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Sodium fluorescein in skull base meningiomas: A technical note

Carlos Eduardo da Silva[a,*], Vinicius Duval da Silva[b], Jefferson Luis Braga da Silva[c]

[a] Department of Neurosurgery and Skull Base Surgery, ICBC – Instituto de Cirurgia da Base do Crânio, Hospital Ernesto Dornelles, Porto Alegre, RS, Brazil
[b] Department of Pathology and Radiation, Pontifical Catholic University of Rio Grande do Sul – PUCRS, Porto Alegre, RS, Brazil
[c] Service of Hand Surgery and Reconstructive Microsurgery, Pontifical Catholic University of Rio Grande do Sul – PUCRS, Porto Alegre, RS, Brazil

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ABSTRACT

Objectives: Skull base meningiomas are a neurosurgical challenge due to the involvement of neurovascular structures. In this study, the authors present the first study of the trans-operative use of sodium fluorescein (SF) to enhance skull base meningiomas and perform a quantitative digital analysis of the tumors' pigmentation. The goal of the study was to observe the SF enhancement of skull base meningiomas.
Patients and methods: A prospective, within-subjects study was designed and performed. This study included twelve patients with skull base meningiomas. After an initial dissection, digital pictures were taken before and after systematic injections of SF using the same light-source used for the surgical microscope. These pictures were analyzed with software that calculated the wavelengths of the sodium fluorescein before and after the injection of the dye.
Results: The meningiomas in the sample included the following types: 1 cavernous sinus, 1 olfactory groove, 3 petroclival, 1 tuberculum sellae, 3 sphenoid wings, 1 anterior clinoid, and 2 temporal floor. The SF enhancement in all tumors was strongly positive.
Conclusions: The low cost, universal availability and safety of SF indicate that this dye should be examined in further studies, and its applications in skull-base meningioma surgeries should be further assessed.

1. Introduction

Skull base meningiomas are neurosurgical challenges due to the neurovascular structures involved in the treatment of these lesions. Numerous surgical advances and skull base techniques have been developed for the management of such complex tumors as these meningiomas.

Sodium fluorescein (SF) was first used for the identification of different types of brain tumors in 1948 [1]. Subsequently, the use of SF and others fluorescent markers, particularly those that address the surgical treatment of glioblastoma multiforme and metastatic disease in the brain, have been described in the literature [2–4]. In 2010, we described the use of SF as an adjuvant for the surgical resection in a small sample of these skull base lesions [5].

Here, the authors present the first study of the transoperative use of SF for skull base meningiomas and performed a quantitative digital analysis of the enhancement of the tumors due to SF. This study examined the enhancement patterns caused by the application of the fluorescent marker SF in skull base meningioma surgery.

2. Materials and methods

A prospective study was designed and carried out. This study included twelve patients with skull base meningiomas who underwent operations between December 2008 and December 2011. The criteria for inclusion in the trial included the following: presentation with tumors meeting the radiological criteria for meningiomas; tumors located in the anterior, medial or posterior cranial base; and the involvement of at least one cranial nerve with the lesions. The patients were informed about the trans-operative use of sodium fluorescein to view the tumors during the surgical procedure. After being informed, the patients provided written consent prior to the procedure.

The initial dissections were performed and, after the exposure of the tumors and determination of their relations to the cranial nerves and vascular structures, an initial digital photo was manually taken through the optical lens of the microscope. The digital camera used was a SONY model DSC-W90 with 8.1 megapixels; macro activation was on, and the internal flash was off. The light-source for the pictures was the same as that used for the

* Corresponding author at: Department of Neurosurgery and Skull Base Surgery, Hospital Ernesto Dornelles, Av. Ipiranga 1801, Box 26, 90160-093 Porto Alegre, Brazil. Tel.: +55 51 32276208; fax: +55 51 32276208.
E-mail addresses: carlos@icbc-neurocirurgia.com.br, dasilvacebr@yahoo.com.br (C.E. da Silva).

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microscope, and the captured images were visualized by the surgeon without the use of any special filters.

A dose of 1 g of 20% SF was injected into a peripheral vein. The second picture was obtained 10 min after SF injection using the same technique described above.

The pictures were saved in JPEG format with minimal compression and divided into pre- and post-SF injection image groups. The images were analyzed with the Image-Pro Plus 4.5.1 program (Media Cybernetics, Silver Spring, MD, USA). First, the SF post-injection image was submitted to the program for analysis. The area of interest was defined using a rectangular frame around the tumor and neurovascular structures. The manual selection of colors was performed using level 4 sensitivity (range: 1–5). The color red was defined to highlight the wavelength (WL) of the sodium fluorescein in the picture. Next, the area of SF enhancement was saved, and the program calculated the total area of the picture that exhibited the SF wavelength. The absolute value obtained by this statistical analysis of the program was then saved in an Excel (Microsoft Redmond, WA, USA) spreadsheet. Subsequently, the SF pre-injection image from the same case was analyzed. The same rectangular frames were applied around the tumor and neurovascular structures without SF. The specific SF wavelength of the post-injection picture recorded by the program was applied to the same selected area of the pre-injection picture and then the program calculated the area that exhibited the SF wave length. The data were saved in the Excel database for statistical analyses.

The non-parametric Wilcoxon test was used for the statistical analyses, which compared the SF wavelength values obtained from the pre- and post-injection pictures.

Table 1
The values measured by the IMAGE PRO PLUS program of the area with the correspondent wave length of the SF.

Meningiomas by site	Pre-SF inj. wave length	Post-SF inj. wave length
Cavernous sinus	1009	109,576
Olfactory groove	232	1776
Petroclival	29,343	287,548
Petroclival 2	40,287	64,670
Petroclival 3	0.37	21.60
Tuberculum sellae	66,882	366,531
Sphenoid wing 1	33,989	687,244
Sphenoid wing 2	91,692	141,215
Sphenoid wing 3	6496	22,373
Clinoidal	5243	114,175
Temporal fossa 1	25	1555
Temporal fossa 2	31,988	45,041

$P = 0.002$.

3. Results

The group of twelve meningiomas was composed of the following types of tumors: 1 cavernous sinus, 1 olfactory groove, 3 petroclival, 1 tuberculum sellae, 3 sphenoid wing, 1 anterior clinoid, and 2 temporal floor.

Table 1 presents the areas with SF wavelengths as measured by the Image-Pro Plus program.

Figs. 1 and 2 illustrate four examples of the clinical effects observed under the surgical microscope.

Fig. 3 shows the effects of the SF injections on the capture of SF WL via both pre- and post-injection measures. The non-parametric Wilcoxon test resulted in $P = 0.002$.

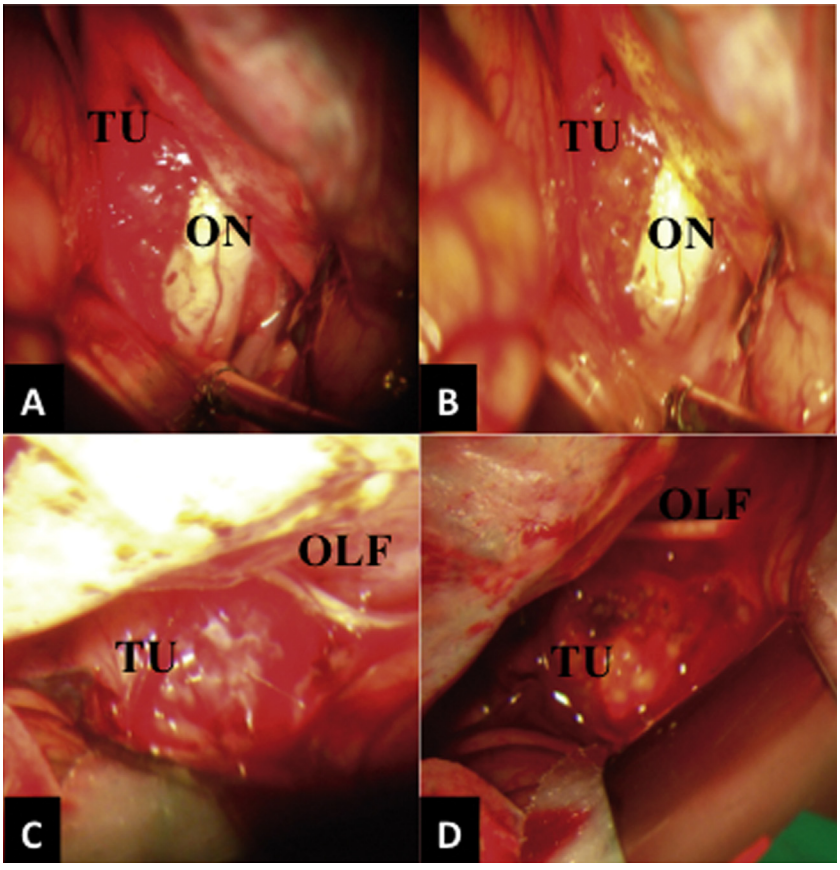

Fig. 1. A – Tuberculum sellae tumor, pre-SF injection. B – Tuberculum sellae tumor, post-SF injection. C – Olfactory groove tumor, pre-SF injection. D – Olfactory groove tumor, post-SF injection. TU – tumor. ON – optic nerve. OLF – olfactory nerve.

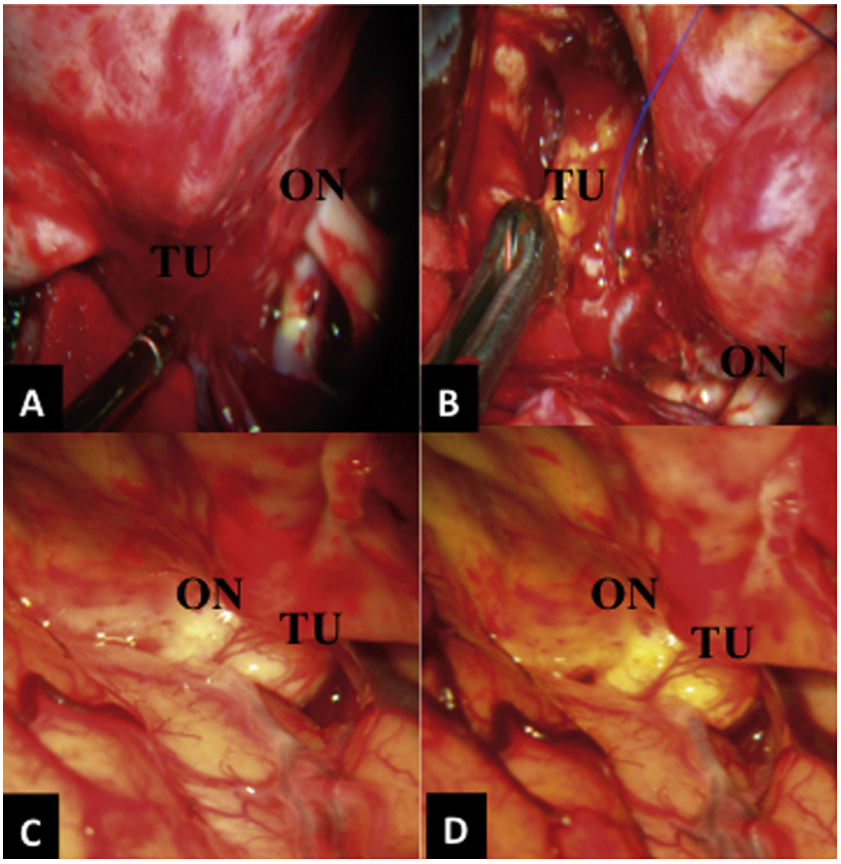

Fig. 2. A – Left cavernous sinus tumor, pre-SF injection. B – Left cavernous sinus tumor, post SF injection. C – Right anterior clinoid tumor, pre-SF injection. D – Right anterior clinoid tumor, post-SF injection. TU – tumor. ON – optic nerve.

4. Discussion

Moore et al. first investigated the use of sodium fluorescein in neurosurgery in 1948 [1]. Several authors have tested the applicability of SF to the surgical removal of glioblastoma multiformes and metastatic brain tumors [2–4]. Other fluorescent markers, such as 5-ALA, have been used as important tools for improving tumor resections [6]. Skull base tumors involve critical neural and vascular structures in the majority of cases. Meningiomas are the most frequently found tumor lesion in the base of the cranium. Advances in surgical techniques have progressively improved the resectioning of such cases [7–20,1,21–29]. However, the morbidities associated with dissections around the cranial nerves and arterial and venous vessels remain a constant concern during the surgical management of skull base meningiomas [7–17,20,24,27,28].

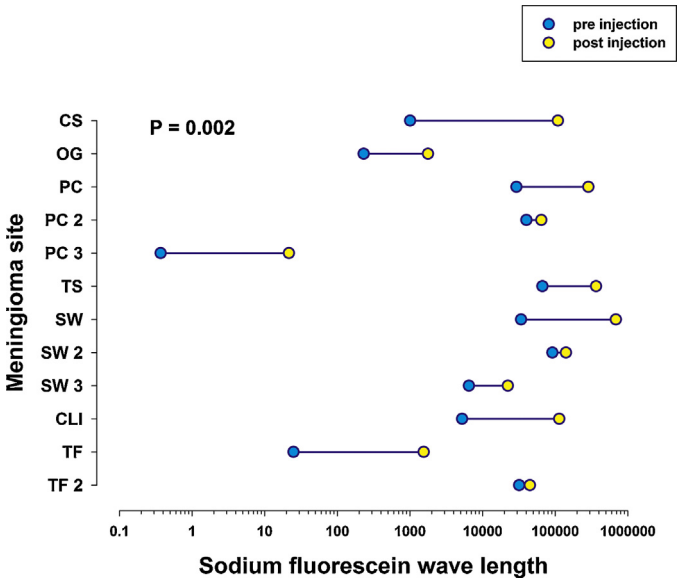

Fig. 3. SF wavelengths pre- and post-SF injection. CS: cavernous sinus; OG: olfactory groove; PC: petroclival; PC2: petroclival 2; PC3: petroclival 3; TS: tuberculum sellae; SW: sphenoid wing; SW2: sphenoid wing 2; SW3: sphenoid wing 3; CLI: clinoidal; TS: temporal fossa; TS2: temporal fossa 2.

The application of sodium fluorescein during cranial base meningioma surgery can be likened to an extension of a previous study that used SF for skull base tumors [5]. In this study, the clinical effect of enhancing the skull base tumors with SF was found to be strongly positive. In the initial group of 6 tumors, three patients presented with meningiomas. Therefore, these findings suggested that this group of lesions may have been strongly enhanced by SF and provided the motivation for further investigation of an expanded version of this hypothesis that included skull base meningiomas.

In the present study, no special filters were applied to the surgical microscope. Using only a standard white-light microscope, the enhanced illumination of the tumors was made obvious by the yellow pigmentation that was present after the injection of SF; thus, the injection of SF produced an evident and important effect (Figs. 1 and 2). The tumors examined showed marked enhancement by gadolinium on MRIs, and this finding could provide an explanation for the strong capture of SF by the meningiomas because disruption of the BBB plays a role in the gadolinium enhancement of tumors on MRI [5].

The simple arithmetical sums of the areas of the SF WLs calculated by the software varied widely; this finding was possibly the

result of variability in the light conditions while taking the pictures manually through the lens of the microscope. Table 1 illustrates this issue; however, the differences between the pre- and post-SF injections remained unaltered despite the external light variations.

The dye was evident 10 min after SF injection and persisted for several hours throughout the durations of the tumor dissections. This finding validates the first study's initial observations of fluorescence in tumors located at different sites that involved other skull base lesions [1,5].

SF was also present in the CSF, particularly in the first hour. Furthermore, constant irrigation and suction to clean the surgical field made the effect of tumor enhancement effect even more evident.

Interestingly, SF enhancement of the dura surrounding the tumors was observed. In most cases, the limits of the meningiomas were clearly defined, and the fluorescent markers were less important during the mass resectioning than they are during glioma surgery. Nevertheless, if a dural tail could be identified for SF enhancement, the dye marker could alter the extent of radical removal. This hypothesis should be tested in further studies.

SF did not enhance the cranial nerves. The contrast between the enhanced mass and the nerves was interesting and aided with the microsurgical dissection of these structures.

The patients included in this series did not present with any adverse reaction to the application of SF. The dye was eliminated, primarily through the urine, in approximately 36 h.

SF is inexpensive, safe, and universally available. The method described herein does not require any special microscope or device. Indeed, this method can be reproduced in any department using a standard white-light microscope.

5. Conclusions

The enhancement of skull base meningiomas by SF was strongly evident. Additional applications of this method should be tested in further studies; particularly promising potential applications include the use of SF to improve cranial nerve preservation and as a dural tail marker.

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Conflict of interest

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

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