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Introduction

The BLUE 400 filter system (Carl Zeiss Meditec, Oberkochen, Germany) has provided visualization of 5-ALA-induced fluorescence-guided surgery for more than 20 years.

Nevertheless, constraints, e.g. limited background discrimination during hemostasis, obstruct fluency of surgery.

A novel filter with improved background visualization was developed, requiring validation regarding fluorescence discrimination.

The aim of this study was to determine diagnostic accuracy and perception of PPIX discrimination of a novel filter system with higher background illumination (BLUE 400 AR) compared to the gold standard, BLUE400.
Methods

A surgical microscope equipped with both BLUE 400 and BLUE 400 AR was used.

Comparisons were performed on a biological basis and on the visual perception of margins. High-resolution images were compared during and after surgery by senior neurosurgeons.

In a predefined biopsy algorithm, four biopsies per patient at tumor margins of PPIX fluorescence and adjacent brain were acquired using BLUE 400 AR only from regions intended for resection and assessed for cell count and density.
Results

Thirty-two patients with malignant gliomas were included in this study.

BLUE 400 AR markedly enhanced the brightness of the surgical field, allowing superior discrimination of brain anatomy.

A total of 128 biopsies from fluorescence margins were collected.

PPV was 98.44% (95% CI, 90.06-99.77%) for malignant glioma.

Residual median cell density in non-fluorescent tissue was 13% (IQR 13 to 31).

Perception of the location of fluorescent margins on HD images was equivalent for both filter combinations.
Results

Fig. 1 - Intraoperative microscopic view of a superficial glioblastoma under a) BLUE 400 conventional filter and b) filter BLUE 400 AR. Fine cortical vessels are well depicted under the novel filter system, as well as sulci and adjacent brain tissue.
Results

Fig. 2 - Box plot analyses comparing a cell count/cm² and tumor cell density between fluorescent and non-fluorescent biopsies. Both demonstrated a highly significant difference between the compared groups (p < 0.0001).

Box plot - n=31 Patients

- Fluorescent tissue
- Non-fluorescent tissue

Sig. (2-sided) p<0.00001

Cell count / cm²

Cell density %
**Results**

**Fig. 3** - Microscopic view of a fluorescent and b non-fluorescent tissue demonstrating the high and low cellularity within these tumor regions.
Results

Fig. 4 - Description of diagnosis of biopsies among the analyzed specimens (n = 128), from both fluorescent (n = 64) and non-fluorescent tumor infiltration zones (n = 64). Note that only one case of reactive brain tissue could be found within biopsies acquired from the fluorescent tumor tissue observed under the novel filter BLUE 400 AR.

Fig. 5 - Comparison of acquired data with BLUE 400 AR during this study with older data generated for BLUE 400 [14], demonstrating an overall good correspondence regarding PPV and specificity when comparing means with their corresponding 95% CI. Furthermore, NPV and hereto-related sensitivity appeared higher.
Conclusion

BLUE400 AR demonstrated superior background compared to conventional BLUE 400 in malignant glioma surgery but comparable fluorescence margins and PPV.

Therefore BLUE 400 AR can be considered safe and effective in supporting malignant glioma surgery.

This article has been accepted for publication in "Acta Neurochirurgica" and is currently “in press”.
Thank you for your attention!

Fluorescence real-time kinetics of Protoporphyrin IX after 5-ALA administration in low-grade glioma
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