EXTENDING THE INDICATIONS OF 5-AMINOLEVULINIC ACID FOR FLUORESCENCE-GUIDED SURGERY FOR DIFFERENT CENTRAL NERVOUS SYSTEM TUMORS: A SERIES OF 255 CASES IN LATIN AMERICA

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Introduction: Fluorescence guidance with 5-aminolevulinic acid (5-ALA) is a safe and reliable tool in total gross resection of intracranial tumors, especially malignant gliomas and cases of metastases. In the present retrospective study, we have analyzed 5-ALA-induced fluorescence findings in different central nervous system (CNS) lesions to expand the indications of its use in differential diagnoses.

Objectives: To describe the indications and results of 5-ALA fluorescence in a series of 255 cases.

Methods: In 255 consecutive cases, we recorded age, gender, intraoperative 5-ALA fluorescence tumor response, and 5-ALA postresection status, as well the complications related to the method. Postresection was classified as '5-ALA free' or '5-ALA residual'. The diagnosis of histopathological tumor was established according to the current classification of the World Health Organization (WHO).

Results: There were 195 (76.4%) 5-ALA positive cases, 124 (63.5%) of whom underwent the '5-ALA free' resection. The findings in the positive cases were: 135 gliomas of all grades; 19 meningiomas; 4 hemangioblastomas; 1 solitary fibrous tumor; 27 metastases; 2 diffuse large B cell lymphomas; 2 cases of radionecrosis; 1 inflammatory disease; 2 cases of gliosis; 1 cysticercosis; and 1 immunoglobulin G4-related disease.

Conclusion: Fluorescence with 5-ALA can be observed in lesions other than malignant gliomas or metastases, including meningiomas, hemangioblastomas, pilocytic astrocytomas, and lymphomas. Although there is need for further evidence for the use of 5-ALA beyond high-grade gliomas, it may be a safe and reliable tool to improve resection in positive tumors or to guide the histopathologic analysis in biopsies.

Table 1 Tumors classified by types, 5-aminolevulinic acid (5-ALA) response, and removal status

Pilocytic astrocytoma, grade	Diagnosis	Total	5-ALA positive	5-ALA removal
Difuse astrocytoma, grade 24 6	Astrocytic and oligodendroglial			
1	Pilocytic astrocytoma, grade I	4	2	2 5-ALA free
Anaplastic astrocytoma, grade III 6 3 1 1 5-ALA free Anaplastic oligodendroglioma, grade III 10 9 7 5-ALA free Cilioblastoma, grade IV 108 104 59 5-ALA free, 7 biopsies Astroblastoma 1 1 1 5-ALA free Diffuse midline glioma 1 1 1 1 biopsy Ependymal	Difuse astrocytoma, grade II	24	6	4 5-ALA free
Anaplastic oligodendroglioma, grade III 10 9 7 5-ALA free Glioblastoma, grade IV 108 104 59 5-ALA free, 7 biopsies Astroblastoma 1 1 1 1 biopsy Ependymal 1 1 1 biopsy Subependymoma, grade II 8 5 3 3-ALA free Ependymoma, grade II 8 5 3 3-ALA free Anaplastic ependymoma, grade II 1 1 5-ALA free Mixed neuronal-glial 1 1 1 5-ALA free Ganglioglioma 4 0 —— Rosette-forming glioneuronal tumor 1 0 —— Weningiomas 1 0 —— Weningioma, grade II 17 17 16 5-ALA free Atypical Meningioma, grade II 2 2 2 2 5-ALA free Mesenchymal non-meningothelial 1 1 1 1 5-ALA free Mesenchymal non-meningothelial 1 1 1 1 5-ALA free Mesenchymal non-meningothelial 1 1 1 1 5-ALA free Melorastric 1 1 1 1 5-ALA free Meloracarcinoma, breast 1 10 6 4 5-ALA free Adenocarcinoma, lung 1 2 12 7 5-ALA free Adenocarcinoma, lung 1 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenocarcinoma, lung 1 1 1 5-ALA free Other tumors Diffuse large Becell lymphoma 3 2 15-ALA free Other tumors Diffuse large Becell lymphoma 3 2 2 5-ALA free Galiosis 6 2 2 5-ALA free Gilosis 6 2 2 5-ALA free Gilosis 6 2 2 5-ALA free	Oligodendroglioma, grade II	7	1	1 5-ALA free
108	Anaplastic astrocytoma, grade III	6	3	1 5-ALA free
Astroblastoma 1 1 1 1 1 15-ALA free Diffuse midline glioma 1 1 1 1 1 biopsy Ependymol 1 1 1 1 biopsy Ependymol 1 1 1 1 biopsy Ependymoma, grade I	Anaplastic oligodendroglioma, grade III	10	9	7 5-ALA free
1	Glioblastoma, grade IV	108	104	59 5-ALA free, 7 biopsies
Subpendymal	Astroblastoma	1	1	1 5-ALA free
Subependymoma, grade 3	Diffuse midline glioma	1	1	1 biopsy
Sependymoma, grade Sependymoma	Ependymal			
Anaplastic ependymoma, grade III 1 1 1 5-ALA free Mixed neuronal-glial Ganglioglioma 4 0 0 — Rosette-forming glioneuronal tumor 1 0 — Dysplastic cerebellar gangliocytoma 1 0 — Meningiomas —— Meningiomas —— Meningioma, grade I 17 17 16 5-ALA free Atypical Meningioma, grade II 2 2 2 2 5-ALA free Atypical Meningioma, grade II 2 1 1 1 1 1 5-ALA free Mesenchymal non-meningothelial —— Hemangioblastoma 4 4 4 4 4 5-ALA free Solitary fibrous tumor 1 1 1 1 1 5-ALA free Metastatic —— Adenocarcinoma, breast 10 6 4 4 5-ALA free Adenocarcinoma, lung 12 12 7 7 5-ALA free Small cells, kidney 2 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 1 5-ALA free Other tumors —— Diffuse large B-cell lymphoma 3 2 1 5-ALA free Non-neoplastic —— Radionecrosis 2 2 2 2 2 5-ALA free 2 3 1 5-ALA free 2 5-ALA free 3 7 5-ALA free 4 5-ALA free 4 5-ALA free 4 5-ALA free 4 5-ALA free 5 7 5-ALA free 6 2 2 5-ALA residual 1 15-ALA free 1 5-ALA free	Subependymoma, grade I	3	1	1 5-ALA free
Mixed neuronal-glial	Ependymoma, grade II	8	5	3 5-ALA free
A	Anaplastic ependymoma, grade III	1	1	1 5-ALA free
Rosette-forming glioneuronal tumor	Mixed neuronal-glial			
Dysplastic cerebellar gangliocytoma	Ganglioglioma	4	0	_
Meningiomas 17 17 16 5-ALA free Atypical Meningioma, grade I 2 2 2 5-ALA free Mesenchymal non-meningothelial 4 4 4 5-ALA free Metangioblastoma 4 4 4 5-ALA free Solitary fibrous tumor 1 1 1 5-ALA free Metastatic 4 4 5-ALA free Adenocarcinoma, breast 10 6 4 5-ALA free Adenocarcinoma, lung 12 12 7 5-ALA free/2 biopsies Melanoma 5 2 2 5-ALA free Small cells, kidney 2 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenocarcinoma thyroid 1 1 1 5-ALA free/1 biopsy Carcinoid tumor, lung 1 1 1 5-ALA free/1 biopsy Christian the product of the tumors 1 1 1 5-ALA free Diffuse large B-cell lymphoma 3 2 1 5-ALA free, 1 biopsy Schwannoma 1 0 - No	Rosette-forming glioneuronal tumor	1	0	_
Meningioma, grade I 17 17 16 5-ALA free Atypical Meningioma, grade II 2 2 2 5-ALA free Mesenchymal non-meningothelial 4 4 4 5-ALA free Hemangioblastoma 4 4 4 5-ALA free Solitary fibrous tumor 1 1 1 5-ALA free Metastatic	Dysplastic cerebellar gangliocytoma	1	0	_
Atypical Meningioma, grade II 2 2 2 2 5-ALA free Mesenchymal non-meningothelial	Meningiomas			
Mesenchymal non-meningothelial 4 4 4 5-ALA free Solitary fibrous tumor 1 1 1 5-ALA free Metastatic	Meningioma, grade I	17	17	16 5-ALA free
Hemangioblastoma	Atypical Meningioma, grade II	2	2	2 5-ALA free
Solitary fibrous tumor	Mesenchymal non-meningothelial			
Metastatic 10 6 4 5-ALA free Adenocarcinoma, breast 10 6 4 5-ALA free Adenocarcinoma, lung 12 12 7 5-ALA free/2 biopsies Melanoma 5 2 2 5-ALA free Small cells, kidney 2 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenoneuroendocrine carcinoma 3 3 1 5-ALA free Adenoneuroendocrine carcinoma 3 3 1 5-ALA free Other tumors 0 1 1 5-ALA free Other tumors 0 - 0 Diffuse large B-cell lymphoma 3 2 1 5-ALA free, 1 biopsy Schwannoma 1 0 - Non-neoplastic 2 2 2 5-ALA residual Inflammatory 2 1 1 5-ALA free Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1	Hemangioblastoma	4	4	4 5-ALA free
Adenocarcinoma, breast Adenocarcinoma, lung 12 12 13 7 5-ALA free 7 5-ALA free 2 5-ALA free Small cells, kidney 2 1 1 15-ALA free Adenocarcinoma, colon 1 1 1 15-ALA free Adenocarcinoma, thyroid 1 1 1 15-ALA free Adenocarcinoma, thyroid 1 1 1 15-ALA free Adenoneuroendocrine carcinoma 3 3 15-ALA free Other tumors Diffuse large B-cell lymphoma 3 2 15-ALA free, 1 biopsy Schwannoma 1 0 — Non-neoplastic Radionecrosis 2 2 2 25-ALA residual Inflammatory 2 1 15-ALA free Gliosis 6 2 25-ALA residual, 1 biopsy Cysticercosis 1 15-ALA free	Solitary fibrous tumor	1	1	1 5-ALA free
Adenocarcinoma, lung 12 12 7 5-ALA free/2 biopsies Melanoma 5 2 2 5-ALA free Small cells, kidney 2 1 1 15-ALA free Adenocarcinoma, colon 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenoeuroendocrine carcinoma 3 3 15-ALA free Adenoneuroendocrine carcinoma 1 1 1 15-ALA free Other tumors Diffuse large B-cell lymphoma 3 2 15-ALA free, 1 biopsy Schwannoma 1 0 — Non-neoplastic Radionecrosis 2 2 2 2 5-ALA residual Inflammatory 2 1 15-ALA free Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1 1 1 5-ALA free	Metastatic			
Melanoma 5 2 2 5-ALA free Small cells, kidney 2 1 1 5-ALA free Adenocarcinoma, colon 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenoneuroendocrine carcinoma 3 3 1 5-ALA free Adenoneuroendocrine carcinoma 1 1 1 5-ALA free Carcinoid tumor, lung 1 1 1 5-ALA free Other tumors 2 2 1 5-ALA free, 1 biopsy Schwannoma 1 0 — Non-neoplastic 2 2 2 5-ALA residual Inflammatory 2 1 1 5-ALA free Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1 1 1 5-ALA free	Adenocarcinoma, breast	10	6	4 5-ALA free
Small cells, kidney	Adenocarcinoma, lung	12	12	7 5-ALA free/2 biopsies
Adenocarcinoma, colon 1 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 1 5-ALA free Adenocarcinoma, thyroid 1 1 1 1 5-ALA free Adenoneuroendocrine carcinoma 3 3 3 15-ALA free Other tumors Diffuse large B-cell lymphoma 3 2 15-ALA free, 1 biopsy Schwannoma 1 0 — Non-neoplastic Radionecrosis 2 2 2 2 2-ALA residual Inflammatory 2 1 1 5-ALA free Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1 1 5-ALA free	Melanoma	5	2	2 5-ALA free
Adenocarcinoma, thyroid 1 1 1 5-ALA free Adenoneuroendocrine carcinoma 3 3 1 5-ALA free Adenoneuroendocrine carcinoma 1 1 1 15-ALA free Other tumors Diffuse large B-cell lymphoma 3 2 15-ALA free, 1 biopsy Schwannoma 1 0 — Non-neoplastic Radionecrosis 2 2 2 25-ALA residual Inflammatory 2 1 15-ALA free Gliosis 6 2 25-ALA residual, 1 biopsy Cysticercosis 1 1 5-ALA free	Small cells, kidney	2	1	1 5-ALA free
Adenoneuroendocrine carcinoma 3 3 15-ALA free/1 biopsy Carcinoid tumor, lung 1 1 1 15-ALA free Other tumors Diffuse large B-cell lymphoma 3 2 15-ALA free, 1 biopsy Schwannoma 1 0 - Non-neoplastic Radionecrosis 2 2 2 25-ALA residual Inflammatory 2 1 15-ALA free Gliosis 6 2 25-ALA residual, 1 biopsy Cysticercosis 1 1 5-ALA free	Adenocarcinoma, colon	1	1	1 5-ALA free
1	Adenocarcinoma, thyroid	1	1	1 5-ALA free
Other tumors 1 1.5-ALA free, 1 biopsy Diffuse large B-cell lymphoma 3 2 1.5-ALA free, 1 biopsy Schwannoma 1 0 — Non-neoplastic Radionecrosis 2 2 2.5-ALA residual Inflammatory 2 1 1.5-ALA free Gliosis 6 2 2.5-ALA residual, 1 biopsy Cysticercosis 1 1 1.5-ALA free	Adenoneuroendocrine carcinoma	3	3	1 5-ALA free/1 biopsy
Diffuse large B-cell lymphoma 3 2 1 5-ALA free, 1 biopsy Schwannoma 1 0 - Non-neoplastic Radionecrosis 2 2 2 5-ALA residual Inflammatory 2 1 1 5-ALA free Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1 1 1 5-ALA free	Carcinoid tumor, lung	1	1	1 5-ALA free
5chwannoma 1 0 — Non-neoplastic Radionecrosis 2 2 2 5-ALA residual Inflammatory 2 1 1 5-ALA free Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1 1 1 5-ALA free	Other tumors			
Non-neoplastic 2 2 2 5-ALA residual 1 1 1 1 1 1 1 1 1	Diffuse large B-cell lymphoma	3	2	1 5-ALA free, 1 biopsy
Radionecrosis 2 2 2 5-ALA residual Inflammatory 2 1 1 5-ALA free Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1 1 1 5-ALA free	Schwannoma	1	0	
1	Non-neoplastic			
Gliosis 6 2 2 5-ALA residual, 1 biopsy Cysticercosis 1 1 1 5-ALA free	Radionecrosis	2	2	2 5-ALA residual
Cysticercosis 1 1 5-ALA free	Inflammatory	2	1	1 5-ALA free
-,	Gliosis	6	2	2 5-ALA residual, 1 biopsy
Demyelinating disease 2 1 1 biopsy	Cysticercosis	1	1	1 5-ALA free
	Demyelinating disease	2	1	1 biopsy



Fig. 1 Illustrative case of a grade-II ependymoma: (A) preoperative magnetic resonance imaging (MRI) scan. (B) intraoperative finding; (C) positivity for 5-aminolevulinic acid (5-ALA); (D) histopathological finding; (E) postoperative MRI.

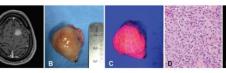


Fig. 2 Illustrative case of a grade-I meningioma: (A) preoperative MRI; (B) intraoperative finding; (C) 5-ALA positivity; (D) histopathological finding: (E) postoperative MRI.

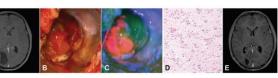


Fig. 3 Illustrative case of a pilocytic astrocytoma: (A) preoperative MRI; (B) intraoperative finding; (C) 5-ALA positivity; (D) histopathologic finding; (E) postoperative MRI.

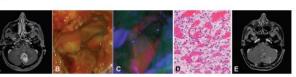


Fig. 4 Illustrative case of a hemangioblastoma: (A) preoperative MRI; (B) intraoperative finding; (C) 5-ALA positivity; (D) histopathologic finding; (E) postoperative MRI.



Fig. 5 Illustrative case of Solitary fibrous tumor: (A) preoperative MRI; (B) intraoperative finding; (C) 5-ALA positivity; (D) histopathologic finding; (E) postoperative MRI.

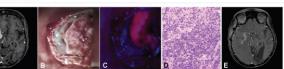


Fig. 6 Illustrative case of a diffuse large B-cell lymphoma: (A) preoperative MRI; (B) intraoperative finding; (C) 5-ALA positivity; (D) histopathological finding; (E) postoperative MRI.

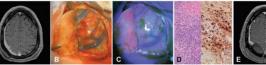


Fig. 7 Illustrative case of immunoglobulin G4-related disease: (A) preoperative MRI; (B) intraoperative finding; (C) 5-ALA positivity; (E histopathological finding (left) with immunochemistry (right); (E) postoperative MRI.