Biopsies and neuropathology

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In their study, Dr. Shooman and colleagues describe their streamlined cost-saving approach for stereotactic biopsies in which the procedure is performed with the patient awake and without intraoperative neuropathology support. They also advocate early discharge if a 6–10-hour postprocedure CT scan shows unremarkable findings. They argue that with this paradigm, a stereotactic brain biopsy can be done expeditiously, safely, and with high diagnostic accuracy. Indeed, this report documents excellent results in 134 biopsies with a diagnostic yield of 99% and a complication rate of 2.2%. Approximately one-third of patients were discharged the day of surgery. The authors conclude that when considering global cost-benefit balance, intraoperative neuropathological consultation may not be justifiable.

The concept of safe same-day surgery for stereotactic biopsies has already been well documented in the literature. Often whether a patient can be discharged early depends more on practical issues of patient travel and institutional systems and facilities. The more interesting conclusion worth exploring is whether intraoperative neuropathological examination is still valuable in the modern age of high-resolution stereotactic instrumentation. While we concur that modern image-guided biopsy techniques have markedly improved our ability to safely obtain diagnostic specimens in a high number of CNS lesions, we believe that the main conclusion suggested—that there is no need for intraoperative neuropathological examination—should be taken with great caution. Our perspective is based on our experience with an intraoperative neuropathology consultation practice that encompasses nearly 200 stereotactic brain biopsies per year. Through the practice of intraoperative smears, a wide spectrum of operative diagnoses is evaluated, extending well beyond the typical radiographic glioblastoma multiforme (GBM) to a wide array of diseases falling under categories that include neurodegenerative, inflammatory, and obscure neurooncology lesions such as intravascular lymphoma.

Although the authors’ positive diagnostic rate is impressive, one should not forget that what might work in the hands of a single gifted and experienced neurosurgeon at a single specialized institution and for a specific set of patients may not work in a different setting. In addition to guiding brain biopsy to potentially improve diagnostic yield, intraoperative examination allows the neuropathologist to acquire important information that might allow optimal triaging of a limited amount of diagnostic tissue and early planning of ancillary studies (such as immunohistochemistry and, less frequently, electron microscopy) required to reach a definitive diagnosis in a timely manner even in the most critical, difficult, and/or unexpected diagnostic dilemmas. As it pertains to diagnostic accuracy, it is also critical to remember the important role of the exchange of clinical and imaging information between the neurosurgeon and the neuropathologist at the time of the biopsy, which may be invaluable to the interpretation of the biopsy findings. This exchange may be considerably more difficult and/or completely lacking when the pathologist simply receives a biopsy core in a jar.

The results presented here were obtained in a highly selected patient population, with imaging abnormalities considered highly suspicious of neoplasm and in which the possibility of craniotomy and resection was never considered, attesting to the malignant stage of most lesions. Nearly all lesions (97%) were supratentorial, the majority being high grade (80%). All lesions were sampled according to a systematic 4-quadrant biopsy technique starting from the first and deepest site with progressive withdrawal toward the peripheral superficial portion along a single trajectory. There is neither surprise nor expected obstacle in reaching a diagnosis of GBM in an elderly patient presenting with a large enhancing intraaxial lesion, and in front of a “grossly abnormal set of biotic cores” intraoperative neuropathology indeed may seem perfunctory. But what about a biopsy targeting a small and minimally enhancing lesion in the thalamus of a neurologically intact 30-year-old woman or a deep-seated midbrain lesion in an adolescent in whom even the limited bleeding secondary to taking an additional biopsy core could be dramatic? Why expose such a patient to the additional risk of even one more biopsy that may turn out to be nondiagnostic? Although the authors may suggest that intraoperative neuropathological evaluation may be limited to these difficult cases, which would theoretically result in significant time and cost savings,
this rationale may not be well founded. As in every aspect of medicine, pathology expertise, accuracy, and reliability are largely built on personal experience and daily diagnostic practice. How could one expect that this same neuropathologist, who may now only rarely be called to perform an intraoperative smear and may have never built true diagnostic expertise, be able to guide and support the surgeon in these most difficult cases?

In an environment in which limited health care resources pose significant challenges, we should not forget the quality equation—that the ultimate goal should be to provide safe, high-quality care at a reasonable cost to each of our patients. It is therefore important to balance safety with cost. As we look at health care value in a comprehensive way, in our opinion this does not appear to be the time to shelve intraoperative neuropathologists in jars of formalin. Given the well-known shortage of general and specialized pathology services in the United Kingdom, it is understandable that the authors’ practice may have evolved to not depend on the support that many of us take for granted. One must question whether the neurosurgery community of the United Kingdom should advocate for the training and services of dedicated surgical neuropathologists.

Reference


Response

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We are grateful to the Journal of Neurosurgery for publishing this work, which many might consider controversial. We agree with many comments made in the editorial, and we value the opportunity to defend the conclusions that we have drawn.

Unfortunately, in most modern health care systems resources are limited, and as responsible clinicians we are challenged with utilizing these resources as efficiently as possible. Of course, in doing so it is of paramount importance not to compromise on quality of patient care, outcomes, or safety. In addition, as technology advances and as surgeons become increasingly specialized, there may be opportunities for innovative challenges to conventional practice, and these should be encouraged but audited carefully. We set out with a hypothesis that modern frameless biopsy techniques that involve high-resolution imaging, in the hands of a recently formed, dedicated neurooncology team, might negate the traditional requirement for the routine use of intraoperative neuropathological examination, while maintaining low levels of nondiagnosis and high levels of safety. We believe that this study supports this theory.

The editorial raises issues of the applicability of our results to other units. However, we are using standard techniques employed in many centers around the world. We are working in a regional neurosciences center serving a population of approximately 3 million, again comparable to many centers in the United Kingdom and overseas. All patients were treated by a single neurosurgeon (P.L.G.) in the first 3 years of independent (consultant) practice. As we discussed in the publication, one reason we may have achieved these results may be partly explained by the recent subspecialization, such that these operations are now only performed by dedicated neurooncology surgeons. The technique of multiple sampling along a single trajectory may also increase yield without increasing risk. It would, therefore, seem very likely that our results would be reproducible by other surgeons working in this field.

The comment that intraoperative examination of tissue might somehow allow triaging of a limited amount of diagnostic tissue and early planning of ancillary studies is not something we consider beneficial. Indeed, one might argue that tissue “lost” to smear or frozen section might well have been of more diagnostic value if formally processed and subjected to the ancillary studies alluded to. Formal H & E–based diagnosis is usually available within 48 hours and routine immunohistochemistry within 72 hours in many units, and we are not certain how results from intraoperative tests would enable this process to be more time efficient.

We absolutely accept the comments that communication between neurosurgeon and neuropathologist is of great importance in the interpretation of some biopsy specimens. It is for this reason that it is our routine practice to discuss every case in a combined multidisciplinary team meeting before surgery, in line with national guidelines in the United Kingdom. This affords the opportunity for discussion between neuroradiologist, surgeon, and neuropathologist prior to surgery (and again postoperatively when the histological results are discussed and a management plan is formalized). If this practice is followed then, this may obviate the need for discussion during a procedure. We would argue that careful consideration of a differential diagnosis and the targeting of lesions in this prospective manner may be a more optimal strategy.

In regard to the comments about our “highly selected patient population,” we would like to reiterate that we reported on consecutive patients referred to our neurooncology multidisciplinary team meeting for tissue diagnosis in whom resection was not considered possible. It is perhaps not surprising that the majority of the lesions were supratentorial high-grade gliomas as these are the most common tumors we manage. Our unit policy is to offer diagnosis to all patients with tumors in whom treatment may be advocated (including the treatment of suspected low-grade gliomas considered for serial scanning alone). We would not routinely recommend biopsy for extremely elderly patients in whom a diagnosis of GBM is highly
likely on MR imaging and in whom active treatment is not being considered. Thus, we consider these results applicable to other units with similarly organized and dedicated neurooncology teams. We have perhaps included fewer inflammatory conditions in our series (2 of 134) than some others, but biopsy of inflammatory cerebral pathologies in modern neurosurgical practice is relatively rare in our experience unless exclusion of malignancy is required. Indeed, in our unit patients with suspected inflammatory conditions for biopsy are still most frequently referred to the neurooncology team due to the desire to exclude tumor and due to our experience with biopsy techniques.

Of course, we modify our technique depending on the size and location of a lesion, as indicated by the examples in the editorial and discussed in the paper. For very small lesions in locations such as the brainstem we would also simply target the lesion and not take serial samples along a trajectory, but we would take more than one sample, as discussed. The editorial asks why we would expose patients to the risk of more than one biopsy. We believe this question was reviewed in the paper and has been discussed by others. There does not appear to be increased risk to obtaining multiple biopsies, and there is some evidence, including this, that the yield may be higher if this is done.1,3,6 Of course, tumors are also frequently heterogeneous and a solitary core from a single location may lead to undergrading of a tumor.

We accept the argument that elimination of all intraoperative pathological examinations may lead to attenuation of the skills of pathologists, but biopsy procedures represent only a small fraction of our neurooncology surgical practice. We often send samples during resection procedures in which ample opportunity is afforded to maintain intraoperative diagnostic skills without substantially lengthening the duration of the procedure (unlike the case with biopsy). If other groups were of the belief that this minor loss of intraoperative workload was to have a negative impact on training, then tissue could simply be sent fresh postoperatively to pathology for processing.

We are fortunate to work in a unit with excellent, continuous in-house neuropathology cover and we have absolutely no intention of shelving “intraoperative pathologists to the formalin jar.” However, the question explored by this paper was whether we could still achieve satisfactory biopsy results without undertaking intraoperative pathological examination as this would save operating room time, increase efficiency, and reduce costs. We have concluded, not unreasonably, that in our practice this is possible and it is likely to be possible in many other neurooncology units around the world.

References

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