

## Technical Note

# Convexity meningiomas enhanced by sodium fluorescein

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## Abstract

**Background:** The resection of the meningiomas surrounding the dura is an important goal during the removal of a convexity meningioma. The authors present the first application of sodium fluorescein (SF) as a tool for tumor and dural tail identification in convexity meningiomas.

**Methods:** Five frontal convexity meningiomas operated on between December 2012 and April 2013 were included. After initial dissection a dose of 1 g of the SF, 20% was injected into a peripheral vein. Tumor and dural tail were removed using the correlation between magnetic resonance imaging (MRI) findings and transoperative SF enhancement.

**Results:** Simpson Grade 1 removal was obtained in three cases, grade 2 in one atypical meningioma and grade zero in one case. SF dural tail enhancement was positive in all cases and histologic analysis evidenced involvement of the dura by tumors.

**Conclusion:** SF enhancement was evident in meningiomas and dura surrounding the lesions. Histologic analysis confirmed dural involvement. SF could represent an universally available fluorescent tool for meningioma surgery.

**Key Words:** Fluorescent marker, grade zero removal, meningioma, surgical resection

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## INTRODUCTION

The recognition of the meningiomas and surrounding dural tail limits is one of the most challenging goals during a meningioma resection. Further, the possibility of better tumor control depends on the extension of the tumor to be removed and includes the dura around the mass. Sodium fluorescein (SF) was first used for the identification of different types of brain tumors in 1948.<sup>[9]</sup> Since then, the use of SF and others fluorescent markers have been described in literature particularly that dealing with glioblastoma multiform resection.<sup>[2,7,8,10]</sup> Recently, the SF application in skull base tumors was described.<sup>[3]</sup>

The authors present five introductory cases using a new application of SF in convexity meningiomas showing a visual analysis of the tumor and the surrounding dural enhancement given by the substance.

## MATERIALS AND METHODS

### Illustrative cases

#### Case 1

A 72-year-old male with recurrence of an atypical meningioma, involving both frontal convexity and superior sagittal sinus (SSP). A partial removal of the bifrontal mass with residual tumor in the SSP, with

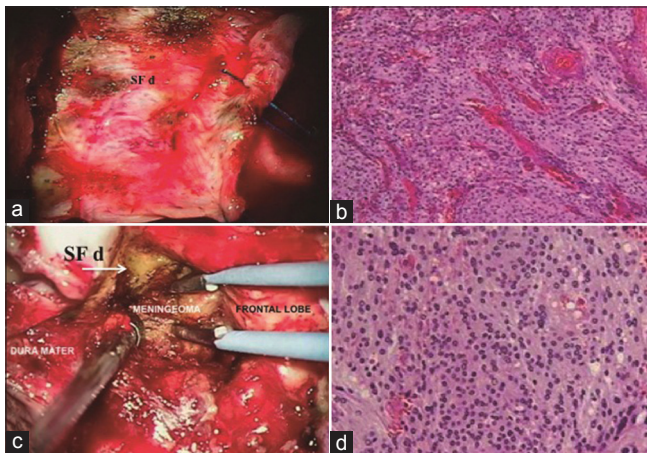
transoperative SF administration, showed strong evidence of dural and tumoral dye enhancement [Figures 1a and 2]. Dural removal at the surrounding meningioma site was also enhanced by SF; there was evidence of meningioma presence in the histological analysis [Figure 1b]. Cytogenetic analysis showed sexual chromosome Y deletion. The patient had a good neurological outcome.

*Case 2*

A 62-year-old male with headache and seizures, presenting a large left frontal cystic meningioma on magnetic resonance imaging (MRI) went through a radical removal, with SF transoperative tumor and surrounding dura enhancement. Histological analysis showed evidence of meningothelial meningioma and the dural surrounding area was negative, even with SF irregular enhancement. The patient was discharged without neurological abnormalities.

*Case 3*

A 60-year-old female with headaches showing a meningioma in the left motor area on MRI.



**Figure 1:** (a) SF enhanced dura; (b) Histologic atypical meningioma; (c) Tumor and surrounding dura enhancement by SF; (d) Histologic psammomatous meningioma; SFd - SF enhanced surrounding dura

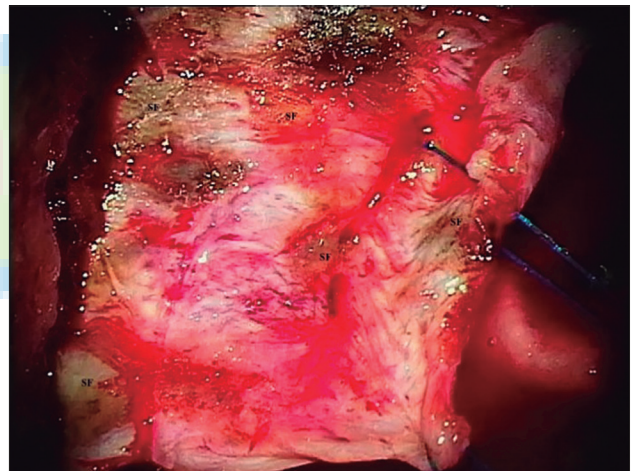
Transoperative SF administration was used, as described below, with positive tumor and a surrounding dura enhancement [Figure 1c]. On histological examination evidence a psammomatous meningioma was seen [Figure 1d]. The dural tail surrounding the meningioma area was equally tumoral.

*Case 4*

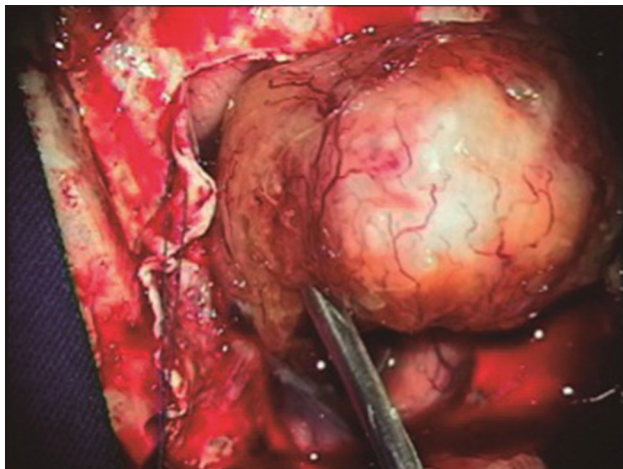
A 37-year-old female with headaches showing a meningioma in the right frontal lobe on MRI. Transoperative SF administration enhanced tumor and a surrounding dura [Figures 3 and 4]. On histological examination a transitional meningioma was seen. The dural tail surrounding the meningioma area was involved by the disease. Cytogenetic analysis showed a 22 monosomy.

*Case 5*

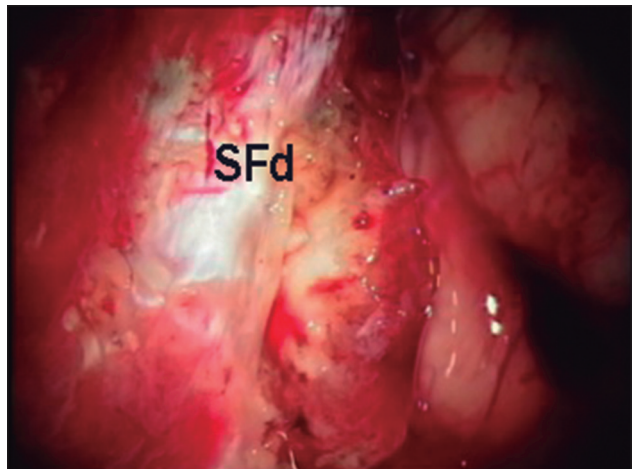
A 57-year-old female with headache and a meningioma in the right frontal lobe on MRI. Trans-operative SF administration enhanced tumor and dural tail [Figure 5 left]. Histologic examination evidenced a transitional meningioma.



**Figure 2:** Larger view of the Figure 1A. SF - sodium fluorescein



**Figure 3:** Convexity meningioma SF enhanced



**Figure 4:** SFd - SF enhanced dura

### Transoperative SF administration

The initial dissections were performed, and after exposure of the tumors and their relative positioning within the cortical and vascular structures, a dose of 1 g of the SF 20% was injected into a peripheral vein and included pictures were obtained 10 min after SF administration. Digital photos were taken using digital camera MediLive Carl Zeiss 1 CCD. The light source of the pictures was the same as the microsurgical field, manual white balance was proceeded, capturing images visualized by the surgeon at the microscope without any special filters.

### RESULTS

SF enhanced all convexity meningiomas. Dural tail as indicated by MRI findings correlated with transoperative SF dural enhancement was also positive according to the histologic analysis. Table 1 summarizes the series characteristics.

### DISCUSSION

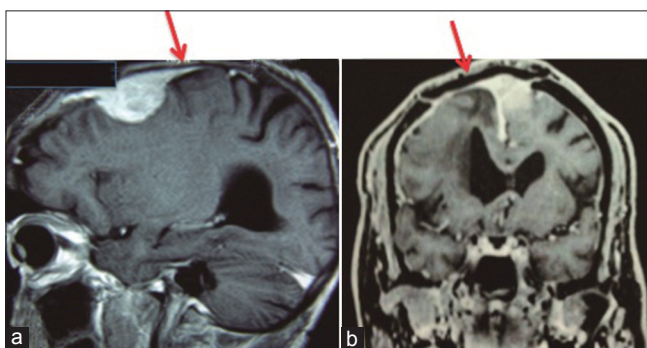
The work of Simpson, seminal, which was undertaken during the second half of the last century, taught that the objective and goal for surgically treated meningiomas was to achieve the most radical removal possible.<sup>[1,4,5,13]</sup> Some authors believe that even with a long-term follow up, the more aggressively removed meningiomas will regrow, possibly because of remaining cells or the molecular biology of the tumors. The MIB-1 index was evaluated as a possible predictor of meningiomas with a higher

risk of recurrence.<sup>[11]</sup> In addition, cytogenetics aspects involved in the recurrence and progression of World Health Organization (WHO) grade I meningiomas are well known, including losses in 1 p and other chromosomal abnormalities and play an important role in the recurrence of the meningioma.<sup>[1,12]</sup> The relevance of Simpson grade I and II resection as a sole predictor of recurrence in meningiomas surgery was diminished in the work of Sughrue *et al.*<sup>[15]</sup> In spite of these important aspects and results, other authors observed consistent relation between radical removal (Simpson 1) and the retreatment-free survival rates in WHO grade I convexity meningiomas.<sup>[4]</sup> Other authors extended the area of dura resection, in order to obtain a grade zero resection. It is a clear consideration of the importance of radical removal for control of the recurrence in meningiomas.<sup>[5]</sup>

Considering the aspects in some cases of convexity meningiomas, those in which the resection could be enlarged with no compromise of the quality of life, and applying the original concept of extensive resection for better disease control, we research a new application of SF in this introductory series.

Fluorescent markers have been used to improve identification of the tumor limits, especially during the resection of gliomas.<sup>[7,8]</sup> SF was first investigated by Moore and more recently in studies of gliomas removal.<sup>[8,9]</sup> Metastatic lesion were also enhanced by SF.<sup>[9]</sup> The 5-ALA has been used in glioma surgery and recent studies applied in Sylvian and spinal meningiomas.<sup>[2,16]</sup>

The present study about the application of SF in convexity meningioma surgery was the first investigation of the fluorescent marker for such lesions. Actually, it represents an extension of the previous experience using this substance in skull base tumors.<sup>[3]</sup> The initial study presented a strongly positive and digitally confirmed analysis of the SF enhancement of the tumors.<sup>[3]</sup> In this study, the use of the 1 g of SF 20% was the same as that of the former study on skull base tumors. During the application of the dye in skull base meningiomas, SF dura mater adjacent to the tumors was also enhanced, pointing to the possibility of the dural tail, which could be involved in such a find. Efforts to achieve a radical resection with dural margin are not suitable in many cases of skull base meningiomas, because of the neurovascular structures around the tumors. However,



**Figure 5: Preoperative MRI. (a) Frontal meningioma and dural tail (red arrow); (b) atypical recurrent meningioma invading superior sagittal sinus (red arrow)**

**Table 1: Convexity meningioma series**

Meningioma site	Sex	Age (years)	Meningioma histology	Citogenetic	SF Enhancement of the dural tail	Simpson grade
Frontal	Male	72	Atypical	Sexual Y deletion	Positive	2
Frontal	Male	62	Menigothelial	-	Positive	1
Frontal	Female	60	Psamommatous	-	Positive	1
Frontal	Female	37	Transitional	22 monossomy	Positive	0
Frontal	Female	57	Transitional	-	Positive	1



in convexity meningiomas, the goal should be tumor resection plus excision of the dural tail and, if possible, an additional dural margin of 2 cm, that is, a grade zero removal.<sup>[4,5,14]</sup>

The dural tail was the most relevant aspect observed in the present study, in order to achieve radical removal. This could be influenced by SF enhancement. All cases presented SF enhancement of the dura around the meningiomas, in an irregular fashion. Surgical resection was oriented by SF enhancement and MRI preoperative images and histological analysis was evident to the dural involvement by the tumor in all cases [Figures 1-4]. It is probably that the positive results for meningioma in histologic analysis of the dura was due to a relationship between MRI images and dural enhancement.

The transoperative dural SF enhancement helped the radical removal. The only exception was in the case 1, a recurrent atypical meningioma, with invasion of a patent superior sagittal sinus, which was preserved [Figure 5 right].

This introductory series points to a relationship between dural enhancement by SF around the mass and the presence of meningioma in histopathology. In contrast, it is possible that distant portions of dura, which were not enhanced by SF, could be involved by tumor also. The limits of any markers and the understanding of what they are enhancing should be considered when analyzing the applicability of fluorescent methods. Kubben *et al.* presented an interesting study about the correlation between contrast enhancement in an intraoperative MRI and histopathology in GBM, where they concluded that the absence of contrast enhancement was a bad predictor for the absence of tumor.<sup>[6]</sup> Considering the differences in the methods and neoplasms, what should be remembered is that any marker present limits and false negatives could be a dangerous bias. In the present series, the enhancement of the dura presented a spot fashion, as illustrated in Figure 2. The irregular enhancement points to the importance of considering that the meningioma could be present in a less enhanced dura. What we advocate is that SF should be used as a complimentary tool to the MRI images during the surgical removal of a dural tail, and the resection should be extended if the MRI indicates such a need. Neuronavigation is an additional tool, which should be included, when available, for dural tail identification.

The concern about important dural sinuses, venous channels and eloquent areas involvement during convexity meningiomas dissection is also a reason for researching the applicability of SF. In cases where dural sinuses were supposed to be invaded by the tumors, as the case 1 included in the present study, SF could help as an auxiliary method for transoperative investigation and decisions. In the case illustrated, meningioma

was enhanced in the wall of the superior sagittal sinus and the preservation of the sinus was helped by the dye [Figure 4]. The initial results suggest the possibility of expanding research in SF enhancement of tumors around the dural sinuses.

SF staining during brain tumor surgery is probably related to blood– brain barrier (BBB) disruption.<sup>[3,7-9]</sup> BBB disruption plays a principal role in the gadolinium enhancement of the tumors on MRI. Meningiomas included in the series were also enhanced by gadolinium on MRI [Figure 5]. This aspect could be involved in transoperative SF enhancement by the meningiomas. In convexity meningiomas, there is no difficulty in identification of tumor limits and irregular enhancement of different portions of the tumors are less important in the surgical removal of the mass [Figure 3]. In contrast, vascular abnormalities in dural involvement by a meningioma could be very important in achieving a more aggressive removal. In this regard, SF could represent an interesting marker.<sup>[3-5]</sup>

In convexity meningiomas with pial invasion and edema surrounding the lesions, BBB disruption permitted a strong enhancement of the tumor [Figure 1c] This is another interesting research question, which should be evaluated in a future and larger series, in order to observe whether SF would help to improve more extended removal of pial invading meningiomas.

In the original work of Moore black light was used to enhance the fluorescein penetration.<sup>[9]</sup> In the present study, the visual perception of the tumor yellow pigmentation promoted by SF enhancement was achieved using a standard white-light surgical microscope. In fact, it was observed in the previous study on skull base tumors.<sup>[3]</sup> Such an aspect is a crucial contribution to the study, because the results could be reproduced in any department without any additional device, using just simple microscopes. Nevertheless, it is possible that the development of special filters, helping the SF wavelength identification could improve the contrast between the tumor and dura mater and surrounding tissues enhanced by the dye. The use of black light or other colored light sources could be tested in future studies in order to observe if the fluorescence effect can be improved.

The study presents the limitation of small number of patients. Also, we prefer to use standard white light instead of black light or special filters. The fluorescence could be improved with such devices. In fact, a recent study tested the SF guided removal of malignant tumors under YELLOW 560 nm surgical microscope filter with interesting results and lower doses of SF.<sup>[13]</sup>

The use of SF is very simple. The substance is safe, presents low cost, and it is a universally available option. The method presented does not require any special techniques or devices, which includes SF as a

considerable fluorescent tool for convexity meningiomas surgery.

## CONCLUSION

The initial results of the enhancement by SF of convexity meningiomas and surrounding dura were positive. Further larger studies should evaluate the dye as an alternative for fluorescence-guided convexity meningiomas surgery in order to improve the radical removal.

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