Wavelength-specific lighted suction instrument for 5-aminolevulinic acid fluorescence-guided resection of deep-seated malignant glioma: technical note

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Surgery guided by 5-aminolevulinic acid (ALA) fluorescence has become a valuable adjunct in the resection of malignant intracranial gliomas. Furthermore, the fluorescence intensity of biopsied areas of a resection cavity correlates with histological identification of tumor cells. However, in the case of lesions deep within a resection cavity, light penetration may be suboptimal, resulting in less excitation of 5-ALA metabolites, leading to decreased fluorescence emission. To address this obstacle, the authors report on the use of a 400-nm wavelength fiber-optic lighted suction instrument that can be used both during resection of a tumor and to provide direct light to deeper areas of a resection cavity. In the presented case, this wavelength-specific lighted suction instrument improved the fluorescence intensity of patches of malignant tissue within the resection cavity. This technique may further improve the utility of 5-ALA in identifying tumor-infiltrated tissue for deep-seated lesions. Additionally, this tool may have implications for scoring systems that correlate 5-ALA fluorescence intensity with histological identification of malignant cells.

KEY WORDS glioma; 5-ALA; fluorescence-guided resection; lighted suction; oncology; surgical technique

For all these tumor types, this approach involves the administration of 5-ALA, a nonfluorescent prodrug form, which is then metabolized to fluorescent protoporphyrin IX that accumulates within malignant cells. Under violet-blue light, protoporphyrin IX fluoresces, allowing for immediate identification of tumor cells. Yet, there are challenges that still remain with fluorescence-guided tumor resection. The diagnostic accuracy of 5-ALA is dependent on the intensity of emitted tissue fluorescence, a factor that correlates with the actual presence of histologically diagnosed tumor in a given location. In turn, the emitted tissue fluorescence is greatly dependent upon exposure of protoporphyrin IX to light. This is important to consider when resecting subcortical or deep-seated lesions such as tumors in the insula where the exposure to light may be diminished, even under a microscope. Patches of tumor cells may not fluoresce intensely and, thus, be discredited as normal brain tissue.

One avenue to improve upon fluorescence-guided resection is to incorporate an intense excitation wavelength light source into instruments that already aid in the removal of
these tumors. In this technical report, we demonstrate the use of a 400-nm fiber-optic light source incorporated into a surgical suction instrument that simultaneously allows for removal of blood products and improvement of tumor fluorescence by providing necessary wavelength-specific illumination to deeper areas of a resection cavity.

**Methods**

**Lighted Suction Instrument and 400-nm Light Source**

Because a suction instrument is critical for the resection of tumors as it removes blood products and allows for better visualization in the operative field, it was selected as the instrument of choice for placement of an additional light source. In the current case, a Spetzler Lighted Suction Tube (5-Fr, Kogent Surgical) was used (Fig. 1A). This device has achieved FDA premarket approval (FDA 510[k] no.: K141781). Light is delivered to an acrylic diffuser at the distal end of the suction cannula that radiates the light in chandelier fashion with an additional component of direction illumination (Fig. 1C and D). Additionally, the device does not generate a significant amount of heat, which is a concern for light-generating devices that are used near brain parenchyma.

The Spetzler Lighted Suction Tube was connected to a custom-designed 400-nm wavelength emitting light source, built using a Luxtec model LX-300 fiber-optic illuminator (Integra) with a 400-nm filter (product no. #84–781, Edmund Optics) installed in the optical path (Fig. 1B). Of note, the proposed setup could have been used in conjunction with other commercial lighted suction devices and is not limited to use with the Spetzler Lighted Suction device. Additionally, the maximum intensity of light emitted was not increased and was limited by the preexisting settings on the Luxtec model LX-300 fiber-optic illuminator. A spectrogram of the light source output demonstrated a peak at 400 nm (Fig. 2A), and illumination of a Zeiss Blue 400 test target demonstrated a fluorescence emission peak at 625 nm (Fig. 2B).

**5-ALA Dosing, Administration, and Postoperative Care**

Patients gave consent for the use of 5-ALA during the operation under an ongoing clinical trial (clinicaltrials.gov no.: NCT01116661). Approximately 3 hours prior to surgery, a single administration of 5-ALA at a dose of 20 mg/kg of body weight was given to patients orally by dissolving the dye in approximately 100 ml of drinking water or juice. Precautions were taken to protect the patient from the effects of skin photosensitivity during surgery and during the postoperative period. Additionally, patients received instructions on how to protect themselves and minimize exposure to sunlight and indoor lighting for up to 72 hours after administration of 5-ALA. The 5-ALA dye was provided by DUSA Pharmaceuticals/Sun Pharma.

**Surgical Procedure**

During surgery, image-guided microsurgical resection of the tumor was undertaken. During the course of tumor resection under light microscopy, the tumor bed was illuminated with violet-blue light via a high-pass optical filter in the microscope’s light source. Additionally, the 400-nm lighted suction instrument was used during the resection of the tumor, both for removing blood products and tumor tissue as well as to illuminate areas of the deep resection cavity to probe for remaining areas of 5-ALA positivity. Images were obtained via the microscope.

**Illustrative Case**

The case presented is of a 68-year-old woman found to have a right temporal parietal mass. The patient presented with worsening headaches and ptosis that had developed over several weeks, and MRI at the time of her initial presentation demonstrated a small nonenhancing abnormality in the right parietal lobe. She was followed with serial imaging but suffered a seizure 3 years later. Imaging at that time demonstrated a dramatic increase in the lesion’s size, prompting a right parietal craniotomy for resection of

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**FIG. 1.** Components and setup of lighted suction instrument. A Spetzler lighted suction tube (A) was connected to a Luxtec model LX-300 fiber-optic illuminator modified with a 400-nm filter (B). The blue light is directed through the acrylic diffuser (clear portion) both around and in the direction of the suction tip (C and D).
the mass that was noted on pathological evaluation to be a WHO Grade II infiltrating glioma most compatible with oligoastrocytoma. The patient subsequently underwent adjuvant treatment with external beam radiation therapy and temozolomide. Two years after the initial surgery, the patient suffered another seizure with imaging demonstrating enhancement at the site of the previous resection. Otherwise, she had no neurological deficits on physical examination.

The patient underwent a right parietal craniotomy for tumor resection with motor mapping and 5-ALA fluorescence guidance. During resection, 5-ALA–positive areas were encountered, at which time the lighted suction instrument was used to assess for improvements in fluorescence intensity. Fig. 3 demonstrates that areas deep within the resection cavity that were minimally fluorescent greatly increased in intensity upon illumination with the lighted suction instrument. However, the light emanating from the instrument did not cause autofluorescence when no 5-ALA–positive tissue was present (Fig. 4). Furthermore, no evidence of photo-bleaching or tissue damage was observed intraoperatively in areas in which the fluorescent light was used. The tumor was removed in its entirety with the aid of subcortical mapping.

Overall, the patient recovered from surgery without any residual neurological deficits. Histological analysis of the specimens demonstrated a WHO Grade IV glioblastoma. Postoperative MRI demonstrated gross-total resection of the previously enhancing lesion compared with preoperative imaging, without evidence of tissue damage or excessive cerebral edema other than expected postoperative changes (Fig. 5).

Discussion

During glioma resection, 5-ALA fluorescence is typically observed upon exposure to the violet-blue light source most commonly produced by the intraoperative microscope. However, a number of factors may result in potentially inconsistent exposure of the area of interest.
to this source of light. Barriers may include the depth of the surgical field, presence of overhanging tissue, shadows created by instruments, magnification and focus settings of the microscope, and even patient positioning. In addition, the assessment of fluorescence has typically been performed in a semiquantitative fashion and is subject to user discretion. Placing the light source directed over the region of interest provides a more consistent and uniform exposure. Thus, with the technique described in this report, one could potentially be more confident that light is consistently available to tissues of interest, resulting in improved fluorescence visualization.

More recently, light sources have been incorporated into neurosurgical instruments, including suction and bipolar devices, aiding in the resection of brain tumors and vascular lesions. These modified instruments provide a valuable adjuvant source of light in the removal of deep-seated lesions where light penetration directly from the microscope is suboptimal. Yet, there has been a paucity of reports demonstrating the technical advantages of using such instruments and how they may be used in conjunction with other operative techniques. To the best of our knowledge, this is the first report detailing the use of wavelength-specific light through a lighted suction instrument to improve 5-ALA fluorescence-guided resection of an intracranial glioma.

There have been groups that have modified other surgical devices to improve fluorescence-guided resection of a deep-seated lesion. Tamura et al. reported on a 5-ALA fluorescence-guided endoscopic biopsy procedure for a malignant glioma within the third ventricle. An ultraviolet cutoff filter was inserted between the ocular lens of the fiberscope and the camera to allow for visualization of dye fluorescence on a screen. Similarly, Rapp et al. reported on a modified endoscope emitting blue light to improve detection of 5-ALA–positive areas after microsurgical removal of brain tumors in 9 patients. Their endoscopic-assisted approach was able to locate tissue at an average depth of 5 cm from their corticectomy. Our current technique offers an alternative approach because it does not require extensive time to set up, does not require
the surgeon to repeatedly switch between instruments to inspect the tumor bed for 5-ALA fluorescence, and can simultaneously be used in the actual removal of the lesion.

Another impact that this technique may have is on refining the sensitivity to detect tumor tissue. Lau et al. previously demonstrated a correlation between ALA fluorescence intensity and tumor cellularity on histological analysis. The authors examined intraoperative biopsies during 5-ALA fluorescence-guided resection of WHO Grade III and IV gliomas. Biopsies were graded on separate 4-point fluorescence intensity and cellularity scales (Grades 0–3) based on 5-ALA fluorescence intensity and pathological examination. The authors found that Grade 3 5-ALA intensity strongly correlated with Grade 3 cellularity, with a positive predictive value ranging from 86% to 100%. However, in nonfluorescent (Grade 0 5-ALA) biopsies, 62.3% had tumor cells present. It was suggested that light penetration to deep resection cavities might account for their findings, further suggesting that methods such as a light-augmented suction are needed to increase the sensitivity of detecting 5-ALA fluorescent tumor.

Conclusions

The use of a wavelength-specific modified lighted suction instrument is a novel technique to enhance the extent of resection when used in conjunction with intraoperative 5-ALA fluorescence guidance. This technique has the potential to improve detection of 5-ALA positive areas, especially in the context of deep-seated lesions such as in the insula. Furthermore, future fluorescence-intensity grading systems may benefit from the use of this technique to improve the correlation between tissue fluorescence and histologically present malignant tissue.

Acknowledgments

We would like to thank Richard Fechter for the construction of the 400-nm light source and for detailing its design.

References

as corroborated by spectrometry and histology and postoperative imaging. Neurosurgery 74:310–320, 2014

Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Morshed.

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