Ultrasound-guided endoscopic surgery


However, a special aspect should be mentioned when using this particular technique for the evacuation of hematomas. It has been shown that an acute hemorrhage within an intracranial cavity is not always hyperechogenic on ultrasound1,2 and can be mistaken for rinsing liquid. Rebleeding appears as visible movement of small particles within an increasing cavity and can be observed only after several minutes of ultrasound monitoring. It should have been emphasized that, especially when the endoscope has been removed, continuous ultrasound monitoring with knowledge of the aspect of a rehemorrhage would offer more safety for the patient.

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References

Disclosures
The author reports no conflict of interest.

Response

We are grateful to Prof. Mursch for the comments on our paper. We have also noted rebleeding that was initially observed as a low echoic lesion that then changed to a high echoic lesion after a few minutes. We agree that continuous ultrasound monitoring is needed after endoscopic surgery to confirm that there is no rebleeding. We thank Prof. Mursch for pointing out this important issue.

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Bibliometrics

TO THE EDITOR: We read with interest the article by Lozano et al.6 (Lozano CS, Tam J, Kulkarni AV, et al: The academic productivity and impact of the University of Toronto Neurosurgery Program as assessed by manuscripts published and their number of citations. J Neurosurg 123:561–570, September 2015).

The use of bibliometrics, especially variations of the h-index, has received much interest and attention in the neurosurgical literature in recent years. A quick search of the literature on the topic provides references dating back to 1990, in which Davis and Cunningham analyzed the citations of the earliest American neurosurgeons.2 More recently, analyses have looked at comparisons of academic departments (residency and fellowship) in the United States,3,4,7 North America,5 and Great Britain and Ireland;10 gender;8 funding;9 and fellowship- versus non–fellowship-trained neurosurgeons.1

These publications establish bibliometric benchmarks for groups of researchers, which can then be used to conduct comparative analyses, both now and in the future. To our knowledge, no recent paper has focused solely on a single institution as does the recent paper by Lozano et al.6 Using our methodology, they compared their program’s publications, citations, and h-index (as well as other indices) with those of other institutions in our paper and conclude that “it is therefore likely that the neurosurgery
program at the University of Toronto ranks first in the world in academic output as measured here.”

The University of Toronto Neurosurgery Program is blessed with many high-achieving neurosurgeons, and their contributions to our field are well recognized. However, we feel the authors missed a clear opportunity to provide a detailed bibliometric analysis of all 14 Canadian neurosurgical programs, which could have served as a natural complement to our analysis of 103 American programs.

The authors do provide the reader with some insight on how their program is structured in order to achieve their high academic output. Programs such as University of Toronto and University of California, San Francisco, undoubtedly have a well-developed culture and environment that support and place high expectations on research. The dissemination of research through publications that result from “chatter” among other researchers—and ultimately the citations that these publications can generate—is the goal of such a culture. Further details of the University of Toronto’s efforts to build and sustain this environment would have been valuable for the reader. Exactly how does Toronto engage their residents and faculty in research? Is there an annual research requirement, and if so, how is it monitored and enforced? Do they provide protected research time? How do faculty balance research with clinical duties? Is there a financial incentive or reward for publishing beyond academic promotion?

We again congratulate the University of Toronto on their remarkable past academic achievements and look forward to their future contributions.

References


Disclosures
The authors report no conflict of interest.

Response

We thank Dr. Klimo and colleagues for their questions and comments on our work. They have asked 2 questions: 1) Why didn’t we include a bibliometric analysis of all 14 Canadian neurological programs? 2) Can we provide some insight into how the Toronto program is structured to achieve high academic output?

As it relates to the first question, our intent was to document and validate the academic productivity of our own program. Bibliometric analyses, particularly third party ones, are often plagued by inaccuracies. For example, many publications are missed due to variations in spelling, misattributions, and omissions. On the other hand, other publications are inappropriately added because of the ambiguity and similarity in an author’s last name. We wanted to produce a data set for our program that could be verified and be as accurate as possible. Our own feeling is that each center should compile and report its own appraisal of its productivity. That would not only serve as a measure of where it stands in the neurosurgical community, but would also be more likely to be accurate and validated and less likely to be contested than one produced by an outside party.

The second question relates to what is our “secret sauce” in reaching this level of academic productivity. We do not have direct cause and effect data, and this question can only be answered with speculation. First and foremost is our clearly defined objective that values research from our residents and faculty. To execute this vision, we preferentially recruit residents who show strong promise in the research realm and target the recruitment of faculty who have successful and sustained research as a major component of their career.

Second, we have created an infrastructure that encourages and supports research. Our residents’ research rotations are a fundamental component incorporated within the residency program in their PGY4. We have a longstanding Surgeon-Scientist Training Program at the University of Toronto that guarantees the full salary of our residents for multiple years while they are conducting their postdoctoral research, which can be up to 5 years. Removing the uncertainty of salary support is, we feel, a major enabler for our residents to pursue research.
With respect to our faculty, there are various income-sharing mechanisms that promote research. We realize that to be a successful program, we need to have excellence across clinical work, teaching, and research. We value each of these components and have revenue allocations to recognize contributions in research and teaching—activities that are not as well monetized. Although those with the highest clinical volumes often earn more, the disparity among our faculty who have predominantly busy clinical practices and those who have a practice with a strong research component is relatively small.

We cannot overemphasize the importance of culture in promoting research. The idea that each program member subscribes to is that we are here not only to treat our current patients, but also to push forward the frontiers of science in neurosurgery and to foster innovation.

We feel fortunate to be in a work environment where research is not just encouraged, but enabled. While these various external factors provide important permissive conditions, it boils down to having the right people with the talent, drive, and commitment to push forward the academic mission of our program and of neurosurgery.

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Disclosures
The authors report no conflict of interest.

Response
We thank Prof. John D. Pickard and Dr. Alonso Pena for their interest and insightful comments regarding our paper. We wish to clarify that in our study we modeled communicating hydrocephalus, and we regret that this point was unclear in the paper. We agree that brain deformation in communicating hydrocephalus can occur without the development of a measurable TPG, which has been conventionally defined as the difference between CSF pressure in the subarachnoid space and cerebral ventricle. We also believe that for hydrocephalic brain deformation to occur, a major change in the mechanical properties of the brain must occur, as suggested by Prof. Pickard and Dr. Pena.

Changes in stiffness (i.e., elasticity or compliance) across a continuum of brain tissue have been suspected to be an essential component for the development of communicating hydrocephalus. One possible cause of the observed reduction in brain stiffness may be a decrease in interstitial fluid (ISF), which saturates the brain. The change in the ISF saturation level, which would directly impact brain elasticity, may be caused by the disruption in the pressure distribution equilibrium across the cerebral mantle. As stated in our Appendix, “The porohyperelastic model describes the brain as a hyperelastic solid matrix, saturated with interstitial fluid.”

In our study, TPG was redefined as the difference between CSF pressure and capillary pressure (in our model, the ventricular fluid pressure and the pressure at cerebral convexity, respectively), rather than the CSF pressure at the subarachnoid space. Based on these definitions, the subsequent brain deformation in communicating hydrocephalus was simulated, similar to the previous work of Peña et al.

Intracranial hypertension, similar to hydrocephalus, is a generic term that encompasses numerous etiological factors that lead to common clinical manifestations. A major common factor is increased intracranial pressure, which should always be confirmed using appropriate monitoring methods. Chronic brain edema caused by obesity, venous outflow obstruction, endocrinological changes, and other factors can all potentially influence intracranial pressure. Treatment depends on an accurate diagnosis, and includes drugs, shunting, and venous stenting; all treatment options have specific success and failure rates. Regarding IIH simulation, we have not designed or constructed a specific finite element (FE) model for simulating well-known IIH features (e.g., dilated optic nerve sheaths, dilated sulci, partially empty sella). Instead, we were intrigued by recent studies stating that a close relationship exists between IIH and hydrocephalus; therefore, we investigated this relationship by inducing the exact opposite change to the same FE model that was used to simulate hydrocephalus (hence the “counterintuitive” negative TPG). The simulation resulted in decreased ventricle size and increased cortical subarachnoid space and water accumulation around the brain, which we interpreted as cerebral (to be specific, interstitial) edema.

Although the results showed a slit-like ventricle as an IIH characteristic, the size of IIH ventricles can vary but rarely appear slit-like. However, small ventricles do exist in IIH and, as previous studies have suggested, reduced ventricles can be a late IIH manifestation.

The presence of cerebral edema, whether interstitial or intracellular, has long been observed in IIH. The conventional understanding regarding the presence and the extent of edema in IIH is being contested, rather than dismissed. For this reason, along with other findings from the simulation, we concluded that the changes in our FE model should be interpreted as the development of IIH. Nonetheless, IIH does not necessarily involve an extensive degree of brain deformation as appears in hydrocephalus, and the results of our work regarding the IIH simulation may be slightly exaggerated because we induced the exact same degree of mechanical stress as would occur during hydrocephalic conditions but not in IIH. We also acknowledged this point in the paper by mentioning that “a very small or even negative transmantle pressure gradient level” would exist in IIH.

Current studies regarding IIH pathogenesis have focused on the worsening of the venous sinus system. Increased venous pressure due to venous stenosis is commonly observed in IIH and may cause a decrease in cerebral compliance and prevent ventricular dilation, overstressing the slit-like ventricle in the FE model with restrictive boundary conditions. Thus, to increase the reliability and accuracy of FE simulations for IIH, greater detail must be incorporated into the brain models.

We agree that a multidisciplinary approach is needed, and we invite Prof. Pickard and Dr. Pena to cooperate with our group in the future.

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References


Evaluation of neurosurgical innovation using patent database

TO THE EDITOR: We read with great interest the article by Marcus et al.10 (Marcus HJ, Hughes-Hallett A, Kwasnicki RM, et al: Technological innovation in neurosurgery: a quantitative study. J Neurosurg 123:174–181, July 2015). In their paper, they attempt to elucidate the process of neurological innovation by using a data-driven method. Their core methodology is derived from earlier work.5 Beginning with a query of the DOCSDB international patent database, comprising the years 1960–2010, a Boolean combination of a number of selected neurosurgery-related terms is used to yield a list of patents. The top 50 patent codes from this list are then manually grouped into “technology clusters.” The neuromodulation cluster is examined separately and in special detail. In parallel with this patent-based analysis, the results of a Boolean MEDLINE publication data search performed using the same terms is used to compare academic publications against patent activity.

Although the authors have done a good job in discussing some of the study limitations, we have some comments and recommendations from a methodological standpoint.

1) Patents versus commercialization as primary marker of “innovation.” The authors loosely equate patents with innovation. In reality, a significant proportion of life science patents lie fallow and do not translate to innovations in the marketplace. Public funding agencies, such as the NIH, have joined academia and industry in identifying this as a looming systemic problem with technology transfer.11,12 Moreover, a patent can only reasonably be said to represent “innovation” if it protects a commercialization activity within 20 years of its issuance, something the authors’ analysis did not take into account. In recent years, creative responses to this inefficient translational process have emerged. Direct attempts to achieve the goals of neuroscience commercialization have resulted in private sector initiatives such as the NeuroLaunch startup accelerator (http://www.neurolaunch.com), university-based initiatives such as the NeuroLaunch startup accelerator (http://www.neurolaunch.com), university-based initiatives such as the Center for Innovation in Neuroscience and Technology,9 and public-private partnerships such as the Neuro Startup Challenge (http://www.neurostartupchallenge.org).

2) Forward citations as the sole measure of “impact”/“top performance.” In academic research, forward citations are a proxy for impact because the aim of research is to seed additional knowledge and discoveries. With a patent, by contrast, the most meaningful measure of impact is the ability to foster commercialization activity.11,12 This paper focuses its analysis almost exclusively on forward patent citations. It would be more relevant (although more challenging) to analyze historical data on neurosurgery startup company formation, product launches, or funding

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Neurosurgical forum


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events. Licensing events would also be a better marker of impact than patent citations, although these data are privately held. Previous attempts to study licensing events within a disciplinary subdomain have met with partial success due to incomplete cooperation from the licensor institutions surveyed.1

3) Source of inventions. It would be valuable to analyze the source of neurosurgical innovations. For instance: what proportions of neurosurgical patents are filed by large device companies, versus individual neurosurgeons or small companies? Are these proportions changing over time? Previous literature suggests an evolving role for individual neurosurgeons in the generation of intellectual property.1,5

4) Limited examination of data peaks. It is remarkable that innovation in neurosurgery, as measured by Marcus et al., has not increased monotonically. Instead, it has peaked at 3 points: around the year 2000, in the mid-2000s, and in the late 2000s. Equally interesting, publications in neurosurgery (normalized) peaked in the early 1960s, early 1970s, and in the 1990s to early 2000s. Would a closer examination of these data peaks reveal underlying insights?

5) Additional markers of impact for patents. Litigation activity may be a theoretical, if infrequently applied, surrogate marker of patents that have led to meaningful commercialization after issuance. CourtLink (LexisNexis), which reflects the government courts database PACER along with additional features, permits searching all federal district and appeals courts by patent number, and could be used for this analysis.

A deepened understanding of the innovation process is critically important for continued technological improvement within our specialty. We applaud all those who seek to facilitate the future of neurological innovation by analyzing its past. It is our hope that future work in this area will continue to hone the necessary methodology while maintaining rigor and relevance. We appreciate the review work done by Marcus et al. on the topic of neurological innovation, and this will serve as a good starting point for further studies and analyses.

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Response

We would like to thank Drs. Amadio and Ahmad for their interest in our study, and the Editor for allowing us the opportunity to respond.

We defined technological innovation within health care as any innovation that initiates a change in clinical practice. We would agree that for a particular patent to truly represent a technological innovation, it must be commercialized. In our study, we analyzed the patent class codes of more than 10,000 patents filed relating to neurosurgery. Although many of the patents will not have been commercialized, the top performing technology clusters over the last 50 years are likely to remain valid. Moreover, for each of these technology clusters we then searched for related peer-reviewed publications in healthcare journals as a measure of translation.

We performed a more detailed analysis of patents relating to neuromodulation devices. Patents were scored according to their year of publication, their number of forward citations, and their family size. Most patent databases do not contain information on whether patents have been commercialized, but previous studies have demonstrated that these other patent quality indicators are positively correlated to commercialization.2

Within patents relating to neuromodulation, the most common applicant was Medtronic. A more detailed analysis of innovators, and the relative contributions of small and large companies, was beyond the scope of our study. Nonetheless, we would welcome such work as interesting and useful additions to the literature.

We would strongly agree with Amadio and Ahmad that any attempt to facilitate the introduction of technological innovation should be predicated on a better understanding of the process of innovation. To this end, we hope that our study spurs further research in this important area.

References


Disclosures

Dr. Ahmad is a consultant for DePuy-Synthes. Dr. Amadio is a co-founder and partner in NeuroLaunch.
Career satisfaction and burnout among neurosurgeons

TO THE EDITOR: “Burnout” often feels like a verbosen concept, despite its threatening reality and potentially detrimental outcomes. Its wide-ranging effects can impact nearly every aspect of our lives, both personally and professionally. As a current resident and member of the American Association of Neurological Surgeons (AANS), my interest was captured by the article by McAbee et al. (McAbee JH, Ragel BT, McCartney S, et al: Factors associated with career satisfaction and burnout among US neurosurgeons, results of a nationwide survey. J Neurosurg 123:161–173, July 2015). Having completed the survey, and having recently had the question “Would you encourage your children to pursue a career in neurosurgery?” posed to me at a conference, I found myself truly contemplating the sacrifices and gains within our career. Burnout is synonymous throughout practice and residency alike, with increasing notoriety due to its shocking prevalence in healthcare. Bringing this topic to the forefront, the current article examined factors associated with satisfaction and burnout within neurosurgery.

Cross-sectional data from a national survey implicated significant self-reported burnout (56.7%). The strongest predictors of burnout in multivariate analysis, by odds ratio, include uncertainty about future earnings and health care reform (OR 1.96; 95% CI 1.41–2.72) and complaint of malpractice (OR 1.60; 95% CI 1.16–2.20). Predictors of satisfaction include a good work/life balance (OR 10.0; 95% CI 4.9–20.3), being challenged at work (OR 4.6; 95% CI 2.9–7.4), having children (OR 2.4; 95% CI 1.2–4.8), and completing > 300 cases per year (OR 1.77; 95% CI 1.03–3.03). Perhaps more important was the collective endorsement of job satisfaction (80%) among neurosurgeons, with approximately 70% reporting that they would choose this career again. Despite laborious demands and uncertain future benefit, neurosurgeons may experience a type of intrinsic fulfillment that extends beyond the limitations of burnout. Identifying occupational pros and cons, such as gratification and burnout, may aid in mitigating factors of exhaustion.

Burnout is highly prevalent amongst residents as well, with the largest study of 15,000 residents showing a prevalence of 51.5% (27%–75% depending on specialty). Largely, burnout is ignored or underrecognized. Acknowledgment of burnout in self-reflection or identification of burnout in colleagues is the first step to improvement. The Maslach Burnout Inventory (MBI) is a well-validated instrument to measure burnout in self-survey form. A shorter and nonproprietary method has been developed for use based on response to a single item. When burnout is identified, physicians should seek assistance. No specialized help currently exists for physicians in burnout, but assistance can be obtained through medical staff offices and counseling departments. In a study of 212 surgeons, assistance-seeking behaviors differed drastically; men tended to seek help from colleagues or friends, whereas women tended to seek help from professional counselors. Regardless of the mechanism of assistance, recognizing and addressing burnout will make us better and more satisfied physicians.

Learning how to avoid this state and to cope with burnout should begin early. Teaching identification of and coping mechanisms for burnout is the focus of intervention at the residency level. Neurosurgeons in academia will know that the US Accreditation Council for Graduate Medical Education (ACGME) has done much work in regard to burnout. Education about burnout and implementing mechanisms to avoid burnout has been a great focus of the ACGME’s Clinical Environmental Review (CLER) Program. Work stress can be categorized into 6 domains, of which CLER seeks to improve workload, control, community, fairness, values, and balance between work and reward. Workload, perhaps commonly perceived to be the foremost factor in burnout, is a complex contributor and involves much more than merely work hours, including patient complexity and documentation efficiency. Hiring physician extenders may assist with the clerical demands of patient care. Meeting with counselors for emotional fatigue may help to process emotions associated with observing suffering and death. Yet, seeking assistance and learning coping mechanisms early in training is of utmost importance.

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References

Disclosures
The authors report no conflict of interest.

Response

My coauthors and I would like to thank Dr. Smith and Ms. Glusman for their thoughtful letter regarding our paper on burnout among US neurosurgeons. As a fourth-year medical student and past president of my school’s AANS Medical Student Chapter, this project was a timely and invaluable experience for me. My medical school class has completed multiple surveys that assessed burnout during different stages of our education. We found that the highest levels of burnout occurred after completing our third year. The research is clear that all current and future physicians are at risk for burnout. From premedical students to department chairpersons, we all have an innate drive to succeed academically, to provide for the care of patients (either on a volunteer basis or as a part of one’s paid profession), and to establish positive relationships with colleagues and societies. But we often neglect self-care and self-reflection in many instances. Thus, there is a need for education on identification, prevention, and treatment of burnout at all levels of medical education and practice, because unchecked burnout has serious consequences for health care workers, their families, colleagues, and for the patients in their care.

To date, there have been several trial programs created to teach mechanisms for coping with burnout and to provide avenues for health and wellness support. For example, the Department of Neurosurgery at the Medical University of South Carolina has recently implemented a wellness program for its residents that provides protected time each week for moderate-intensity team-based exercise, free healthy meal options each day, and a health and wellness lecture series. The goal of the program is to teach, encourage, and support healthy living in an effort to reduce burnout and increase commitment to self-care. A similar study at the Mayo Clinic demonstrated a higher quality of life and lower levels of burnout for residents and physicians who participated in an incentivized exercise program. A required health course for medical students at Northwestern University encouraged them to identify an area for self-improvement and work toward achieving behavior change in that area. At the conclusion of the course, the majority of the students who participated in the program felt healthier and believed they could achieve future goals with similar strategies. These studies demonstrated that interventions need not directly address burnout to provide benefits and career longevity; rather they can simply promote an environment in which health care workers are encouraged to be mindful of the importance of self-care, maintaining a healthy lifestyle, and achieving a favorable work/life balance.

In addition to promoting healthy living, several interventions have focused on enhancing emotional, mental, and spiritual well-being through discussion groups, mindfulness training, and relaxation techniques. The Mayo Clinic Department of Radiology implemented a Stress Management and Resiliency Training (SMART) program for its physicians and saw improvements in stress, anxiety, quality of life, and mindfulness 12 weeks after a brief 90-minute group intervention with optional follow-up calls. A longer, facilitated small-group curriculum was developed and implemented for practicing physicians in the Mayo Clinic Department of Medicine that focused on mindfulness, reflection, shared experience, and small-group learning. Every other week, program participants received paid time off from clinical duties to attend group sessions. Increased empowerment and engagement at work as well as decreased depersonalization, emotional exhaustion, and overall burnout occurred for program participants, and was sustained for months after the intervention. Interestingly, participants in the trial control arm who received the same amount of paid time off from clinical duty, which they could use in any way they chose, also demonstrated a slight decrease in burnout levels compared with those physicians who did not receive any paid time off at all.

Individualized coaching sessions may also hold promise by coaching physicians in self-care areas, such as boundary setting and prioritization, self-compassion and self-care, and self-awareness. Many of these programs, and mindfulness training in general, attempt to teach physicians how to monitor their own lives for signs of burnout, to place more priority on self-care, and to implement stress reduction strategies as a mechanism to improve both their personal and professional lives. They also teach physicians how to deal mentally and emotionally with challenging situations by viewing difficult events of the human experience through a lens of gratitude, compassion, acceptance, meaning, and forgiveness.

Because burnout is a problem for potentially all health care workers, institutional changes will need to be made. The study mentioned above that allows for periodic paid time off suggests that physicians may benefit from protected professional time spent doing what they perceive to be valuable. It is easy to imagine how this method could help physicians be more productive, achieve better work/life balance, and reduce stress. Other possible institutional policies include granting residents time off during business hours to access personal and family health care. By allowing residents to access the care they need, a healthier and more energized clinical team could emerge. Results from the Healthy Work Place Study involving primary care physicians in the upper Midwest and New York City showed that interventions centered around improved communication, changes in clinic work flow, or targeted quality improvement projects can decrease burnout, increase satisfaction, and decrease intention to leave.

It is becoming increasingly obvious that institutional and organizational interventions are needed to improve burnout prevention in physicians, but such interventions can only occur with the support of hospital and departmental leadership. Not only is support necessary, but hos-
pital leadership must lead by example, because the leadership characteristics of physicians’ supervisors have a direct impact on burnout rate. Physicians who rated their supervisors favorably had less burnout and more satisfaction than those who rated them unfavorably. Thus, leadership development courses may be useful for helping leaders to foster an atmosphere of support and empowerment for their subordinates struggling with burnout.

Burnout is a real and potentially debilitating syndrome that threatens the modern physician. In a field as challenging and demanding as neurosurgery, the threat is even greater. By raising awareness of this syndrome, its signs, and its potential prevention strategies, we can better identify those at risk at an earlier stage in their career. By developing interventions, support groups, and organizational resources, we can provide the necessary treatment for those suffering from burnout and more effectively assist them in achieving their personal and professional goals. Finally, by creating an atmosphere in which physicians can pursue help for themselves or their colleagues without fear of judgment or penalty, we may be able to realize a system in which we are able to identify and address burnout long before it becomes detrimental to physicians or their patients.

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References

Sudden death following cranioplasty: autoregulatory failure?

TO THE EDITOR: I read with interest the recent article by Sviri in which three patients died due to massive uncontrolled cerebral swelling following an uneventful cranioplasty (Sviri GE: Massive cerebral swelling immediately after cranioplasty, a fatal and unpredictable complication: report of 4 cases. J Neurosurg 123:1188–1193, November 2015). There are two points upon which I would like to comment. The first is a minor correction. In Table 1 it states that the outcome in two patients in the 2011 publication was not reported. This is incorrect. The publication was entitled “Sudden death following cranioplasty: a complication of decompressive craniectomy for head injury” and in the last line of the introduction it is stated, “Each patient failed to recover despite immediate return to theatre for removal of the bone flap.” I only point this out to highlight that the incidence may be higher than previously appreciated, and although I agree it may be a rare occurrence, it may be that it is just underreported. Indeed, a recent publication listed death following bone flap replacement on the outcome algorithm for patients who have had a decompressive craniectomy following ischemic stroke.

The second point is regarding the possible pathophysiology. I agree that this is yet to be determined, but I would suggest that it may relate to the severity of the brain injury and failure of autoregulation.

Autoregulation Following Traumatic Brain Injury

A number of studies have demonstrated that autoregulation can be impaired in patients who have sustained a trauma.
matic brain injury (TBI), and this can occur over a variable time course.\textsuperscript{5,9}\textsuperscript{10} When cerebrovascular pressure reactivity is impaired, cerebral blood volume, and therefore intracranial pressure, will increase or decrease passively (in the same direction) in response to changes in intracranial pressure. It is this loss of autoregulation that reduces the ability of the brain to control adequate blood flow in the presence of hypo- or hypertensive episodes.\textsuperscript{2,3}\textsuperscript{12} This increased vulnerability of the injured brain to secondary hemodynamic impairments has increased our awareness of maintaining a perfusion pressure in TBI, and targeted perfusion pressure therapy has gained wide acceptance.\textsuperscript{1}

A number of studies have demonstrated that impaired autoregulation is correlated with poor outcome and an increased mortality rate, and they have also shown that the pressure reactivity index (PRx) is one of the most important predictors.\textsuperscript{2,5}\textsuperscript{12} It has also been demonstrated that loss of autoregulation can evolve over the first 24 hours. It is at its lowest after 36–48 hours postinjury and thereafter slowly recovers.\textsuperscript{5,12} While there are limited data on long-term time course of autoregulation recovery, it would appear to remain impaired in a small number of severely injured patients.\textsuperscript{5,12} Based on these studies, it could be postulated that certain patients who survive a serious TBI by undergoing a decompressive craniectomy may do so not only with poor neurological function but also with residual impairment in cerebral autoregulation.

Current Literature

Most patients in whom this complication has occurred have sustained either a severe TBI of an extensive ischemic stroke. While it was not demonstrated preoperatively that these patients had impaired autoregulation, it would be difficult to attribute the massive and uncontrolled cerebral swelling to any other mechanism. Notwithstanding this assumption, the question remains as to how the clinical management of these patients may have been altered.

At our institutions we have had no further episodes of sudden death following cranioplasty, and this may due to a heightened awareness of this problem. There is now close attention to seizure prophylaxis and, in certain cases, preoperative electroencephalography is performed in order to detect subclinical seizure activity. There is also close attention to avoiding hypertension in the immediate postoperative period, and while we still use suction drains, we do not place them on high suction in order to prevent significant pressure differentials. Currently we do not perform any type of preoperative autoregulatory assessment, but this may be an interesting avenue of future research. If it is established that autoregulation is impaired, it may be necessary to consider a period of postoperative sedation and ventilation whereby the intracranial pressure and blood pressure are closely monitored in much the same way that patients are managed following removal of large arteriovenous malformations.\textsuperscript{8}

Future Directions

There appears little doubt that the use of decompressive craniectomy will become increasingly common for patients with neurological emergencies. If this is the case, then there may be a significant number of patients who survive not only with poor neurological function but also with some degree of cerebral autoregulatory impairment. It may be that these patients need to be identified preoperatively so that measures may be put in place to prevent this complication occurring following cranioplasty.

References


Disclosures

The author reports no conflict of interest.

Response

I would like to thank Dr. Honeybul for his letter to the editor.

I cannot state that the occurrence of this phenomenon of fatal massive brain edema after cranioplasty is related to the severity of the initial brain injury. All my patients actually recovered quite well from the initial injury and...
were ambulatory; some were independent at the time of cranioplasty.1 Definitely there are autoregulation impairments after head injury that are related to the severity of the initial injury, but the fact that, at the time of the cranioplasty surgery, all of the 4 reported patients recovered quite well from the initial injury indicates that the initial injury was not as severe as might be expected and was probably more focal than diffuse. These patients usually show a fast recovery of autoregulation and definitely should have intact autoregulation reactivity at the time of the cranioplasty surgery several months or more after the initial injury.

The massive fatal brain edema may have been related to some autoregulation impairments and may have been associated with reduction in the cerebral perfusion pressure as the edema was global and resembled an acute severe hypoxic injury. The trigger can be vasomotor impairments initiated by the elimination of the atmospheric pressure, which leads to a significant reduction in the cerebral perfusion pressure and increased resistance to blood flow.

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References

Specialists and survival times

TO THE EDITOR: We read with interest an article by Khan et al.4 (Khan UA, Bhavsar A, Asif H, et al: Treatment by specialist surgical neurooncologists improves survival times for patients with malignant glioma. J Neurosurg 112:297–302, February 2015). The authors are to be commended for a comprehensive review of the practice at their center, but the potential benefits of patients having surgeries performed by specialist neurooncology surgeons remain unclear. We have a number of reservations about the methodology, data analyses, and conclusions from the study.

Firstly, the patients’ comorbidities were not correctly adjusted using the Cox regression and hazards models, and this undoubtedly affected the results. These were neither part of the Medical Research Council (MRC) prognostic index1 nor were they a part of the multivariate modeling undertaken by the authors. It would have helped to have the entire results of the proportional hazards multivariate model in a tabulated form for the readers to understand this better. The authors state that they used the MRC prognostic index, as well as type of surgeon, extent of resection, and so on, to control for case mix—this is counterintuitive because extent of resection is already part of the MRC index. It seems that the authors have also used the Karnofsky Performance Scale (not explicitly clarified in the manuscript), which runs in tens, so a median score would have been more appropriate than a mean score, which somewhat confuses the issues since there is no Karnofsky Performance Scale score of 51 or 45 as mentioned by the authors.

Secondly, the exact location of the tumor in each patient was not disclosed. This is extremely important. Location has a huge bearing on resectability (biopsy vs partial vs gross macroscopic resection) and hence prognosis and survival.7 Were the generalists attempting resections of tumors located in areas where a complete resection was not possible? Were these tumors in eloquent or inaccessible regions? The answers again would have a direct impact on whether a gross-total or subtotal resection was achieved and whether what was achieved was in line with what was intended. This factor would also impact on patients’ length of stay and rates of immediate postoperative deaths/ complications, which appear to be higher among the generalists.

Thirdly, as is the case in our center and other centers in the UK, most surgeons will obtain an immediate postoperative scan to assess the extent of tumor resection.1,3,8 In this study, Khan et al.4 stated that gross resection was higher in the specialist group but the extent of resection was assessed, on some occasions, only by radiotherapy-planning scans, presumably several weeks after the surgery (usually within 1–3 weeks as per standards of the Christie NHS Foundation Trust quoted by the authors). Delaying this scan until a patient is seen by an oncologist several weeks after the initial surgery does not necessarily provide an accurate assessment of the extent of tumor resection. It has been suggested that early postoperative MRI overestimates residual tumor after resection of gliomas.2 However, the optimal timing of postoperative MRI has yet to be determined, and the general consensus favors obtaining an early postoperative scan. Sometimes, radiotherapy-planning scans are just CT scans, and therefore it is likely that there was a significant variability in the method and accuracy of judging postoperative extent of resection. This cannot be accurately used to highlight differences in extent of tumor resection among surgeons as the measurement criteria for scans obtained immediately after surgery and those acquired for radiotherapy planning are very different. The authors also failed to mention whether postoperative resections were assessed on CT or MRI scans. It would have been helpful to know when the radiotherapy scans were obtained and how many extent-of-resection scans were assessed in this manner in each group and with what modality. In addition, a proportion of the patients did not have any adjuvant chemotherapy or radiotherapy. When were their postoperative scans done in these cases? While they were still inpatients? In the outpatient department? Or by oncologists?

In Table 1, when stating the extent of resection, the authors used the total number of surgeries performed as a denominator; however, the authors themselves stated in the results that 14 and 17 biopsies were carried out by specialists and generalists, respectively. It would make sense to

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exclude these cases when assessing extent of resection, as resection was never the intention in any of these operations performed for obtaining a tissue diagnosis.

Furthermore, neuronavigation was only used in 21 patients in the specialist group and 19 in the nonspecialist group. This means that only 40 of 135 surgeries used neuronavigation, which is a small number, and contrary to National Institute of Clinical Excellence guidelines.6 Also, it is likely that all biopsies would have used neuronavigation (n = 31), therefore suggesting only 9 resections were guided by neuronavigation, which is an exceptionally small number. The authors stated that neuronavigation did not offer any benefit to the extent of tumor resection in 22 of the 105 operations across both groups—it is not quite clear how this number was determined.

Importantly, it is unclear whether we are talking of a 2-, 3-, or a 4-year study when the authors stated “2006–2009.” Was it December 2006 to January 2009 (2 years), January 2006 to December 2009 (4 years), January 2006 to January 2009 (3 years), or something completely different? It would have helped to clarify the duration, as this has a direct bearing upon the number of expected patients with this pathology during the study period. There were a total of 306 cases seen between 2006 and 2009, of which only 135 patients had surgery. For a larger neurooncology center based in the UK, this figure seems low, partly due to the unclear time duration involved. Does this data set account for all of the patients operated on in this unit?

Despite careful organization and execution, we believe this study has a number of failings, which do not accurately support the conclusions the authors have drawn. Subspecialization in neurooncology has clear advantages, but it is likely that these are due to ease of access to services under one umbrella, leading to greater patient satisfaction and improved continuity of care with patients being followed up by the same team of health care professionals. This outcome advantage does not have much to do with the technical aspect of surgery as such, which remains a “core skill.” From this study, we find it difficult to conclusively accept that a group of “specialist” neurooncological surgeons, who perform fewer resections than “nonspecialists” in a given period and do not use any more modern adjuncts, are able to outperform the generalists in every way just by virtue of being part of the “neurooncology” multidisciplinary team.

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Disclosures
The authors report no conflict of interest.

Response
We would like to thank Drs. Kalsi and Mukerji for their comments on our article and are pleased to respond to them. We feel our analysis, within the limitations of this cohort, is robust and still provides an important insight into a rapidly evolving area of neurosurgery. The study included 135 patients operated on from April 2006 to November 2009 and should not be discredited due to its sample size. A statistical difference was noted and therefore Type II error is low. This is likely to persist with a larger cohort, as demonstrated by multiple similar multivariate survival analyses assessing extent of resection in both small cohorts (n = 46,14 107,1 128,2 126,2 and 170 patients11) and larger cohorts (n = 4169 and 949 patients12).

Our regression analysis included some of the most important, verified confounding variables when assessing survival in this cohort, such as the MRC prognostic index. Incorporating multiple patient comorbidities would introduce a considerable number of variables, which could obscure the survival analysis, reducing parsimony and prediction accuracy. Moreover, it could inadvertently result in statistically significant variables by chance, influencing the model’s validity. This is likely the reason that such data were excluded from survival analyses in previous similar studies.10,11 Furthermore, the robust MRC prognostic index does not include patient comorbidities and still maintains accuracy. We therefore do not agree with Kalsi and Mukerji that omitting comorbidities from the multivariate analysis has undoubtedly affected the results.

As in our analysis, it is better to include such variables when assessing heterogeneity of groups. We have included morbidity scores, such as the externally validated Waterlow score,13,16 a patient handling score, and a falls risk assessment score. These scores incorporate factors such as
body mass index, medical history, medications, continence, sensory deficit, mobility, falls history, and comprehension. There was no statistical difference when comparing these scores between groups, and therefore comorbidities did not result in an unfair disparity between cohorts.

The exact location of tumors was not assessed in the analysis and could be useful. It is expected that greater surgical morbidity exists in patients with tumors involving eloquent areas of the brain. Therefore, this limitation is overcome, to some degree, by comparing postoperative deficits by using morbidity scores, which measure mobility, consciousness, cognition, continence, and gait. Importantly, they showed no difference between groups, making it unlikely that one cohort was more debilitated from surgery and iatrogenic neurological deficit resulting in longer inpatient stay or influencing mortality. Therefore, as implied by Kalsi and Mukerji, it is imprudent to suggest that generalists were attempting resections in predominantly eloquent brain, resulting in higher perioperative death, complications and inpatient stay.

Interestingly, factors that may influence the extent of resection, such as the surgeon’s ability to judge residual tumor and how aggressive one may be at removing gliomas, may have indirectly become apparent in this analysis.

To some degree, the MRCP prognostic score, notably which includes performance status and history of seizures, may have captured patients with tumors involving eloquent brain. This may also indicate why the MRCP prognostic score is valid despite not specifying tumor location as part of the index. As we have used it to adjust for case mix, discrepancies among groups would have been accounted for.

Indeed the MRCP prognostic index includes the extent of surgery as well as history of seizures, age, and performance status. As the index incorporates a number of factors and assigns a score to each, it is not equivalent to a statistical categorical multivariate assessment of one of its constituents, as suggested by Kalsi and Mukerji.

The study used the WHO performance status. Table 1 should show the MRCP prognostic scores. The mean of the MRCP prognostic score was 20 and 21 for specialists and generalists respectively (p = 0.250, Student t-test). The WHO performance status score ranged from 1 to 3 with a median of 1 (p = 0.551, chi-square test).

The extent of resection in our cohort was confirmed by postoperative MRI scans, the majority of which were acquired within 72 hours of surgery. Confirmation of subtotal resection was verified for some of the patients on radiotherapy planning MRI scans, which usually were obtained within 2 weeks of surgery. As illustrated in Table 1, the denominator is not the total number of surgeries; rather, it is the number of partial resections. Due to the nature of malignant glioma, there is some evidence to suggest no survival advantage from debulking the lesion compared to biopsies, and therefore, on a spectrum of surgical intervention, it may be appropriate to view subtotal resection and biopsy as similar entities when assessing survival.

More importantly, there was no statistical difference between groups regarding the number of biopsies; therefore this factor would not influence the fundamental outcome of survival, or even an independent comparative assessment of extent of resection. In addition, since biopsies are part of the MRCP prognostic score, any subtle differences between groups would have been accounted for.

The surgeries in which neuronavigation was used were compared with surgeries in which it was not, and we found no difference in the extent of resection or survival. Indeed, in our study this number is small and therefore remains an observation; it is not the best when understanding the merits of neuronavigation.

Although our study represents a single-center retrospective analysis, we feel it gives insight into pertinent factors (both assessed directly or those that warrant further investigation) that may influence the survival of these patients. Kalsi and Mukerji suggest that the most important advantage from subspecialization is the ease of access to services, resulting in greater patient satisfaction and continuity of care. This is unlikely as these services are available to all surgeons and would not result in a disparity in survival. We know that, in other areas of neurosurgery, including complex spine, vascular neurosurgery, and pediatric neurosurgery, both operative and nonoperative skills are important to providing optimal patient care, and thus fellowships are offered to improve or develop an identified area of neurosurgical practice. It is unlikely that an evolving, complex area of neurosurgery such as neurooncology is any different. Although our article provides an initial assessment of the subject, there are likely factors outside the scope of this study that would influence the survival of these patients. We feel there are advantages to the management of brain tumor patients by surgeons who have a specific interest in the subject and are familiar with current research. Their job plan allocates dedicated time to the management of their oncology patients. In addition, they are more closely engaged with the whole multidisciplinary team when making important management decisions. Unfortunately, this can only be assessed in future studies, which may prove difficult as the care of these patients is rapidly shifting toward specialists. Mitigating for the heterogeneous nature of these patients and their tumors will always be difficult.

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J Neurosurg Volume 124 • March 2016 889

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TO THE EDITOR: We read with great interest the article by Maissan et al.1 (Maissan IM, Dirven PJAC, Haitasma IK, et al: Ultrasonographic measured optic nerve sheath diameter as an accurate and quick monitor for changes in intracranial pressure. J Neurosurg 123:743–747, September 2015), in which the authors measured intracranial pressure (ICP) and optic nerve sheath diameter (ONSD) before, during, and after tracheal suctioning in adult head injury patients with Glasgow Coma Scale (GCS) scores of 9 or less and found the ultrasonographic measurement of ONSD to be an accurate and quick method of identifying changes in ICP. We would like to address a few points that we believe warrant discussion. The authors did not describe the position of their patients (i.e., supine-horizontal, head elevated 30°, or other), orientation of the ultrasound probe (along the transverse or longitudinal axis or both), the distance of the site of measurement from the globe (e.g., 3 mm posterior), the use of sedatives and/or muscle relaxants prior to tracheal suction, the timing of the last dose of mannitol, timing of the test (i.e., day or night), the status of patients with a GCS score of E1M1V1 (i.e., brain dead or not), the association with cervical trauma (cervical collar use) or polytrauma, status of autoregulation (impaired vs intact), or cerebral perfusion pressure (CPP) and mean arterial pressure (MAP) before, during, and after tracheal stimulation. We had studied ONSD in 100 patients with head injuries, as published (Goel et al.)3 in the journal Injury in 2008. In that study, we compared the data with CT findings instead of ICP. We obtained false-positive results in 2 patients who had frontal extradural hematomas (EDHs). Frontal EDH with pressure on the optic nerve could be the reason for these false positives. We also had 1 false-negative result. This case involved an elderly patient, and we hypothesize that the false negative could be due to brain atrophy. There may be subarachnoid septations around optic nerves, and these septations could increase with age. We realize that it is not possible to discuss or quote all papers, but discussion of specific findings could be helpful in interpreting results.

After publication of our article, many studies were done to correlate ONSD as a marker of ICP in different conditions. These studies showed differing results. In sharp fluctuation of ICP, ONSD correlated with change in ICP in the study by Maissan et al.1 but not in the study by Rajaej et al.8 Autoregulation status; CPP and MAP before, during, and after tracheal stimulation; and muscle relaxant use were not described by Maissan et al.1 Perhaps these details could help to identify the cause of sharp fluctuations in ONSD and ICP after tracheal stimulation. Studies involving patients with endoscopic third ventriculostomy failure, ventriculoperitoneal shunt failure,2,4 and aneurysmal subarachnoid hemorrhage without raised ICP1 as well as studies of brain-dead patients8 show interesting results. Further studies of patients with hypotensive and cerebral injury are needed, as cerebral sympathetic block has been found to cause an increase in ONSD.3 Patients with diffuse axonal injury (DAI) may show interesting results, as DAI is not associated with elevated ICP.

The upper limit of normal ONSD is 5 mm for adults, 4.5 mm for children aged 1–15 years, and 4.0 mm for infants up to 1 year of age.3 It would be useful to assess ONSD in adults as Grade 0 (< 5 mm), Grade 1 (5mm), Grade 2 (> 5 mm but < 7 mm), and Grade 3 (≥ 7 mm) and discuss results according to these grades, especially with respect to the use of ONSD as a prognostic marker in neurosurgical patients. ONSD grading should be correlated with ICP grades and CT scan midline shift grades, and it could be standardized and used in formulating treatment protocols.

We believe that ultrasonic measurement of ONSD has the potential to be a useful ancillary tool in the neurointensivist’s armamentarium—not only in caring for patients with head injuries but also in managing other neurosurgical and medical conditions. We also believe that a prospective, blinded study of the correlation between ICP and ONSD could be of great help in standardizing the use of

**Optic nerve sheath diameter as ICP marker**


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this tool—particularly if the study were to include analysis of multiple factors. It is important to identify indications for, limitations of, and misunderstandings related to the ultrasonic measurement of ONSD in order to optimize patient care. To avoid mechanical and thermal side effects, the procedure should be performed quickly, and one can expect that there would be a learning curve; accuracy and efficiency are likely to improve with experience. In summary, we believe that this new technology is appealing and that further assessment is needed to evaluate the efficacy of the technique.

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References

Disclosures
The authors report no conflict of interest.

Response
We thank Ravishankar S. Goel and Pooja Goel for their comments on our paper. We also believe that ultrasonographic measurement of ONSD has the potential to be a useful tool, especially in prehospital settings and at the emergency department, where invasive ICP monitoring is often impossible. We compared 2 tests to determine ICP: the noninvasive sonographic measurement and the invasive gold standard, use of an ICP probe. Furthermore, we were interested in a tool to be used in the prehospital setting to assess instantaneous changes in ICP more than static ICP measurements. In our prospectively designed study we found a strong correlation between ICP changes and ONSD changes. ONSD was measured 3 mm behind the retina in a transverse axis. We used the international definition of ONSD as the distance inside the hyperchoic dura mater.

All patients who suffered severe brain injury were treated according to our hospital protocol “raised ICP after traumatic brain injury.” This includes elevated head position (20°–30°), heavy sedation and analgesia, management of hyponatremia and osmolality administration 6–12 times a day, depending on baseline ICP. Mean arterial pressure was titrated to 80–100 mm Hg in patients with a baseline ICP < 20 mm Hg to guarantee cerebral perfusion pressure of at least 60 mm Hg. If baseline ICP exceeded 20 mm Hg, the treatment was intensified. No additional sedatives or muscle relaxants were administered prior to suctioning the endotracheal tube. All study measurements were done during daytime shifts (8:00 AM to 6:00 PM; Amsterdam time, i.e., Greenwich Mean Time + 1 hour).

Our results are in contradiction with the suggestions made by Rajajee et al. in their retrospective analysis of their data.1 They observed a rapid response of ONSD to ICP increase but a delayed return to normal ONSD after ICP had already lowered to baseline levels. However, they included patients with raised ICP due to causes other than brain injury. Furthermore, the delayed return may be the result of brain edema in their patients, and this may explain the difference in results. In our study, we focused on the value of ONSD in brain-injured patients as a tool in the prehospital setting. We do realize that our population was rather specific and small but believe our study should be interpreted as a proof of principle. We fully agree that more studies should be done in larger groups and in different circumstances to assess the efficacy and the place of this noninvasive technique.

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