УДК 616.31-006.04-076-072:681.784.8
DOI: 10.35693/2500-1388-2020-5-3-181-185

Identification of the site for biopsy in oral mucosa cancer diagnostics

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Abstract

Aim – to refine the method of incisional biopsy in the diagnosis of oral mucosa cancer using the auto-fluorescent stomatoscopy.

Materials and method. The study was conducted on the base of the Samara Regional Clinical Oncology Center. The inclusion criterion for patients was the diagnose of the oral mucosa cancer of various localization. Patients were divided into 2 groups. The main group included patients (n=43), who were being diagnosed for cancer with the help of optimized incisional biopsy of the oral mucosa formations, using the "AFS-400" autofluorescence complex and glasses with a green light filter for identification. The patients of the control group (n=46) received the standard biopsy procedure under direct vision.

Results. The first incisional biopsies revealed cancer in 25 (54%) patients of the control group and in 36 (84%) patients of the main group. A histological verification of the diagnosis was necessary in 7 (16%) patients of the main group and required the second biopsy. In the control group, for the same purpose, 17 (37%) patients underwent the second biopsy and 4 (9%) patients required the third biopsy procedure. Exophytic-papillary forms of cancer were the most complex for histological verification. The primary biopsy of these cases was effective in 16 (37%) patients in the main group and in 8 (17%) patients in the control group (p = 0.036). In patients with initial stages of cancer (I-II), with the first incision biopsy, the histological verification of cancer was achieved in 16 (37%) cases in the main group and in 8 (17%) cases in the control group (p = 0.036).

Conclusion. The use of the "AFS-400" autofluorescent complex and glasses with a green light filter for incisional biopsy of oral mucosal formations allows histological verification of cancer with the first biopsy in 84% of cases, including in stages I - II – in 16 (37%) cases and in exophytic papillary forms – in 16 (37%) cases. The significant difference was registered for the similar indicators of the control group (p = 0.036).

Keywords: oral mucous membrane, incisional biopsy, histological verification, autofluorescent stomatoscopy.

Conflict of interest: nothing to disclose.

Citation
Orlov AE, Gabrielyan AG, Kaganov OI , Postnikov MA, Trunin DA, Denisova YuL. **Identification of the site for biopsy in oral mucosa cancer diagnostics.** *Science & Innovations in Medicine.* 2020;5(3):181-185 doi: 10.35693/2500-1388-2020-5-3-181-185

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Received: 20.04.2020
Revision Received: 12.05.2020
Accepted: 15.05.2020

Идентификация локализации участков для забора материала при выполнении биопсии в диагностике рака слизистой оболочки полости рта

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Аннотация

Цель – оптимизировать методику инцизионной биопсии с применением аутофлуоресцентной стоматоскопии при диагностике рака слизистой оболочки полости рта.

Материал и методы. Работа выполнена на базе ГБУЗ «Самарский областной клинический онкологический диспансер». В исследование вошли больные с установленным диагнозом «рак слизистой оболочки полости рта» различных локализаций. Пациенты были разделены на 2 группы. В основной группе (n=43) для диагностики рака применена оптимизированная методика

инцизионной биопсии образований слизистой полости рта с использованием в качестве идентификации аутофлуоресцентного комплекса «АФС-400» и очков с зеленым светофильтром. В контрольной группе (n=46) применялась стандартная методика под контролем глаза.

Результаты. После выполненных однократных инцизионных биопсий в контрольной группе рак выявлен у 25 (54%), а в основной группе – у 36 (84%) пациентов. В контрольной группе для получения гистологической верификации (ГВ) диагноза проводились дву- и трехкратные биопсии – 17 (37%) и 4 (9%) соответственно, в основной – только двукратно у 7 (16%) пациентов. Наиболее сложной группой пациентов были больные с экзофитно-папиллярными формами. В основной группе ГВ при первичной биопсии была получена у 16 (37%) больных, в контрольной у 8 (17%) больных (p=0,036). У пациентов с начальными стадиями (I-II) при однократной инцизионной биопсии ГВ рака достигнута в основной группе в 16 (37%) случаях, в контрольной в 8 (17%) случаях (p=0,036).

Заключение. Применение аутофлуоресцентного комплекса «АФС-400» и очков с зеленым светофильтром для инцизионной биопсии образований слизистой полости рта позволяет уже при первой биопсии в 84% случаев получить ГВ, с учетом наличия I-II стадий – в 16 (37%) случаях и экзофитно-папиллярной формы – в 16 (37%) случаях. Это значимо отличается от аналогичных показателей контрольной группы (p=0,036).

Ключевые слова: слизистая оболочка полости рта, инцизионная биопсия, гистологическая верификация, аутофлуоресцентная стоматоскопия.

Конфликт интересов: не заявлен.

Для цитирования:
Орлов А.Е., Габриелян А.Г., Каганов О.И., Постников М.А., Трунин Д.А., Денисова Ю.Л. **Идентификация локализации для забора материала при выполнении биопсии в диагностике рака слизистой оболочки полости рта.** *Наука и инновации в медицине.* 2020;5(3):181-185
doi: 10.35693/2500-1388-2020-5-3-181-185

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СОПР – слизистая оболочка полости рта; ИБ – инцизионная биопсия; АФС – аутофлуоресцентная стоматоскопия; ГВ – гистологическая верификация.

Рукопись получена: 20.04.2020
Рецензия получена: 12.05.2020
Решение о публикации принято: 15.05.2020

INTRODUCTION

Annually, more than 355 thousand new cases of malignant neoplasms of the oral mucous membrane (OMM) are registered worldwide [1]. In 2018, OMM cancer, according to oncological morbidity, ranks 18th in the Russian Federation. In 2018, 9,518 patients were diagnosed with OMM cancer in Russia, including 199 patients in the Samara region. In all patients with malignant neoplasms of the OMM registered in the Russian Federation, the diagnosis was verified histologically in 97.9% of the cases [2].

Knowledge of the morphology and type of tumor growth is necessary when selecting treatment for patients with OMM cancer. From the standpoint of evidence-based medicine, cancer can be diagnosed only with biopsy sampling, followed by highly reliable histological examination [3]. Biopsy sampling should be performed according to strict indications, as it can lead to a number of adverse events. Diagnostic errors in OMM cancer, when obtaining a histological conclusion, can be made when taking study materials.

Biopsy of OMM formations is an invasive method of taking tissue specimens for histological examination for differential and definitive diagnoses [4]. This procedure is performed mainly in specialized health care institutions and is included in the standard and algorithm for examining patients with suspected oncopathology. The establishment of a correct diagnosis, subsequent timely treatment, and disease prognosis depend on the histological conclusion obtained [5].

Indications for biopsy of OMM formations should be justified and based on both subjective and objective data. Biopsy of OMM formations is performed by both incisional biopsy (IB), with removal of a part of the pathological tissue, and excision, with total removal of the pathological tissue and subsequent histological examination for verification and diagnosis. Excisional biopsy is performed when the tumor is small or the pathology is not yet verified after repeated IBs.

Difficulties in the morphological verification of a malignant process are largely associated with the biopsy technique, incorrect section of the macro preparation, and interpretation by a morphologist of an atypical tumor growth [6, 7, 8]. A recent study revealed that epithelial tumors of the OMM are most often diagnosed (98.5%) and represented by keratinizing squamous cell carcinoma [9].

The autofluorescent stomatoscopy (AFS) method has proven itself well for diagnostics of early forms of OMM cancer and demonstrated a high sensitivity in a number of studies. The use of autofluorescent methods for diagnosing cancer is currently promising because of its availability, non-invasiveness, and simplicity. According to scientific publications, in AFS rays, the precancer and cancer foci have a distinctive glow in the form of a dark spot [10, 11, 12, 13]. Since 2017, at the Samara Regional Clinical Oncology Center, to verify the diagnosis of cancer, materials for histological examination were examined using an autofluorescent lamp (AFS-400, Polironik, Moscow), glasses with a green light filter, and otorhinolaryngological conchotomes.

AIM

This study aimed to optimize the technique of IB using AFS in the diagnosis of OMM cancer.

MATERIAL AND METHODS

In this study, 89 outpatient records of patients examined at the Samara Regional Clinical Oncology

Center in the period from 2017 to 2019 were analyzed; the patients had established diagnosis of OMM cancer of various localizations after IBs.

The inclusion criteria were patients initially referred to an oncologist for biopsy; exophytic papillary, ulcerative, and mixed forms of tumors; and verified OMM cancer.

The patients were distributed into two groups depending on the technique of IB and the histological verification (HV) of OMM cancer.

Patient groups were distributed by localization and histological type of the structure of the malignant process (**Tables 1, 2**). Indicators such as the biopsy rate, type of tumor growth, and disease stage were assessed. IB of OMM formations was performed to the main group (n = 43) under AFS until cancer was established histologically. Patients of the control group (n = 46) underwent single, second, and third IB of the OMM formations under direct vision until cancer was established histologically.

The patients were 27–87 years old. The male-to-female ratio was 3:1 in the main group and 3:1 in the control group ($p = 0.737$). In both groups, IB was performed under local application, infiltration, and/or conduction anesthesia.

Localization	Group			
	Control n = 46		Main n = 43	
	n	%	n	%
Tongue	29	**63**	27	**62**
Alveolar part of the upper jaw	1	**2**	-	**-**
Alveolar part of the lower jaw	3	**7**	3	**7**
Oral cavity floor	8	**17**	7	**16**
Hard palate	3	**7**	2	**5**
Soft palate	1	**2**	2	**5**
Cheek	1	**2**	2	**5**
Total	46	**100**	43	**100**

Критерий Пирсона 2,221; p=0,988 [Pearson's criterion 2,221; p=0.988]

Таблица 1. *Распределение больных по группам и локализации опухоли*
Table 1. *The distribution of the patients by group and location of the tumor*

Biopsy results	Group			
	Control n = 46		Main n = 43	
	n	%	n	%
Keratinizing squamous cell carcinoma	36	**78**	33	**77**
Non-keratinizing squamous cell carcinoma	9	**20**	9	**21**
Adenocystic cancer	0	**0**	1	**2**
Adenocarcinoma	1	**2**	0	
Total	46	**100**	43	**100**

Критерий Пирсона 2,221; p=0,988 [Pearson's criterion 2,221; p=0.988]

Таблица 2. *Распределение больных в группах по полученным гистологическим результатам злокачественного процесса*
Table 2. *Distribution of patients in groups by the resulting histological data of the malignant process*

In the control group, IB with tissue removal from the pathological focus for histological examination was performed using otorhinolaryngological conchotomes at random under direct vision from the surface and along the edge of the pathological formations (**Figure 1**). In the main group, AFS was performed using an AFS-400 device and glasses with a green light filter. When using the lamp, precancer and cancer signs were assessed on a light scale, where a dark glow (dark spot effect) indicated the precancer and cancer foci.

In the main group, biopsy was performed using otorhinolaryngological conchotomes under AFS control, and tissue samples were obtained from sites of pathological glow (dark spot) (**Figure 2**).

After single IB in the control group, the diagnosis of cancer was confirmed in 25 (54%) patients, and after second and third incisions, the diagnosis was confirmed in 17 (37%) and 4 (9%) patients, respectively. In the main group, the AFS-400 lamp was used to identify more suspicious areas of the malignant process; after a single IB, the cancer was verified in 36 (84%) patients, and after repeated IB, it was verified in 7 (16%) patients (**Figure 3**).

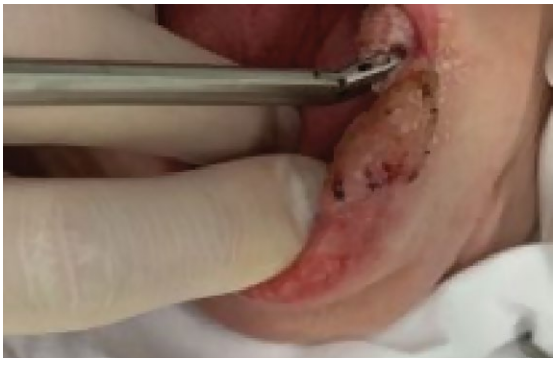

Рисунок 1. *Инцизионная биопсия опухоли слизистой щеки под контролем глаза с использованием оториноларингологического конхотома.*
Figure 1. *Incisional biopsy of cheek mucosa tumor under eye-control using an otorhinolaryngologic conchotome.*

Рисунок 2. *Инцизионная биопсия опухоли слизистой ретромолярного пространства с использованием лампы «АФС-400», очков с зеленым светофильтром и оториноларингологических конхотомов.*
Figure 2. *Incision biopsy of retromolar mucosa tumor using "APS-400" lamp, glasses with green light filter and otorhinolaryngological conchotomes.*

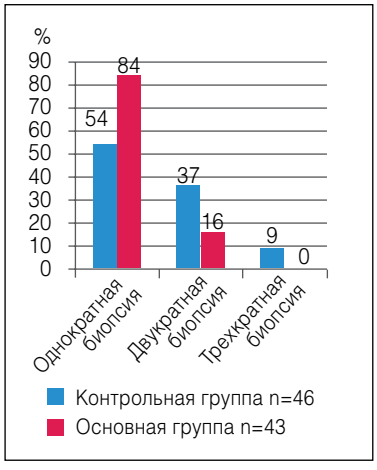

Рисунок 3. *Кратность биопсий и верификация диагноза.*
Figure 3. *Number of biopsies and diagnosis.*

Рисунок 4. *Кратность биопсий и верификация диагноза при смешанном типе опухолевого роста.*
Figure 4. *Number of biopsies and diagnosis verification for mixed tumor growth.*

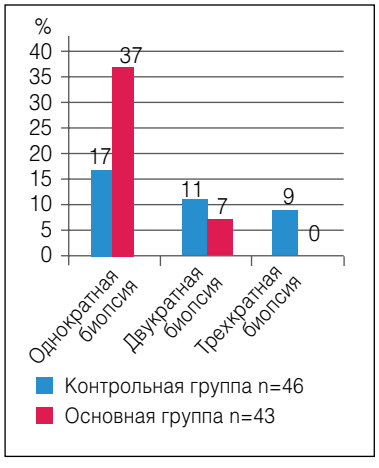

Рисунок 5. *Кратность биопсий и верификация диагноза при экзофитно-папиллярной форме опухолевого роста.*
Figure 5. *Number of biopsies and diagnosis verification in exophyte-papillar form of tumor growth.*

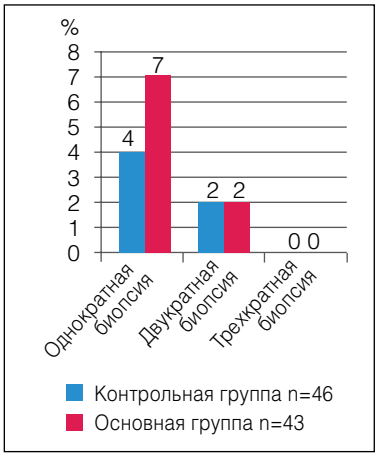

Рисунок 6. *Кратность биопсий и верификация диагноза при экзофитно-язвенной форме опухолевого роста.*
Figure 6. *Number of biopsies and diagnosis verification in the exophite-lumen form of tumor growth.*

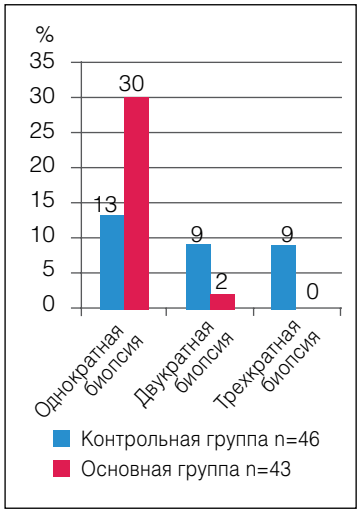

Рисунок 7. *Кратность биопсий и верификация диагноза при I стадии.*
Figure 7. *Number of biopsies and diagnosis verification in stage I.*

Рисунок 8. *Кратность биопсий и верификация диагноза при II стадии.*
Figure 8. *Number of biopsies and diagnosis verification in stage II.*

After single IB, HV of the tumor was made mainly in cases with a mixed type of tumor growth, i.e., in 17 (40%) and 15 (33%) cases in the main and control groups, respectively ($p = 0.497$) (**Figure 4**).

HV of exophytic-papillary tumor growth, which was the most difficult to verify, was obtained in 16 (37%) patients in the main group during primary biopsy and in 8 (17%) patients in the control group ($p = 0.036$) (**Figure 5**). Exophytic and ulcerative forms were diagnosed after a single IB in 3 (7%) and 2 (4%) cases in the main group, respectively ($p = 0.591$) (**Figure 6**).

The number of biopsies was also assessed depending on the stage of disease prevalence. After a single IB, HV of stage I–II cancer was achieved in 16 (37%) patients in the main group and in 8 (17%) patients in the control group ($p = 0.036$) (**Figures 7, 8**). After a single biopsy, the HV in patients with stages III–IV was diagnosed in 20 (47%) patients in the main group and in 17 (37%) patients in the control group ($p = 0.361$) (**Figures 9, 10**).

DISCUSSION

Recent research has revealed that the mucous membrane of the tongue is most often affected by cancer, and the percentage of advanced stages of OMM cancer is quite high. In our cases, tongue lesion was noted in 29 (63%) patients in the control group and in 27 (62%) in the main group ($p = 0.981$), and advanced stages were registered in 29 (63%) and 24 (56%) cases ($p = 0.488$), respectively [5]. A high percentage of malignant neoplasms of the OMM was represented by epithelial keratinizing squamous cell carcinoma in 36 (78%) cases in the control group and in 33 (77%) cases ($p = 0.864$) in the main group, which does not contradict published data [2, 4, 10].

Applying an optimized technique enabled HV of OMM cancer with a mixed type of growth in both groups without marked differences, with the exception of exophytic-papillary forms, which were found in 16 (37%) and 8 (17%) patients in the main and control groups, respectively ($p = 0.036$). HV of malignant tumors with exophytic-papillary forms and an initial stage of OMM cancer in the control group was difficult because the true pathological focus was not identified and elements of inflammation are present, which was demonstrated

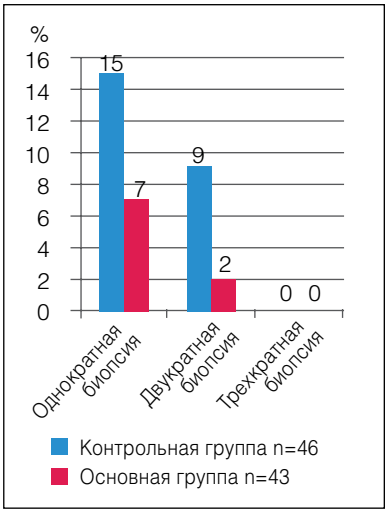

Рисунок 9. *Кратность биопсий и верификация диагноза при III стадии.*
Figure 9. *Number of biopsies and diagnosis verification in stage III.*

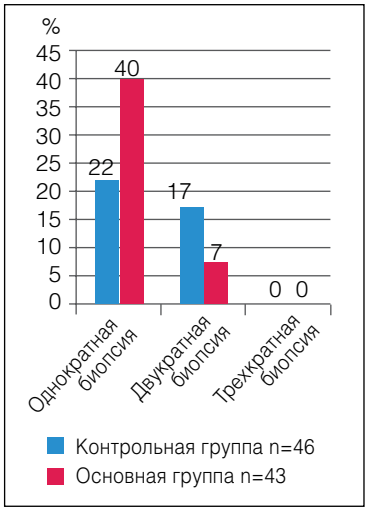

Рисунок 10. *Кратность биопсий и верификация диагноза при IV стадии.*
Figure 10. *Number of biopsies and diagnosis verification in stage IV.*

контрольная группа	control group
основная группа	main group
однократная биопсия	single biopsy procedure
двухкратная биопсия	second biopsy procedure
трехкратная биопсия	third biopsy procedure

by the results obtained in the main group [10]. Moreover, after a single IB, the rate of verified cancer in initial stages in the main group was significantly higher than that in the control group, at 16 (37%) and 8 (17%), respectively (p = 0.036). To verify the diagnosis of cancer in initial stages, a third biopsy was required [10].

CONCLUSIONS

The autofluorescent complex AFS-400 and glasses with a green light filter for IB of OMM formations enable identification of suspicious sites for tissue sampling for histological examination and to obtain HV at the first biopsy in 84% of cases, taking into account the presence of stage I–II cancer in 16 (37%) patients and exophytic-papillary forms in 16 (37%) patients. This differs significantly from similar indicators in the control group (p = 0.036) and reduces the number of repeated IB.

Conflict of interest. *The authors declare no conflict of interest.*

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