and impact upon neurosurgical training (1–4).

New advances in imaging, computer vision, image-processing technologies, and multidimensional rendering of neuroanatomical models have introduced extended-reality educational tools, such as virtual and augmented reality, into neurosurgeon training (2–6). Photogrammetry and related technologies may complement advanced tomographic neuroimaging studies (e.g., magnetic resonance imaging [MRI] and computed tomography [CT]) by providing detailed surface information of neuroanatomical structures. Stereoscopy, which is commonly used for neurosurgical education (7–9), is the process by which two 2-dimensional (2D) photographs of the same object taken at slightly different angles are viewed together, creating an impression of depth and solidity. Photogrammetry is a technique in which 2D photographs of an object are taken at varying angles (up to 360°) and then overlaid using computer software to generate a 3D reconstruction (10). In a previous study (1), a 3D model of a real cadaveric brain specimen was created using photogrammetry and 360° spanning. Although this technique is very practical and useful, it is limited to objects that can be scanned in 360°. Unfortunately, in most surgical scenarios, the surgeon or trainee can only visualize a portion of the surgical anatomy, usually through a narrow corridor. Thus, more practical photogrammetric approaches are needed to overcome this barrier. Recently, an artificial intelligence (AI)-based tool was developed to estimate monocular depth, which potentially makes it possible to convert 2D photographs into 3D images. We believe that this tool can be used to overcome limitations and bridge the gap between neuroimaging and photogrammetry scanning technologies.

In this proof-of-concept study, we brought together the spatial accuracy of 3D reconstruction of cadaveric neuroimaging data with the realistic texture of 3D photogrammetry to create high-fidelity neurosurgical simulations for education and surgical planning. The method sought to merge the spatial accuracy of medical MRI and CT images with 3D textural features obtained using advanced photogrammetry techniques. We hypothesized that current imaging, photography, computer vision, and rendering technologies could be effectively combined to maximize the use of cadaveric specimens for education, surgical planning, and research. This innovative approach aimed to not only enhance neurosurgical anatomy training but also create a new digital interactive cadaveric imaging database for future anatomical research. If this attempt is successful, a cadaveric specimen would no longer have to be discarded after fixation and dissection. A cadaver could instead be digitalized and passed along from generation to generation in the same condition in which it was first dissected. Herein, we describe and validate our novel methodological paradigm to create qualitatively and quantitatively accurate 3D models.

MATERIALS AND METHODS

Study Design

No institutional review board approval was required for this study. This proof-of-concept study included two phases: development and validation. In the first phase, a methodological pipeline was developed to combine various imaging, modeling, and visualization techniques to create integrated, multilayered, immersive 3D models for cadaveric research and education (**Figure 1**). After the development phase, the second phase of the study included validation of this novel methodological approach by matching agreement between surface maps. Four embalmed and injected cadaver heads were used for method development ($n = 3$) and quantitative validation ($n = 1$). We initially used 3 heads to optimize the methodological pipeline. Once optimized, we applied this pipeline to produce the virtual model in 1 head for this proof-of-concept study. Importantly, all heads used in this study were of the highest anatomical quality.

Neuroimaging

All cadaver heads underwent MRI and CT scans. A 3T MR-system machine (Ingenia, Philips Healthcare, Best, Netherlands) was used for volumetric imaging (1.0 mm), with the 3DT1 MPRAGE and 3DT2 FSE sequences. A LightSpeed VCT 64-slice CT scanner (General Electric Company, Boston, MA, USA) was used for thin-cut (0.65-mm) axial CT images.

3D Rendering

All 3D planning and modeling studies were performed with Mimics Innovation Suite 22.0 Software (Materialise, Leuven, Belgium). DICOM files (in all axial, coronal, and sagittal planes) were imported into Mimics. The masking process was undertaken using Hounsfield unit (HU) values on 2D radiological images, and segmentation of various anatomical structures was performed according to defined anatomical borders visualized on MRI scans. Bone was segmented based on CT scans, whereas MRI was used for all other structures (i.e., soft tissue). The 2 imaging modalities were merged and aligned with the Align Global Registration module.

Three-dimensional surface-rendered models of different anatomical structures were created. The design module feature (3-matic 14.0, Materialise, Leuven, Belgium) was used for fine-tuning and model details. Segmented structures included the skin, temporal muscle, bone, cerebrum, cerebellum, brainstem, and ventricles (**Figure 2**).

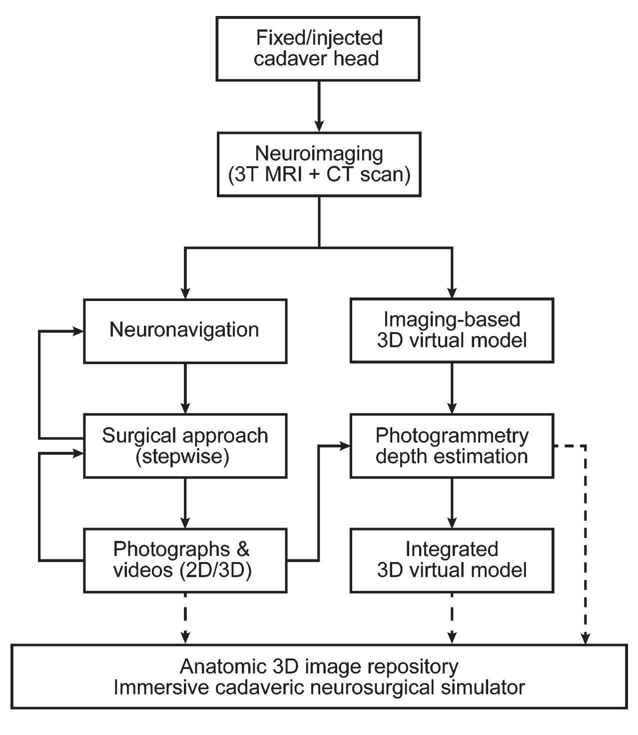

FIGURE 1 | The methodological pipeline to fully digitalize the cadavers. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

Pterional Craniotomy Model

To create a 3D pterional craniotomy model, neuronavigation used during a stepwise surgical procedure was combined with photogrammetry (**Figure 3A**).

Surgical Procedure

A cadaver head was placed and fixed in the Mayfield 3-pin head holder. Neuronavigation registration was performed using surface landmarks (**Figure 3B**). A pterional craniotomy was performed in a stepwise manner. Surgery was divided into 5 steps: (1) skin incision and dissection, (2) muscle incision and dissection, (3) burr holes and craniotomy, (4) durotomy, and (5) the intradural phase (exposure of brain) (**Figure 3C**).

Neuronavigation

Medtronic StealthStation S7 (Medtronic PLC, Minneapolis, MN, USA) was used for neuronavigation. Volumetric MRI scans were imported. Registration was performed using surface landmarks. Cartesian coordinates (x, y, z) were acquired and recorded for all registration points and assigned points in 3D space using the navigation probe. Each step of the surgical procedure included the acquisition of 3 to 8 different points corresponding to anatomical structures in the surgical field. For each point, screenshots of the navigation system were obtained verifying and illustrating the corresponding coordinates on axial, coronal, and sagittal planes as well as the 3D reconstructed image on the neuronavigation system (**Figure 3B**).

Photography

All stages of surgery were photographed with a professional camera (Canon EOS 5DS R, Canon Inc., Ota City, Tokyo, Japan) and a smartphone (iPhone 12, Apple Inc., Cupertino, CA, USA). Each acquired point in the surgical field was tagged with a 5×5-mm paper marker indicating an alphabetic-numeric code (e.g., S1 for the first point of skin incision) and photographed for further cross-validation.

Importing Neuronavigation Data to the 3D-Rendered Virtual Model

After the surgery was performed and the Cartesian coordinates for each point were obtained and verified with navigation, all points were imported into a 3D virtual model environment. The original landmarks for neuronavigation registration were used to register the point cloud of the 3D virtual model space. Integrating neuronavigation coordinates and photography data allowed surgical steps to be simulated on the 3D model. All pertinent surgical steps and layers of a pterional craniotomy were included, such as skin incision, muscle incision, burr

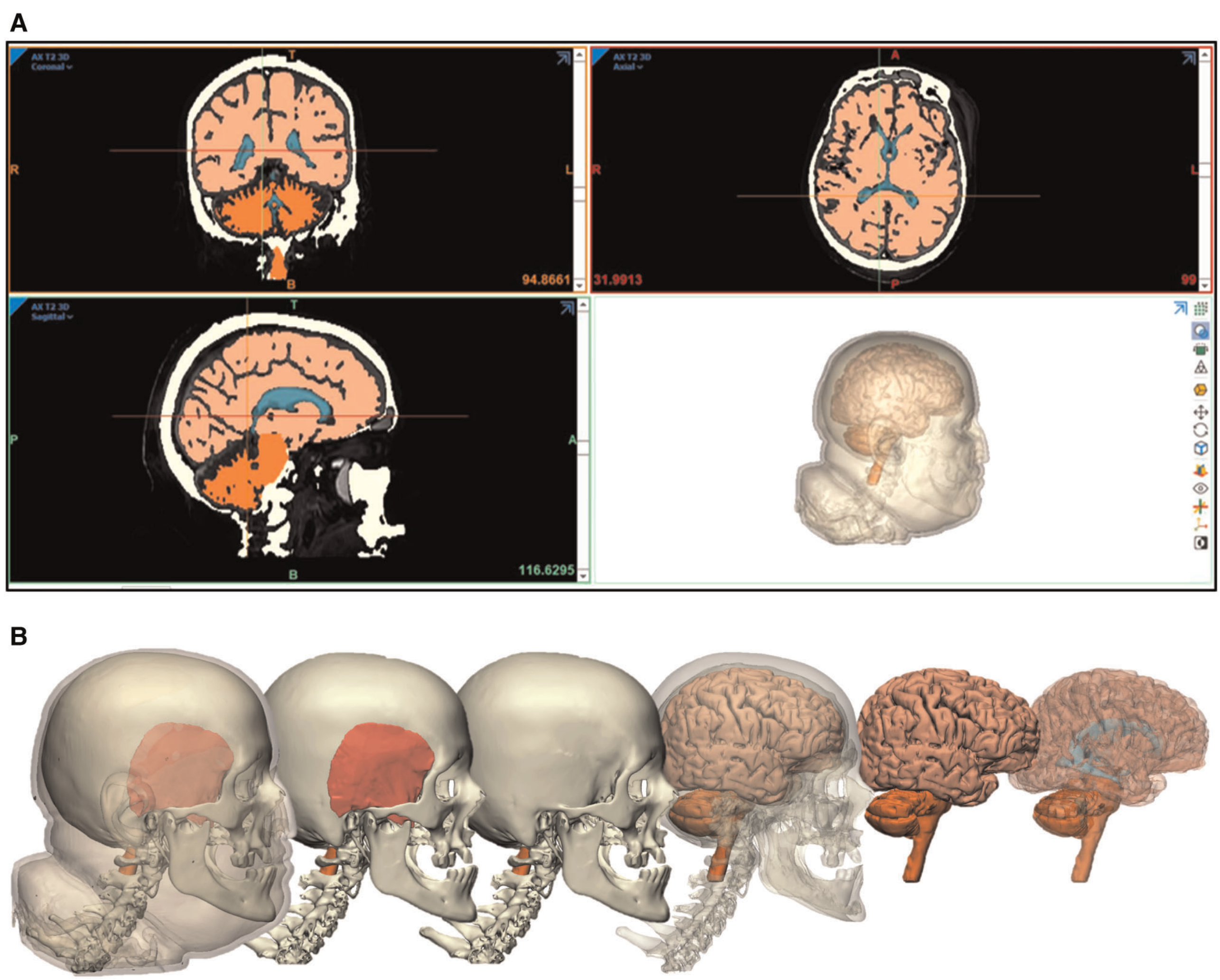

FIGURE 2 | Segmentation and rendering process. (**A**) Neuroimaging data used for 3D rendering of segmented anatomical structures. (**B**) 3D rendering of segmented anatomical structures. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

holes and craniotomy, dura incision, and brain exposure (**Figure 3C**). Points relevant to each step were added to the 3D virtual environment.

Machine Learning–Assisted 3D Reconstruction of 2D Photographs

Traditional photogrammetry tools use multiple photographs of an object to create 3D representations, whereas a novel AI-based depth-estimation tool developed to produce accurate 3D reconstructions of single 2D photographs provides a new form of photogrammetry. Intel ISL MiDaS v2.1 (Intel Labs, Santa Clara, CA, USA) is a neural network–based platform for robust depth estimation from 2D images that was used to create depth maps. Depth maps are images where every pixel is assigned an intensity value on a specific color-range scale according to its location on the z-axis (i.e., depth axis). Open3D library (an open-source library (11)) was used to create a point cloud from depth maps. MeshLab software (Visual Computing Lab, Pisa, Italy) was used for quality improvement and simplification of 3D modeling and surface reconstruction. The Sketchfab (Epic Games, Cary, NC, USA) website platform was used to visualize and share 3D reconstructed photographic images.

Quantitative Validation Studies

In theory, neuronavigation and imaging-based 3D modeling should demonstrate inherently excellent spatial accuracy because of their reliance on high-resolution volumetric MRI and CT imaging. However, the validity of 3D reconstructed photographs has not been reported previously in the neuroanatomical literature. Therefore, we used the 3D space of the image-based reconstructed model as the ground truth and validation for other modalities (e.g., neuronavigation coordinates of the surgical field and depth maps of 3D reconstructed images) (**Figure 4**). In other words, the 3D

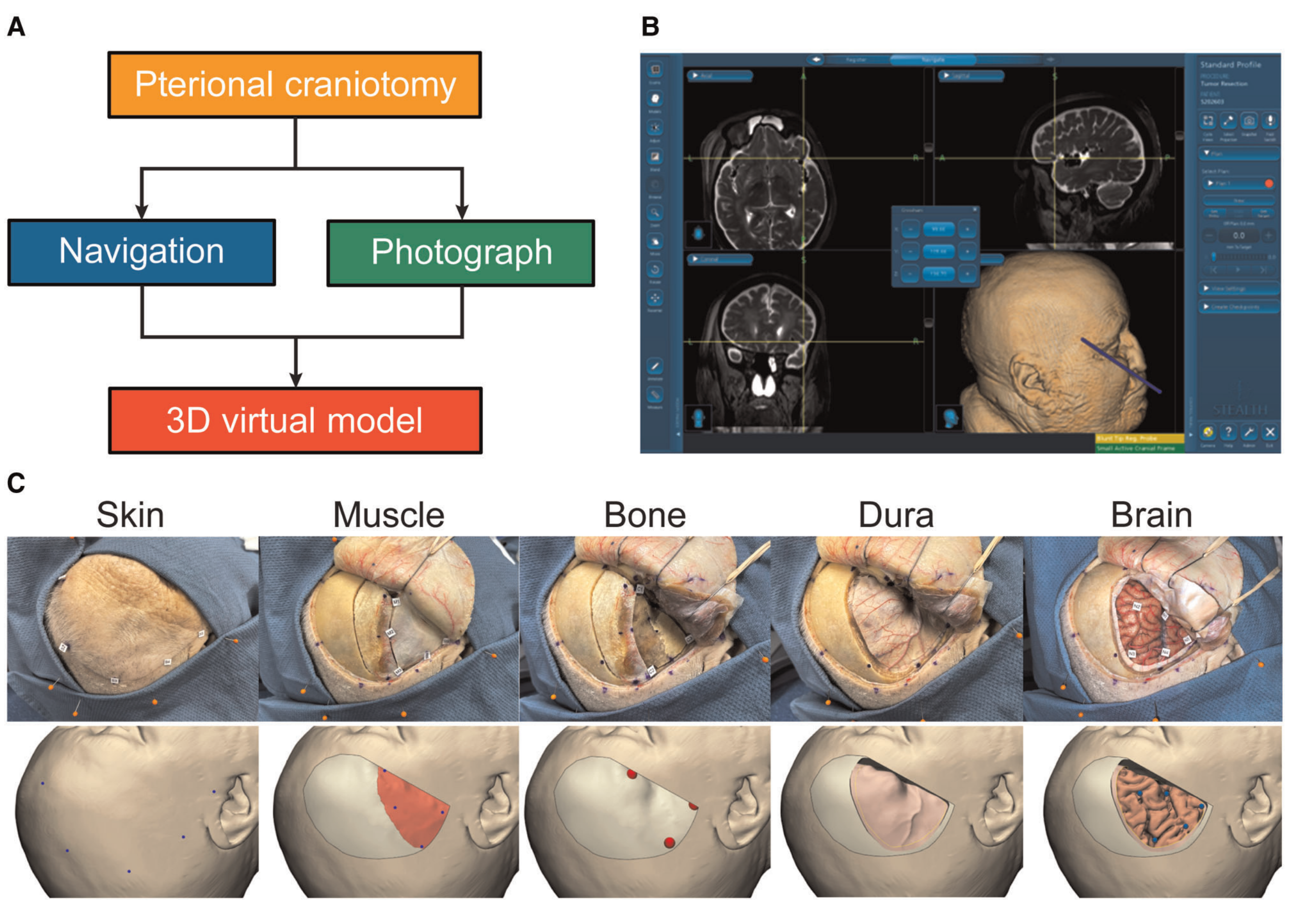

FIGURE 3 | Creation of virtual pterional craniotomy model. (**A**) Steps to create 3D pterional craniotomy model. (**B**) Synchronous data acquisition through neuronavigation. (**C**) Stepwise pterional craniotomy with images in the real-world setting (top panels) and 3D virtual model (bottom panels). *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

reconstructed surface rendered from standard medical imaging served as the true reference values.

Cross-Validation Studies

Pairwise comparisons of the two modalities were used for cross validation. Geomagic software (3D Systems, Rock Hill, SC, USA) was used to quantitatively measure how well two surfaces (neuroimaging-based 3D model vs. depth map of 3D rendered photograph) matched. The software also produced a color-scale deviation map (**Figure 4**). The use of neuronavigation also served as a valuable conduit to accurately rebuild the "invisible" anatomical details on the 3D virtual model (e.g., superficial sylvian vein, cortical arteries, etc.) by converting qualitative information of photography into quantitative data.

RESULTS

Feasibility of the Methodological Pipeline

A variety of alternative photogrammetry and 3D-rendering methods were tested. **Figure 1** demonstrates our proposed pipeline, which was found to be feasible and effective after a few iterations on different cadaver heads during the development phase.

Generation of Neuroimaging-Based 3D Virtual Models

We created displays of successful reconstruction and segmentation of 3D virtual models, using volumetric imaging data (**Figure 2**). Highly accurate and realistic features of skin, bone, dura, and brain surface models were created. Sulci and gyri anatomy of the brain mirror those seen in photographic views.

Unlike in vivo human brains, cadaver neuroimaging lacks a clear visualization of vascular structures; therefore, this 3D virtual model does not show vasculature. However, the casts of injected major arteries and veins can still be traced and rendered manually with the software, or a contrast medium can be used for injection if desired. Alternatively, microvasculature or other fine anatomical details can be added manually by using photographic information (**Figure 5**).

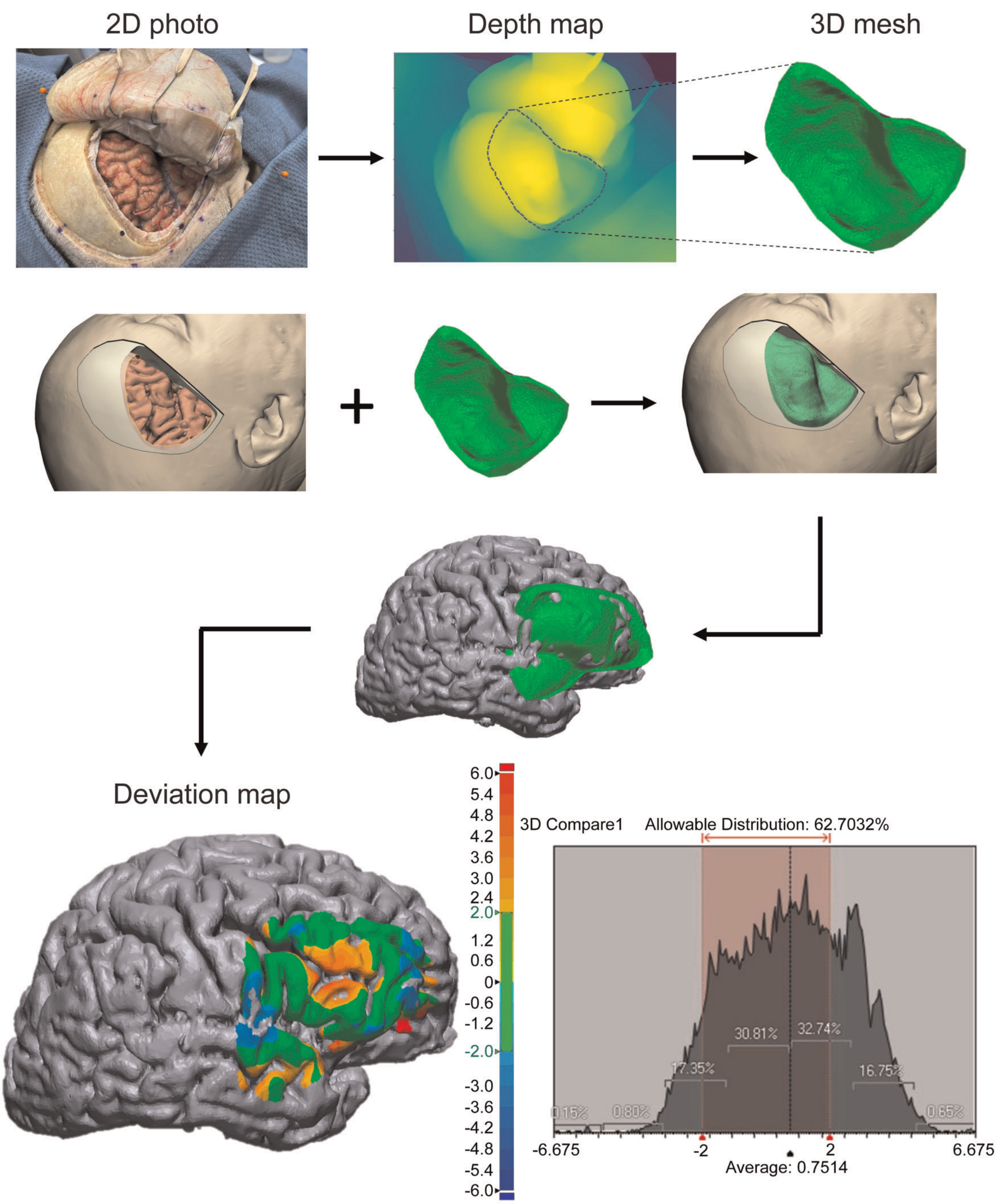

FIGURE 4 | Validation of monocular-depth estimation technique using the 3D virtual model. A single operative photograph was used to create a depth map and corresponding 3D mesh. This mesh was then imported into the 3D virtual model space as an object. Two models (3D mesh of the photographic depth map and 3D virtual model) were aligned, and the deviation map between 2 surfaces was created. The deviation map shows that almost two-thirds of the entire surface area matches almost perfectly between the 2 models (within 2-mm limits). The epicenter and edges show the highest degrees of distortion. Colored scale bar indicates the degree of distortion in millimeters. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

Cross-Validation of Neuronavigation with a Neuroimaging-Based 3D Model

After we constructed an imaging-based 3D model, we assessed the accuracy and validity of the model using the neuronavigation tool in the real-world setting. Co-registration of the 3D space from the neuronavigation system with the 3D virtual model allowed us to quantitatively measure the distortions arising from the surgical procedures on a cadaver (i.e., brain shifting). We measured the differences between the "true" model (image-based 3D reconstruction) and the

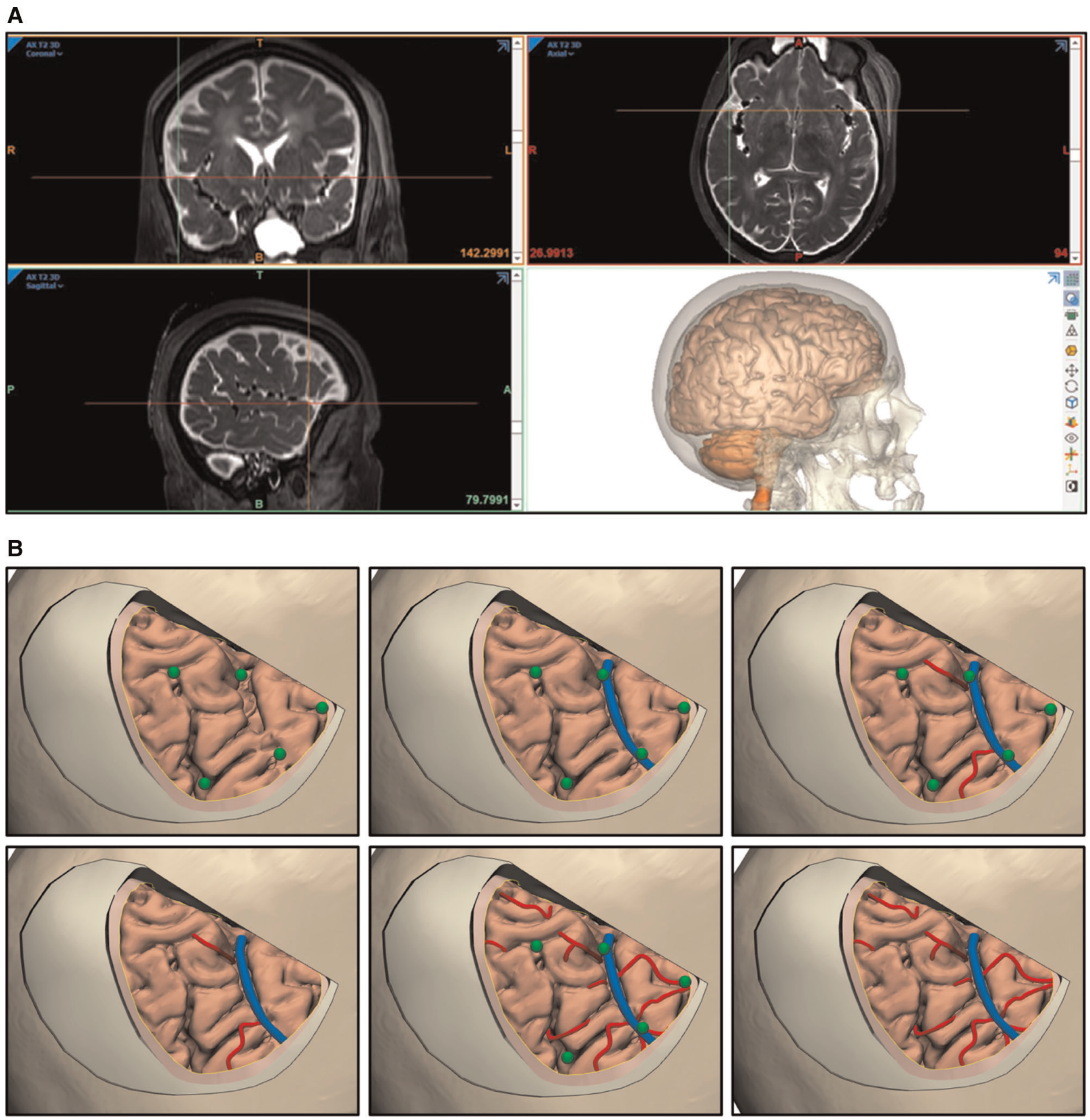

FIGURE 5 | Adding vasculature to 3D virtual models. (**A**) Vascular structures are visible on MRI (coronal, top left; axial, top right; sagittal, bottom left). However, the delineation of vascular structures in 3D models (bottom right) is not practical or accurate unless a contrast medium is used before the vessels are injected. (**B**) An alternative method is to artificially add or draw arteries (*red lines*) or veins (*blue lines*) using certain anatomical landmarks acquired via neuronavigation and photography (*green dots*). *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

measured (navigation) coordinates of prespecified points at each step of the surgical procedure. Overall, mean distortion was calculated as 3.3 ± 1.5 mm (range, 0–7 mm) for all 29 points acquired during the surgical procedure. Measurements in the 3D virtual model perfectly matched (defined as deviation <2 mm) that of real measurements on cadaveric specimens (**Figure 6**).

Validation of 3D Images Reconstructed from Single 2D Photograph

The validity of machine learning–based 3D reconstruction (a novel form of photogrammetry, using monocular-depth estimation) of a single 2D photograph was assessed. The first validation step involved analyzing the depth map (seen in

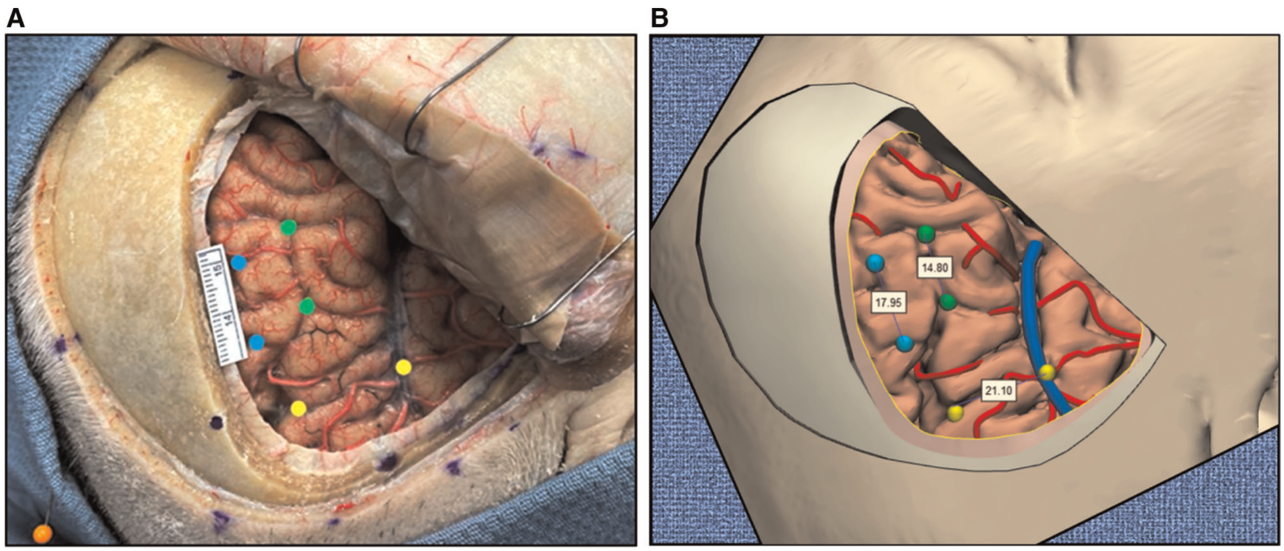

FIGURE 6 | Measurements in the real-world setting using a photograph (**A**) correspond to the 3D virtual model (**B**). Ruler and values shown are millimeters. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

Figure 4). The results showed that the depth map accurately represented relative depths of anatomical structures in the surgical field.

The second step was a quantitative analysis of the same depth map with reference to the 3D model's cortical surface exposed through the pterional craniotomy. The mean (SD) distortion was 0.7 ± 1.9 mm (range, −6.7 to 6.7 mm). Overall, within the craniotomy window, 63% of surface maps were perfectly matched (deviation <2 mm). Notably, the central area (around the inferior frontal sulcus) showed the largest distortion, whereas the match at the peripheral cortical surface was nearly perfect (<2 mm distortions). However, distortions increased again toward the edges.

The third step was qualitative validation. Real-time inspection of the 3D images created by texture mapping yielded accurate 3D perception in a wide range (up to 45° in all directions from the perpendicular axis of neutral image). Furthermore, qualitative validation was demonstrated objectively by comparing the same angle visualization of both the 3D photograph and the 3D virtual model (**Figure 7**).

Feasibility of Multimodality Integration

Our findings support the feasibility and applicability of the virtual models to be used as simulation tools for education, research, and surgical planning. The capability of supplementing the 3D model with anatomical details invisible to neuroimaging is demonstrated in **Figures 5–7**.

DISCUSSION

In this study, we introduced and validated a novel methodological pipeline that integrates various imaging and modeling technologies to create an immersive cadaveric simulation. We combined cadaveric dissections, virtual reality, surgical simulation, and postdissection analysis and quantification. Our findings suggest the following. First, neuroimaging and 3D modeling technologies can successfully digitalize precious cadaveric materials with a breadth of volumetric information and segmentation options. Second, various forms of photogrammetry technology can supplement these 3D models with more realistic surface information, such as fine anatomical details, color, and texture. Third, neuronavigation can be used as a medium to connect, communicate, calibrate, and eventually combine these two 3D technologies. Lastly, all these technologies could potentially pave the way for more integrated and immersive neurosurgical simulations. To the best of our knowledge, ours is the first neuroanatomical study to show the feasibility of combining the spatial accuracy provided by standard medical imaging (i.e., CT and MRI) with overlaid realistic textural features to a 3D reconstructed model.

Cadaveric Dissection as a Training Tool

Historically, cadavers have been considered the best material to use for studying human anatomy from both training and research perspectives. Also, cadaveric dissection is the gold standard for training neurosurgeons because it allows surgical techniques to be demonstrated, provides a unique experience with a wide range of sensory inputs, and creates necessary surgical skills (12, 13). These skills include depth perception, 2D and 3D vision orientation, sensitive movements in limited environments (14), bimanual coordination, and hand-eye coordination (15, 16). In fields such as chess, music, sports, and mathematics, studies on human performance have shown that attaining an expert performance level requires about

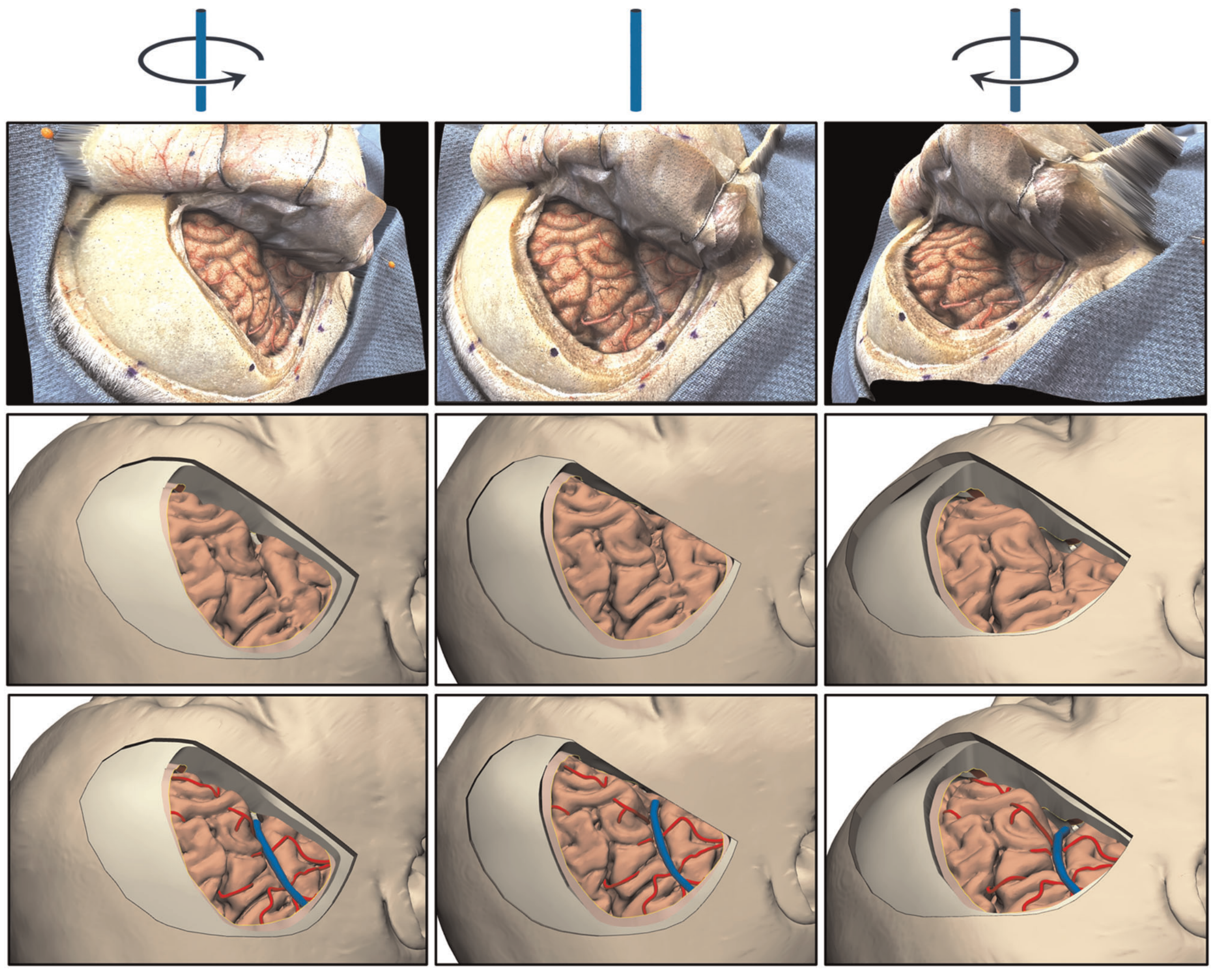

FIGURE 7 | Three rotations (columns) of real-world and two 3D models. Cadaveric photographs are shown in the top row. Both the 3D images obtained from a single 2D photograph via monocular-depth estimation technique (middle row) and the 3D virtual model generated from neuroimaging data (bottom row) can be rotated and matched in 3D space. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

10,000 hours of focused practice (17, 18). To obtain 10,000 hours of practice in a certain field, a person would have to dedicate 5 hours/day, 6 days/week, 48 weeks/year for 6.9 years (18). This equates to the time needed to graduate from a neurosurgical residency in the United States (7 years). A significant percentage of hours can be efficiently spent in a cadaveric dissection laboratory. However, access to such laboratories is limited due to a global shortage of cadavers, increasing costs of cadaver materials, and fewer dedicated anatomy laboratories, as well as the recent coronavirus pandemic. All these factors have contributed to decreased availability and use of cadavers worldwide (19–23). As a result, these recent limitations have paralleled the rapid adoption of new technologies to replace cadavers in anatomical training and international collaborations to maximize the use of the existing cadaver supply (19, 20, 24–26).

Virtual 3D Models and Simulators for Training

Three-dimensional virtual models are not unique to the field of neurosurgery or medicine. Use of these models began in the 1950s and 1960s as computer-aided design systems for military simulators and the aerospace and automobile industry (27–29). Later, mathematical algorithms were created to define virtual 3D solid models (27, 30). Now, with the emergence of advanced neuroimaging modalities and volumetric reconstruction, the means of teaching neurosurgical anatomy has been markedly influenced, opening the possibility for learning anatomy and simulating surgical interventions through virtual reality (13, 31, 32).

Neurosurgical education and training have been gradually moving toward virtual reality (5, 33). The COVID-19 pandemic further accelerated this trend. In fact, distant (i.e., remote) learning has become the mainstay of education during the pandemic (34). As a result, we believe now is the most opportune time to supplement neurosurgical training worldwide with 3D virtual reality.

The process of creating 3D virtual models in medicine requires the segmentation of CT or MRI, then volume rendering (35), which produces surface models with high spatial resolution. This technique is currently useful for identifying a pathologic location and surgical planning; however, the current 3D models lack color, texture, and fine anatomical details, such as fine blood vessels, cranial nerves, and arachnoid membranes, which cannot be reproduced (5). The next step in the evolution of 3D anatomical and virtual simulations is the development of models that are both spatially accurate and have fine anatomical detail and realistic textures.

Photogrammetry as a Supplement to Anatomy Training

Neuroimaging-based 3D reconstruction models capture anatomical features with high spatial accuracy, but as noted above, they lack fine anatomical details and realistic textures. A possible solution to this limitation is to incorporate photogrammetry into building the models. Photogrammetry creates 3D representations using multiple 2D photographs of an object and has long been used in anatomy to bring 3D perception to 2D photographs or to create virtual 3D representations of anatomical specimens (1, 5, 10, 36–38). De Benedictis et al. (36) reported quantitative validation of photogrammetry for the study of white matter connectivity of the human brain. Although their study used a relatively sophisticated setup, our group recently showed the applicability of a freely available 360° photogrammetry tool for neuroanatomy studies (1). In addition, Roh et al. (5) also incorporated photogrammetry into a virtual 3D environment to create realistic texture details of cadaveric brain specimens, but their study lacked quantitative validity. Nonetheless, these studies clearly show the potential of this rapidly developing technology in enhancing neurosurgical and neuroanatomy training.

Monocular-Depth Estimation as a Novel Form of Photogrammetry

Although photogrammetric technology has advanced tremendously in recent years, the various tools that are available continue to involve very complex hardware or software. However, the proposed monocular-depth estimation tool detailed in this study, which can also be regarded as a novel form of photogrammetry (Intel ISL MiDaS v2.1), appears to be a revolutionary game-changer. The technique provides spatially accurate features by AI-based and machine learning–guided 3D reconstruction of a single 2D image. When this tool is trained with a massive database of 3D films, it outperforms competing methods across diverse data sets (39). Indeed, we have demonstrated that this tool has a surprisingly high accuracy of estimating depth, even on a complex surface like the human brain. The potential for applying this novel photogrammetry tool in neuroanatomy training and research is enormous, and researchers will likely rapidly explore this technology in the near future.

Integrating Various Technologies for Immersive Simulations

All the technologies mentioned in this study are valuable instruments on their own, but each has its own limitations. Nevertheless, each technology can potentially complement another's weaknesses; therefore, when combined, they may offer an immersive, realistic simulation that is both quantitatively and qualitatively accurate. Thus, we believe the proposed methodological pipeline can be used not only for cadaveric dissections but also for real surgical scenarios. Images taken from surgical microscopes can be exported and implemented in our proposed pipeline. Some microscopes even support robotic and tracked controlled movements that can acquire stepwise stereoscopic imaging to postprocess into a 3D environment showing real tissue color, texture, and surgical approach anatomy (40). In addition, one can supplement the fine anatomical details that are usually missed when reconstructing standard MRI or CT images. This refinement is achieved using neuronavigation as a registration tool during cadaveric dissections and pinpointing the exact location of a structure that is "invisible" on neuroimaging.

Overall, we believe our proposed integrative approach can maximize the utility of cadavers and offers endless virtual dissection possibilities. In other words, a cadaver intended for dissection can be digitalized, so that it can remain an educational instrument forever rather than simply being destroyed when it can no longer be used. Physical models provide the advantage of real anatomical substances, but they are subject to decay and manipulation and require preservation and constant maintenance. In contrast, virtual models can be shared electronically, yield joint diagnostics and collective expertise, and eliminate geographical limitations (27). High-quality neurosurgical training and education can be continued in the comfort of a training neurosurgeon's home or office rather than a cadaveric dissection laboratory.

Supplementing 3D Virtual Models with Cadaveric Dissection and Live Surgery

Given the proposed pipeline, in what ways can 3D virtual models supplement neurosurgical training through cadaveric dissection and live surgery in real patients? In theory, the 3D methods can apply to both cadaveric heads and live heads, but one is inherently more pragmatic. The construction of an accurate and realistic 3D virtual model requires time, physical (i.e., surgical) dissection, and multiple measurements of different anatomical structures using neuronavigation. Unless an anatomical structure is related to the underlying pathology of a live patient, it will not be exposed in surgery, and under no circumstance will unnecessary dissection be performed on a live patient to expose distant structures. In addition, live patients will have blood and cerebrospinal fluid (CSF) in the surgical field, brain shift due to CSF removal, and brain pulsations that can interfere with the quality and precision of intraoperative imaging and registration. Fixed, injected cadaveric heads do not have limitations created by the real surgical environment. Working with cadaveric heads creates no immediate time limit. Cadavers can be dissected to show all desired anatomical structures. Also, using a cadaver creates no interference in measurements or registration caused by blood, CSF, brain shift, or pulsations as in live surgery.

Cadaveric tissue also has inherent limitations. Digitalizing a cadaver head before the irreversible physical dissection process allows for its repeated use via virtual dissections. This digital copy also provides an opportunity to continually improve the virtual model by acquiring cadaveric photos, even in standard 2D format with smartphones, professional cameras, or microscopes. While the actual cadaveric specimen is damaged from repeated use over time, it will give rise to a more complete and enriched digital cadaveric model dataset. Having such a dataset of cadaveric images and models will also enable novel anatomical measurements, simulation of different surgical approaches, and virtual dissections.

Although the purpose of surgical dissection in a live patient is to treat a certain pathology and not create a realistic 3D model, we believe that our proposed pipeline can be effectively used under certain circumstances in intraoperative situations without interfering with treatment. For example, serial surgical exposure images (both macroscopic and microscopic) can be co-registered with neuroimaging data using either neuronavigation registration points or more reliable anatomical landmarks (e.g., superficial veins). Then, machine learning algorithms can be used to train AI with the overwhelming intraoperative photographic data so that the algorithm can accurately predict the texture and surface details of MRI-based 3D-rendered virtual models.

However, it should be noted that surgical exposure will always be limited by a craniotomy performed at one specific time in a live patient, whereas a cadaveric specimen can be freely explored through many craniotomies and approaches at different time points. Furthermore, when using a cadaveric specimen, more aggressive retraction and dissection can be performed to reach distant anatomical targets that are deemed not safe in a real patient or are being tested for feasibility. Virtual models can support learning by allowing numerous rehearsals, with skills then confirmed by actual dissections in a laboratory. Eventually, with optimization of our pipeline and future advances in 3D virtual technology, we believe that accurate and realistic 3D virtual models can be effectively applied to both cadaveric and real-life specimens. Our technology is developed and exists to augment neurosurgical training; we have no doubt that considerable practice dissecting the cranium and brain is mandatory to achieve technical excellence for the progressing neurosurgeon.

Study Limitations

This study describes and validates a novel methodological pipeline for neurosurgeons and neuroanatomists worldwide. It includes both modifications in already known technologies (3D modeling, navigation, and photogrammetry) and the introduction of new technology (AI-based monocular-depth estimation) into the field. However, the model has certain limitations. This model development pipeline is supported by our preliminary, proof-of-concept study and should be validated with a larger number of specimens and by other groups. The process requires some expensive materials and tools, such as cadavers, neuroimaging, neuronavigation, and modeling software. However, we believe this methodology can be implemented in laboratories that already have these capabilities and resources, and those laboratories could then share their resources and outputs with others across the world who are in need of these valuable and innovative educational materials. Although merging 2 technologies to complement each other provides an exciting opportunity, this process may not be as easy as thought due to the complexity of underlying technical substrates and operational principles of each technology. This potential training tool will require the collaborative effort of surgeons, anatomists, imaging scientists, software developers, computer vision and image recognition specialists, and even graphic designers. The image processing procedures described in this study still require human effort and expertise, which restricts their efficiency but allows for personalization, revision, and modification. AI applications will likely generate more automatic or semiautomatic processes in the near future.

CONCLUSIONS

Our report represents the first time multiple 3D rendering technologies have been integrated and validated for the fields of neuroanatomy and neurosurgery. We were able to successfully merge the 3D reconstructions from standard medical imaging (CT and MRI) and photogrammetry (including a novel technique not yet applied to any form of anatomy) with high accuracy. As a result, we produced a 3D virtual model that is both quantitatively and qualitatively accurate. We believe our methodological pipeline can supplement both neurosurgical training and education globally, especially in a setting where cadaveric dissection or operating room access is limited. With 3D virtual technology, we envision a future where neurosurgeons can learn relevant anatomy and practice surgical procedures in the comfort of their own homes and at the pace of their choosing.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

SH: Conceptualization, Methodology, Investigation, Format Analysis, Data Curation, Visualization, Writing – Original draft preparation; NGR: Methodology, Software, Resources, Visualization; GM-J: Methodology, Investigation, Writing – Original draft preparation; OT: Software, Formal analysis, Resources, Visualization; MEG: Validation, Investigation, Data Curation; IA: Validation, Data Curation; YX: Validation, Data Curation; BS: Validation, Formal analysis; II: Validation, Resources; IT: Validation, Resources; MB: Supervision; MTL: Supervision; MCP: Resources, Writing – Review & Editing, Supervision, Project administration. All authors contributed to the article and approved the submitted version.

ACKNOWLEDGMENTS

This study was supported by the Newsome Chair in Neurosurgery Research held by Dr. Preul and funds from the Barrow Neurological Foundation. We thank the staff of Neuroscience Publications at Barrow Neurological Institute for assistance with manuscript preparation.

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frontiers | Frontiers in Surgery

ORIGINAL RESEARCH
published: 19 May 2022
doi: 10.3389/fsurg.2022.882063

Shadows and Lights: Perspectives of Training and Education in Neurosurgery for Undergraduate Students

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OPEN ACCESS

Edited by:
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Reviewed by:
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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: 23 February 2022
Accepted: 04 April 2022
Published: 19 May 2022

Citation:
Zoli M, Zenesini C, Bassani G, Colangelo A, Fayel E, Labanca Lima G, Maestri M, Pinto G, Scibilia A, Conti A and Mazzatenta D (2022) Shadows and Lights: Perspectives of Training and Education in Neurosurgery for Undergraduate Students. Front. Surg. 9:882063. doi: 10.3389/fsurg.2022.882063

Introduction: Neurosurgical education should start during medical school to involve more students, favoring the recruitment of the most prepared and motivated ones and spreading this subject to the future medical generations. Despite multiple investigations, a dedicated educational plan does not exist. This study aims to assess the undergraduates' interests, needs, and perceptions of this subject.

Materials and Methods: The survey was structured to collect demographic data of the participants, and to explore their interest in neurosurgery, their consideration of its importance in medical school, their opinions about the role of this subject in medical education, their needs in this training, and, the usefulness of this subject for their future career.

Results: A total of 156 students participated in the survey. Interest in neurosurgery was shown by 76 (48.7%) participants, however, this subject was also perceived as intimidating by 86 (55.1%). Attending the first 2 years of medical school ($p < 0.02$), previous interest in neuroscience ($p < 0.01$), and in a surgical subject ($p < 0.01$) were the factors associated with a greater interest in this subject. Neurosurgery should be included in all students' education, according to 117 (75.0%) participants and practical operating room training should involve all students, according to 96 (61.5%). The most effective learning methods were considered internship (134, 85.9%), followed by participation in meetings or seminars (113, 72.4%). Online seminars were considered useful by 119 participants (76.3%). Neurosurgery was assessed as a potentially interesting career by 99 students (63.5%), who also considered that it can increase their preparation for other subjects (116, 74.4%).

Conclusions: Neurosurgery was positively considered by medicals students, who, however, also perceived it as intimidating and hardly approachable. Demonstration that knowledge of neurosurgical concepts can improve their preparation also in general medical settings and, not only in the field of neuroscience, can be useful to promote their interest toward this subject. A combination of lectures and practical internships is considered an effective learning method, which can be fruitfully associated with new technologies.

Keywords: education, training, medical students, undergraduates, new technologies, social media

INTRODUCTION

Among all neuroscientific and surgical sciences, neurosurgery has a peculiar long learning curve, which makes its training a continuous process that mostly starts during the last years of medical school, continues during the residency, and goes on as long as the entire professional life. Indeed, the complex challenges are given by neurosurgical diseases and the need to develop both specific manual and intellectual skills for the correct patient management, which is not limited to the surgery but extended to Pre-operative planning and the entire follow-up, lengthening the time necessary to complete this education and training. Most of the studies investigating the educational methods in neurosurgery are focused on residents and Post-residency young surgeons, not inquiring about the interests, needs, requests, and aspirations of medical students, who, conversely, are of paramount importance for this discipline, representing the next generation of neurosurgeons or, as we would say in football jargon, our "primavera" (1, 2). Moreover, despite multiple investigations, a validated and accepted model aimed at building an educational plan focused on the best education and training and neurosurgical basic principles, and at improving students' skills in managing patients affected by neurosurgical issues still does not exist (3–8).

Indeed, on one hand, neurosurgery education for undergraduates is perceived as important both by medical students and neurosurgery training programs directors, with up to 78% of undergraduates who would be interested in this career, as reported by Akhigbe et al. (8). However, on the other hand, the amount and type of neurosurgical education reserved for medical students is very variable, with a rate ranging from 5.8 to 80% of undergraduates who reported not having received any neurosurgical training in their formative experience in the United Kingdom (3, 4). The factors influencing positively or negatively medical students in their consideration of neurosurgery have been extensively investigated: poor work-personal life balance, competitiveness, male-dominant environment, and neurophobia were the main deterrents in this choice, while social prestige, remuneration, practical aspects (innovation and technology), and research opportunities were the most appealing factors (3–8).

Furthermore, over the last years, multiple innovative learning instruments have become available, coupling traditional books and surgical atlases with interactive software, virtual reality tools, dedicated web channels, social media pages, webinars, and online educational events (9). The recent COVID-19 pandemic has been a strong booster toward the implementation of these new complementary learning models, with which medical students are quite familiar due to their younger age and more natural informatic background (9). The impact of these tools on neurosurgery tuition in medical schools, possibly not only favoring early exposure to this subject but also improving the quality of this first approach experienced by students, is yet to be fully determined (9, 10).

With this study, we have explored in our context the medical students' point of view about neurosurgery to assess their interest, needs, and perception of this subject, but also of understanding their consideration of the importance of neurosurgery in their education and training programs, and defining how useful they consider this specialized surgical discipline to be in their future career.

MATERIALS AND METHODS

An online electronic survey was prepared in the English language and was sent to 1,500 undergraduate students of the School of Medicine and Surgery, of the University of Bologna, Italy. The survey was distributed *via* e-mail along with regular reminders.

Questionnaire Preparation

The survey was structured into question groups including demographic and personal data of the participants (questions 1–6), their interest in neurosurgery and similar subjects and how this attitude has changed during medical school (questions 7–10.3), their consideration of the importance of neurosurgery in medical school (questions 10.4–10.7), their opinions about the role that neurosurgical education and training should have in medical school (10.8–10.13), their needs in neurosurgical training (10.14–10.22) and, finally, how useful they think this education could be for their future career (10.23–10.27) (**Supplementary Table S1**).

Questions were prepared and revised by all authors using a Likert scale. They were initially presented to a selected group of 10 medical students (5 males and 5 females, mean age 22 years old, all attending the 6 years of medical school in both the Italian and English course of our University, 4 had attended the neurosurgical department and 6 had not yet). Based on their answers and comments, the authors revised each question. The authors and a selected group of 10 students were not invited to participate in the survey. Data were collected prospectively. After receiving all the responses, Cronbach's alpha test was performed to measure the internal coherence between data and was found to be 0.85.

Outcome

The main outcome is the degree of medical students' personal interest in neurosurgery. Secondary outcomes were: (1) their consideration of the importance of this subject in medical school; (2) their opinions about the role of neurosurgical education and training in medical school; (3) the analysis

TABLE 1 | Features of the participants to the survey.

	N.	%
Sex		
Males	65	41.7%
Females	89	57.1%
Prefer not to declare	2	1.2%
Mean age	22 ± 2	
Year of medical school	4th ± 2	
Attemption to neurosurgical course		
Yes	52	33.3%
Not	104	66.7%
Exposure to a neurosurgical enviroment for more than 20 h		
Yes	6	3.8%
Not	150	96.2%
Influence of media in the image of neurosurgeon work		
Nothing at all	21	13.5%
Low	31	19.9%
Neutral	42	26.9%
High	50	32,0%
Very high	12	7.7%

of their needs for neurosurgical education; (4) and the consideration of its usefulness for their future medical career. Other collected data were age, sex, year of medical school, having attended the neurosurgery course (in the 4th year in our University), time spent in a neurosurgical unit and/or operating room, the influence of media on the view of the neurosurgeon work and interest in another subject in the field of neurosciences or surgical sciences. These features were correlated with the primary and secondary outcomes to assess the influencing factors determining the personal interest, consideration, role, and perceived usefulness of neurosurgery.

Statistical Analysis

In the descriptive analysis, we presented the continuous variables with mean and standard deviation and the categorical variables with absolute (n) and relative frequency (%). Chi-square or Fisher's exact test was used to evaluate the associations between the two outcomes and the characteristics of the interviewees described above. Kruskal-Wallis test, based on median and interquartile range, has been used for continuous variables. Multivariable logistic regression models were used to evaluate the associations with the variables significant in univariate analysis and those outcomes, which presented more than one significant association in univariate analysis. For this analysis we aggregated the items "high" and "very high" vs. items "nothing at all", "low", and "neutral". The results were presented as Odds Ratio (OR) and 95% Confidence Interval (95% CI). p-Values < 0.05 were considered significant. Statistical analysis was conducted using Stata SE version 14.2.

RESULTS

A total of 156 medical students responded (10.4%): 65 were males (41.7%), 89 (57.1%) females and 2 (1.2%) preferred not to declare their sex. The mean age was 22 ± 2 years old and they were enrolled in the 4th ± 2 of 6 years of medical school (**Table 1**). The neurosurgery course in the 4th year of the University of Bologna had been already attended by 52 (33.3%) participants and only 6 (3.8%) had spent more than 20 h (corresponding in our educational system to a rotation of about a week) in a neurosurgical environment (operating room, in- or outpatient facilities). Sixty-two (39.7%) responders revealed that their view of neurosurgical work is mostly influenced by media (TV series, movies, news, etc.).

Personal Interest in Neurosurgery and Similar Subjects by Medical Students

A large number of participants (76, 48.7%) had a high/very high personal interest in neurosurgery, among them 91 (58.3%) stated to be interested also in other subjects in the field of neuroscience (i.e., neuroradiology, neurology, neuropathology, neurobiology, neuropsychiatry, etc.), and 89 (57.1%) also in another surgical subject (**Table 2**). This interest has increased during the years of medical school for 49 (31.4%) students, and only 23 (14.7%) stated to have reduced their initial interest in this topic over the years (**Figure 1**). Seventy-four (47.4%) students considered that the neurosurgery course or personal studies of this discipline increased their interest in this subject (**Table 2**).

In univariate analysis, younger age ($p = 0.02$), attending the first 2 years (Pre-clinical) of medical school ($p < 0.01$), previous interest in neuroscience ($p < 0.01$), and in a surgical subject ($p < 0.01$) were positively associated with a greater interest in neurosurgery. In multivariate analysis, the attending the first 2 years of medical school (p: 0.02), previous interest in neuroscience ($p < 0.01$), and in a surgical subject ($p < 0.01$) confirmed their association with developing an interest in neurosurgery.

Importance of Neurosurgery in Medical School

Neurosurgery was considered a relevant part of medical students' education by 118 participants (75.6%), however, it was perceived as an intimidating subject by 86 of them (55.1%) (**Table 3** and **Figure 2**). A large number of students (84, 53.8%) disagreed that, despite its fascinating aspects, neurosurgery has limited importance in medical students' education and only 32 (20.5%) considered this subject too advanced for undergraduates (**Table 3**).

In univariate analysis, younger age (p: 0.02), attending the Pre-clinical years of medical school ($p < 0.001$), previous interest in neuroscience ($p < 0.001$) and in a surgical subject ($p < 0.001$) were directly associated with a more positive consideration of the importance of neurosurgery in medical school. In multivariate analysis, previous interest in neuroscience ($p < 0.01$), and a surgical subject (p: 0.01) were directly associated with this positive consideration of the importance of neurosurgery.

TABLE 2 | Personal interest in neurosurgery and similar subjects.

	Nothing at all (%)	Low (%)	Neutral (%)	High (%)	Very high (%)
Interest in NS	12 (7.7%)	19 (12.2%)	49 (31.4%)	38 (24.4%)	38 (24.4%)
Interest in other neurosci. subjects	12 (7.7%)	22 (14.1%)	31 (19.9%)	43 (27.6%)	48 (30.8%)
Interest in other surgical subjects	18 (11.5%)	22 (14.1%)	27 (17.3%)	23 (14.7%)	66 (43.3%)
Positive increase of interest toward ns along years	23 (14.7%)	21 (13.5%)	63 (40.4%)	37 (23.7%)	12 (7.7%)
Negative increase of interest toward ns along years	62 (39.7%)	24 (15.4%)	47 (30.1%)	20 (12.8%)	3 (1.79%)
Increased by NS course or study	10 (6.4%)	18 (11.5%)	54 (34.6%)	51 (32.7%)	23 (14.7%)

NS, Neurosurgery; Neurosci., Neuroscience.

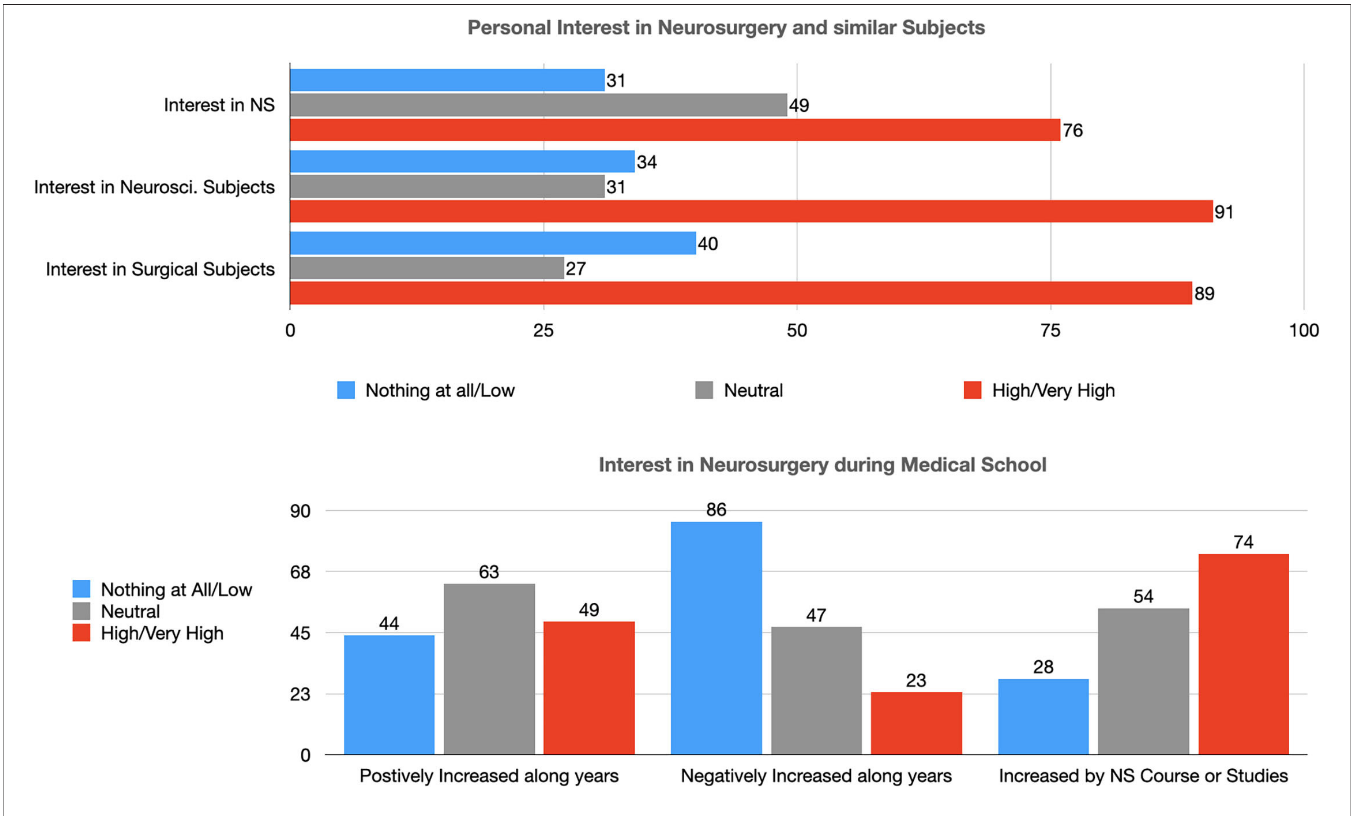

FIGURE 1 | Personal interest in neurosurgery and similar subjects (NS, Neurosurgery; Neurosci., Neuroscience).

Role of Neurosurgical Education and Training in Medical School

The vast majority of participants (117, 75.0%) considered that a neurosurgery course should be included in the educational plan of all undergraduate students, a large proportion (102, 65.4%) disagreed that it should be offered only to a selected group of interested ones (**Table 4**). Only 32 (20.5%) stated that this subject should be reserved only for Post-graduates (**Table 4** and **Figure 3**).

Moreover, 90 (57.7%) thought that also practical training in the operating room to teach basic neurosurgical procedures should be included in all medical student's education; a large number of them disagreed that it should be reserved for a selected group of students (77, 49.3%) or only to Post-graduates (121, 77.6%) (**Table 4** and **Figure 3**).

In statistical analysis, attending the last 2 years (when the clinical specialties are taught) of medical school ($p < 0.04$) was positively associated with the consideration that

TABLE 3 | Importance of neurosurgery in medical school.

	Nothing at all (%)	Low (%)	Neutral (%)	High (%)	Very high (%)
NS is a relevant subject for MS	4 (2.6%)	5 (3.2%)	29 (18.6%)	66 (42.3%)	52 (33.3%)
NS is an intimidating subject for MS	16 (10.3%)	29 (18.6%)	25 (16.0%)	60 (38.5%)	26 (16.7%)
NS is a fascinating subject but of limited importance for MS	32 (20.5%)	52 (33.3%)	45 (28.8%)	18 (11.5%)	9 (5.8%)
NS is too advanced for MS	22 (14.1%)	49 (31.4%)	53 (34.0%)	25 (16.0%)	7 (4.5%)

NS, Neurosurgery; MS, Medical Students.

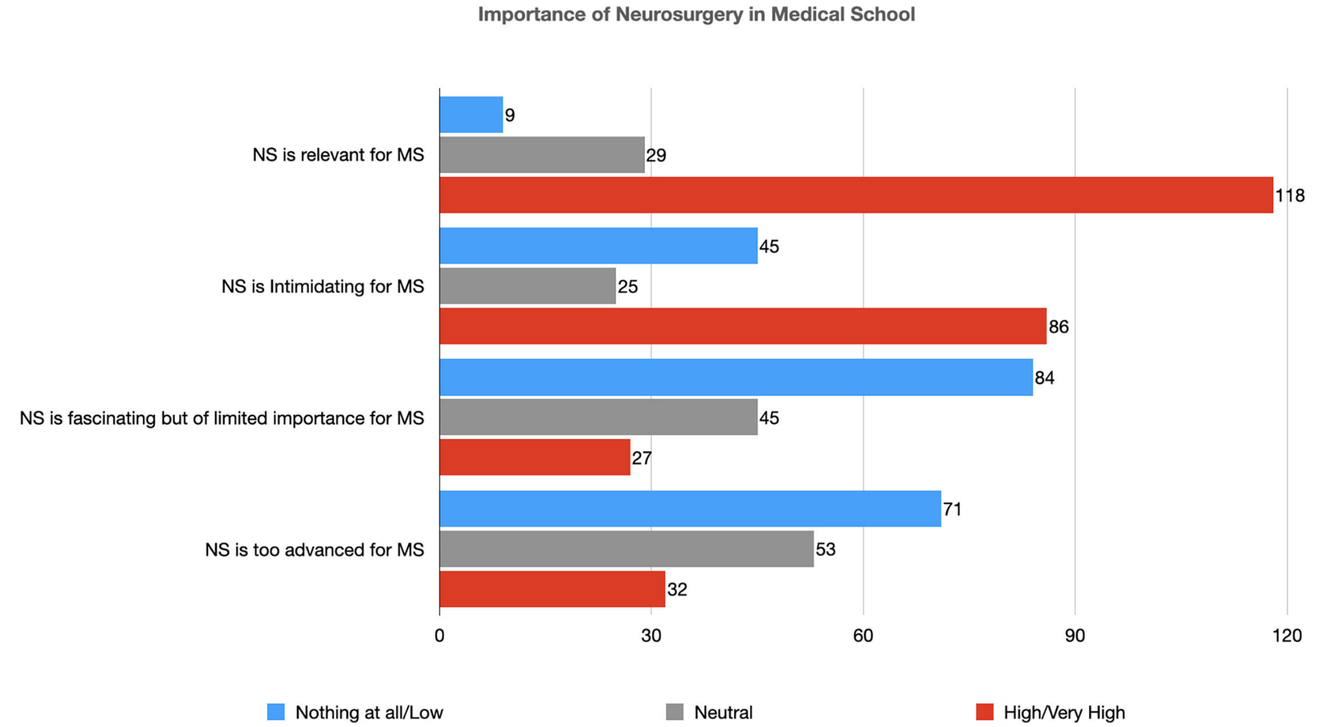

FIGURE 2 | Importance of neurosurgery in medical school (NS, Neurosurgery; MS, Medical Student).

neurosurgical education should be provided to all medical students. Moreover, previous interest in a surgical subject ($p < 0.001$) was directly associated with the consideration that practical training in the operating room should be offered to all medical students.

Needs in Neurosurgical Education and Training by Medical Students

The teaching modality considered most useful has been internships or clerkships in neurosurgical departments (137, 87.8%), followed (117, 75.0%) by the active involvement of medical students in neurosurgical patients' management and decision-making process, a high number of patients visited and seen under supervision (113, 72.4%) and participation in local or national/international meetings or seminars (113, 72.4%) (**Table 5** and **Figure 4**). Learning by doing was considered an effective teaching modality by 106 (67.9%) students and participation in operating room sessions by 111 (71.1%) (**Table 5**). Conversely, classroom lectures were considered effective for learning neurosurgery by 28 (17.9%) undergraduates. A large number of them (119, 76.3%), also, reported that online seminars, educational events (also remotely accessible), and the use of virtual reality instruments in classroom teaching can ameliorate this traditional educational system (**Table 5**). Mentoring and tuition were considered an important part of neurosurgical teaching by 82 (52.6%) students (**Table 5**).

TABLE 4 | Role of neurosurgical education and training in medical school.

	Nothing at all (%)	Low (%)	Neutral (%)	High (%)	Very high (%)
Neurosurgical education should be offered to all MS	4 (2.6%)	10 (6.4%)	25 (16.0%)	68 (43.6%)	49 (31.4%)
Neurosurgical education should be offered to a restricted group of interested MS	52 (33.3%)	50 (32.1%)	21 (13.5%)	24 (15.4%)	9 (5.8%)
Neurosurgery should be not included in MS education	22 (14.1%)	49 (31.4%)	53 (34.0%)	25 (16.0%)	7 (4.5%)
Neurosurgical OR training should be offered to all MS	8 (5.1%)	23 (14.7%)	35 (22.4%)	51 (32.7%)	39 (25.0%)
Neurosurgical OR training should be offered to a restricted group of interested MS	42 (26.9%)	35 (22.4%)	32 (20.5%)	37 (23.7%)	10 (6.4%)
Neurosurgical OR training should be not included in MS Education	82 (53.6%)	39 (25.0%)	20 (12.8%)	11 (7.1%)	4 (2.6%)

MS, Medical Students; OR, Operating Room.

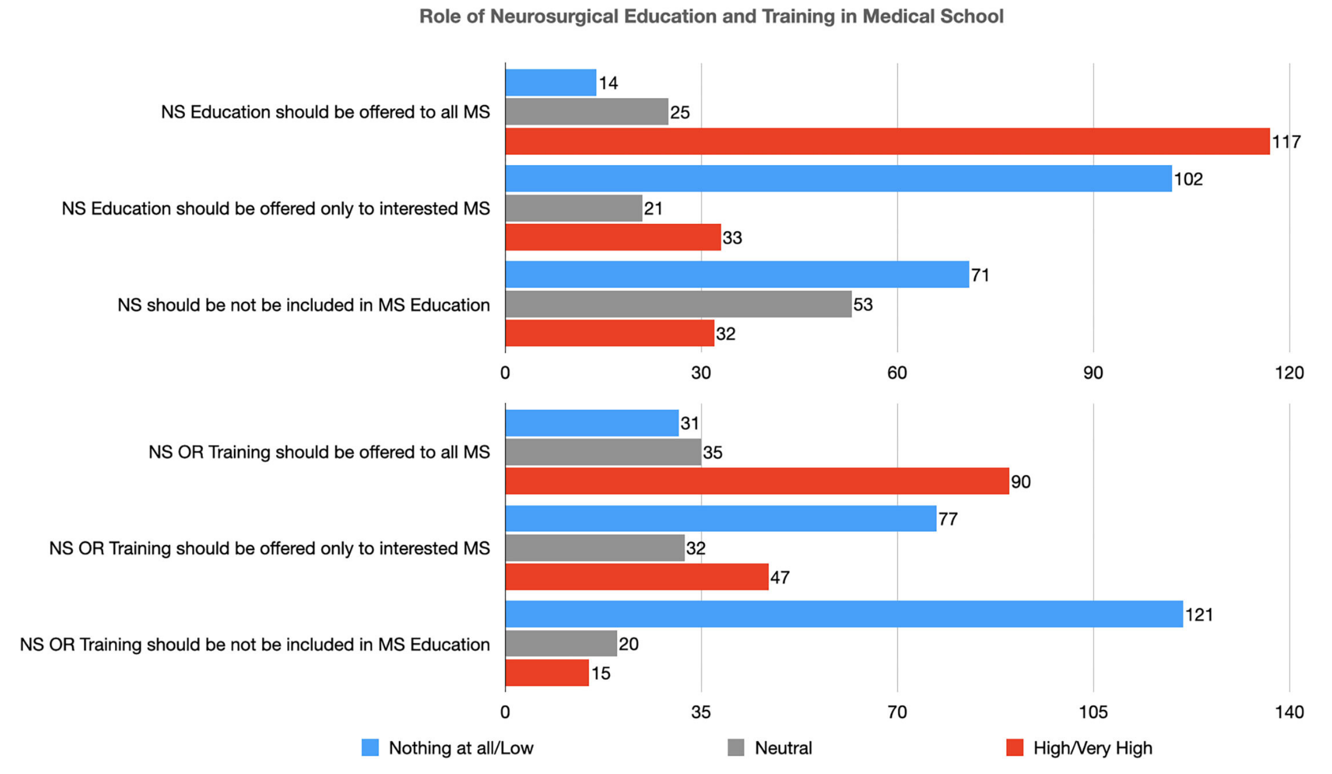

FIGURE 3 | Role of neurosurgical education and training in medical school (NS, Neurosurgery; MS, Medical Student; OR, Operating Room).

Usefulness of Neurosurgery in Medical Students' Career

Neurosurgery was considered a potentially interesting career by 101 students (64.7%) (**Table 6** and **Figure 5**). They also stated that neurosurgical education can increase their preparation for other neuroscience subjects in 116 (74.4%) cases, for other surgical subjects in 106 (67.9%), and other Non-neuroscience subjects in 67 (42.9%) (**Table 6**). Only 20 (12.8%) reported that neurosurgery is a subject with limited potential usefulness in their future career (**Table 6**).

At univariate analysis, previous interest in neuroscience ($p < 0.001$) and in surgery ($p < 0.001$) were directly associated with a more positive consideration of neurosurgery as a potential future career (**Table 7** and **Supplementary Material 2**). In multivariate analysis, both these variables (previous interest in neuroscience, $p < 0.01$, and interest in a surgical subject, $p < 0.01$) confirmed

TABLE 5 | Needs in neurosurgical education and training by medical students.

	Nothing at all (%)	Low (%)	Neutral (%)	High (%)	Very high (%)
Clerkships or internships are important to learn NS	1 (0.6%)	1 (0.6%)	17 (10.9%)	64 (41.0%)	73 (46.8%)
Active Involvement of MS in patients' management is important to learn NS	0 (0.0%)	8 (5.1%)	31 (19.9%)	67 (42.9%)	50 (31.1%)
High number of patients seen is important to learn NS	0 (0.0%)	7 (4.5%)	36 (23.1%)	70 (44.9%)	43 (27.6%)
Participation to meetings or seminars is important to learn NS	2 (1.3%)	4 (2.6%)	37 (23.7%)	58 (37.2%)	55 (35.3%)
Learning by doing is important to learn NS	6 (3.8%)	13 (8.3%)	31 (19.9%)	58 (32.2%)	48 (30.8%)
Participation to OR sessions is important to learn NS	2 (1.3%)	5 (3.2%)	38 (24.4%)	72 (46.2%)	39 (25.0%)
Classrooms are important to learn NS	6 (3.8%)	63 (40.4%)	59 (37.8%)	27 (17.3%)	1 (0.6%)
Online seminars, didactical events and virtual reality instruments are important to learn NS	0 (0.0%)	9 (5.8%)	28 (17.9%)	68 (43.6%)	51 (32.7%)
Mentoring and tuition are important to learn NS	2 (1.3%)	11 (7.1%)	61 (39.1%)	63 (40.4%)	19 (12.2%)

MS, Medical Student; NS, Neurosurgery; OR, Operating Room.

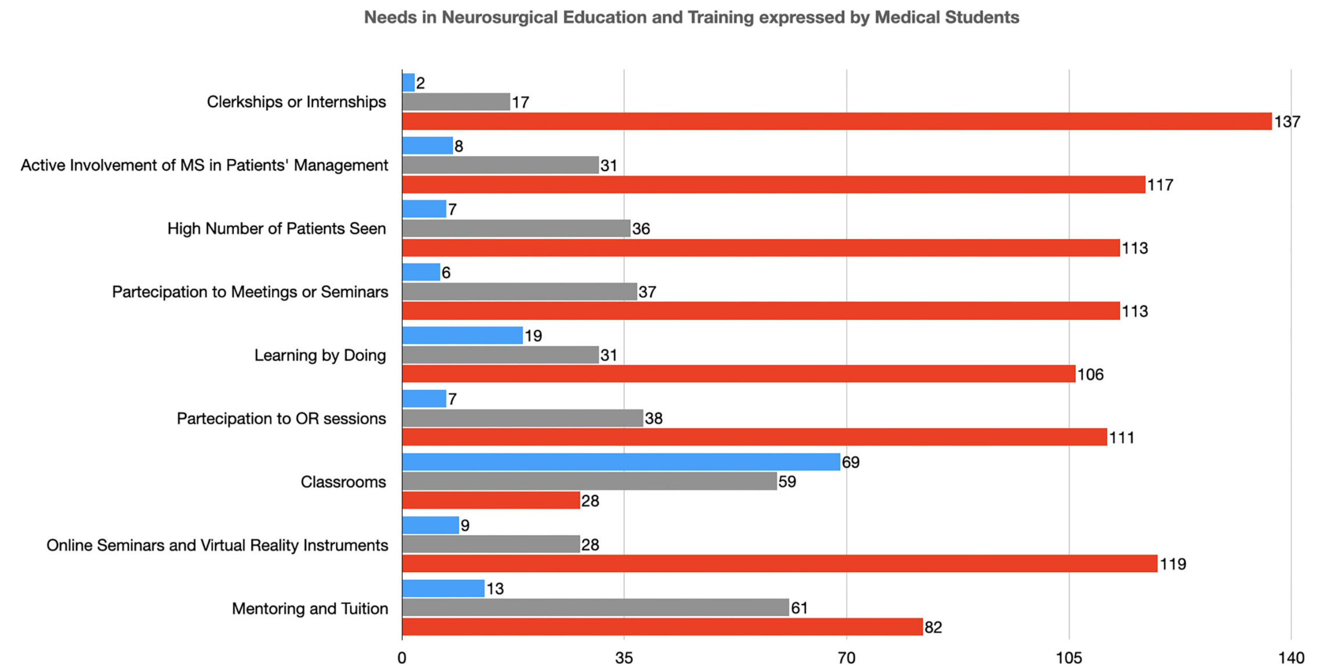

FIGURE 4 | Needs in Neurosurgical Education and Training expressed by Medical Students (MS, Medical Student; OR, Operating Room).

their association with the consideration of neurosurgery as a potentially interesting career (**Table 8**).

DISCUSSION

Similar to other dedicated reports, neurosurgery is considered, on one hand, fascinating and potentially interesting, but on the other, many deterrents prevent undergraduates from dedicating their passion and energy to this field (3–8). Our study underlines the presence of these shadows and lights, finding that 48.7% of medical students have a personal interest in neurosurgery and 64.7% consider it a potential future career, but also that 55.1% of them consider this subject as intimidating. To explore the reasons at the base of these ambiguous considerations, many

TABLE 6 | Usefulness of neurosurgery in medical students' career.

	Nothing at all (%)	Low (%)	Neutral (%)	High (%)	Very high (%)
NS education is of limited usefulness of MS	36 (23.1%)	48 (30.8%)	52 (33.3%)	20 (12.8%)	0 (0.0%)
NS education increases MS preparation for other neurosci. subjects	1 (0.6%)	11 (7.1%)	28 (17.9%)	76 (48.7%)	40 (25.6%)
NS education increases MS preparation for other Non-neurosci. subjects	9 (5.8%)	28 (17.9%)	52 (33.3%)	53 (34.0%)	14 (9.0%)
NS education increases MS preparation for other surgical subjects	2 (1.3%)	11 (7.1%)	37 (23.7%)	72 (46.2%)	34 (21.8%)
NS is a potentially interesting career for a MS	12 (7.7%)	16 (10.3%)	27 (17.3%)	56 (35.9%)	45 (28.8%)

MS, Medical Student; NS, Neurosurgery; Neurosci., neuroscience.

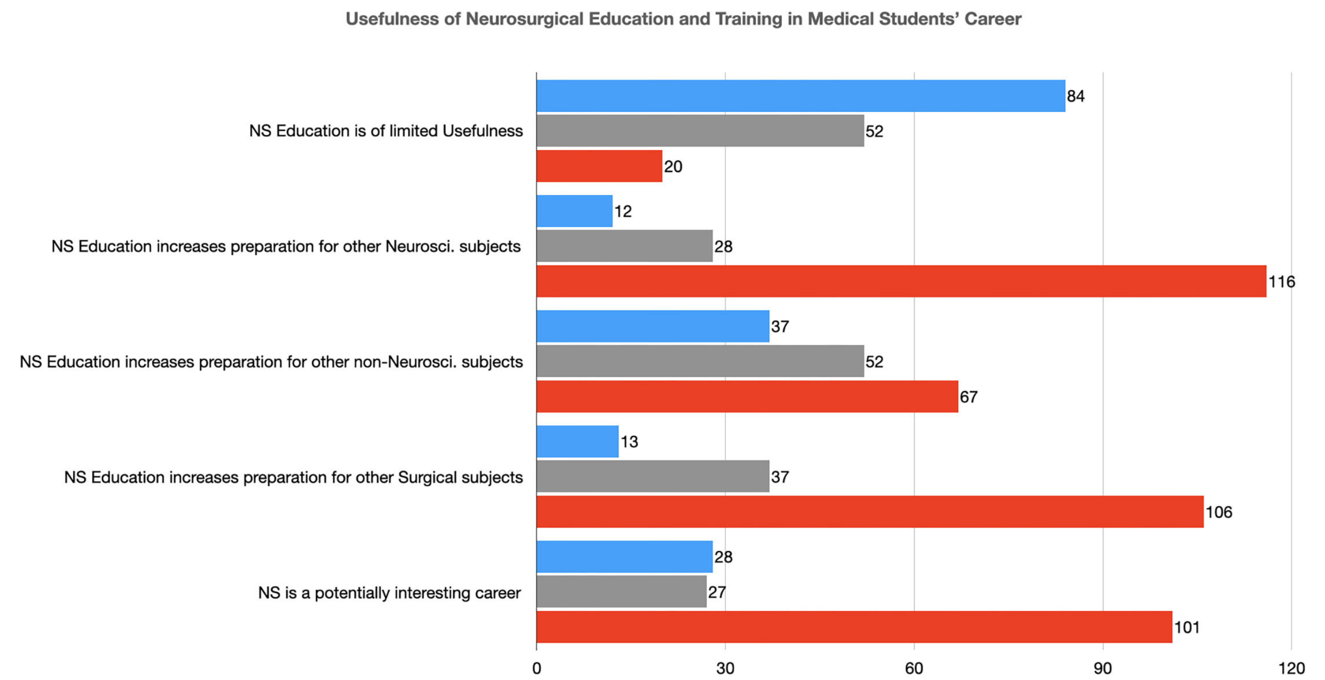

FIGURE 5 | The usefulness of Neurosurgical Education and Training in the Medical Students' Career (NS, Neurosurgery; Neurosci., Neuroscience).

studies (mostly from the USA and the UK, only a few from continental Europe, and a very low number from middle/low-income countries) have analyzed which characteristics of this subject are most commonly focused on by medical students (3–8). Particularly, DeZee et al. analyzed the impact of lifestyle on the conception of a medical specialty, observing that the main factor determining the low score of neurosurgery (the third worst, followed only by general surgery and obstetrics-gynecology) was the lack of a controllable lifestyle (according to the definition by Schwartz et al. i.e., the possibility by the physician to control the number of hours devoted to the specialty) (11). The long and emotionally draining training required to acquire sufficient self-confidence in managing neurosurgical patients, a possibly unfriendly or unwelcoming environment due to the high pressure on physicians and residents, and a gender gap, with a prominent male dominance in most neurosurgical centers have proven in the study by Balogun et al. to be the main features reducing the appeal of neurosurgery (6). A further factor to be considered in determining the perception of neurosurgery by medical students is neurophobia (12). It represents a well-documented phenomenon, firstly described by Jezefowicz as "the inability to productively integrate and thus properly understand and apply basic science and clinical knowledge of neuroscience and clinical neurology" coupled with the perception that clinical neurosciences are seldom curative (12). Because of neurophobia, neurosurgery is seen as an inaccessible subject, excessively complicated and it is associated with (often unmotivated) feelings of anxiety, dislike, and disinterest also when a potentially neurosurgical patient is visited in different clinical contexts, as in the emergency room or an internist ward (12).

TABLE 7 | Results of univariate statistical analysis.

	Age	Sex	Year of med. school	Interest in neurosci.	Interest in surg.	Attempted NS course	Time in NS unit/OR	Influence of media
Personal interest in NS	***p*: 0.02**	*p*: 0.86	***p* < 0.01**	***p* < 0.01**	***p* < 0.01**	*p*: 0.34	*p*: 0.20	*p*: 0.47
Relevance of NS in MS education	***p*: 0.02**	*p*: 0.66	***p* < 0.01**	***p* < 0.01**	***p* < 0.01**	*p*: 0.17	*p*: 0.37	*p*: 0.14
Involvement of all MS in NS education	*p*: 0.45	*p*: 0.11	***p*:0.04**	*p*: 0.15	*p*: 0.37	*p*: 0.12	*p*: 0.35	*p*: 0.79
Involvement of all MS in OR NS training	*p*: 0.90	*p*: 0.12	*p*: 0.22	*p*: 0.51	***p* < 0.01**	*p*: 0.09	*p*: 0.10	*p*: 0.39
Usefulness of NS as potential career	*p*: 0.26	*p*: 0.72	*p*: 0.08	***p* < 0.01**	***p* < 0.01**	*p*: 0.96	*p*: 0.18	*p*: 0.77

NS, Neurosurgery; MS, Medical study; OR, Operating room; med., medicine; neurosci., neuroscience; surg., surgery. Statistical significant results are in bold.

TABLE 8 | Results of multivariate statistical analysis.

	Odds ratio	Std. error	*Z*	*P* > [z]	95% Confidence interval	
Personal interest in neurosurgery						
Age	1.04	0.12	0.33	0.75	0.83	1.29
Year of medical school	**0.68**	**0.11**	**−2.29**	**0.02**	**0.49**	**0.95**
Interest in neurosci.	**12.89**	**6.65**	**4.96**	**<0.01**	**4.69**	**35.41**
Interest in surg.	**14.14**	**7.27**	**5.15**	**<0.01**	**5.16**	**38.75**
Relevance of neurosurgery as part of medical students education						
Age	0.89	0.11	−0.91	0.36	0.70	1.14
Year of medical school	0.78	0.13	−1.44	0.15	0.56	1.09
Interest in neurosci.	**5.18**	**2.33**	**3.66**	**<0.01**	**2.15**	**12.51**
Interest in surg.	**4.19**	**1.88**	**3.19**	**0.01**	**1.74**	**10.09**
Usefulness of neurosurgery as potential career						
Interest in neurosci.	**4.89**	**2.03**	**3.82**	**<0.01**	**2.17**	**11.05**
Interest in surg.	**7.71**	**3.21**	**4.91**	**<0.01**	**3.41**	**17.44**

neurosci., neuroscience; surg., surgery. Statistical significant results are in bold.

To tackle these deterrents, many educational strategies have been proposed, which have been summarized by Stumpo et al. in the triad: early exposure, research involvement, and mentoring (12). In our study, we have observed that 31.4% of students state that their interest in neurosurgery has grown over the years of medical school and that the neurosurgery course in the 4th year has increased this positive attitude. Also, other courses in similar subjects (such as neuroanatomy, neurophysiology, neuropathology, neuroradiology, neurology, and others), rotations or clerkships in other departments, or exposure to neurosurgery in other environments, such as international exchange programs (i.e., Erasmus program and others) could have turned on the curiosity and eventually the interest of students for neurosurgery. Interestingly, media (TV series, movies, news, etc.) showed no specific role in increasing the students' consideration or interest in this subject in our study. Conversely, it is relevant that attendance in Pre-clinical years (1st and 2nd) is associated with a greater interest in neurosurgery. This confirms the importance of exposure to this subject to tackle the possible deterrents and suggests also that this exposure should occur as early as possible, mainly to avoid the development of neurophobia (13, 14). Indeed, most basic science and Pre-clinical notions, essential for the comprehension of clinical neuroscientific principles, are illustrated in the first years of medical school. Then, due to the low number of teaching hours for neuroscientific subjects, they are not re-called anymore in the following semesters, which are mainly based on general medical and surgical subjects. This progressive feeling of remoteness and difficulty with basic neuroscientific principles can be at the base of the development of neurophobia. Therefore, early exposure to neurosurgery can fight this mechanism, keeping the interest toward this subject alive (13, 14). This can be confirmed also by our observation that students already interested in other disciplines in the field of neuroscience and surgical sciences, i.e., which have developed and kept alive a stronger familiarity with principles common also to neurosurgery, are more interested also in this subject.

In our study, we have observed that 74.4% of medical students consider that neurosurgical education can increase their preparation for other neuroscience subjects, 67.9% also for other surgical subjects, and, interestingly, a not negligible number of students (42.9%) state that it can improve their knowledge also for Non-neuroscience subjects. We think that these data can give us a further perspective to implement neurosurgical training. Even if its main aim is the development of a positive attitude toward this subject, which could permit the recruitment of the best, hardworking, scientifically brilliant students, it should also promote the dissemination of the knowledge of the basic principles of this discipline to "contaminate" the largest number of future physicians and to avoid that neurosurgery would be considered an isolated, self-referential subject with no multidisciplinary links (15). In order to achieve this secondary, but not less important, aim, our study suggests the relevance of demonstrating the importance of understanding neurosurgical principles for managing patients also in general environments, outside the traditional neurosurgical settings, such as emergency room, primary care, or others. In their study, Horan et al. observed that students would benefit greatly from lectures given by other specialists, who would demonstrate the practical role of neurosurgery in their daily work, confirming our suggestions (16).

Indeed, in our study neurosurgery teaching was considered relevant for undergraduates by 75.6% of participants, who were strongly convinced that it should be offered to all medical students, not only to a restricted group of interested ones. It is interesting to note that the value of neurosurgical education was perceived as more relevant by students in the last 2 years of medical school (when the clinical specialties are taught), confirming that its role is better appreciated when students are close to the end of medical school and are getting prepared to manage patients more autonomously. This confirms that this subject should be included in the core of curricular studies. However, it is debated in literature which the most effective method is to teach neurosurgery to undergraduates (17–21). In our study, students considered internships or clerkships in neurosurgical departments as the most effective teaching method (85.8%), to actively involve students in neurosurgical patients' management and decision-making process and to permit them to visit and see the largest number of patients possible. Participation in local or national/international meetings or seminars was considered an effective method also by 72.4%. The low rate of students who considered classroom lectures an optimal educational tool (17.9%), can be affected by a limited number of participants who already attended the neurosurgery course. These data are in line with current literature, which emphasizes that the teaching of a practical subject, such as neurosurgery, should be performed by combining both lectures (involving the use of modern technology to improve their interactive aspects, when possible) and internships (possibly in a protective environment, to avoid over-exposure of students, which could have a negative impact) (17–21). Interestingly, it has been recently assessed a positive impact in stimulating students' interest in neurosurgery on their involvement in specific scientific projects during medical school (10). However, these Authors demonstrated how this exposure failed in providing a full insight into this specialty, not permitting to entirely replace the combination of teachings and internships, which remains the gold standard in undergraduates' education (10). Learning by doing was appreciated by 67.3% of students this result can be an expression of their ambiguous feelings toward neurosurgery, requiring supervision or tuition to feel protected by the challenges of the field, as suggested by 52.6%, who positively evaluated the role of mentorship for learning this subject (22). The low number of students, in our study, who have performed an internship is an effect of the recent COVID-19 pandemic, which has strongly hampered the possibility of medical students attending neurosurgical department activities in the last 2 years. As a consequence, we have observed that 76.3% of students would benefit from online seminars and other educational events accessible remotely, which in our country have been promoted also by the Italian Society of Neurosurgery (SINch). Recent studies have analyzed these innovative instruments, proposing that they could have a positive impact, increasing students' knowledge and self-confidence in managing neurosurgical patients (23, 24).

In our study, the students' expectations about practical training to learn basic neurosurgical procedures were high. Not surprisingly, most of the students with this positive attitude were those already interested also in other surgical subjects (25). However, 71.2% of students consider participation in operating room sessions an effective way to approach neurosurgery. Possibly, new technologies would be helpful to achieve this goal, overcoming possible limitations due to the low number of students that could be present during a surgical procedure. Indeed, the large availability of neurosurgical videos on social media, YouTube channels, national scientific societies websites, but also of simulators and of exercises to improve manual skills with daily use objects (i.e., eggs, chicken wings, etc.) would permit a larger number of students to be exposed also to the most technical parts of the neurosurgical activities (23–25). However, we consider that such exposure requires to be guided and commented on by a mentor, to avoid the risk that students would wrongly consider the challenges of this surgery (22).

The limits of this study are the relatively low number of students who have responded to the survey. As a consequence, the participants' sample could be not fully representative of the entire medical student cohort, and results could be possibly biased by the fact that only the most interested students would have participated. Moreover, the low number of students who have attended to the neurosurgery course has prevented the possibility of fully analyzing its role in undergraduate training and education. A further limitation is that the study is monocentric and it gives a description only of the situation at the University of Bologna, possibly not representing the entire national or international context. Finally, all reported results are subjective and self-reported, without the possibility to have an objective control.

CONCLUSIONS

In our context, neurosurgery has been considered by medical students as an interesting subject with a good possibility for a future career, and they believe that its training and education should include all undergraduates. However, it was also felt intimidating and hardly approachable. Despite its limitation, our study confirms that a combination of both lectures and internships (possibly in a protective environment, to avoid students' over-exposure) are still considered the most effective way to learn neurosurgery and tackle the deterrents that prevent undergraduates from approaching this subject.

We suggest that demonstration of the usefulness of neurosurgical knowledge in general medical settings and not only in the field of neuroscience can be useful to promote students' interest toward this subject.

New technologies, such as interactive software, virtual reality tools, dedicated web channels, social media pages, webinars, and online educational events, which have largely developed in the last years, can be become even more relevant in the future to spread the neurosurgical education as much as possible to all medical students.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

MZ: study design and draft preparation. CZ: data analyses. GB, AnC, EF, GL, MM, and GP: data collection. AS: draft preparation. AlC and DM: study supervision and manuscript revision. All authors contributed to the article and approved the submitted version.

FUNDING

The manuscript published fee has been covered thanks to Fondo Ricerca Corrente, found by IRCCS Istituto delle Scienze Neurologiche di Bologna, Italy.

ACKNOWLEDGMENTS

We thank all Medical Students of University of Bologna, Italy who participated to the survey. Although it was completely, the following accepted to leave on separate file their names to be listed in this acknowledgment list: Sara Alban, Kamia Ashouri, Alessandro Bacchiocchi, Alessandro Benini, Francesco Pio Bettoni, Alessio Bianchi, Alessia Bonfissuto, Giulia Bonini, Irene Bosi, Andrea Carà, Paolo Checcaglini, Francesca Ciritella, Alberto Dalsass, Emily Degiovanni, Fabio Desimoni, Elif Hesna Erim, Sara Fusco, Giulia Galletto, Federica Giofrè, Alice Gori, Hakim, Mersedeh, Laura Iangone, Ehsan Keshtkar, Efstratios Kinalis, Laura Lenzi, Anna Giulia Longanesi, Chiara Longo, Manuel Lucchin, Chiara Marchesini, Sofia Marfoq, Paride Melli, Fernando Henrique Mizuno, Mario Mouratai, P. Nefeli, Alessia Pasella, Lorenzo Perrone, Thiago Piffanelli, Matteo Piovaccari, Matteo Pironi, Alessandro Pisani, Federica Prodi, Caterina Ragazzi, Angelo Semeraro, Nicolò Sensi, Usama Sikandar, Luna Sissa, Camillo Tancredi Strizzi, Leticia Sueiro, Elisa Suzzi, Wasim Tayeb, Alam Maisha Tesnova, Lia Torre, and Arianna Vignaroli. We thank Dr. Cecilia Baroncini (IRCCS Istituto delle Scienze Neurologiche di Bologna, Italy) for her English revision of the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2022.882063/full#supplementary-material

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The handling editor CZ declared a past co-authorship with the authors MZ and DM.

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ORIGINAL RESEARCH
published: 19 May 2022
doi: 10.3389/fsurg.2022.862948

Virtual-Augmented Reality and Life-Like Neurosurgical Simulator for Training: First Evaluation of a Hands-On Experience for Residents

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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: 26 January 2022
Accepted: 04 April 2022
Published: 19 May 2022

Citation:
Petrone S, Cofano F, Nicolosi F, Spena G, Moschino M, Di Perna G, Lavorato A, Lanotte MM and Garbossa D (2022) Virtual-Augmented Reality and Life-Like Neurosurgical Simulator for Training: First Evaluation of a Hands-On Experience for Residents. Front. Surg. 9:862948. doi: 10.3389/fsurg.2022.862948

Background: In the recent years, growing interest in simulation-based surgical education has led to various practical alternatives for medical training. More recently, courses based on virtual reality (VR) and three-dimensional (3D)-printed models are available. In this paper, a hybrid (virtual and physical) neurosurgical simulator has been validated, equipped with augmented reality (AR) capabilities that can be used repeatedly to increase familiarity and improve the technical skills in human brain anatomy and neurosurgical approaches.

Methods: The neurosurgical simulator used in this study (UpSurgeOn Box, UpSurgeOn Srl, Assago, Milan) combines a virtual component and a physical component with an intermediate step to provide a hybrid solution. A first reported and evaluated practical experience on the anatomical 3D-printed model has been conducted with a total of 30 residents in neurosurgery. The residents had the possibility to choose a specific approach, focus on the correct patient positioning, and go over the chosen approach step-by-step, interacting with the model through AR application. Next, each practical surgical step on the 3D model was timed and qualitatively evaluated by 3 senior neurosurgeons. Quality and usability-grade surveys were filled out by participants.

Results: More than 89% of the residents assessed that the application and the AR simulator were very helpful in improving the orientation skills during neurosurgical approaches. Indeed, 89.3% of participants found brain and skull anatomy highly realistic during their tasks. Moreover, workshop exercises were considered useful in increasing the competency and technical skills required in the operating room by 85.8 and 84.7% of residents, respectively. Data collected confirmed that the anatomical model and its application were intuitive, well-integrated, and easy to use.

Conclusion: The hybrid AR and 3D-printed neurosurgical simulator could be a valid tool for neurosurgical training, capable of enhancing personal technical skills and competence. In addition, it could be easy to imagine how patient safety would increase and healthcare costs would be reduced, even if more studies are needed to investigate these aspects. The integration of simulators for training in neurosurgery as preparatory steps for the operating room should be recommended and further investigated given their huge potential.

Keywords: simulator, training, virtual reality, life-like actuation, brain, neurosurgery, residents

INTRODUCTION

In recent years, growing interest in simulation-based surgical education has led to various practical alternatives for medical training (1). Factors such as the cost-effectiveness of the operating room, medico-legal and ethics implications, the actual restrictions for residents in terms of hours spent on work-related activities, and reduced time availability for surgical instruction during surgical activities are the elements most likely connected with a reduction in operative case volume during residency (2). After recent changes in disease management and technological advances, especially for surgical subspecializations, a growing attention has been paid to patient safety during surgical care, keeping back residents from the operating rooms while redirecting them into more administrative mansions (3).

On the other hand, up to 50,000 additional neurosurgeons are estimated worldwide to face the critically growing needs in surgical care (4). A net discrepancy between the need for new experienced neurosurgeons and their actual surgical experience is coming to light over time.

Traditionally, practical solutions for surgical training implementation include cadaveric and animal models and abroad fellowships (2, 3). However, some drawbacks and limitations must be taken into account. Neurosurgical anatomy is highly specific for human brain and does not compare well with animal specimens. Moreover, the management of cadaveric models entails ethical concerns and high maintenance costs, as well as specific and highly equipped structures for their preservation. In all these cases, practical training on these models allows only a partial anatomical practice, excluding the pathologic aspects of neurosurgical experience.

Nowadays, international training for surgical residents is considered desirable for a complete neurosurgical education in this particular medical field (5). Unfortunately, after the COVID-19 pandemic outbreak, surgical activities and international exchange programs have been dramatically reduced (6–8).

To counter the lack of surgical exposure, more recently, courses based on virtual reality (VR) and three-dimensional (3D)-printed models are available (2, 3). In particular, we validated a hybrid (virtual and physical) neurosurgical simulator equipped with augmented reality (AR) capabilities that can be used repeatedly to increase familiarity and improve technical skills in human brain anatomy and neurosurgical approaches.

MATERIALS AND METHODS

The neurosurgical simulator used in this study (UpSurgeOn Box, UpSurgeOn Srl, Assago, Milan) combines a virtual and a physical component with an intermediate step to provide a hybrid solution. The virtual part is based on an application which allows for the interactive exploration of 3D anatomical models and animations, both in a purely virtual environment and in an AR projection of the physical simulator (hybrid). These tools are designed to be integrated into a 3-step training sequence: mental training (based on a virtual environment), hybrid training (based on virtual models projected onto the physical simulator through a mobile device), and manual training (based on the physical simulator).

Virtual Reality

Through the "Neurosurgery" mobile application, it is possible to explore the different surgical approaches using a smartphone or tablet.

A total of 9 surgical approaches (pterional, mini pterional, frontal monolateral, supraorbital, temporal, mini temporal, retrosigmoid, mini retrosigmoid, interhemispheric, and suboccipital) and 2 pathological modules for brain aneurysms and pituitary adenomas are available. Each virtual exploration uses 3D anatomical models and animations to support a Mental Training system aimed at understanding a patient's positioning according to a specific craniotomy and a specific intradural target.

The study of each approach in 3D mode is divided into 6 phases (**Figures 1A–D**) as follows:

1. Craniotomy selection: One can select among pterional, mini pterional, frontal monolateral, supraorbital, temporal, mini temporal, retrosigmoid, mini retrosigmoid, interhemispheric, and suboccipital approach.
2. Target selection: One can select specific anatomical (non-pathological) structures visible from the craniotomy previously selected.
3. Patient positioning: An artificial intelligence (AI)-based system calculates in real time a range of correct patient's body/head positionings according to the craniotomy and the target selected.
4. Surgical approach: This step involves an interactive 3D animation of the surgical steps of the approach.
5. Microsurgical exploration: This step simulates the microscope view using the gyroscopic technology of the hardware. Furthermore, tissues can be deformed by tapping the screen to expose the deep anatomy.
6. Closure: An interactive step that explains, through an animation, the reconstruction technique.

Augmented Reality

The application software presents a module dedicated to the use of AR able to project 3D anatomical models and animations on

FIGURE 1 | (A–E) Training steps. **(A)** Training laboratory set up; **(B)** suturing exercise; **(C)** augmented reality (AR) for craniotomy and approach planning; **(D)** dura opening on the pterional approach simulator box; **(C)** microscopic intradural phase through pterional approach with gentle brain retraction; **(E,F)** microscopic exploration and dissection through pterional approach of the carotid artery, optic nerve, and sylvian vessels.

the physical simulator, acting as a guide to plan the hands-on surgical approach (**Figure 2**).

This phase, defined by the term "Hybrid Training," includes:

1. Patient positioning in AR: using AR it is possible to view the patient's entire skull on the simulator and modify the position of the head on the three axis. The AR system also allows to view the position of the target on the screen, before visualizing it on the physical simulator.
2. Craniotomy planning in AR: the Application projects on the physical skull several possible craniotomies.
3. Surgical steps in AR: the software reproduces the surgical approach step by step to understand which tasks will be carried out on the physical model.

Physical Simulator

The simulator is designed to reproduce different surgical approaches (pterional, temporal, retrosigmoid, interhemispheric, suboccipital, and transsphenoidal) and different patient positions *via* a semi-spheric support. Through interchangeable skulls, one can perform multiple craniotomies and dural openings using the same deep microanatomical scenario, which can be explored

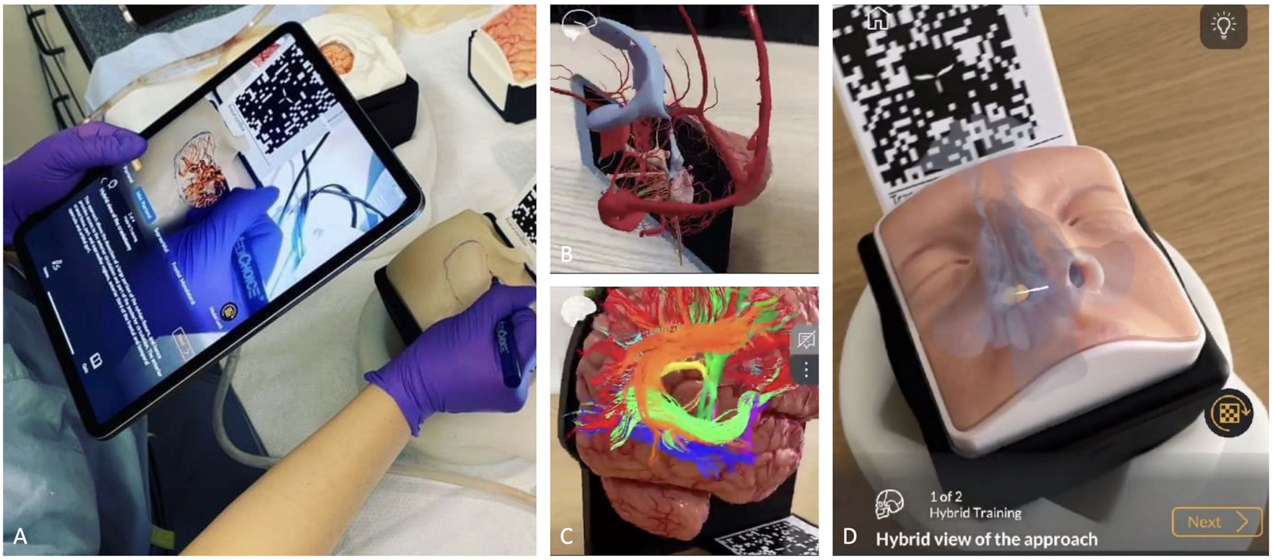

FIGURE 2 | (A-D) The role of AR and the hybrid simulation. **(A)** AR of a pterional approach. Before performing the craniotomy, it is possible to see the vessels and the brain under the skull by framing the specific QR code through tablet and/or smartphone app; **(B)** brain parenchyma has been hidden to allow better evaluation of dural venous system and ventricular system; **(C)** AR used to better evaluate white matter fiber anatomy; **(D)** application of AR in endoscopic endonasal approach allows to identify anatomical landmarks before entering the nose.

FIGURE 3 | Workstation set up with microscope and simulator.

under the microscope/exoscope/endoscope once the skull and dura are opened (**Figures 1E,F**, **3**).

Once the craniotomy has been performed, it is then possible to replace the skull and start again.

Data Collection

The first reported and evaluated practical experience on the anatomical 3D-printed model was conducted at the Department of Neuroscience "Rita Levi Montalcini" in Turin, Italy.

A total of 30 neurosurgery residents were involved. The first phase of the workshop consisted in using the AR application. The residents had the possibility to choose a specific approach (pterional, subtemporal, retrosigmoid), to focus on the correct patient positioning, and to go over the chosen approach step-by-step by interacting with the model through AR application.

Next, each practical surgical step on the 3D model was timed and qualitatively evaluated by 3 senior neurosurgeons. The training comprehended 4 standardized surgical moments: craniotomy, opening of the dura mater, reaching the pre-assigned target, and closing of the dura mater. Surgical loupes and a surgical microscope were available. For the pterional approach, optic nerve, middle cerebral artery (MCA), and III cranial nerve were identified as the principal targets of interest. Similarly, the IV cranial nerve and posterior cerebral artery (PCA) were chosen for the subtemporal approach, while VII-VIII, V cranial nerves, and superior cerebral artery (SCA) were identified for the retrosigmoid approach.

At the end of the workshop, quality and usability-grade surveys were filled out by participants. The second questionnaire was a modified version of the System Usability Scale (9). Each answer was graded by a 5-point scale (Likert score) (10). Incomplete questionnaires were excluded, and a total of 28 forms were considered for the assessment.

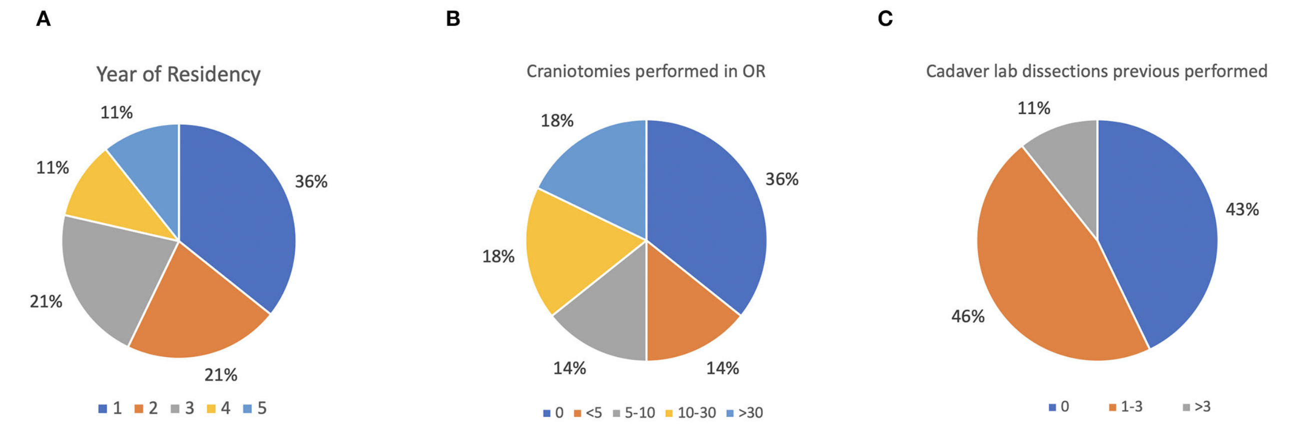

FIGURE 4 | (A–C) Baseline assessment of the audience. **(A)** Stratification by year of neurosurgery residents; **(B)** assessment of performed craniotomies; **(C)** assessment of attended cadaver labs.

TABLE 1 | Survey results about teaching effectiveness and quality of the model.

Survey #1 item	Strongly disagree (1)	Disagree (2)	Neutral (3)	Agree (4)	Strongly agree (5)
The Application and the AR simulator help to develop the orientation skills needed during neurosurgical approach	0.0	3.6	7.1	28.6	60.7
The BrainBox had appropriate surface anatomy	0.0	0.0	10.7	39.3	50.0
Neurovascular structures and skull base anatomy were realistic and appropriately detailed for surgical orientation	0.0	0.0	3.6	64.3	32.1
The tactile feedback and response on manipulation was realistic	0.0	3.7	44.4	37.0	14.8
Skills to handle the craniotomies and dissection instruments were representative of those required to perform the real procedure	0.0	0.0	15.4	38.5	46.2
The drilling experience is similar to the real skull	0.0	3.6	7.1	46.4	42.9
Dural opening and suturing was realistic	3.7	14.8	40.7	22.2	18.5
Using this model helps to increase competency when applied to neurosurgical training	0.0	0.0	14.3	17.9	67.9
I feel more confident using neurosurgical instruments after training with this model	0.0	0.0	21.4	35.7	42.9
Using this model can facilitate the process of using the surgical microscope	0.0	0.0	7.1	25.0	67.9
The study of the surgical approach and surgical anatomy in a virtual way (App) passing through augmented reality and then the BrainBox is an effective method of learning	0.0	0.0	3.6	39.3	57.1
This model of training should be part of a standard curriculum	0.0	0.0	14.3	25.0	60.7

RESULTS

Descriptive results regarding stratifications by year of neurosurgery residents who participated in the surveys are reported in **Figure 4A**. In addition, the number of craniotomies and the number of previous cadaveric labs performed were assessed to define the experience level of the audience (**Figures 4B,C**). The results of the survey about teaching effectiveness and quality model are summarized in **Table 1**. More than 89% (agree and strongly agree) of the residents assessed that the application and the AR simulator were very helpful in improving the orientation skills during neurosurgical approaches. Indeed, 89.3% of the participants found brain and skull anatomy highly realistic during their tasks. Moreover, workshop exercises were considered useful in increasing the competency and technical skills required in operating room, by 85.8 and 84.7% of residents, respectively.

On the other side, tactile feedback of the brain tissue and dura mater consistency were found as relative weaknesses of anatomical models with a mean score of 3 points (neutral). In particular, the most critical issue found was the lower elasticity and higher hardness and tension of the anatomical model compared to normal parenchyma.

Interestingly, when the residents were asked, 85.7% agreed with the possibility to include this kind of training into a standard surgical training for neurosurgeons (4 and 5 scores).

Data collected with the second survey confirmed that the anatomical model and its application were intuitive, well integrated, and easy to use. The results of grade of usability questionnaire about anatomy models are summarized in **Table 2**.

Moreover, although the aim of the study was not a quantitative analysis, data regarding length of exercises and performance qualitative evaluation are reported in **Tables 3**, **4**. Results showed that residents attending the last 2 years of residency performed the various skills quicker and with higher quality than younger residents. However, no significant comparisons or analysis could be made on these data because of the heterogeneity of surgical approach among different groups of residents.

DISCUSSION

Neurosurgery residency is characterized by high levels of competence and an intense hands-on experience. Due to monetary restrictions, infrastructure conditions, and recent work time restrictions (11), it is hard for a resident to reach an adequate operative case volume over the education program (3). To counter these drawbacks in neurosurgical training, cadaveric specimen (12) and animal model courses (13) are some of the common alternatives for the improvement of surgical skills in neurosurgery, even if their high maintenance costs and ethical issues represent some of the principal limitations to date (14). Some abroad experiences or post-graduate surgical courses are still valid options, but recently, after the COVID-19 pandemic, international exchange programs have been dramatically reduced (6, 7). Also, learning new surgical skills is different from perfecting them, which implies that they have to be repeated with constancy over time (15). The neurosurgical learning curve is still too long and dominated by conventional mentor–apprentice relationships (16).

In this scenario, neurosurgical simulators are becoming increasingly important. Among the modern surgical training solutions, interest in VR or AR and 3D models has been growing (16, 17). Our experience with hybrid AR and 3D-printed neurosurgical simulator showed that the combination of such learning methods could lead to interesting results. Specifically, hybrid AR represents a helpful tool to guide young neurosurgeons from notional knowledge to practical experience. Indeed, after an anatomical revise, residents can focus on the correct patient positioning and go over the chosen approach step-by-step by interacting with the model through AR application. In the second phase of the simulation, high detailed 3D-printed neurosurgical models allow trainees to obtain immediate feedback of the previous theoretical topics.

Winkler-Schwartz et al. (18) have already described 17 students' and residents' training experience with a VR simulator. Their results suggest the possibility to categorize participants'

TABLE 2 | Evaluation of the anatomical model through the System Usability Scale.

Survey #2 item	Strongly disagree (1)	Disagree (2)	Neutral (3)	Agree (4)	Strongly agree (5)
I think that I would like to use UpSurgeOn box frequently	0.0	0.0	14.3	42.9	42.9
I found UpSurgeOn box unnecessarily complex	35.7	50.0	7.1	7.1	0.0
I thought UpSurgeOn Box was easy to use	0.0	0.0	14.3	28.6	57.1
I think that I would need the support of a technical person to be able to use UpSurgeOn box	35.7	21.4	35.7	0.0	7.1
I found the various functions in UpSurgeOn box were well integrated	0.0	0.0	10.7	46.4	42.9
I found consistency between the functions of the UpSurgeOn box	0.0	0.0	0.0	28.6	71.4
I found the UpSurgeOn box very intuitive to use	0.0	0.0	14.3	32.1	53.6
I would imagine that most people would learn to use UpSuregOn box very quickly	0.0	0.0	0.0	14.3	85.7
I felt very confident using UpSurgeOn box	0.0	0.0	14.3	35.7	50.0
I needed to learn few things before I could get going with UpSurgeOn box	0.0	0.0	0.0	28.6	71.4

TABLE 3 | Descriptive results regarding time, procedures, and quality of exercises.

Residency Y	Approach	Time (Min:Sec)	Quality (1–5)
Craniotomy			
1	Retrosigmoid	14:43	2
1	Retrosigmoid	13:10	2
1	Subtemporal	12:20	3
1	Pterional	16:45	3
2	Pterional	11:12	2
2	Subtemporal	15:10	3
2	Pterional	10:40	3
2	Subtemporal	08:20	4
2	Pterional	09:50	4
3	Pterional	08:38	4
3	Pterional	07:12	3
3	Retrosigmoid	06:24	4
4	Subtemporal	09:30	4
5	Retrosigmoid	05:34	5
5	Pterional	03:10	4
Dural opening and suspension			
1	Retrosigmoid	15:30	2
1	Retrosigmoid	12:45	1
1	Subtemporal	19:35	1
1	Pterional	23:45	2
2	Pterional	18:40	2
2	Subtemporal	14:20	3
2	Subtemporal	16:45	2
2	Pterional	17:10	3
2	Pterional	13:00	3
3	Pterional	09:20	3
3	Pterional	06:40	2
3	Retrosigmoid	05:50	4
4	Subtemporal	06:35	4
5	Retrosigmoid	04:00	4
5	Pterional	04:30	5
Microscopic target			
1	Retrosigmoid	09:40	1
1	Subtemporal	07:20	1
1	Retrosigmoid	08:30	2
1	Pterional	06:40	2
2	Pterional	11:10	2
2	Pterional	09:10	3
2	Subtemporal	06:10	2
2	Subtemporal	05:40	2
2	Pterional	08:30	3
3	Pterional	08:10	3
3	Retrosigmoid	06:05	4
3	Pterional	05:25	4
4	Subtemporal	02:40	4
5	Retrosigmoid	02:50	5
5	Pterional	02:20	4
Dural closure			
1	Pterional	16:50	1

(Continued)

TABLE 3 | Continued

Residency Y	Approach	Time (Min:Sec)	Quality (1–5)
1	Subtemporal	13:15	3
1	Retrosigmoid	15:10	2
1	Retrosigmoid	15:40	3
2	Subtemporal	10:35	3
2	Pterional	11:35	4
2	Pterional	12:10	3
2	Pterional	11:25	3
2	Subtemporal	10:40	2
3	Pterional	09:10	5
3	Retrosigmoid	07:50	4
3	Pterional	10:15	3
4	Subtemporal	05:20	5
5	Retrosigmoid	04:20	5
5	Pterional	05:40	5

TABLE 4 | Descriptive results stratified by year of residency.

Resident Y	Average time	Quality
Craniotomy		
1	14:14	2.50
2	11:02	3.20
3	07:24	3.67
4	09:30	4.00
5	04:22	4.50
Dural opening		
1	23:53	1.5
2	15:59	2.6
3	07:16	3
4	06:35	4
5	04:15	4.5
Microscopic target		
1	08:02	1,5
2	08:08	2,4
3	06:33	3,67
4	02:40	4
5	02:35	4,5
Dural closure		
1	15:13	2.25
2	11:17	3
3	09:05	4
4	05:20	5
5	05:00	5

technical abilities and use this tool to develop and maintain psychomotor skills. Licci et al. (2) developed a synthetic simulator based on patient-specific computed tomography (CT) data set, and different realistic skull models were produced by a 3D printer, including vascular structures and some soft tissue portions mimicking ventricle tumors. Neurosurgical trainees were invited to a neuroendoscopic workshop and qualitatively assessed afterwards. They found that this training empowered the development of specific surgical skills.

Joseph et al. (19) developed and used a physical simulator that was able to reproduce the experience of clipping intracranial aneurysms based on 3D-printed models of skull, brain, and arteries. They judged this simulator as a reliable and useful tool for neurosurgical training.

Chawla et al. recently reported a systematic review addressing 4 major neurosurgical skills using various modalities of training, assessed by face, content, and construct validity. An increased use of simulation models in neurosurgical training was found. Currently, synthetic models have been found to be the most convenient and practical, especially during the pandemic breakdown, but VR models are found promising due to the visual realism and improved haptic feedback technology (20).

The topic of burnout among neurosurgery residents is widely covered in scientific literature (21, 22). Training outside the operating room provides the possibility of practical education based on constructive criticism in a stress-free field. Surgical simulation allows the residents to perform a constant self-assessment of their growth from a technical and cognitive point of view. Personal growth and intellectual reward could be a real solution for the burnout issue. Furthermore, the repetitive use of a 3D model associated with AR would allow to standardize the surgical act in the different years of residency. More than 85% of residents agree or strongly agree (**Table 1**) to make this kind of simulation a part of the standard curriculum in neurosurgery. Our next target will be to create a surgical portfolio based on hybrid simulation to complete before joining the procedure in the operating room.

The 3D anatomic model allows to recreate even complex pathological conditions such as tumors and cerebral aneurysm. Indeed, senior residents were asked to perform an extra trial: clipping exercise on few 3D models enhanced with saccular aneurysm of middle cerebral artery (MCA), anterior communicating artery (ACoA) and posterior communicating artery (PCoA). This is certainly an important strength of the simulator that human or animal cadaveric specimens cannot provide. It is conceivable that it will be possible to perform the same procedure several times on the same patient in a simulated way before arriving at the day of the planned surgery.

On the other side, the texture and tactile feedback of the brain tissue and dura mater can still be improved. These characteristics were assessed with a mediocre scores in about 40% of the responses (3 out of 5 points). Furthermore, the arachnoid and the cisterns, which constitute some of the anatomical references for the surgery of the skull base, are not represented. These are the current limits of the tool.

The hybrid simulation with AR and 3D model represents a constant, modular, and repeatable training tool, while the surgeon will be the only variable. This new way of learning could change the old rules of knowledge transmission in neurosurgery centered on the mentor–apprentice relationship.

Limitations

The main limitation of this study is its purely qualitative nature and lack of quantitative analysis. However, as reported in the method section, this study was a preliminary experience with this new hybrid simulation, and the purpose of the study was primarily to assess the usability and liking of the tool. Therefore, despite its qualitative nature, the encouraging results that emerged from the survey could be considered a driving force for further quantitative studies aimed at analyzing the actual possibility of improving the learning curve of residents outside the operating room, using a reproducible and less expensive tool. To this end, the authors are developing a standardized 1-year surgical training program, tailored to the needs of different residency years, in which the residents' skills are assessed with quantitative scales in order to evaluate their growth curve.

CONCLUSION

The hybrid AR and 3D-printed neurosurgical simulator could be a valid tool for neurosurgical training, which is capable of enhancing the technical skills and competence of the residents. In addition, it could be easy to imagine how patient safety would increase and healthcare costs would be reduced, even if more studies are needed to investigate these aspects. The integration of simulators for training in neurosurgery as preparatory steps for the operating room should be recommended and further investigated given their huge potential.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

SP: writing draft. FC: editing and writing. FN: conceptualization and reviewing. GS: conceptualization and supervision. MM: conceptualization and data collection. GD: editing and data collection. AL: data collection. ML and DG: supervision and reviewing. All authors contributed to the article and approved the submitted version.

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Conflict of Interest: FN is Founder and CEO of UpSurgeOn. GS is Co-founder of UpSurgeOn. MM is Lead Bioengineer at UpSurgeOn.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The handling editor declared a past co-authorship with several of the authors FC and DG.

frontiers | Frontiers in Surgery

ORIGINAL RESEARCH
published: 06 June 2022
doi: 10.3389/fsurg.2022.920252

Comparative Learning Curves of Microscope Versus Exoscope: A Preclinical Randomized Crossover Noninferiority Study

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OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

Received: *14 April 2022*
Accepted: *12 May 2022*
Published: *06 June 2022*

Citation:
Layard Horsfall H, Mao Z, Koh CH, Khan DZ, Muirhead W, Stoyanov D and Marcus HJ (2022) Comparative Learning Curves of Microscope Versus Exoscope: A Preclinical Randomized Crossover Noninferiority Study. Front. Surg. 9:920252. doi: 10.3389/fsurg.2022.920252

Background: An exoscope heralds a new era of optics in surgery. However, there is limited quantitative evidence describing and comparing the learning curve.

Objectives: This study aimed to investigate the learning curve, plateau, and rate of novice surgeons using an Olympus ORBEYE exoscope compared to an operating microscope (Carl Zeiss OPMI PENTERO or KINEVO 900).

Methods: A preclinical, randomized, crossover, noninferiority trial assessed the performance of seventeen novice and seven expert surgeons completing the microsurgical grape dissection task "Star's the limit." A standardized star was drawn on a grape using a stencil with a 5 mm edge length. Participants cut the star and peeled the star-shaped skin off the grape with microscissors and forceps while minimizing damage to the grape flesh. Participants repeated the task 20 times consecutively for each optical device. Learning was assessed using model functions such as the Weibull function, and the cognitive workload was assessed with the NASA Task Load Index (NASA-TLX).

Results: Seventeen novice (male:female 12:5; median years of training 0.4 [0–2.8 years]) and six expert (male:female 4:2; median years of training 10 [8.9–24 years]) surgeons were recruited. "Star's the limit" was validated using a performance score that gave a threshold of expert performance of 70 (0–100). The learning rate (ORBEYE -0.94 ± 0.37; microscope -1.30 ± 0.46) and learning plateau (ORBEYE 64.89 ± 8.81; microscope 65.93 ± 9.44) of the ORBEYE were significantly noninferior compared to those of the microscope group ($p = 0.009$; $p = 0.027$, respectively). The cognitive workload on NASA-TLX was higher for the ORBEYE. Novices preferred the freedom of movement and ergonomics of the ORBEYE but preferred the visualization of the microscope.

Conclusions: This is the first study to quantify the ORBEYE learning curve and the first randomized controlled trial to compare the ORBEYE learning curve to that of the microscope. The plateau performance and learning rate of the ORBEYE are significantly noninferior to those of the microscope in a preclinical grape dissection task. This study also supports the ergonomics of the ORBEYE as reported in preliminary observational studies and highlights visualization as a focus for further development.

Keywords: microscope, exoscope, neurosurgery, learning curve, innovation, education, surgery

INTRODUCTION

The operating microscope pioneered in the 1950s by Yasagil (1) remains the gold standard for microneurosurgery. More recently, an "exoscope" system has been introduced as a potential alternative to the microscope (2). Suggested benefits of an exoscope include improved ergonomics and being a valuable educational tool (2–5). A newly developed exoscope is an ORBEYE (Olympus, Tokyo, Japan, 2017), equipped with 3D optics, 4 K imaging quality, and comparable field of view and depth of field to those of the microscope.

The safe introduction of novel technology into clinical practice is central to reducing patient harm (6, 7). Surgeons gain procedural competence as their experience increases with a device (8, 9). This relationship between learning effort and the outcome can be represented using learning curves (10, 11). Factors that affect the learning curve are the initial skill level, the learning rate, and the final skill level achieved—known as the learning plateau (10, 12, 13). Understanding learning curves, both at individual and system levels, is crucial for assessing a new surgical technique or technology, informing surgical training, and evaluating procedures in practice (14, 15). Previous comparative studies suggest the presence of a learning curve for experienced surgeons with the ORBEYE, but there has been no attempt at quantification of the learning curve nor a direct comparison of the learning curve for both the microscope and ORBEYE in relation to novice surgeons (5, 16–18).

We explored the learning rate, learning plateau, and cognitive load of novice surgeons performing a validated microsurgical grape dissection task.

We performed a microsurgical grape dissection task to explore the learning rate, learning plateau, and cognitive load of novice surgeons with limited experience of both the microscope and OREYE; the learning curve of the ORBEYE is not inferior to that of the traditional microscope.

METHODS

Protocol and Ethics

The protocol was registered with the local Clinical Governance Committee and was approved by the Institutional Review Board. The Consolidated Standards of Reporting Trials Statement (19) (CONSORT) with noninferiority extension was used.

Participants

Novice and expert surgeons were recruited from a university hospital. Novice surgeons had not performed any operative cases on either the microscope or the ORBEYE. Expert surgeons had completed their neurosurgical training (20, 21). Informed written consent was obtained.

Sample Size

A target sample size of 12 novices was set. Owing to pragmatic constraints and the lack of applicable pilot data, no power calculation was undertaken, but such a number was deemed appropriate based on previous similar studies (20–23).

Randomization

Novice surgeons were randomly allocated to start on either optical device before crossing over. Permuted blocked randomization (block size 2 and 4) using a computer-generated sequence. One author (ZM) performed sequence generation and implementation. Blinding was not possible due to the nature of optical devices.

Interventions

Microsurgical Grape Dissection Task: "Star's the Limit"

Participants performed a validated microsurgical task "Star's the limit" (24). A standardized star is drawn on a grape using a stencil with a 5 mm edge length. Participants cut the star and peeled the star-shaped skin off the grape with microscissors and forceps while minimizing damage to the grape flesh (**Figure 1**). Each novice repeated the task 20 times consecutively before changing the device and repeating the

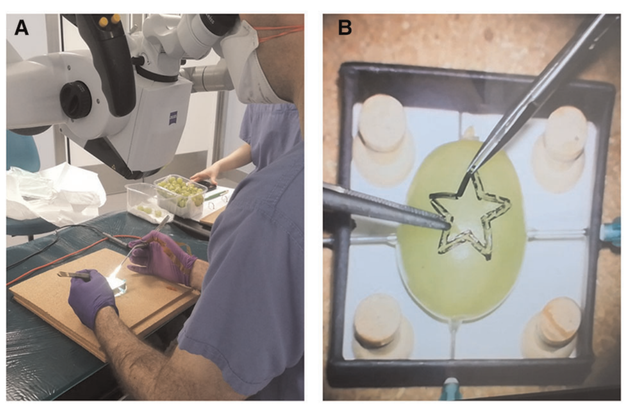

FIGURE 1 | Microsurgical grape dissection task "Star's the limit" setup. (**A**) Microscope trial. (**B**) "Star's the limit." Note the grape has a homogeneous shape, drawn on by stencil, and secured using needles to ensure constant position across the trials.

task a further 20 times consecutively. The microsurgical task was validated by experts who repeated the task 20 times consecutively using the microscope only. No feedback or teaching was provided to the participants during the task. If participants were not able to finish within 5 min, they were told to stop, and the next repetition would begin. The microscopes used were an OPMI PENTERO or a KINEVO 900 (Carl Zeiss Co, Oberkochen, Germany).

Outcomes

Primary Outcomes: Learning Plateau, Learning Rate, and Learning Curves

The performance of participants in the task was assessed using a five-item rubric: (1) time to completion; (2) completeness of dissection; (3) degree of grape flesh attached to the star; (4) number of edges incised within the drawn lines; and (5) perforation of grape flesh with the instruments (**Table 1**). The same assessor (ZM) prepared all 820 grapes and assessed all 17 novice and 7 expert surgeons to reduce scoring intravariability. The raw scores were combined into a composite performance score for each repetition. There was a modification to the performance score algorithm from the original protocol (OpenEd@UCL repository; https://open-education-repository.ucl.ac.uk//620/). The performance score was calculated as follows:

$$\text{Performance score} = 90 - 0.3 \times (\textit{Time taken}) + 0.5 \times \textit{Edge score}$$

Numerous different learning curve models were tested (**Appendix 1**). The best-fitting curve was selected using log-likelihood. All curves tested are characterized by the rate of improvement decreasing over time (**Appendix 1**). The curves were fitted with nonlinear mixed-effects models. Fixed effects were used to

1. investigate the difference between the microscope and ORBEYE and
2. establish the coefficients of the curves.

Random effects were used to account for

1. nonindependence of the data from the same subject and
2. random variations in coefficients between subjects.

The fixed effects of the model output gave the curves averaged across each group. These fixed-effects outputs were used to test the noninferiority of the asymptote and the learning rates of the ORBEYE group compared to thosed of the microscope group. The inferiority threshold was set *a priori* at 20%, and a one-tailed *t*-test was used against this inferiority margin to give the plateau performance.

Finally, crossover analysis was performed to evaluate whether the starting optical device (ORBEYE or microscope) had an impact on novices' performance. The final five trials before and after crossover were considered. The performance score was investigated before and after crossover (fixed-effects), and the difference between each group (fixed-effects) was taken into account by the subject (random-effects). The analysis was performed using linear mixed-effects regression.

TABLE 1 | Microsurgical grape dissection task "Star's the limit" grading rubric.

Items	Descriptions
Time to Complete	The time to completion (seconds) is recorded, up to 5 min for each repetition; otherwise, participants are told to stop
Completeness of the Dissected Star	Defined as star-shaped grape skin is obtained 0 for failure 1 for success
Clean Star with No Flesh – "flesh score"	The dissected star needs to be "clean skin" without flesh attached 0 points for a lot of flesh or no star obtained 1 point for some flesh 2 points for no flesh
Edge within Limit – "edge score"	Incision needs to be made within the drawn line Both the dissected star and the remaining grape is examined; 1 point for the existence of the blackish on each edge If no star obtained, up to 10 points since only the main grape can be assessed If star obtained, up to 20 points
Perforation	The number of perforations made is recorded 1 point deduction for every perforation into the deep grape flesh

Secondary Outcomes: Subjective Impression of Optical Devices

The perceived workload was assessed using the NASA Raw Task Load Index (NASA R-TLX) (25, 26) (**Appendix 2**). Within the NASA R-TLX are six domains: mental, physical, and temporal demands, performance, effort, and frustration, and these are rated using a 20-point scale. Participants completed the NASA R-TLX immediately after finishing the task. The domain score and total score were used for the secondary outcome. Novice surgeons also reported their subjective impression of the microscope and ORBEYE (**Appendix 3**).

Statistical Methods

Curve fitting was performed using R *v4.1.2* (27); linear mixed-effects regression analysis was made using packages lme4 v1.1 (28), lmerTest v3.1 (29), and nlme v3.1 (30). Noninferiority testing of the learning curves was conducted using the outputs for the estimates, standard errors, and the degrees of freedom of the growth curve coefficients by utilizing the base R functions for Student's *t* distributions. Subjective impression analysis was conducted using JASP v0.14.1 and GraphPad Prism v9.2.0. Data are expressed as mean ± 95% confidence intervals or median ± IQR. The threshold for statistical significance was set at $\alpha < 0.05$. Adjustments for multiple comparisons were made using the Benjamini–Hochberg method for false discovery rates.

RESULTS

Participants

Seventeen novice and seven expert surgeons were recruited (**Appendix 4**). The novice surgeons (male:female 12:5) had completed a median of 0.4 years of training (0–2.8 years). No novice surgeon had not performed any microsurgical cases using either the ORBEYE or a microscope. The expert surgeons (male:female 4:2) had a median 10 years of training (8.9–24 years) and completed the "Star's the limit" task using the microscope only to validate the grape dissection model.

Validation of the Composite Performance Score

The time to task completion was the slowest during the first attempts and plateaued by the 16th attempt (**Appendix 5**). To compare "absolute novice" and "absolute expert" for validation purposes, the first five attempts for novices and the final five attempts for experts were considered. The time taken for task completion by novices and experts demonstrates that participant 2 (expert) and 10 (novice) are outliers and was excluded from the validation analysis.

The Akaike information criterion (AIC) was used to select the best predictive model for discrimination between novice and expert (**Table 2**). The best performing model was time taken to task completion alone (AIC: 13.1) and the second-best performing model was time taken + edge score (AIC: 15.0). We elected to utilize the latter model despite the higher AIC value to ensure penalization for a fast performance if performed poorly. A validated performance score was created with a threshold of expert performance of 70 (0–100) (**Appendix 6**).

Investigating the Learning Curve

We evaluated the seven different models, and the best fit was the modified Weibull function (AIC 2389.013; log-likelihood −1181.506) (**Figure 2**; **Appendix 7**). The primary outcome of the learning rate (ORBEYE -0.94 ± 0.37; microscope -1.30 ± 0.46) and learning plateau (ORBEYE 64.89 ± 8.81; microscope 65.93 ± 9.44) of the ORBEYE was significantly noninferior compared to that of the microscope group ($p = 0.009$; $p = 0.027$, respectively) (**Figure 3**). If considering participants crossing over to the ORBEYE from the microscope, the plateau is not (but nearly significant) noninferior ($p = 0.055$). ANOVA analysis demonstrates that performance significantly improved after crossover in both groups (microscope to ORBEYE and ORBEYE to microscope).

TABLE 2 | Summary of best selective model function for discrimination between novice and expert performances.

	AIC	logLik
(1−Total time/300)	13.14999	−3.574996
(1−Total time/300)+Edge	15.01496	−3.507481
(1−Total time/300)+Accuracy score	15.05006	−3.525028
(1−Total time/300)+Clean star	15.14999	−3.574994
(1−Total time/300)+Clean star + Edge	16.79633	−3.398165
(1−Total time/300)+Edge + Perforations	17.01496	−3.507480

AIC, Akaike information criterion; logLik, log likelihood ratio.

Workload Assessments

The NASA R-TLX demonstrates that mental demand, performance, effort, and frustration scores were not statistically different between the ORBEYE and the microscope (**Figure 4A**). Analysis of variance (repeated-measure two-way ANOVA) showed no significant main effect of device and group assignment on the workload scores, and a significant interaction was only found in the temporal demand score ($p < .05$). However, post-hoc comparisons with FDR adjustments did not find significant results.

Subjective Impression

Novice surgeons answered the subjective questionnaire following task completion on each device (**Figure 4B**; **Appendix 8**). For Q1, 75% (12/16) of novices strongly preferred or preferred the microscope compared to the ORBEYE regarding visualization. Further, 55% (9/16) strongly preferred or preferred the microscope compared to the ORBEYE for task completion. Novices strongly preferred or preferred the greater movement (55%; 9/16) and comfortable ergonomics (63%; 10/16) of the ORBEYE compared to the microscope. Seven novices compared to five novices would prefer to use the microscope rather than the ORBEYE in the future (**Figure 4B**).

DISCUSSION

Interpretation

This preclinical, randomized, crossover noninferiority trial provides robust data that quantifies for the first time that the learning curve of the ORBEYE is statistically noninferior regarding the learning rate and learning plateau compared to that of the traditional operating microscope in novice surgeons (**Figure 3**).

The modified Weibull function was the best fit to model learning curves using the composite performance scores. The microsurgical task was satisfactory at discriminating between novice and expert surgeons using the composite performance score. This adds validity to the modeled learning curves as representatives of real-world learning curves.

There was no significant difference in the cognitive workload of the optical devices using the NASA R-TLX. The total workload score was 61 (IQR: 44.75–72.75) for the ORBEYEE and 53 (IQR: 38.75–63) for the microscope. Analysis of variance demonstrated no significant difference in the scores depending on the optical device the novice surgeon started on.

Subjective assessment of the optic devices found that novices preferred the visualization, ease of task completion, and preferential future use of the microscope, while they preferred the ergonomics and greater freedom of movement of the ORBEYE.

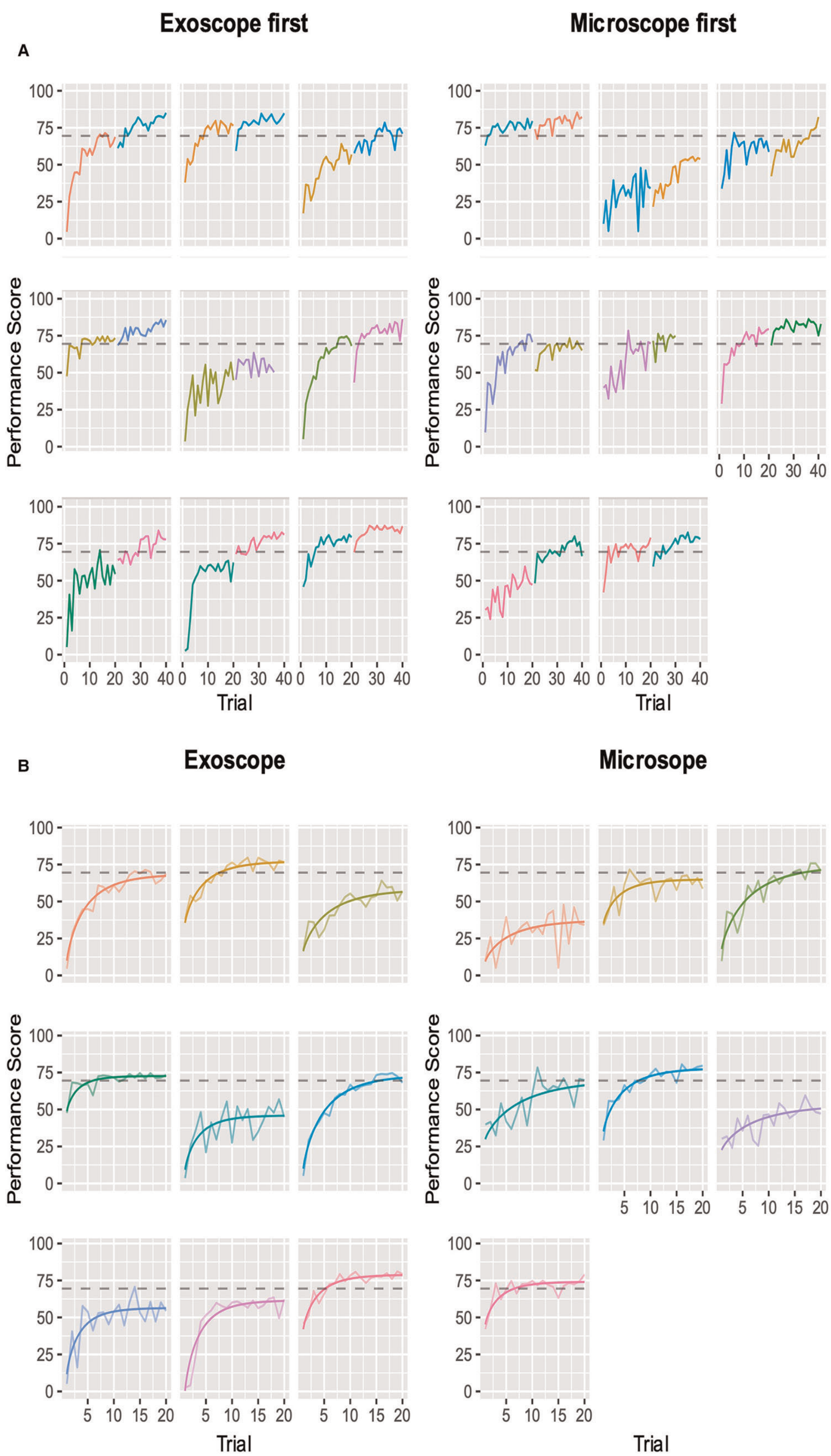

FIGURE 2 | Composite performance score of novice surgeons completing the microsurgical grape dissection task with a threshold for expert performance (gray dashed line 70; 0–100). Each graph represents a separate novice. In total, participants completed 20 repetitions of the task on each device consecutively. (**A**) Novice surgeons' performance scores plotted against the number of trials performed, with the group starting with the ORBEYE and microscope. The first colored graph represents the first device, and the second colored graph represents the crossover to the second device. (**B**) Modeled learning curves using the modified Weibull function.

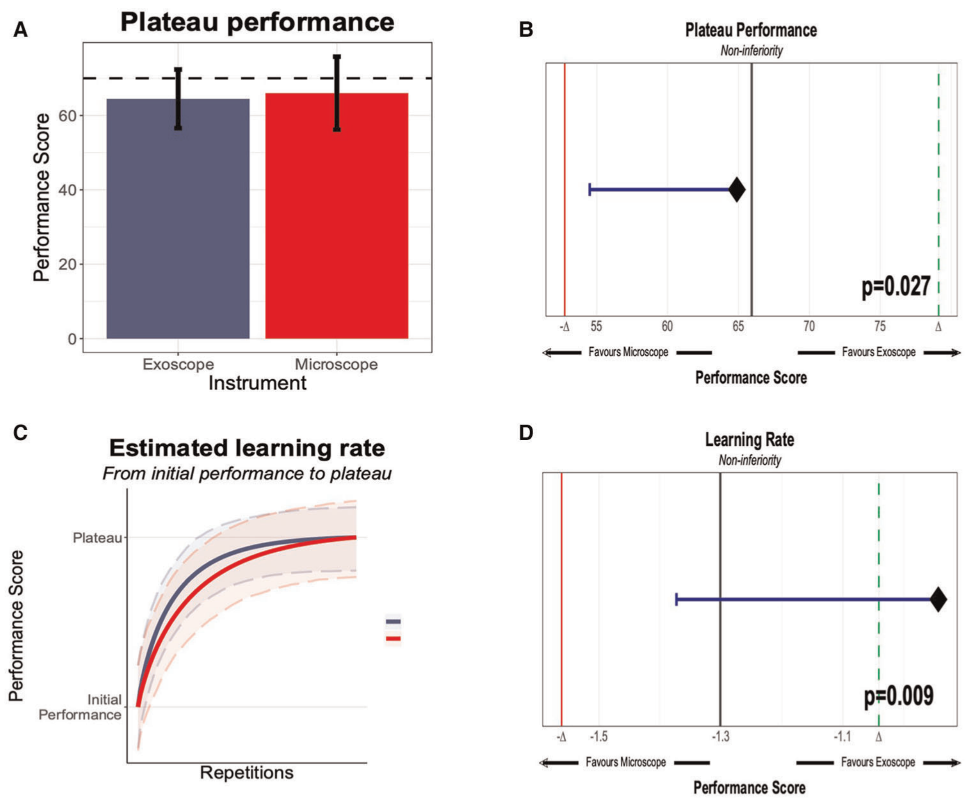

FIGURE 3 | (**A**) Plateau performance between the novices, starting the "Star's the limit" task on the exoscope or the microscope. The performance score was 0–100, generated through methods outlined in section Methods, with an expert threshold score of 70. (**B**) Significant noninferiority of the microscope and exoscope based on novice performance compared against the expert performance. (**C**) Learning rate of novices on the exoscope or the microscope. (**D**) Learning rate and statistical noninferiority of the exoscope compared to the microscope.

Taken together, and considering the microscope has been standard practice for decades, this study does not intend to definitively state that the ORBEYE should replace the microscope. Instead, the ORBEYE has a similar learning plateau and learning rate to the microscope in novice surgeons on a preclinical task; further work must be undertaken to facilitate safe, comparative clinical studies.

Comparison with the Literature

The "learning curve" is frequently used in surgical education literature and represents the relationship between learning effort and the outcome (11, 12, 15, 31). Understanding the learning curve, rate, and plateau provides a mechanism for understanding the development of procedural competency (7, 15). The learning curve is vital when introducing novel technology to surgical practice and should be established before any definitive comparative clinical trials (6, 32, 33). The current ORBEYE literature describes the learning curve subjectively or is inferred from a sample of experienced surgeons (16, 17, 34, 35). The present study provides quantitative data that models the learning curve for novices for both the microscope and the ORBEYE. We demonstrate no significant inferiority for either optical device. This should encourage the international community to ensure trainees develop skills for both optical devices.

The subjective impression from the novice surgeons in this study prefers or strongly prefers the ORBEYE's freedom of movement and comfortable position. This supports existing literature and descriptive studies (35, 35–37). Regarding visualization, participants strongly preferred or preferred the microscope compared to the ORBEYE (**Figure 4**). Microscope preference might have been influenced by obstruction of the line of sight or increased "noise" in peripheral vision while completing novel tasks. The subjective feedback supports future ORBEYE development to enhance their visualization. Future advances to the ORBEYE may add further functionality, including the possibility of augmenting data flow due to the digital nature of the ORBEYE, permitting interoperability with other technological innovations such as augmented reality or computer vision.

Strengths and Limitations

The aim was to compare the learning curves of the ORBEYE and microscope in novices. Previous studies ask experts to perform simulations using the ORBEYE or microscope or ask for subjective feedback after performing surgery with the

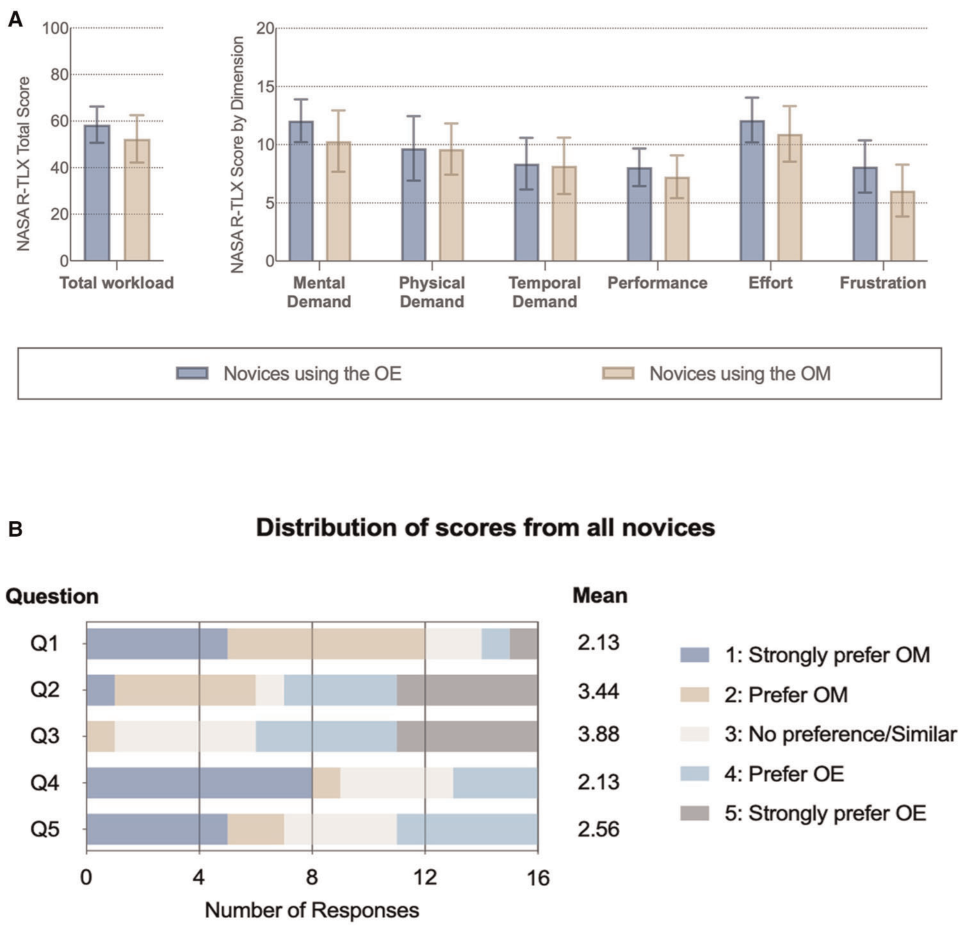

FIGURE 4 | Subjective impression of the optical device. (**A**) NASA Raw Task Load Index (NASA R-TLX) score for each dimension and total workload compared between novices with different instruments. (**B**) Subjective questionnaire (**Supplementary Material Table 2**): Q1: better visualization; Q2: greater freedom of movement; Q3 more comfortable; Q4: easier to perform a task with; and Q5: prefer to use in the future.

exoscope. This introduces bias based on their previous experience and likely established preference. It was therefore considered more robust to use a single, large, homogeneous group of novice surgeons with limited surgical experience, rather than a small group of experts with varying experience of optical device and technical expertise. We did validate the task with expert surgeons to characterize the learning curve for novices. To ensure we avoided any learning curve with the visualization device, we felt it best for expert surgeons to complete the task on the device they were most familiar with, in this case, the microscope. The validated low-fidelity task was also appropriate to characterize the learning curve, as it was not too easy that novices could perform perfectly but not too challenging that a plateau was not achieved at the end of 20 consecutive repetitions. Our methods were also published *a priori*; participants were randomized to reduce the risk of bias and modeled over 60 variants of the performance score.

A limitation was using a low-fidelity microsurgical grape dissection task. Although this has precedence within the literature, our findings require further validation with higher fidelity models when evaluating an expert's learning curve, such as suturing or anastomoses. The novice sample size is small, although again concordant with the literature. Finally, no participant did not crossover; therefore, we cannot control for the effect of switching optical devices.

CONCLUSION

This is the first study to quantify the ORBEYE learning curve and the first randomized controlled trial to compare the ORBEYE learning curve to the microscope. The plateau performance and learning rate of the ORBEYE are significantly noninferior to those of the microscope in a preclinical grape dissection task. This study also supports the ergonomics of the ORBEYE as reported in preliminary observational studies and highlights visualization as a focus for further future development.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article/ **Supplementary Material** will be made available by the authors without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the National Hospital for Neurology and Neurosurgery, London, UK. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

HLH, ZM, CHK, DZK, WM, DS, and HJM conceived, created, and developed the idea and protocol. HLH and ZM led the data collection with CHK, DZK, WM, and HJM assistance. HLH, ZM, CHK, and DZK wrote the first draft of the manuscript. CHK undertook the statistical analysis with support from HLH and ZM. DS and HJM critically reviewed and edited the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

HLH, HJM, CHK, and WM are supported by the Wellcome/ EPSRC Centre for Interventional and Surgical Sciences, University College London. DZK is supported by an NIHR Academic Clinical Fellowship. HJM is also funded by the NIHR Biomedical Research Centre at University College London.

ACKNOWLEDGMENTS

The authors thank the Theatre Staff at the National Hospital for Neurology and Neurosurgery for facilitating this trial. The Olympus ORBEYE was loaned to the National Hospital for Neurology and Neurosurgery as part of a reference center agreement.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://journal.frontiersin.org/article/10.3389/fsurg.2022.920252/full#supplementary-material

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frontiers | Frontiers in Surgery

TYPE Original Research
PUBLISHED 27 July 2022
DOI 10.3389/fsurg.2022.899649

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SPECIALTY SECTION
This article was submitted to Neurosurgery, a section of the journal Frontiers in Surgery

RECEIVED 18 March 2022
ACCEPTED 27 June 2022
PUBLISHED 27 July 2022

CITATION
Mignucci-Jiménez G, Xu Y, Houlihan LM, Benner D, Jubran JH, Staudinger Knoll AJ, Labib MA, Dagi TF, Spetzler RF, Lawton MT and Preul MC (2022) Analyzing international medical graduate research productivity for application to US neurosurgery residency and beyond: A survey of applicants, program directors, and institutional experience.
Front. Surg. 9:899649.
doi: 10.3389/fsurg.2022.899649

Analyzing international medical graduate research productivity for application to US neurosurgery residency and beyond: A survey of applicants, program directors, and institutional experience

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Background: The authors investigated perceived discrepancies between the neurosurgical research productivity of international medical graduates (IMGs) and US medical graduates (USMGs) through the perspective of program directors (PDs) and successfully matched IMGs.
Methods: Responses to 2 separate surveys on neurosurgical applicant research productivity in 115 neurosurgical programs and their PDs were analyzed. Neurosurgical research participation was analyzed using an IMG survey of residents who matched into neurosurgical residency within the previous 8 years. Productivity of IMGs conducting dedicated research at the study institution was also analyzed.
Results: Thirty-two of 115 (28%) PDs responded to the first research productivity survey and 43 (37%) to the second IMG research survey. PDs expected neurosurgery residency applicants to spend a median of 12–24 months on research (Q_1-Q_3: 0–12 to 12–24; minimum time: 0–24; maximum time: 0–48) and publish a median of 5 articles (Q_1-Q3: 2–5 to 5–10; minimum number: 0–10; maximum number: 4–20). Among 43 PDs, 34 (79%) ranked "research institution or associated personnel" as the most important factor when evaluating IMGs' research. Forty-two of 79 (53%) IMGs responding to the IMG-directed survey reported a median of 30 months (Q_1-Q_3: 18–48; range: 4–72) of neurosurgical research and 12 published articles (Q_1-Q_3: 6–24; range: 1–80) before beginning neurosurgical residency. Twenty-two PDs (69%) believed IMGs complete

Abbreviations: AAMC: Association of American Medical Colleges, AANS: American Association of Neurological Surgeons, ECFMG: Educational Commission for Foreign Medical Graduates, IMG: International medical graduate, LMIC: Low- and middle-income countries, LOR: Letter of recommendation, NRMP: National Resident Matching Program, PD: Program director, USMG: US medical graduate, USMLE: United States Medical Licensing Examination.

more research than USMGs before residency. Of 20 IMGs conducting dedicated neuroscience/neurosurgery research at the study institution, 16 of 18 who applied matched or entered a US neurosurgical training program; 2 applied and entered a US neurosurgical clinical fellowship.

Conclusion: The research work of IMGs compared to USMGs who apply to neurosurgery residency exceeds PDs' expectations regarding scientific output and research time. Many PDs perceive IMG research productivity before residency application as superior to USMGs. Although IMGs comprise a small percentage of trainees, they are responsible for a significant amount of US-published neurosurgical literature. Preresidency IMG research periods may be improved with dedicated mentoring and advising beginning before the research period, during the period, and within a neurosurgery research department, providing a formal structure such as a research fellowship or graduate program for IMGs aspiring to train in the US.

KEYWORDS

international medical school graduates, neurosurgery research, neurosurgery residency, neurosurgery residency application, research productivity

Introduction

Professional neurosurgery organizations in the United States (US), such as the American Association of Neurological Surgeons (AANS), Neurosurgery Research and Education Foundation, Congress of Neurological Surgeons, American Board of Neurological Surgery, Society of Neurological Surgeons, and various regional and state associations, continue to advocate for dedicated research time during neurosurgical training, with a full year of research designated within the residency structure. The founding departments of US neurosurgery training programs have been, and continue to be, leaders in neurosurgery and neuroscience research within the US. This trend continued as most other neurosurgery departments and training programs were established. Thus, in addition to developing training technology, the human factor of performing research continues to be of major importance for neurosurgery education and residency applicants to US programs, especially in the ever-more connected international world of neurosurgery. Indeed, applicants may spend years in research before residency, involving significant professional and life planning. International medical graduates (IMGs) with an outlook toward US neurosurgery residency in the next 10 years may already be involved in such career decisions.

The question that follows is, "Why do IMGs apply for neurosurgery training in the US?" The answer is multifactorial, but it can be inferred that the IMGs believe that either the training or quality of life in the US is superior to that of their home country. Previous papers have focused on IMGs' perceptions of neurosurgery residency in their own country, especially in low to middle-income countries (LMICs). Deora et al. (1) sent a questionnaire through social media to all neurosurgical residents in LMICs, asking general questions about their perspectives on their training programs. Significant differences between US and LMIC residency programs were found in work-hour regulations and subspecialty training. Substantial gaps in residency experience were noted; 40% of respondents did not report substantial residency experience in any of the queried subspecialties (i.e., endovascular, epilepsy, deep-brain stimulation/lesioning, minimally invasive surgery, radiosurgery, or deformity surgery). The lack of subspecialty training in a candidate's respective country could be a major factor in their decision to pursue US-based training. The US training system is perceived as organized, complete, and accepting of IMGs. The training programs in LMICs are inherently limited due to local, geographical, infrastructure, and economic factors (2).

In a 2018 study, IMGs represented 24% of the US physician workforce and 1 in 4 trainees in US residency programs (3). These numbers are likely to rise in the coming years as major physician shortages develop due to increased health care demand, workforce shortages due to the recent COVID-19 pandemic and government mandates, and an aging workforce. The projected US physician deficit is 139,160 by 2030. A well-recognized shortage of neurosurgeons is likely to increase similarly, as 46% of practicing neurosurgeons are 55 years of age or older (4, 5).

IMGs account for 13% of practicing physicians, 6% of neurosurgical residents (8% in 2018), and 11% of academic neurosurgeons (3, 6, 7). The need for neurosurgeons is met by USMGs and IMGs, which reflects the competitive nature of the neurosurgery residency match, with 66.8% (211/316) and 65.2% (211/322) of allopathic USMGs matching in 2020 and 2021, respectively. In contrast, 28.6% (18/63) and 25.8% (17/66) of IMGs matched in 2020 and 2021, respectively, as reported by the National Resident Matching Program (NRMP) (8, 9). Among IMGs, 25% (12/48) and 22% (11/50) were non-US

IMGs in the 2020 and 2021 match cycles, respectively. Overall, USMGs, including graduates from both allopathic and osteopathic medical schools, comprised 92.2% (214/232) and 92.7% (217/234) of applicants who matched in 2020 and 2021, respectively. Conversely, US and non-US IMGs comprised only 7.8% (18/232) and 7.3% (17/234) of matches (8, 9). These numbers show the discrepancy between USMGs and IMGs.

Neurosurgery is uniquely intertwined with scientific work, and an overwhelming majority of training programs are affiliated with major academic institutions. This characteristic contributes to neurosurgery applicants having the highest research productivity of all medical specialties in the US (10). IMGs seeking to overcome the difficulty of matching with a US neurosurgical residency program view high-level research as critical to overcoming this difficulty. IMGs perceive higher h-indices and numbers of published articles as an advantage for matching with a US program (11).

Nonetheless, studies have reported biases affecting IMGs in the US neurosurgical matching system (7, 11, 12). Sheppard et al. (12) reported that IMGs are more likely to match at unranked or lower-ranked residency programs compared to USMGs despite high research output, publications, and the research impact. The likelihood of a USMG vs. an IMG matching into a ranked program was almost 3 times higher (OR = 1.7 vs. 0.59). Khalafallah et al. (7) conducted a retrospective review of 2,749 residents spanning 50 years. They reported that IMGs were significantly more likely than USMGs to have completed a research fellowship after medical school and before residency (16% vs. 2%). Chandra et al. (11) reported that from 2009 to 2017, the number of IMG applicants increased without a significant increase in submitted applications or matched IMGs over this period. These individual findings reveal that research productivity is important for matching into a neurosurgery training program. However, IMGs are still limited in their acceptance into a ranked training program (e.g., *U.S. News & World Report* “Best Hospitals for Neurology & Neurosurgery” ranking) (13).

Although the geographical location where IMGs received graduate education and the characteristics of success in their neurosurgical match have undergone recent analysis (6, 11), an investigation into IMGs' neurosurgical research, coupled with the program directors' (PDs) expectations, has yet to be reported. Neurosurgical and basic science laboratories of neurosurgery departments are the mainstay of departmental research productivity and commonly host postdoctoral researchers from home and abroad. We obtained successful IMG matching data for those who conducted dedicated research in our institution's neurosurgical laboratory.

Some researchers have accessed publicly available databases to analyze broad trends and outcomes for IMGs applying to neurosurgery residency programs, which have required large sample sizes (7, 11, 12). However, we desired a more focused and granular study of the features of a successful IMG application to residency programs. We sought to assess the research productivity of IMGs—both from their perspective and that of PDs—using direct, anonymous surveys to understand the personal aspects of researchers that cannot be ascertained from publicly available databases. For this study, IMGs comprise all individuals who received medical degrees outside the US, irrespective of their nationality. This survey was limited to the most recent 8-year span (July 2013 through June 2020) of IMGs currently or recently matched in US neurosurgery residency programs and a separate survey encompassing all 20 IMG neurosurgery research fellows from our institution who applied and were successfully matched into neurosurgery residency programs or who entered neurosurgery clinical fellowships. The findings elucidate the key research period-related components of a successful IMG application and compare the research experience of IMGs with that of USMGs who successfully matched with US-based neurosurgery programs.

Materials and methods

Data collection

No protected health information and no individually identifiable information were collected. No patients were involved in this study. Therefore, no institutional review was sought or required.

A search for all neurosurgical residency training programs in the Directory of the AANS and the Association of American Medical Colleges (AAMC) for the 2020–2021 match cycle revealed 115 training programs. Every PD identified through the AANS directory (14) was provided a survey including qualitative and quantitative questions, focusing on all applicants, their experiences with IMGs in a research environment, and how IMGs relate to USMGs. Later, every PD was contacted again and provided an additional survey, focusing on the importance of different factors associated with an IMG applicant's research productivity.

All Accreditation Council for Graduate Medical Education–approved neurosurgery residency programs in the US listed by the AAMC for the 2020–2021 cycle were identified using the AAMC's online portal (15). All programs older than 7 years (i.e., had graduated at least 1 resident) were then identified, and individual public websites were reviewed for the most updated list of current residents. An IMG was defined as any resident who had completed his or her primary medical degree (MD, MBBS, MBChB, or others) at a medical college outside of the United States. In addition, public residency websites of all identified programs were reviewed for up-to-date information on their current residents. Residents who received their medical degrees abroad were identified, and publicly available information was collected. A search before and after residency graduation in June 2020 revealed 8 residency classes and 79 IMGs. A questionnaire with both qualitative and quantitative questions on their research experiences before and after the neurosurgical match was sent to the 79 IMGs.

Data regarding IMGs who successfully matched in either a US residency program (i.e., neurosurgery or other) or entered a clinical fellowship program and conducted a dedicated research period at Barrow Neurological Institute (Barrow) from 2000 through 2020 were collected with the permission of the Director of Neurosurgery Research at Barrow. All IMGs completed a research fellowship, and some completed an additional integrated interdisciplinary neuroscience PhD program. Research program type, research focus, match specialty (i.e., neurosurgery, other, or clinical fellowship), months of research, geographical region, h-index, and the number of publications associated with Barrow before residency, 1 year after matching, and 2 years after matching into a residency program were collected and analyzed. A retrospective bibliographic search was done for these Barrow IMGs using PubMed. A publication was added to their total count if the IMG was the first author or co-author and the publication was associated with Barrow. The Scopus author profile database (16) was used to determine each author's h-index.

Survey content

The first PD and IMG surveys were delivered between April 2020 and January 2021. The second PD survey was delivered in April 2022. The first PD survey contained 5 questions that assessed: (1) the number of years PDs believe IMGs should spend on research before their residency application; (2) the number of peer-reviewed publications any neurosurgery residency applicant should have published; (3) whether PDs believe IMGs complete more research than USMGs before residency; (4) whether PDs believe IMGs complete more research than USMGs during residency, and (5) whether PDs believe nonresident research fellows (i.e., full-time research fellows) or residents were more productive in scholarly research than US research fellows and residents if their program supported such research programs. The second PD survey contained 1 question, asking the PD to rank from 1 to 4 the importance of the following factors when evaluating an IMG applicant's research productivity: (1) the research institution or associated personnel, (2) the impact of the research, (3) the number of publications, and (4) a structured research period or theme.

The IMG survey contained 12 questions. Two were demographic assessments of sex and country of origin—the country of origin was later categorized as a geographical region (i.e., North America, South America, Europe, Middle East, North Africa, South Africa, South Asia, and East Asia) to protect the identity of residents. Three questions inquired whether the IMG spent time on research in a neurosurgery laboratory, the length of their neurosurgery research experience, and whether they spent time in more than one laboratory. The remaining 7 questions dealt with (1) their training background before obtaining a neurosurgical residency, (2) their motivation in seeking neurosurgery research, (3) the degree this research impacted their future career, (4) if they would recommend dedicated research time to peers and future applicants, (5) what their current position was at the time of the survey, (6) how many papers they published before residency, and (7) how many papers they published after beginning residency.

Analysis

Collected respondent survey data was stored on a password-protected computer and backed up on an encrypted drive. Data of respondents were given an anonymizing number code for identification. Qualitative answers were reported in full whenever their content diverged from others in a meaningful way. Specific sample means in the PD and IMG-directed surveys were analyzed. Data were expressed as medians with first and third quartile ranges (Q_1-Q_3) and absolute ranges and then compared using the Mann-Whitney test. The means, medians, and minimum and maximum responses of the PDs were compared to the responses of the IMGs. GraphPad Prism version 9.3.1 (GraphPad Software, San Diego, California, USA) and Microsoft Excel version 16.58 (Microsoft Corporation, Redmond, Washington, USA) were used for data analysis.

Results

Program directors

Of 115 programs contacted, we received 32 nearly complete responses (28%) to the first PD survey. These PDs responded that neurosurgery residency applicants should spend 12 to 24 months (Q_1-Q_3: 0–12 to 12–24; minimum range, 0–24, maximum range, 0–48 months) on research (**Figure 1**). They also expected the applicants to have published a median of 5 articles (both minimum and maximum medians = 5) (Q_1-Q_3: 2–5 to 5–10; minimum range 0–10, maximum range 4–20) before applying (**Figure 2**). Two PDs stated that the answer to both questions was variable. One suggested taking additional factors into account when evaluating the research capabilities of applicants, such as the research opportunities their medical school offered. Furthermore, 22 (69%) PDs answered that IMGs completed more research than USMGs before residency. When asked whether IMGs are engaged in more research than USMGs once they enter residency, 11 (34%) PDs answered yes. In comparison, 14 (44%) PDs believed that IMGs were not more productive during residency, and 2 (6%) emphasized the IMG's character rather than the residents'

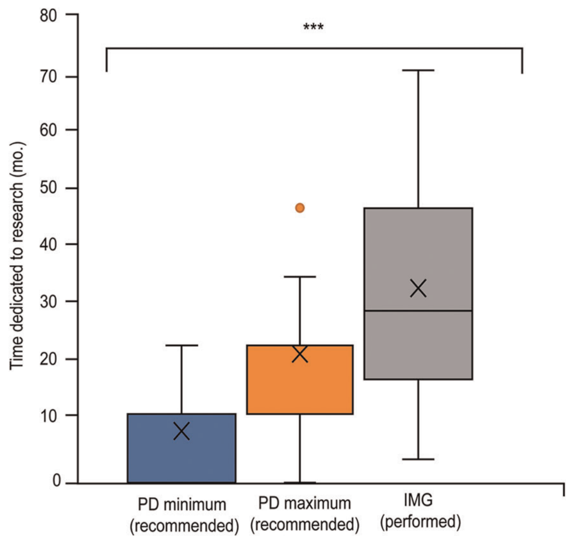

FIGURE 1
Box and whisker plot of the length of dedicated research (months) completed by international medical graduates (IMGs) before matching into neurosurgical residency, compared to the expectations neurosurgical residency training program directors (PDs) have of applicants. The X represents the mean. The horizontal line (if visible) represents the median. Whisker lines represent the maximum and minimum values. Additional dots represent outliers that did not fit the model. (***) Represents statistical significance ($P < 0.05$). *Used with permission from Barrow Neurological Institute, Phoenix, Arizona.*

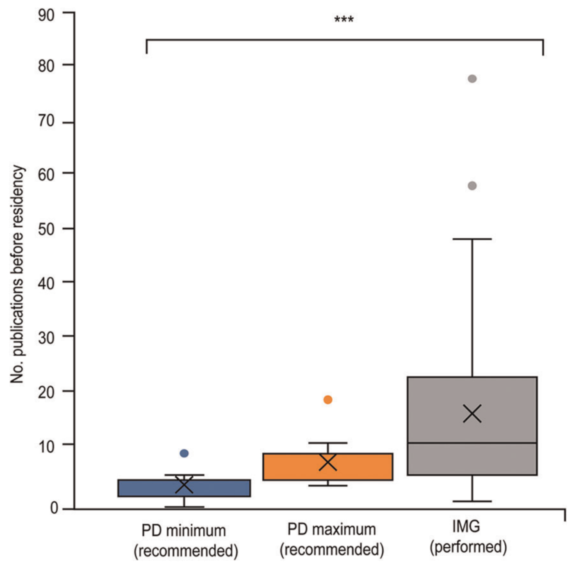

FIGURE 2
Box and whisker plot of the number of publications of IMGs before matching into neurosurgical residency, compared to PD applicant expectations. The X represents the mean. The horizontal line (if visible) represents the median. Whisker lines represent the maximum and minimum values. Additional dots represent outliers that did not fit the model. (***) Represents statistical significance ($P < 0.05$). *Used with permission from Barrow Neurological Institute, Phoenix, Arizona.*

respective medical school location. Seventeen (53%) PDs stated that their program regularly supports research fellows, 10 (31%) PDs responded that research fellows are more productive than residents, while 3 (9%) assessed residents to be more productive than full-time research fellows. Four others (13%) suggested generalization is impossible or that IMGs' and USMGs' productivity did not differ.

In response to the second PD survey of 115 programs, 43 (37%) PDs provided complete responses. Thirty-four of the 43 (79%) PDs responded that the prestige or reputation of the research institution or associated personnel was the most important factor when evaluating an IMG's research productivity. Nine (21%) PDs responded that the impact of research was the most important factor. Twenty-eight (65%) PDs responded that a structured research period or pursuing a thematic research topic was the third most important factor. All 43 (100%) PDs responded that number of publications is the least important factor when evaluating an IMG applicant's research productivity (Table 1).

TABLE 1 Neurosurgical residency training program director ($n = 43$) ranking of research productivity evaluation factors.

Factor	Program director ranking[a] *n* (%)			
	1	2	3	4
Research institution or associated personnel	34 (79)	9 (21)	0 (0)	0 (0)
Impact of research[b]	9 (21)	19 (44)	15 (35)	0 (0)
Structured research period or theme[c]	0 (0)	15 (35)	28 (65)	0 (0)
Number of publications	0 (0)	0 (0)	0 (0)	43 (100)

[a]Ranking: most important (1) to least (4) important.
[b]For example, impact factor of journal or h-index.
[c]For example, graduate program, multiple projects covering same topic.

International medical graduates

Responses came from 42 of 79 (53%) residents contacted for the IMG-directed survey. Of those 42, 13 (31%) were from the Middle East, 12 (29%) from Europe, 7 (17%) from South Asia, 5 (12%) from South America, and 2 (5%) from North Africa; 1 (2%) each was from North America, South Africa, and East Asia (Figure 3). Thirty-nine (93%) respondents were men, and 3 (7%) were women. All respondents participated in resolute neurosurgical or neuroscience research before their match. Twelve (29%) spent time in multiple research laboratories.

Asked about the degree to which their research in a neurosurgical laboratory impacted their future career, 26

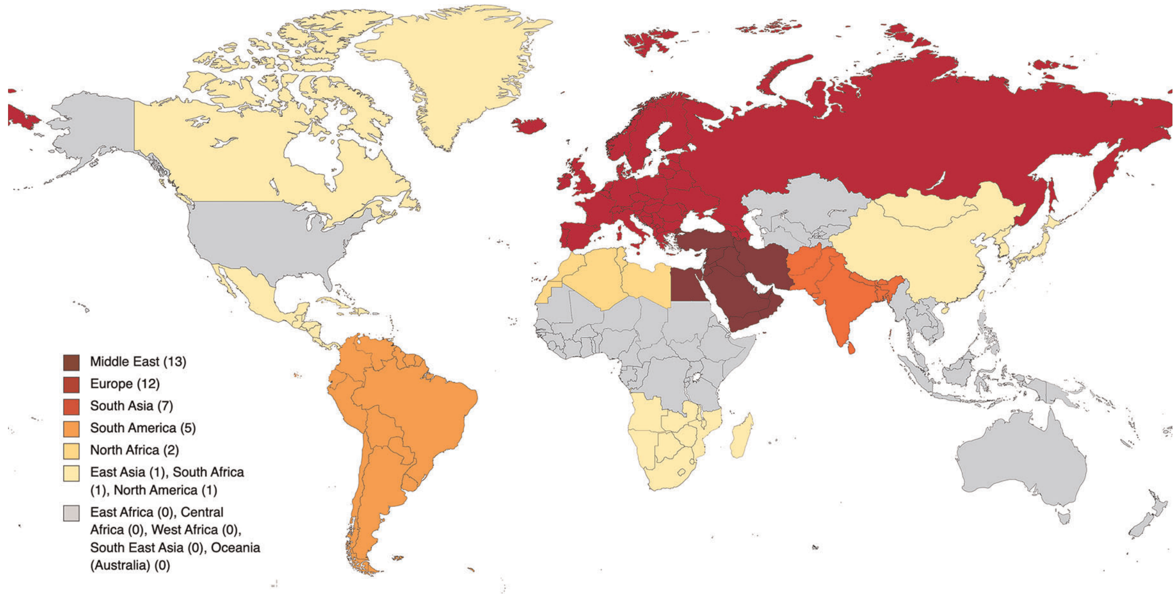

FIGURE 3
Geographic data of IMGs' home countries by region. Small countries of origin were categorized into regions to protect the identities of IMG residents who come from such countries. *Copyright made available under the Creative Commons Attribution-ShareAlike 4.0 International (CC BY-SA 4.0)* (https://creativecommons.org/licenses/by-sa/4.0).

(62%) IMGs responded with "A great deal," and the other 16 (38%) with "A lot." A total of 35 (83%) would recommend dedicated research time to their peers and future neurosurgery applicants, whereas 7 (17%) would not. Their respective year in training (i.e., postgraduate year) was removed from analyses to protect the identity of each respondent. Among the 42 IMGs, 11 (26%) completed a neurosurgery residency training program abroad, and 14 (33%) attended foreign postgraduate training without completing a neurosurgical residency (4 with incomplete neurosurgical training, mandatory rural service, master's degree, or surgical internship). In contrast, 17 (40%) received no postgraduate training before coming to the US to apply to a residency program (**Figure 2**).

When asked about the primary motivation for their research work, 12 (29%) IMGs stated that they wanted to improve their chances of a neurosurgical match, and the remaining 30 (71%) commented on their passion for neurosurgical research. Before beginning their neurosurgical residency, 42 IMGs reported a median of 30 months (Q_1-Q_3: 18–48; range 4–72 months) spent in neurosurgical research and 12 published articles (Q_1-Q_3: 6–24.3; range 1–80), with 1 vacant answer (**Figures 1**, **2**). Thirty IMGs reported their research productivity before and after successfully matching into residency (**Figure 4**). The number of publications differed significantly before and during residency ($P < 0.001$). Of the 30 IMGs reporting this information, 25 (83%) had more publications before than during residency. The median number of publications per year for an IMG before matching was 6.8 (Q_1-Q_3: 3.3–12.5; range 0.2–40), while the median number per year for an IMG during residency was 3 (Q_1-Q_3: 2–4; range 0–6.4). Only 5 of 30 (17%) IMGs published more articles after entering residency (**Figure 4**).

Comparison between PD recommendations and IMG performance

The minimum and maximum recommendations by PDs for months of research and the number of publications before matching were combined and compared to actual IMG performance for each variable. The PDs' median recommended research period was 18 months, and the median recommended number of publications was 5. The median IMG-performed months of research (30 months) and the number of publications (12) before matching were both significantly larger than the recommended PD values ($P < 0.001$ and $P < 0.001$, respectively).

Barrow IMG matching results

Twenty IMGs who spent dedicated research time at Barrow during the study period were evaluated (**Table 2**). All 20

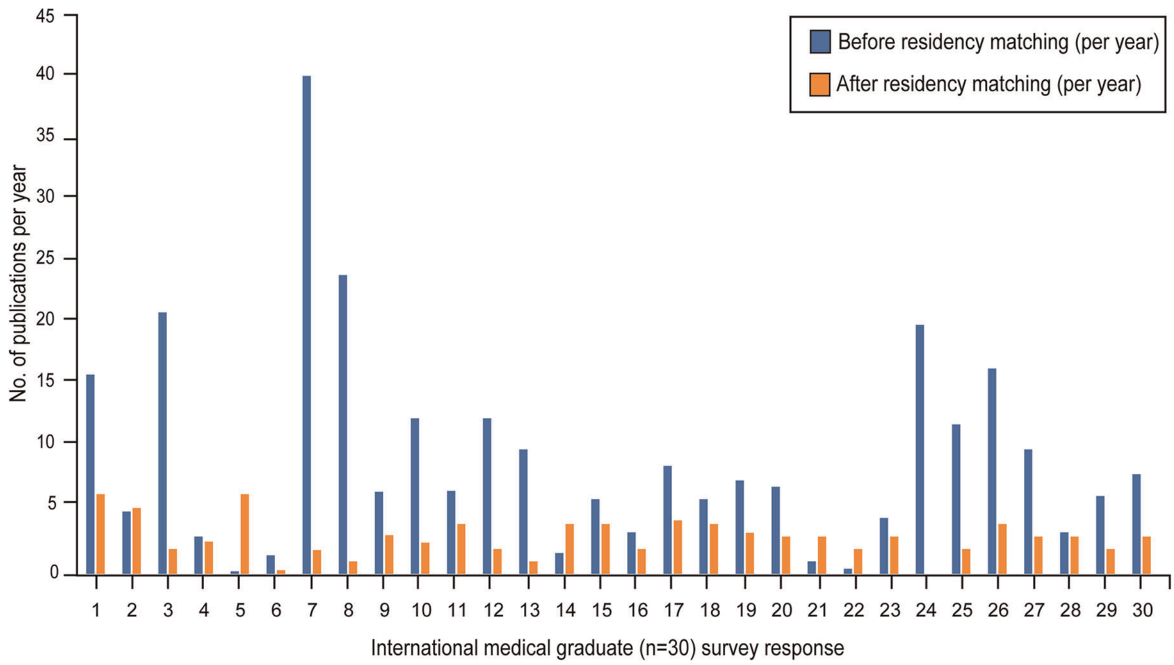

FIGURE 4
Graphical representation of the number of publications per year of IMG residents that were completed before (i.e., during their dedicated research time, *blue*) and after matching into a neurosurgical residency (*orange*). Residents entering postgraduate-year 1 and those who chose not to answer the question were excluded from this analysis. *Used with permission from Barrow Neurological Institute, Phoenix, Arizona*.

completed a named neurosurgery research fellowship of the hospital institution. In addition, 3 (15%) of these IMGs were part of a nationally-ranked integrated interdisciplinary neuroscience PhD program with a local major state university. Sixteen (80%) Barrow IMGs applied to US neurosurgical residency programs, 2 (10%) applied for residency in another medical specialty, and 2 (10%) applied for US neurosurgery clinical fellowships. All 20 IMGs matched or entered the specialty of their choice. All 3 IMGs who completed the PhD program were matched into a US neurosurgery residency program. Three (15%) IMGs were accepted into a residency upon their second application, with two continuing a research fellowship in the meantime. Another was accepted into a preliminary general surgery year and was then admitted 2 years later into a vacated neurosurgery position. Four (25%) of the 16 IMGs who applied to neurosurgery were accepted into the Barrow neurosurgery residency. However, the other 12 (75%) were all admitted to competing top neurosurgery residencies.

For all IMGs at Barrow, the median number of research months was 24 (Q_1-Q_3: 24–36; range: 12–70). The median number of total publications was 31 (Q_1-Q_3: 4.8–55; range: 1–103), with a median number of publications before residency of 6 (Q_1-Q_3: 1.3–39; range: 0–88). The median h-index was 13 (Q_1-Q_3: 9–19; range: 2–43). The data for IMGs who completed a research fellowship only vs. those who completed the PhD program is shown in **Table 3**.

Discussion

Research demographics of IMGs in neurosurgical residency

Matching into neurosurgery is among the most difficult career choices for USMGs, let alone for IMGs, who face additional scrutiny during the residency matching process. Attempting to set themselves apart, IMGs often invest in years of dedicated research after graduating in their home countries. The median number of months IMGs in our study spent performing dedicated research before entering neurosurgery residency was 30 (Q1-Q3: 18–48). They produced a substantial quantity of published research, with the median number of publications per person being 12 (Q1-Q3: 6–24). The largest proportion of IMGs came from the Middle East (31%); 7% of all respondents were women. Thus, our cohort had demographics similar to the previously described demographics of originating countries and those of the American Board of Neurological Surgery-certified practicing neurosurgeons who are IMGs (6%). Currently,

TABLE 2 Characteristics and research data of international medical graduates (IMGs) who completed a dedicated research period at Barrow Neurological Institute.

IMG	Research		Match Specialty	Research Time (mo.)	Barrow Publications				h-Index[b]	Region
	Type	Focus			Total[a]	Before Residency	+1 Y	+2 Y		
1	Fellow	SA	NS	24	31	3	3	2	43	South America
2	Fellow	SA	NS	36	7	4	0	2	9	South America
3	Fellow	ET	CF	24	1	1	0	0	6	East Asia
4	Fellow	SA, SBM	NS	24	45	9	3	4	22	Europe
5	Fellow	SCI, BI	NS	24	4	4	0	0	10	North America
6	Fellow	SCI	NS	36	2	0	0	0	23	Europe
7	Fellow	SA	CF	36	30	11	4	1	15	South America
8	Fellow	SBM	NS	24	22	0	2	5	14	North America
9	Fellow	SA	Other	12	2	0	0	0	2	North America
10	Fellow + PhD	FT, SCP	NS	48	58	12	2	6	21	Europe
11	Fellow	ST	NS	12	3	2	0	0	13	South Asia
12	Fellow	SCI, BTI	Other	24	10	4	2	1	11	Europe
13	Fellow + PhD	SA	NS	36	20	8	7	5	13	Middle East
14	Fellow	SA	NS	24	46	0	0	4	9	Middle East
15	Fellow	SA	NS	48	103	88	11	4	8	Middle East
16	Fellow	FT, SA	NS	25	39	28	9	0	11	Europe
17	Fellow	SA	NS	24	59	49	9	1	9	East Asia
18	Fellow + PhD	FT, ST	NS	70	91	80	10	1	17	Europe
19	Fellow	VNTs	NS	24	60	60	0	0	12	South Asia
20	Fellow	SA	NS	24	42	42	0	0	20	Middle East

Abbreviations: BI, brain imaging; BTI, brain tumor immunology; CF, clinical fellowship; ET, endovascular technology; FT, fluorescence technology; NS, neurosurgery; SA, surgical anatomy; SBM, spine biomechanisms; SCI, spinal cord injury; SCP, spinal cord physiology; ST, surgical technology; VNTs, varied neurosurgical topics.
[a]Total number of publications associated with Barrow, even after completion of a dedicated research period.
[b]The Scopus author profile database was used to determine the h-index. This includes publications not associated with Barrow and those published more than 2 years after matching.

about 19% of US neurosurgical residents are women (17). Many IMGs genuinely enjoy their research activities. Despite the short timeframe to produce a competitive body of work, our results show how valuable IMGs perceive their research experience to be and how much their research experience positively impacted their careers.

Program director perceptions

This study is the first to investigate neurosurgical residency PDs regarding their views on the value of research as part of the IMG neurosurgery residency application and to compare their expectations with data from successfully admitted IMGs. IMG residency applicants surpassed PD expectations for dedicated research time (12–24 months) and the number of published articles (5). Additionally, we acknowledge that the numbers of peer-reviewed publications do not consider the academic quality, research productivity, or global impact of the published articles. Nor do these data consider the actual contribution of the applicant to the final work (i.e., first author vs. co-author).

Our assessment goes beyond the NRMP Charting Outcomes in "The Match" report (18) that displays the cumulative number of research experiences, abstracts, presentations, and publications included in successfully admitted IMG applications entered in the Electronic Residency Application Service. According to the 2018 NRMP Charting Outcomes in "The Match," non-US IMGs averaged 3.9 research experiences and 46.6 abstracts, presentations, and publications, whereas USMGs averaged 5.2 research experiences but only 18.3 abstracts, presentations, and publications (19). These data mirror the perceived rise in research productivity of neurosurgery applicants depicted as an "arms race" in the neurosurgery application process (20).

TABLE 3 Data for international medical graduates (IMGs) who conducted research at Barrow Neurological Institute overall and by research fellowship and PhD program participation.

IMG group Metric	Time (months)	Barrow Publications				h-Index[b]
		Total[a]	Before Residency	+1 Year	+2 Year	
All ($n = 20$)						
Mean (SD)	30 (13)	34 (30)	20 (28)	3.1 (3.9)	1.8 (2.1)	14 (8.7)
Median (Q_1-Q_3)	24 (24–36)	31 (4.8–55)	6 (1.3–39)	2 (0–6.3)	1 (0–4)	13 (9–19)
Fellowship only ($n = 17$)						
Mean (SD)	26.2 (8.7)	29.8 (28)	17.9 (26.3)	2.5 (3.7)	1.4 (1.8)	13.9 (9.3)
Median (Q_1-Q_3)	24 (24–30.5)	30 (3.5–45.5)	4 (0.5–35)	0 (0–3.5)	1 (0–3)	11 (9–17.5)
Fellowship + PhD ($n = 3$)						
Mean (SD)	51.3 (17.2)	56.3 (35.5)	33.3 (40.5)	6.3 (4)	4 (2.7)	17 (4)
Median (Q_1-Q_3)	48 (36–70)	58 (20–91)	12 (8–80)	7 (2–10)	5 (1–6)	17 (13–21)

[a]Total number of publications associated with Barrow after completion of a dedicated study period.
[b]The Scopus author profile database was used to determine the h-index. Data included publications not associated with Barrow and those published more than 2 years after matching.

Wadhwa et al. commented on a similar trend. They noted the stark difference between the upward trends of the NRMP-reported research numbers and the actual number of peer-reviewed articles published (20). The 5 published articles that are expected of neurosurgery applicants, according to the PDs surveyed, are similar to the previous report of an average of 5.5 publications per neurosurgery postgraduate-year 1 residents in 2018 (20).

These observations suggest that, on average, across all neurosurgery residents, research expectations for future residents are met at the time of application (20). However, other publications that reported data for USMGs and IMGs noted an average of 2 publications by USMG applicants and 5 in the admitted IMG applicant cohort before residency matriculation (11). Given this evidence, it is reasonable to infer that IMGs markedly affect the overall number of publications of medical students who match into a neurosurgery residency program.

To address the qualitative characteristics of an IMG's research productivity instead of absolute numbers, the PD directors were given a 1-question survey at a later time (**Table 1**). When given the task of ranking research productivity evaluation factors from 1 to 4, most PDs (34/43, 79%) ranked the research institution and its associated personnel as the most important factor. The second most important was the impact of research (i.e., impact factor of journal or h-index). More compelling, all PDs (43/43, 100%) ranked the number of publications as the least important factor. This result brings to light a divergence in the perception of research between IMG and PD that has not been emphasized thus far: the quality of research outweighs the number of publications. This could explain the marked difference in research numbers reported in previous publications, by national databases, and in the present study. Therefore, although an IMG reports a significant amount of research, the data suggests that PDs look beyond the numbers and instead focus on the associated institution and the overall impact and quality of the research work.

Discrepancy in background and experience between match candidates

An IMG's situation is entirely different from that of a USMG applicant for a neurosurgery residency. Certain IMGs aspire to train in the US for various reasons, including some unrelated to training, such as socioeconomic, political, or quality-of-life motives. They opt to enter research posts and spend years improving their portfolio because it is likely necessary in order to become competitive within the US residency matching system. USMGs complete undergraduate degrees before medical school, prolonging their preclinical and potential research period. In addition, the research opportunities and facilities that US students can access during their undergraduate and postgraduate programs are superior to those of candidates who earn their medical degrees in LMIC countries. According to Sheppard et al. (12), applicants from the top 20 or top 40 US medical schools had higher preresidency publication counts. Applicants with higher preresidency publication counts were also matched at residency programs with highly ranked affiliated hospitals.

In addition to published work, as one of the PDs explained, applicants' research opportunities before the residency match vary greatly, and this variability increases the difficulty of evaluating neurosurgical residency applicants. The importance of an applicant's opportunities is supported by the fact that a significant difference is seen in the number of publications by

USMG applicants who graduated from the top 20 medical schools (per *U.S. News & World Report* "Best Research" ranking in 2018), compared to those who did not (9.40 vs. 4.43) (20). In addition, attendance at a top 40 National Institutes of Health–funded medical school was a distinct characteristic associated with successful neurosurgery residency matching (21), with other competitive specialties reporting similar importance of medical school ranking on success in their residency match (22). For example, 40% of US neurosurgery applicants who successfully matched from 2011 to 2018 came from medical schools ranking in the top 40 for research based on the 2018 *U.S. News & World Reports* rankings (12). Furthermore, the opportunities provided by an applicant's medical school are made even more important by a recent change to the United States Medical Licensing Examination (USMLE) Step 1 exam to a pass-fail format. In one study, PDs across all specialties agree that medical school prestige will be considered more important in the evaluation of an application after the change in the USMLE Step 1 scoring format (23). Regarding neurosurgery residency programs, more than half (71%) of the 48 PDs responding to a survey believe that medical school reputation will become more important in resident selection, and 63% of PDs believe it will put IMGs at a disadvantage because of the change (24).

The importance of the research post also translates to the international setting. A higher-ranked medical school seems to similarly impact IMG applicants. In theory, a greater proportion of countries known for their scientific prowess produces more IMGs who are successful in the neurosurgical residency match. The variability of foreign-home institutions, ranging from well-known and research-intensive European centers to those in LMICs with relatively low exposure to scientific work, is represented by applicants (6). In this study, the Middle East accounted for most IMGs in US neurosurgical residency programs (13/42 [31%]). However, about 40% of all Lebanese medical graduates in the past quarter-century have migrated to the United States (25). Arguably this specific example is the exception but again highlights how socioeconomic and environmental aspects, as seen in the Lebanese and Middle East communities, influence international migration. For critical inferences to be made, an analysis of the geographical distribution of all neurosurgical applicants would give a more accurate picture of the country-specific success rates of foreign neurosurgery applicants.

Additionally, while medical school prestige and research opportunities impact a candidate's professional trajectory, elements such as the alignment of foreign medical school curricula to those in the US and collaboration or exchange programs with US institutions, as suggested by Chandra et al. (26), could help explain the observations that specific countries or schools produce more IMGs who successfully enter US neurosurgical residency programs.

More than a subject of professional competency

The subject of international migration based on professional development is complex and multifaceted. While the US has developed an independent assessment of international professionals, other nations have done the same. Labor ideals, such as free movement and working rights in Europe, have mandated that means be established for assessing international candidates equal to their native counterparts (27). Acceptance of foreign applicants impacts the workforce, resources, and service provision aspects of the neurosurgery profession. Professional immigration has also been the subject of political debate.

The situation for IMGs in the US depends on federal policies, where congressional appropriation for medical training results in appropriate and substantive federal input into the fabrication of residency infrastructure given the government's financial contribution. Graduate medical education programs funded by US tax dollars support the development of the nation's citizens, serve the American public, and USMG and US residency programs. This reality emphasizes the infrastructure's educational, financial, and legislative components to determine the appropriate distribution of resources for training. It provides an infusion of new ideas, rewards for diligent and high-quality professional contributions, professional opportunities, and compatibility with the nation's view of immigration.

The visa requirement to enter and study in the US is a critical component of the neurosurgery residency application process for many IMGs. Because of the length of US neurosurgery training programs, IMGs require a permanent residency permit ("green card") or other semi-permanent or permanent work authorization. This type of immigration work status can require months to years to acquire, thus impacting the length of an IMG's research period before applying to a neurosurgery residency program.

It is also important to note that professional associations and boards have specific policies regarding training and acceptance. Comparative frameworks include the European and UK systems. Medical graduates of the European Union and other countries with bilateral agreements, such as Switzerland, Norway, and Iceland, are not considered IMGs when applying for residency in these countries. It is particularly important for IMGs to obtain a work permit and accreditation for their medical degrees. This hurdle is comparable to attaining Educational Commission for Foreign Medical Graduates (ECFMG) certification in the US. These accreditations count as the initial basic requirements for practicing medicine in the US.

A "Kenntnisprüfung" in Germany and the Professional and Linguistic Assessments Board (PLAB) in the UK are required to prove sufficient medical knowledge to practice medicine and are only mandatory for foreign graduates (as of January 1, 2021, the PLAB is required of EU citizens) (28). Language requirements, however, are not bound to labor agreements in the European Economic Area due to its multilingual landscape. In Germany, C1 medical language proficiency and B2 German proficiency as per the Common European Framework of Reference for Languages are required (29). This requirement aligns with the Occupational English Test now required by the ECFMG after it canceled the Step 2 Clinical Skills examination for foreign graduates (30).

Furthermore, in the UK, the concept of "experience limits" is a stark difference from the US system of training doctors. In the UK, postgraduate experiences in a medical specialty that exceed certain limits may lead to the status of overqualification for the applicant and ineligibility for residency training. For neurosurgical training, these limitations are as follows: clinical experiences that do not exceed a timeframe of 24 months, with a maximum of 12 months in neurosurgery, neurology, neuroradiology, and neuro-intensive care combined (31). Such a requirement could pose a significant limitation for IMGs if the US had such a directive. This requirement would affect foreign applicants in our cohort, with 5 residents who received some form of foreign training and 5 who completed a neurosurgery residency before entering US residency. In this scenario, IMGs may view the US as an easier or more accessible pathway into postgraduate training programs. Although a maximal preresidency specialty limitation does not apply uniformly to all tracks that may lead to neurosurgical qualifications in the UK (Certificate of Eligibility for Specialist Registration (CESR), CESR-Combined Program), it pertains to the main national training curriculum of an 8-year neurosurgical residency.

The UK exercises annual recruitment for neurosurgical residency similar to the US matching system. As pointed out by Solomou et al. (32), obtaining a neurosurgical specialty training position in the UK was highly competitive in 2018 with 152 applicants for 34 positions and in 2019 with 157 applicants for 24 positions. They noted that proof of early interest in the neurosciences, substantive academic productivity, and undergraduate achievements constituted significant components of a competitive application. Conversely, in Germany, a standardized national process for hiring residents does not exist, and prospective IMGs need to focus on acquiring their work permit and medical accreditation before directly applying to training programs.

The path to residency training for IMGs in the US is well structured. European models appear less well delineated in their residency trajectory. Poorly delineated application processes for achieving professional competency can also hinder international migration and deter potential candidates who favor a more formal approach.

Benefit of IMG research years beyond their research period

Not only do the research opportunities before the residency application substantially contribute to a successful application, but also factors such as a well-established faculty for mentorship play a role. This point is in line with reports that letters of recommendation (LORs) for the neurosurgical match hold more importance as an admission criterion than the applicant's research, according to PDs (33, 34). Obtaining a recognized, appropriate, or meaningful LOR, which is often as difficult to obtain as for IMGs in their home country, is an additional reason to complete dedicated research time in a US neurosurgical department (35). This time is vital for the advancement of research acumen and ancillary reasons such as producing publications and presentations, attending conferences, networking, building relationships, and time spent as a clinical observer within the research period. IMGs are also evaluated during a research period because the IMG represents an unknown, especially not having been through the standard USMG progression to residency application. These evaluations may include assessments of seriousness, dedication, and persistence—essentially a test of whether the IMG is a good fit for a program. Often, a USMG who does not match may be in a similar situation. Many IMGs enter a US academic environment inexperienced in quality research. Thus, a central question is: "How do IMGs learn research?" Centers should be equipped to offer excellent periods of research where IMGs accomplish research through mentorship and coaching.

Aside from standardized tests for ECFMG certification, it is difficult to determine the quality of international medical curricula and, therefore, the medical education that IMGs receive. In addition, LORs from research mentors abroad are much harder for PDs to evaluate than those from domestic colleagues in the more familiar US neurosurgery community. The time spent on research fellowships in a US neurosurgery department allows an IMG to build rapport with potential future mentors and colleagues and acquire LORs from established US neurosurgeons.

The currently established pathway for IMGs who intend to match into US neurosurgical residency primarily revolves around several dedicated research years. The influences the research years have on the competitiveness of their applications go beyond the quantity of research they produce. Our results suggest that the heavy focus on research might not be warranted or worthwhile in the long term. IMGs often spend onerous time in research that may take on the characteristics of indentured servitude. Thus, the institutional environment must be one of support, mentorship, and positive accomplishment. Information on financial support was not consistent and is variable. Although research project costs are covered, institutions may provide minimal financial living support, requiring the research IMG to establish sufficient personal funds for their stay at the institution. Many institutions now require such individuals to be paid by the institution at levels consistent with National Institutes of Health postdoctoral levels or to establish comparable personal funding, which the US Department of Labor may regulate. IMGs often go into dedicated work positions in laboratories led by a primary investigator working on an established research topic where they are paid from a grant or funded project.

Although most PDs in our survey believed that IMGs produced more work before residency than their USMG counterparts, this impression is not preserved once IMGs enter residency. Although IMG and USMG publication numbers are not available for comparison for the period of neurosurgical residency training, we contrasted the median number of publications by IMGs in residency with those completed before residency (3 articles per year vs. 7 articles per year; **Figure 4**). This decrease in publications is not surprising because IMG residents are bounded by the same clinical duties and time constraints as USMG residents.

Previous studies found that the academic careers of fellowship-trained vascular, endovascular, and oncological neurosurgeons are primarily associated with the h-index during residency (36, 37). Similarly, Daniels et al. reported the number of publications produced during residency was associated with academic career progression in neurosurgery, whereas the number of publications preresidency was not (38). However, residents who devoted a dedicated research period before their application had better academic career trajectories, but this finding was not differentiated between USMGs and IMGs. However, the input of PDs seems to indicate that the research contributions of IMGs have an impact beyond merely the h-index for their publications.

It is difficult to assess and directly compare USMG neurosurgery applicants who do not spend lengthy dedicated time on research but produce research articles and balance medical school duties with IMGs who work full time on research and do not have clinical responsibilities. In an analysis of burnout in neurosurgical trainees, IMGs score high in resilience (39). A study on general surgery interns found their performance to be of equal quality to USMGs (40). Regarding research, there was no difference in h-indices between IMGs and USMGs during or after residency (7). The analysis of this situation may be more about the assessment of the individual background of the IMG, as more than half of the successfully admitted IMGs had previous neurosurgical training (10/17) in addition to their LORs and US-based research period. IMGs who have experienced previous neurosurgery training may understand the demands that are expected of them and may be committed to seeing their opportunity through to completion. US neurosurgery has had a history of training foreign neurosurgeons who have been successful in academic and private practice environments. Foreign neurosurgeons have also become leaders in American neurosurgery.

The interview process, USMLE scores, and LORs are commonly ranked as more important than research, which supports the sentiments that a well-rounded application of every neurosurgery applicant is of the greatest importance. This finding might encourage future applicants to invest more time in clinical and voluntary work or expand upon their professional connections through neurosurgical meetings and observerships. However, starting at the end of January 2022, the USMLE Step 1 will no longer be graded on a 300-point scale. Instead, it will become graded as pass-fail. A recent study conducted by Huq et al. indicates that most PDs expect the involvement in research and the number of publications to increase among the applicant pool due to the change in the USMLE Step 1 exam format (41). Thus, research performed to gain a neurosurgery residency position may become more consequential.

In addition, barriers are increasing to clinical work for temporary or transient foreign neurosurgeons or medical students in US hospitals due to liability and other legal issues. Clinical or clerkship opportunities are uniquely available to IMGs from Caribbean medical schools due to their location and the fact many are US citizens (i.e., US-IMG) (42, 43). Thus, the research period for IMGs continues to be an opportune means to demonstrate the resourcefulness and accomplishment to support a neurosurgical residency application. With a better understanding of expectations in the most personally controlled component, i.e., a dedicated research period, this study clarifies the cardinal aspect of a successful residency application and how the research period impacts the optimal pathway of IMGs toward neurosurgery residency programs.

Contributions of Barrow Neurological Institute to IMG development and matching into a US neurosurgery residency program

Another critical question is: "How can the time spent in research as an IMG be made worthwhile?" Several PDs who responded to our survey noted formal neurosurgery department support of IMGs for their research period to be important. One PD cited their American Council for Graduate Medical Education recognition and accreditation for IMG research time. Most PDs in the second survey ranked a candidate's "institution or associated personnel" as the most important factor when considering research productivity. Because their tenure may be years or at least 1 year, involvement of the IMG in a structured, mentored research fellowship or graduate program may be an answer. In 2012, the neurosurgery research laboratory at Barrow (i.e., The Loyal and Edith Davis Neurosurgical Research Laboratory) was a founding member of an integrated interdisciplinary neuroscience graduate PhD program partnership between the hospital institution (Barrow Neurological Institute) and the major local university (Arizona State University), supporting one of the top neuroscience programs in the country. The laboratory supports 2 funded neurosurgery research fellowships per year, with at least 1 one of these positions dedicated to the support of a research fellow in the neuroscience graduate program that lasts from 3 to 5 years, culminating in a PhD in neuroscience. Other research fellows beyond the two positions must self-fund with support verified by hospital human resources administration and be of an amount in line with NIH postdoctoral levels. The laboratory funds all projects, meetings, presentations, and publications costs.

Additionally, neurosurgery research fellows who spend 1 year at Barrow are enrolled in a named research fellowship of the laboratory and institution and receive a formal certificate of research fellowship at the successful completion of their program. They become part of the heritage of the institution, imparting legitimacy to their work and tenure. Thus far, all 3 graduates of the neuroscience PhD program who applied to neurosurgery residency were readily accepted. Furthermore, all 20 IMGs who have worked in the research laboratory since 2000 and applied for residency or a clinical fellowship have been accepted. The duration spent in research by these IMGs is comparable to that reported in the present survey (both 30 months).

The leadership of an in-depth, research-experienced, chair-endowed neurosurgeon engaged full time without clinical duties who directs and coordinates all phases of the laboratory experience, projects, and collaborations, and who skillfully mentors and assesses the research fellows (both IMGs and USMGs) likely plays a major role in applicant acceptance into a neurosurgery residency. A long-established dedicated international outreach toward education in neurosurgery by Barrow's retired and current institutional directors also supports this success.

With a stance similar to Wilder Penfield's viewpoint for training his first research fellows and later residents, [44–46] he and William Cone, and later Arthur Elvidge, allowed trainees and research fellows to develop according to their strengths and interests while providing support and mentorship to help shape their careers. Indeed, attracting research fellows, i.e., IMGs, to become neurosurgery residents is only the beginning. A program director needs to have the skills and resources to inspire these trainees to come into their own. Otherwise, it is a waste of talent and precious career time. Research fellows in the Barrow program are enveloped in a productive environment that focuses on creativity and promotes resourcefulness and innovation.

Interestingly, of our 3 IMGs who were not admitted to a neurosurgery residency program upon the first application, 1 had just arrived in the US a few months earlier and submitted a late, underpowered application. This applicant submitted an excellent application with guidance the next year and was admitted to a prestigious residency. Another elected to continue after 2 years at another institution, at which 2 applications were necessary for residency admittance, without exact details. The third research fellow did not engage in a concentrated or thematic evolution of research but was admitted to a preliminary postgraduate year of surgery and was then admitted to a vacated neurosurgery residency position 2 years later. The common theme of these 3 and the 13 other first-round successfully matched research fellows from our program experience is that all IMG research fellows who were engaged in a structured or thematic line of excellent research, skillfully mentored, and who submitted excellent applications while at Barrow were admitted upon their initial application to a first-rate residency program. Given the success of the IMGs who conducted dedicated research at Barrow, we believe our current model provides a possible solution to the challenges and biases faced by IMGs who desire to train in the US.

Solutions to possible biases affecting IMG applicants to neurosurgery

IMGs face several institutional biases when applying to a US neurosurgery residency program. These biases result in IMGs being more likely to perform a research fellowship after medical school and matching into an unranked program. In addition, from 2007 to 2019, there has not been a significant increase in the number of IMGs accepted into programs, even though the number of positions has significantly increased and the proportion of IMGs applying has increased.

Although it is beyond the scope of this paper, we believe there are possible solutions to these problems exemplified by our institution. For example, all neurosurgical programs with a dedicated research department or laboratory could foster positions for IMG applicants. This action may even include a graduate program (e.g., PhD program) that extends the IMG's research period and focuses on a specific topic or theme. In our analysis, PDs found this research activity more important than the overall number of publications, which may be on scattered topics or simply one-off clinical papers. Furthermore, these research positions should be more available at highly ranked institutions, which, on average, have more residents per year and resources for performing high-impact research. This outreach may target the bias of not being able to match at a ranked program because from 1968 to 2018, 25% of IMGs who completed a research fellowship stayed at the same institution to complete their residency training (7).

It is somewhat disappointing that only 4 research fellows have been matched into the Barrow residency program, with 2 of them entering vacant positions. Senior staff and faculty believe that the research fellows were not well known by the residents or that the residents do not want to "take a chance" on an IMG in the residency program, perhaps believing they would not fit "the team." Several research fellows expressed disappointment with not being in the top residency position consideration cohort at Barrow when they had been there for years performing outstanding research or performing a clinical rotation, but where other candidates less familiar and experienced were accepted. These research fellows, however, matched into programs where they stated their research and clinical experience were valued. Fifth-year residents at our institution are critical leaders of future resident selections. Many of our research fellows have won major acclaim for their research work and have already fully trained in neurosurgery at demanding foreign programs, such as Russia's renowned Burdenko National Medical Research Center of Neurosurgery, yet are ranked relatively low. None of the research fellows have had personality issues and have been held in the highest esteem and befriended by department and hospital staff.

Notwithstanding the above, the Barrow fellowship program has achieved success with its structure and reputation. Uniquely, the program has matched 2 foreign fellows in the same year to prestigious residency programs on their initial application, and 2 fellows were matched into the same top residency program over successive years. Although research fellows give presentations, attend rounds, institutional, national, and international conferences, and educational and social events with the residents, solutions to this problem at our institution include further integrating the fellows with residents to apprise them of the full scale of fellows' backgrounds and impending residency applications.

Limitations

Although our findings portray an interesting component regarding compelling aspects that have evolved in US neurosurgical residency programs, the data presented are limited. These data concern IMGs in US neurosurgery training programs only. The response rate to surveys was about 50% for IMGs and 28% for PDs; thus, it is reasonable to argue that the opinions obtained do not accurately represent the complete resident demographic and PD opinions and policies. Our data do not derive from social media or publicly available databases, which may yield large numbers but few personal details. However, the data are sufficient. Our sample size is sufficient considering the actual size of the denominator (78 or 79). First, a search before and after residency graduation in June 2020, revealed 8 residency classes and 79 IMGs. Second, after collecting archived data from the NRMP from 2013 to 2020 (8 years), we found that 95 IMGs had been accepted into US neurosurgical residency programs, of which 78 were non-US IMGs. Our study only surveyed non-US IMGs. Lastly, the 79 IMGs (from before and after resident graduation) and the 78 non-US IMGs (from the NRMP archive data) do not accurately represent the number of non-US IMGs who conducted dedicated research as fellows before applying to US neurosurgery residency programs. This number cannot be accurately determined but is less than 78 or 79. Therefore, our already high response rate (53%) for non-US IMGs who successfully matched into US neurosurgery residency programs most likely represents an even more significant percentage of non-US IMGs who conducted research through a fellowship and were accepted into a US residency program, perhaps as high as 80%. In addition, no previous study has included information from neurosurgery residency PDs.

Respondents were cautious with some of their responses to questions (i.e., country of origin and number of publications during residency). As such, the data might not be representative of the cohort due to a lack of responses from some residents. The present paper only describes the results regarding IMG research productivity, and it does not address all the questions given in the questionnaires. Other survey results will comprise additional studies. We used as much accessible NRMP and published literature as possible for comparison. In cases where similarities were identified, the findings suggest the continuity and the legitimacy of the representative trends.

Furthermore, some important questions cannot be addressed by the present study but merit answers. Is the neurosurgical training system in the US the best in the world? If so, does it allow weaker candidates to become excellent neurosurgeons? Is the international community lacking excellent potential neurosurgeons? Regarding the PD role, do PDs require qualities (i.e., aptitude, passion, predisposition, teamwork, or ambition) that cannot be evaluated through an IMG's research productivity? Is a research fellowship necessary for an IMG, or could an IMG and USMG apply under the same conditions? Is neurosurgical attitude associated with the prestige of the home institution of a candidate? Lastly, how can the system be improved to offer all IMGs a similar condition when applying? All these questions are critical and, unfortunately, outside the scope of the present study due to its strict focus on the IMG research period from the perspective of both IMGs and PDs. We acknowledge that a focused editorial on such a topic would be justified.

Conclusions

The IMGs surveyed reported significantly longer periods invested in dedicated research and more published articles before their US neurosurgery residency match than the expected numbers reported by the PDs surveyed. PDs perceive IMGs to be more productive in their research than USMGs until they enter residency. At that time, many PDs stop seeing a difference in research productivity between IMGs and USMGs. This impression is in accordance with our finding that there is an understood decrease in published work by

IMGs upon entering residency. Many IMGs complete a dedicated research period in a US institution before their residency application, unlike USMGs. This dedicated period allowed them to surpass the research productivity expectation of PDs and enhance their neurosurgery residency application. This study highlights that the research requirement is more than satisfactorily achieved by IMGs, and to improve their competitiveness, IMGs may be better served by completing more clinical placements. However, with limitations in clinical positions and neurosurgery's tradition of research involvement, neurosurgery residency training in the next decade will be defined as much by advances in technology as by the opportunities afforded in neurosurgery training and the labor shifts in the overall profession. As neurosurgical education and technology advance worldwide with growing interconnections between neurosurgeons of different countries, potential changes in the requirements and policies of training programs may open training positions for successfully and comparatively educated IMGs in various countries.

In 1928 when he arrived at McGill University's Royal Victoria Hospital under the aegis of Edward Archibald, Wilder Penfield pioneered what would be a remarkable achievement 6 years later with the opening of the Montreal Neurological Institute. He sought nothing in the way of nationalism, only a pursuit of excellence—his first research fellows arriving in 1929 were from San Francisco and London, with one woman—the future famed neuropathologist Dorothy Russell—and his residents were as well international, contributing brilliantly in the next decades to scientific neurosurgery (44, 45). In fact, up until the mid-1990s, McGill had trained more department chairmen of US neurosurgery programs than any other single institution (46). McGill trained the first African American neurosurgeons during a period of intense racial segregation in the US, "enabling subsequent African Americans to enter and enhance the field of neurosurgery." Up until 1997, a unique, close relationship existed between American and Canadian neurosurgery since famous institutions of the two countries were among the founding centers of neurosurgery in North America, with activities, training, faculty, and programs constantly shared. Unfortunately, unresolved training, practice, and economic issues since have designated Canadians as ordinary IMGs to the US neurosurgery system. For many years, Americans went abroad for research at various times related to their residency period, although most returned to the US for clinical training. Although the notion of protecting national interests is crucial and socioeconomic attractions are a powerful attractant to the US medical practice environment, might we take an altruistic lesson from Penfield, that excellence and the deserving, no matter what human form, are just as critical to the progress and improvement of neurosurgery and its training milieu. A delicate balance is also necessary between the workforce and national interests. We hope that our findings will benefit future applicants and PDs alike and encourage further investigation of IMG applicants to neurosurgery training programs.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

Author contributions

*GM-J—primary author, study conception, data generation, data analysis. YX—assistant author, study conception, data generation, data analysis. LMH—assistant author, study conception. DB—assistant author, data generation. JHJ—data generation. AJSK—data generation. MAL—data generation. TFD—study review, secondary author, paper review. RFS—study review, paper review. MTL—study review, paper review. MCP—study conception, supervision, paper revision, paper review, and approval. All authors contributed to the article and approved the submitted version.

Funding

This study was funded by the Newsome Chair in Neurosurgery Research, held by Dr. Preul, and the Barrow Neurological Foundation.

Acknowledgments

We thank the staff of Neuroscience Publications at Barrow Neurological Institute for assistance with manuscript preparation.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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