A Prospective Validation Study of the First 3D Digital Exoscope for Visualization of 5-ALA Induced Fluorescence in High Grade Gliomas

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DISCLOSURE

• I DO NOT have any financial or organizational relationships with commercial interests or other entities. I hereby certify that to the best of my knowledge, no aspect of my current personal or professional circumstances places me in the position of having a conflict of interest with my duties, responsibilities and exercise of independent judgement as an Officer, Member of the Board of Directors, Nominee for Office, Educational Presenter and/or a representative of AANS/NREF/NPA.
INTRODUCTION

• The use of aminolevulinic acid (5-ALA) for intraoperative visualization of high grade glioma (HGG) is well described. Conventional surgical microscopes equipped with blue-light filters require switching between blue- and white-light in order to visualize fluorescence and anatomy, respectively.

• A novel 3D digital exoscope (Olympus Orbeye) was designed to permit enhanced visualization of both fluorescence and anatomy under blue-light.

• We present the first use in the US of a blue-light equipped Orbeye for 5-ALA guided HGG surgery.
METHODS

• An IRB-approved, prospective clinical trial was designed to evaluate the utility and sensitivity/specificity of the Orbeye for 5-ALA guided HGG surgery

• At least 2 tissue specimens were collected from 3 sites for qualitative evaluation of fluorescence: strong, weak, none

• All specimens were reviewed by a neuropathologist in a blinded manner and scored based on tumor cellularity: abundant, scarce, none

• We determined the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of visualized fluorescence
RESULTS

- Twenty patients were consecutively enrolled
  - 16 recurrent lesions, 4 newly diagnosed
  - 12 male, 8 female
- Intraoperative fluorescence was observed in all subjects
- 121 total surgical specimens were collected for histopathological analysis
RESULTS

Fluorescence Score

- **Strong**: 33 samples with abundant tumor cells and 7 with scarce
- **Weak**: 28 samples with abundant tumor cells, 7 with scarce and 5 had none
- **None/Absent**: 14 samples with abundant tumor cells, 11 with scarce and 16 had none
## RESULTS

Table 1. Pathology scores with corresponding fluorescence scores in all collected surgical specimens.

| Fluorescence Score | Pathology Score None/Negative | Pathology Score Scarc 
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<tbody>
<tr>
<td>None</td>
<td>16</td>
</tr>
<tr>
<td>Weak</td>
<td>5</td>
</tr>
<tr>
<td>Strong</td>
<td>0</td>
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<tr>
<td>Total</td>
<td>21</td>
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| Fluorescence Score | Pathology Score Abundant | Total |
|--------------------|---------------------------|
| None               | 14                        |
| Weak               | 28                        |
| Strong             | 33                        |
| Total              | 75                        |

The Kappa coefficient is 0.196 and the asymptotic 95% confidence interval is (0.08, 0.31).
RESULTS

• Robust visualization of both fluorescence and normal anatomy was possible under blue light conditions

• Sensitivity- 75%
• Specificity- 76%
• Positive predictive value (PPV)- 94%
• Negative predictive value (NPV)- 39%
DISCUSSION

• The high PPV (94%) in this study demonstrates the ability of the Orbeye to identify tumor, similar to prior studies with 5-ALA and a standard operative microscope
  • All specimens classified as having “strong” fluorescence accurately predicted the presence of neoplasm

• Falsely fluorescent tissue may be seen more commonly in recurrent gliomas
  • Given that 80% of included cases were recurrent HGGs, compared with only 20% newly diagnosed, this may partially account for the 5 false positive samples
SUMMARY POINTS

• Our experience to date indicates that the 5-ALA equipped Orbeye demonstrates clinical utility

• The high PPV for fluorescence allowed both visualization of neoplastic tissue and associated margins, while permitting much of the resection to be completed while under blue-light conditions