РАЗНОЕ

DOI: 10.37903/vsgma.2025.1.40 EDN: IYXVIR

ВПЕЧАТЛЕНИЯ О СТАЖИРОВКЕ РОССИЙСКОГО НЕЙРОХИРУРГА В ВЕДУЩЕЙ АМЕРИКАНСКОЙ КЛИНИКЕ (UCSF) США ПО ПРОГРАММЕ МЕЖДУНАРОДНОГО ОБМЕНА FULBRIGHT

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Резюме

Цель. Описание стажировки нейрохирурга из России в американской нейрохирургической клинике в течение 5 месяцев.

Методика. Сбор, систематизация и анализ данных собственных наблюдений во время пятимесячной стажировки в ведущей нейрохирургической клинике США.

Результаты. В результате работы выявлены особенности подготовки нейрохирургов в резидентуре и практической работы врачей в ведущей нейрохирургической клинике США. Для американской академической нейрохирургии, как и для российской на базе крупных центров, характера субспециализация. Подробно описаны новые технологии, используемые для лечения пациентов с различной нейрохирургической патологией, включая внутримозговые опухоли (глиомы).

Заключение. Многомесячная стажировка в академическом американском нейрохирургическом отделении позволяет выявить сходства и различия в подготовке врачей при обучении в резидентуре, а также сравнить подходы и уточнить новые технологии в лечении сложной нейрохирургической патологии, включая внутримозговые опухоли (глиомы).

Ключевые слова: ишемия головного мозга, фармакологическая нейропротекция, фармакологические мишени, эндогенные механизмы адаптации

EXPERIENCE OF THE INTERNSHIP OF A RUSSIAN NEUROSURGEON AT A LEADING AMERICAN CLINIC (UCSF) USA UNDER THE FULBRIGHT INTERNATIONAL EXCHANGE PROGRAM

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Abstract

Objective. Description of the internship of a neurosurgeon from Russia at an American neurosurgical clinic for 5 months.

Methods. Collection, systematization and analysis of personal observation data during a five-month internship at a leading neurosurgical clinic in the USA.

Results. As a result of the work, the peculiarities of neurosurgeons training in residency and the practical work of doctors in the leading neurosurgical clinic in the USA were revealed. American academic neurosurgery, like Russian neurosurgery based on large centers, is characterized by subspecialization. New technologies used to treat patients with various neurosurgical pathologies, including intracerebral tumors (gliomas), are described in detail.

Conclusion. A multi-month internship at the academic American Neurosurgical Department allows us to identify similarities and differences in the training of doctors during residency training, as well as

compare approaches and refine new technologies in the treatment of complex neurosurgical pathology, including intracerebral tumors (gliomas).

Keywords: brain ischemia, pharmacological neuroprotection, pharmacological targets, endogenous adaptation mechanisms

Program Fulbright

The Fulbright Program was established in 1947 for international exchange between the United States and other countries of the world in the cultural, scientific and humanitarian fields by American Senator James William Fulbright (1905-1995). I first learned about this program on the website of my Alma mater, Smolensk State Medical University. Every year, 20 people from our country come to the United States to complete their projects as part of a three-stage competition (presentation of a scientific project, an interview in English with the competition committee, and final approval of the project). In 2022 I was lucky enough to become the winner of the competition and, among the other 19 researchers, went on a 5-month internship in the USA. I chose the leading neurosurgical clinic in the USA, the University of California at San Francisco (UCSF), as the venue. The topic of my research project concerned the surgical treatment of brain gliomas. Gliomas are infiltratively growing primary tumors of the central nervous system. The most aggressive of them is glioblastoma, a tumor with an extremely low life expectancy of patients [10]. The main problem of surgical treatment in these patients is the lack of clear boundaries between the tumor and intact brain tissue, which makes it difficult to remove it. My research and internship topic concerned the technique of intraoperative glioma boundary determination for their more complete resection using spectroscopy [8].

Neurosurgery Department of the University of California

The Department of Neurosurgery at the University of California, UCSF, was founded in 1905 by an outstanding neurosurgeon, Professor Howard Naffziger (the author of the famous and named after him access to the posterior cranial fossa) and was the first department of neurosurgery on the West coast of the United States. In the following years, prominent, world-renowned neurosurgeons Boldrey, Adams, Wilson and Professor M. Berger worked there. The department is a forge of neurosurgical personnel for the whole country, and its graduates head neurosurgical departments in academic hospitals in various US cities (professors McDermott, Lawton and others). In general, the prestige of the department is determined by the place occupied by the neurosurgery residency within the framework of the annual national report. UCSF ranks 1st among 117 neurosurgical residency programs in the United States [1].

About my internship supervisor

My supervisor was an outstanding American neurosurgeon and scientist, Professor M. Berger (Fig. 1).

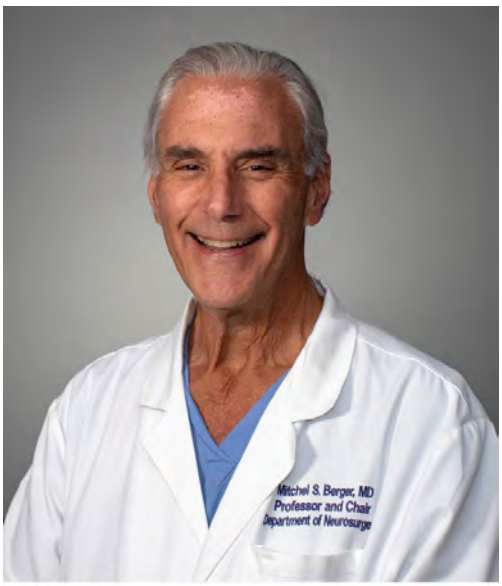

Fig. 1. Professor M. Berger, head of the department of neurosurgery at UCSF university of California (1997-2020), head of the center for the study of brain tumors

His main areas of work are surgical treatment of brain gliomas, fundamental neuro-oncology and brain mapping [3]. A student of the outstanding neurosurgeon J. Ojemann, Professor M. Berger continued his academic traditions and created a unique department where neurosurgeons and scientists work in tandem. The professor was the head of the department from 1997 to 2020 and completely rebuilt its work, where each neurosurgeon specializes strictly in his or her field (subspecialization in neurosurgery), and also gathered a stellar team of doctors and researchers around him. Currently, Professor M. Berger directs the Center for the Study of Brain Tumors, which consists of more than 15 scientific laboratories. This center was established in 1970 and for more than 50 years of its work has won the largest American scientific grants, having the highest rating in the country.

About the traditions of American academic neurosurgery

Academic neurosurgery in the USA has been established in large university centers that compete seriously with each other. American neurosurgery has a serious specialization in which it is impossible for everyone to perform all types of operations. An employee of a department at a large university usually specializes in a certain field – brain tumors (neuro-oncology), spinal pathology, vascular diseases, epilepsy, functional neurosurgery, cranial base surgery, etc., which is generally similar to such traditions at the Center for Neurosurgery. Academician N.N. Burdenko. However, scientific research, including work in laboratories, grants, conference presentations, publications in leading foreign journals, and participation in clinical research, plays an equally important role in the schedule of every academic neurosurgeon. All this together creates a high reputation of the clinic in the professional community.

About neurosurgery residency training in the USA

The duration of residency in American neurosurgery is 7 years (for comparison, most specialties are 5 years), after which the candidate passes a special certification exam (Board certificate). During their studies, 1-year residents have rotations in related fields of neurosurgery (intensive care, plastic surgery, neurology, general surgery), after which they gradually master basic neurosurgical interventions in several university clinics (2-4 years, 6 years). In year 5, residents are free from clinical work for a whole year and spend this time on scientific research, naturally, starting with simpler ones and continuing with more complex ones. During 7 years of training, a report on operations performed by a resident is constantly being filled out in the personal account of the Council for Accreditation of Postgraduate Medical Education (ACGME), which allows us to calculate the achievement of the minimum amount of mastered neurosurgical interventions during training in order to obtain a certificate in the future. An important year is the last, 7th year of residency, where the chief resident oversees the work of junior residents, draws up a schedule of resident assistants to the clinic's doctors, a duty schedule, and solves urgent issues in the clinic.

The total number of clinic residents is 21, with 3 students for each year of the program. After completing the residency, the doctor can additionally complete a 1 or 2-year fellowship program in a narrow area of interest, such as epilepsy, functional neurosurgery, cranial base surgery, and endovascular interventions. An important point in the training of American neurosurgeons is the Grand Round, a weekly meeting of residents with leading clinic staff and invited lecturers, where the most interesting clinical observations are discussed and lectures on all areas of the specialty are listened to. On this day (usually Thursday), residents are released from operating rooms.

The working day of the junior resident (1-3 years old) begins at 4 a.m. with a visit to all patients of the clinic. All appointments must be made before the arrival of senior doctors at 7 a.m. The working day of American neurosurgeons begins very early. Every year, on June 1, the Resident research day is held, where, in the presence of senior doctors, the head of the department and guests from other universities, residents report the results of their research for the previous year.

About new technologies and clinical research in neuro-oncology

An important trend in scientific research in neuro-oncology is the intraoperative visualization of the boundaries of brain tumors. For this purpose, various authors use metabolic navigation (tumor staining), ultrasound, CT and MRI technologies. UCSF Clinic is a leader in the use of intraoperative Raman histology (SRH) to quickly determine the presence of tumor cells in a biopsy [8]. The essence of this system is as follows. When removing a glioma, a neurosurgeon takes several biopsies from its bed in various areas. Each of them is placed on a slide and lowered into the machine. A laser is used to scan a tumor sample, and after 1 minute a picture of the cellular structure of the sample appears on the screen (without using traditional staining with hematoxylin and eosin). The program uses artificial intelligence to immediately determine the index from 0 to 100, which is displayed on the system screen in the lower-left corner. Conventionally, the value of this index of up to 40 units is brain tissue, and more than 40 units is a tumor (Fig. 2). Thus, the neurosurgeon gets the opportunity for a quick intraoperative biopsy without the participation of a pathologist, which makes it possible to perform supratotal resection of glioma (if possible, its localization relative to functional areas). This makes it possible to increase the survival time

of patients. Based on this work, the RANO group in 2023, when analyzing operations of patients with 1001 glioblastoma, revised the classification of tumor resections in the direction of its tightening [9].

Fig. 2. Intraoperative analyzer for urgent biopsy using SRH technology (Invenio, university of California, department of neurosurgery)

All patients with gliomas after surgery at the University of California undergo genome-wide sequencing for 500 genes on the unique UCSF 500 gene panel. Based on the results of this study, a decision is made to include the patient in clinical trials testing new targeted drugs if some of their mutations are detected in this panel. The decision to conduct such a study is made by a neuro-oncological council, which includes the following specialists: a neurosurgeon, a radiologist, a pathologist, and a chemotherapist (neuro-oncologist). The Council meets weekly on Thursdays and discusses treatment tactics for all operated-on patients with brain gliomas. The analysis of each such case begins with a description by the radiologist for colleagues of the MRI before and after the operation.

The manual and technical features of operations in the United States and Russian large centers are very similar. In the operating room, the operating neurosurgeon independently places and positions the patient, fixes his or her head in a Mayfield brace, processes and covers the surgical field. All craniotomies in the USA are performed with the mandatory use of neural navigation. The neurosurgeon is assisted at all stages of the operation by a resident assistant and a medical technician. A large number of new clinical trials of both intraoperative technologies and new drugs are noteworthy. One of the important studies is the study of intraoperative brachytherapy with cesium for the treatment of recurrent brain metastases and glioblastomas. After removing the tumor, the neurosurgeon leaves a caesium wire in its bed and sutures the wounds [2].

An important direction is the emergence of a new class of targeted drugs for the treatment of gliomas with IDH 1 mutation. This mutation is quite common in gliomas with a low degree of malignancy relative to malignant gliomas. In 2023, the FDA approved new drugs for the treatment of certain types of gliomas based on the multicenter INDIGO study conducted by UCSF specialists. These substances (the drug vosaradenib and its analogues) block (inhibit) the IDH 1 mutation, which makes it possible to reduce gliomas in volume [6]. In general, more than 20 clinical trials of new drugs and technologies for neuro-oncological patients are currently being conducted and opened at Klinke. An interesting area is ultrasound exposure to break through the blood-brain barrier, followed by intravenous chemotherapy. For this purpose, a special ultrasound sensor is implanted in the bed of the removed tumor, which is activated after surgery by an external device. After ultrasound exposure, intravenous administration of chemotherapy drugs is performed. This allows them to more actively penetrate into the tumor area and its bed after surgery.

Interesting studies of immunotherapy for patients with glioblastomas are being conducted. An important area is CED (catheter enhance delivery), the delivery of chemotherapy drugs to or near the bed of the removed tumor using an implanted microcatheter. While this area is actively developing, various options for local administration of chemotherapy drugs and their combinations are being used [4].

The Radiotherapy department is conducting a study on the effects of boost. The hypoxia zone is up to 90 Gy for patients with glioblastomas, while the total dose for the entire tumor volume remains the standard 60 Gy, which is safe for the patient and does not increase the frequency of radiation reactions. The hypoxia zone is detected using PET examination with a special substance FMISO, which is tropic to hypoxia zones, followed by a combination of PET and MRI images (fusion) and an individual calculation of the radiation treatment regimen. Why is such attention being paid to glioblastoma hypoxia zones? It has been proven that they contain the most aggressive tumor cells, which need a hypoxic environment to divide [7].

A promising area of new clinical research is the targeted delivery of radioactive isotopes (Y90 – yttrium) to the tumor using angiography and endovascular intervention. Point catheterization of tumor vessels in X-ray surgery conditions allows radioactive isotopes to be introduced into its stroma. This is one of the cutting-edge research areas currently (FRONTIER). So far, this technology has been used in large tumors outside of functionally significant areas of the brain.

About brain mapping and features of neurosurgical operations

The Neurosurgery Clinic at the University of California is a leader in brain mapping – that is, the intraoperative determination of cortical functional areas (primarily motor and speech) and brain pathways (primarily the pyramidal and arcuate tracts). This occurs with the help of intraoperative electrical stimulation, which can be mono or bipolar [3, 5]. Accordingly, the selection of stimulation parameters, current frequency and strength, and mapping techniques is very important. The combination of mono, bipolar stimulation, transcranial and transcortical methods of stimulation of the motor cortex and the pyramidal tract is the essence of the technique of "quadruple" mapping of the motor areas of the brain. This increases the safety of neurosurgical interventions.

During operations on the speech areas of the brain (cortical speech centers and the arcuate tract), brain mapping is performed using the technique of conscious craniotomy. There is continuous contact with patients in the operating room during tumor removal with parallel stimulation of the speech areas of the brain. The same methodology is used at the Burdenko Neurosurgery Center and other major neurosurgical centers in our country.

About some new technologies in clinical research in other sections of academic neurosurgery in the USA

Lyophilized cadaveric nerves are actively used in peripheral nerve surgery. The manufacturer (Oxygen) is actively implementing this technology in clinics in the USA. This avoids taking the donor nerve from the patient as an insertion in case of a large defect in the operated nerve and, consequently, additional trauma and incision. Cadaveric nerves can be of various lengths and diameters. After suturing the cadaveric nerve with the ends of the damaged nerve of the patient, axon regeneration and growth in this insert occurs at a rate of 1 mm per day.

In vascular neurosurgery, the direction of developing new stents in animal experiments is developing in collaboration with manufacturers of these consumables. A simulation of strokes in a vivarium is performed using the endovasal technique. Minimally invasive endoscopic technologies are widely used to remove hypertensive brain hematomas. In the surgery of arterial aneurysms of the brain, approximately half of the operations are performed microsurgically, the rest is endovasally. A similar distribution occurs in the NMITS of Neurosurgery named after him. Academician N.N. Burdenko in our country. However, all neurosurgeons of the department specializing in the treatment of strokes in the USA have both open surgeries and endovasal equipment. In our country, a number of clinics have similarities with this approach (the leading schools of neurosurgery in St. Petersburg at the Russian National Research Institute named after Prof. A.L. Polenov at the Almazov Center and the Kirov Military Medical Academy). At the same time, in some neurosurgical centers, microsurgical and endovasal operations are performed by various doctors (NMIC of Neurosurgery named after Academician N.N. Burdenko, Federal Center of Neurosurgery in Novosibirsk).

In functional neurosurgery, adaptive deep brain stimulation (DBS) systems are being studied in severe extrapyramidal diseases and pharmacoresistant feedback epilepsy. This allows you to conduct stimulation sessions only when necessary, for example, with the development of an epileptic seizure. The rest of the time, the system does not work. A large number of microvascular decompression (MVD) operations are performed for neurovascular conflicts, for example, trigeminal neuralgia, and less often, hemifacial spasm. Elderly patients sometimes undergo minimally invasive puncture surgery for radiofrequency destruction of the Gasser node.

An important part of functional neurosurgery at the University of California is the surgical treatment of pain syndromes, compression neuropathies, and spasticity. For this purpose, various neurostimulators are used (occipital nerves for some forms of severe headache, epidural for back pain, peripheral nerve stimulators). Baclofen pumps are also widely used in severe spastic syndromes. Compression neuropathies include a large number of patients with carpal and cubital syndromes, and compression of the nerves of the lower extremities.

In the field of traumatic brain injury, the TRACK TBI consortium, led by Professor G. Manley, is actively working on the use of biomarkers for the diagnosis and prediction of outcomes of mild and severe TBI. This makes it possible to quickly, in the absence of neuroimaging data, and sometimes by supplementing them, with high accuracy, combined with clinical data and medical history, to suspect the presence of traumatic brain injury and predict its outcomes. This scientific consortium includes more than 20 leading US universities dealing with traumatic brain injury, the head of which is UCSF University of California. A consortium of universities for spinal cord injury research, TRACK SCI, has been created separately. This allows conducting large-scale clinical trials in the field of traumatic brain injury on thousands of patients with the formation of common databases, including CT scans, MRI scans, blood serum, clinic data and disease outcomes [11]. In our country, there is no consortium approach in carrying out scientific research in neurosurgery.

In addition to resective surgery, vagus nerve stimulation (VNS) and invasive EEG diagnostics with implantation of multiple surface grids and deep electrodes (stereo EEG) are actively used in the treatment of epilepsy to search for epileptogenic foci located in various parts of the brain.

A separate area is transnasal endoscopic neurosurgery of tumors of the base of the skull and pituitary adenomas. Its principles are similar to those in our country. These operations are performed by individual neurosurgeons of the clinic together with ENT surgeons.

Spinal neurosurgery occupies a large volume of activity of the university of California department. The clinic employs about 5 spinal neurosurgeons who perform 5-6 operations daily. A feature of this area in the USA is the wider use of spinal stabilization systems (screw structures, plates, cages), including at several levels.

About the organization of clinical research at the academic neurosurgical clinic of the USA

Performing new clinical trials for the clinic is a highly sought-after and prestigious area that attracts new patients not only from the state of California, but also far beyond its borders. The research team includes 6 neuro-oncologists and a staff of assistants who help maintain medical records, call patients for their timely visit to the clinic according to the research protocol. Each project has a responsible researcher and a firm or grant that funds the project. All patients are carefully catamnesized, their MRI data is collected at various stages of treatment for subsequent analysis, and the dates of disease recurrence are specified. Multicenter studies are often conducted with other leading clinics in the USA and Europe. Their value is significantly higher due to the greater accumulation of patients treated according to a single protocol. All the results of such studies are published in high-impact journals on neurosurgery, neuro-oncology and reported at thematic conferences.

About the concept of a neurosurgeon researcher

Professor M. Berger is the author of the unique concept that every neurosurgeon is a researcher and should lead his fundamental laboratory to study applied issues of his specialization – the molecular mechanism of development and treatment of gliomas, aneurysms, neurodegenerative diseases, epilepsy. At the same time, an American neurosurgeon working in an academic institution must allocate at least 1 day a week for research work in the work schedule. The concept of a neurosurgeon researcher is also expressed in the very careful and serious attitude of American colleagues towards their scientific publications, citations of works, and presentations at scientific conferences.

About constant reading of scientific journals

All american resident neurosurgeons and staff doctors constantly read monthly periodicals of leading neurosurgical journals such as Journal of Neurosurgery, Neurooncology, Spine and others. Constant work with such journals both in residency and throughout the professional life of a neurosurgeon allows them to be at the forefront of all new knowledge in the specialty and to be a widely educated doctor in their specialty.

About the virtual anatomy of the central nervous system

The university has a neuroanatomical laboratory that conducts research and creates a collection of drugs in virtual execution by scanning and photographing brain preparations, vascular network and base of the skull using high-resolution scanners and special computer programs. At the same time, the virtual neuroanatomical collection is freely available on the university's website. The technologies of

preservation of drugs without the use of formalin are used according to the technique of the Egyptian neuroanatomist Enlady.

About memorial lectures
The department has a wonderful tradition of giving annual memorial lectures. Every year, a memorial lecture is held in honor of doctors who worked in the department of neurosurgery at UCSF hospital in the past, where the best neurosurgeons of the department and the world speak. In memory of this event, a plaque with the lecturer's name is hung after each performance.

About the department's annual traditional scientific conference
Another interesting tradition of the department is the annual neurosurgical reporting conference, where both department staff and invited guests make presentations. In 2024, it was held in a small village of Napa, a wine valley in California. The program covers the most interesting issues of neurosurgery: neuro-oncology, vascular neurosurgery, vertebrology, functional and pediatric neurosurgery. At the end of the sections, the moderator makes a short message – the 3 most important breakthroughs in each of the listed areas over the past year that every neurosurgeon should know.

Conclusion

The training of a neurosurgeon and the work of our colleagues in the USA and Russia have similarities and differences. Important differences are the longer duration of the residency program (7 years), more extensive theoretical training, and the mandatory implementation of scientific and clinical research by practicing physicians. The fastest growing and most complex field of modern neurosurgery in the USA is neuro–oncology. It is necessary to strive to introduce new promising technologies for both drug therapy of brain tumors based on molecular profiling and local treatment methods (brachytherapy, catheter drug delivery, endovasal treatment methods, intraoperative rapid determination of tumor boundaries).

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Conflict of interest: the authors declare that there is no conflict of interest.

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Конфликт интересов: авторы заявляют об отсутствии конфликта интересов

Поступила 20.02.2025

Принята к печати 20.03.2025