

# Methylene Blue Test in Assessing Disease Free Margins in Lingual Carcinoma Resection

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*Lingual squamous cell carcinoma is one of the most frequent localization of the oral carcinomas. The tongue neoplasia represents nearly 40% of the oral carcinomas. Recent studies showed an increasing trend of lingual carcinoma in young patients. Several staining tests have been described to early detect the disease. After detection, disease free margins resection will increase the survival rate. This study aims to analyze the methylene blue staining test in achieving disease free resection margins in lingual squamous cell carcinoma.*

**Keywords:** Lingual squamous cell, oral carcinomas, free margins resection, methylene blue

Head and neck neoplasms represent approximately 2% of all cancers [1]. In Romania the incidence of the pharyngeal cancer is 15.5 (100.000), so we are in the third place in Europe. From that, oral cancers represent almost 50% of the head and neck carcinomas, and squamous cell carcinoma represents nearly 90% of the cases. Alcohol and smoking abuse are responsible for 40% of the cases being located in the lingual area [2]. The most common topographic localization of the tumor will be on the posterior, lateral and ventral border of the tongue.

Recent studies showed an increased number of young adults affected by lingual carcinomas, probably due to the exposure to tobacco, alcohol abuse and also environmental factors, including pollution of food and air. Tongue cancers are responsible for high mortality rates, more than 9000 deaths every year. Screening protocols are recommended by the American Cancer Society for all head and neck cancers. Patients with ages between 20-40 year old must be scanned every three years, asymptomatic patients with age over 40 year old must be scanned once per year [3]. If alcohol and tobacco abuse are detected, the patient will enter in a high-risk group, and they must be examined every year no matter what their age is.

Various modalities of assessing disease free resection margins are mandatory to the patient's overall survival.

The purpose of this paper is to analyze the value of the methylene blue staining test in determining disease free resection margins in squamous cell carcinoma located on the tongue.

## Experimental part

Nowadays we are trying to assess lingual cancer in very early stages. Conventional hemiglossectomies or total glossectomies require reconstruction of the lingual area so that our patient will regain oral continence, deglutition and prevent aspiration [4, 5]. In initial stages tongue neoplasia will have limited resection areas that usually do not require reconstruction of the defect and usually primary closure is possible.

In those cases, it's hard to assess disease free margins, so additional tests may help the surgeon to define the lesion better.

Prior surgery, a complete evaluation of the lingual tumor is done using bucopharyngoscopy and fiberoptic nasopharyngolaryngeal exam.

Intraoperatively we propose a protocol that will include the methylene blue staining test to assess the disease free resection margins better.

We included in our study two hospitals, Prof. Dr. Dorin Hociota Institute of Phonoaudiology and Functional ENT Surgery and Gen. Dr. Aviator Victor Anastasiu Institute of Aeronautical and Spatial Medicine.

We enrolled 23 patients confirmed with tongue carcinoma by the histopathologic exam. The age of the patients was between 46 and 69 year old. The group consisted of 17 men and 6 women. Tumor staging revealed 5 patients with T1 and 18 patients with T2 confirmed cancer. A CT scan was performed on the cervical and thoracic areas prior surgery.

We performed the surgery under general anesthesia with transoral intubation.

We exposed the tongue by mounting two silk sutures, 0 diameters of 30 cm length. By pulling the wires the tongue is better exposed, and the mouth is opened easily (fig. 1).

It is mandatory to have a good cooperation with the anesthesiologist to have a proper relaxation of the patient,

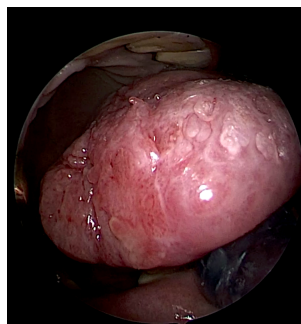


Fig.1. Intraoperative view - extensive lingual tumor

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otherwise it is hard to open the mouth and to expose the lingual lesion.

We aspirated the saliva and the tried to dry the surface of the lingual mucosa. We cleaned the lingual mucosa with 1% acetic acid solution, and then we dried one more time the mucosa. We stained the surface of the tongue with 1% methylene blue solution, and then we waited for 5 minutes. The surface of the tongue is cleaned afterward with saline solution. We resected the area of the tongue that remained stained by methylene blue in the tumoral perimeter (fig. 2). We collected multiple biopsies from the remained margins of the defect, and we compared our results with the histopathological result.



Fig. 2. Intraoperative view - lingual tumor after the methylene blue staining test, the limits of the tumor and the vascular design are emphasized

Due to the complex geometry of the lesion, we collected some 10-12 biopsies in every case.

### Results and discussions

We created a map with the location of every 10-12 biopsies collected from the lingual area. The specimens were positioned in the same place in the remnant margins of the defect.

Comparing our results from the staining test with the paraffin sections from the histopathological exam we found a correlation of 98.4% between them.

The obtained results concluded that the methylene blue staining test is a simple and valuable method of getting disease free resection margins in tongue neoplasia.

### Conclusions

The methylene blue staining test is a helpful way of assessing disease free margins in tongue cancer. Methylene blue is a cheap substance highly available [6, 7]. The method of staining the tissue with methylene blue is easy to perform. The test can be quickly executed; no surgical time is prolonged. Methylene blue is a substance that was

used as an antiseptic [8-13]. High correlation figures obtained comparing with the paraffin histopathological results support the conclusion that methylene blue staining test is a reliable test for assessing disease free resection margins. It does not require special abilities, it is simple to be performed, and the learning curve is easy to achieve. A multitude of therapies exists for cancers, from local to systemic delivery [14]. However, all these therapies are more efficient when the resection associates disease free margins, which is why our efforts aim to achieve this goal

### References

1. ALI H, SINNOTT S-J, CORCORAN P, DEADY S, SHARP L, KABIR Z. *BMC Cancer*. **16**, 2016, p. 950.
2. RAM H, SARKAR J, KUMAR H, KONWAR R, BHATT MLB, MOHAMMAD S. *Journal of Maxillofacial & Oral Surgery*. **10**, nr. 2, 2011, p. 132-137
3. GAJENDRA S, CRUZ GD, KUMAR JV. *Journal of cancer education/ : the official journal of the American Association for Cancer Education*. **21**, nr. 3, 2006, p. 157-162.
4. REITER M, HARREUS U. *Anticancer Res*. **37**, nr. 8, 2017, p. 4233-4237
5. NAVACH V, ZURLO V, CALABRESE L, MASSARO MA, BRUSCHINI R, GIUGLIANO G, ANSARIN M, CHIESA F. *Br J Oral Maxillofac Surg*. **51**, no. 3, 2013, p. 217-23
6. STEFANESCU D.C., CEACHIR O., ZAINEA V., HAINAROSIE M., PIETROSANU C., IONITA I.G., HAINAROSIE R. *Rev. Chim.(Bucharest)*, **67**, no. 8, 2016, p. 1558-59
7. HAINAROSIE, R., ZAINEA, V., CEACHIR, O., HAINAROSIE, M., PIETROSANU, C., STEFANESCU, C.D.. *Rev. Chim. (Bucharest)*, **68**, no. 1, 2017, p. 16-17
8. STECZKO J, ASH SR, BREWER L, GUILLEM A. *J Infect*. **60**, nr. 1, 2010, p. 36-43.
9. OBSTOY B, SALAUN M, VERESEZAN L, et al. *BMC Pulmonary Medicine*. **15**, 2015, p. 30.
10. WARNECKE A, AVERBECK T, LEINUNG M, SOUDAH B, WENZEL GI, KREIPE HH, LENARZ T, STOVER T. *Laryngoscope*. **120**, nr. 2, 2010, p. 253-8.
11. C. NITIPIR, M.A. BARBU, L.G. POPA, M.M. MIHAI, I. RADU, D., MIREA, C. GIURCANEANU, R.V. SCAUNASU, *Revista Farmacia*, **63**, nr. 6, 2015, p. 805-810.
12. C. NITIPIR, M.G. ALBU, G. VOICU, A. FICAI, M.A. BARBU, L.G. POPA, D. MIREA, C. LEVAI, S. LAZAR, M.V. GHICA, *Journal of Chemistry*, **66**, nr. 8, 2015.
13. M.V. GHICA, M.G. ALBU, D.A. KAYA, L. POPA, S. OZTURK, L.C. RUSU, C. DINU-PIRVU, C. CHELARU, L. ALBU, A. MEGHEA, C. NITIPIR, *Korean Journal of Chemical Engineering*, **33**, nr. 4, 2016, p. 1325-1330.
14. YIPEL M., GHICA M., ALBU M.G. et al. *Current Organic Chemistry*, **20**, nr. 28, 2016, p. 2934-2948

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