

To the Chairman of the Scientific Jury,  
appointed by order of  
The executive director of Ajibadem  
City Clinic UMBAL Tokuda Sofia,  
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## **REVIEW**

By Prof. Dr. Anton Yordanov Jorov, MD  
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Subject: Dissertation work for the award of the educational and scientific degree "Doctor of Philosophy" in professional direction 7.1 Medicine, doctoral program Neurosurgery  
Topic: "Minimally invasive extended lateral orbital approach for intraorbital and intracranial pathology"

Author: Lili Naskova Laleva, PhD student on independent training at the Neurosurgical Department

Research supervisor: Assoc. Dr. Vladimir Stefanov Nakov, MD

### I. Biographical data and career development of the dissertation student

Dr. Laleva was born in Sofia on July 29, 1985. She graduated from Medical University - Sofia in 2010 as a Master of Medicine. Since May 2011 she works at Neurosurgery Clinic in Acibadem City Clinic UMBAL Tokuda. In 2016 has a master's degree in "Health Management", and in 2017 she acquired a specialty in "Neurosurgery". Dr. Laleva takes part in numerous educational courses, conferences, seminars, clinical internships and international scientific projects. There are also several academic awards and scholarships.

### II. Relevance of the topic of the dissertation

According to modern trends for minimal invasiveness and standards for good surgical results, the operative approach used should be "large enough and at the same time as small as possible". Choosing the most appropriate approach for the individual case is a balance between the above mentioned, the specific pathology, and the judgment and experience of the surgeon. The orbit is a structure located between the facial and cranial lobes of the skull. It opens up new possibilities for anatomical corridors to intracranial areas and allows approach to neurosurgical pathology. It is expected to overcome some of the complications and achieve a better postoperative cosmetic result. Lateral orbital approach with a transpalpebral incision is routinely used in ophthalmology and maxillofacial surgery with proven good results. Multiple reports indicate that it allows approach to anterior, middle, and even posterior cranial fossa lesions. In the recent decades, the concept of "keyhole" type craniotomy has been developed, together with the introduction of endoscopic technique for additional visualization, but there is a lack of clear definition of approach limits and systematization of possible operative corridors. All this makes the chosen topic "Minimally invasive extended lateral orbital approach for intraorbital and intracranial pathology" by Dr. Laleva theoretically and clinically relevant and up to date.

### III. Quantity and structure of the presented dissertation work

The dissertation is written on 158 pages and is illustrated with 32 figures (which include 8 author's illustrations), 6 tables and 10 diagrams. The literature review is on 249 titles, of which 11 Bulgarian authors and 238 foreign ones. Through it, the unsolved problems brought out by the dissertation are logically as follows:

- There are few anatomic studies in the literature describing lateral orbital approach for intracranial pathology. There is insufficient data for clear and easily recognizable anatomical landmarks.
- There are no clear criteria for the indications and contraindications for the application of approach.
- Clinical trials are few, with a small number of patients and a short follow-up period. There are no publications on the subject in the Bulgarian neurosurgical literature.
- The specific details of its technical details (techniques and instrumentation, endoscopic technique, neuronavigation) are not described.
- There is a lack of comparison of the advantages and disadvantages of lateral orbitotomy compared to other approaches in clinical settings, as well as formed criteria for the application of this approach in practice.

Based on this, Dr. Laleva formulated the goal: "to study and describe the anatomical and clinical application of extended lateral orbital approach as a minimally invasive anterolateral approach in neurosurgical practice during operative interventions for tumor and vascular intracranial pathology". For the achievement of this aim are formulated the following tasks:

1. Anatomic description of extended lateral orbital approach with definition of anatomical landmarks, approach -specific details, and possible intracranial surgical corridors.
2. Clinical study of the application of the extended lateral orbitotomy as a surgical approach in intracranial pathology with the formulation of indications and limitations for its application.
3. Evaluation of the results of the application of approach according to the outcome of the treatment of intracranial tumor and vascular pathology.
4. Evaluation of the approach application according to its minimal invasiveness, adequacy, technical difficulty, clinical and cosmetic result. Comparison of results with control groups.
5. Tracking approach -associated surgical complications and deficiencies.
6. Comparison of the results with control groups of patients with similar pathology who underwent surgical treatment in the clinic during the same period, but with another anterolateral approach.
7. Analysis of details of the technical implementation of the approach and their relation to the clinical outcome.

#### IV. Materials and methods

The present study consists of two main stages: a descriptive anatomical study and a prospective clinical study.

The anatomical part was performed on three fixed cadaver heads through six approaches at the Neurosurgical Anatomy Laboratory of the Medical University of Barcelona, Spain. Initially, the imaging studies were performed, which were transferred to the laboratory workstation and the markers were co-registered to the neuronavigation. Dissections begin with a standard transpalpebral skin incision in the crease of the upper eyelid. Dissections were performed microscopically and endoscopically. The lateral orbital wall, orbital roof, and sphenoid crest were removed, allowing exposure of the periorbita, temporal, and frontal dura. The main anatomical landmarks are presented and four extradural endoscopic routes after extended lateral orbitotomy are classified: anteromedial, posteromedial, posterior, and inferior. Each

one of them targets a different anatomical area: optic nerve, lateral wall of cavernous sinus and posterior trigeminal ganglion, petrous apex, pterygopalatine and infratemporal fossa.

The clinical study was conducted in the period December 2016-October 2020 at the Neurosurgical Department of Acibadem CityClinic UMBAL Tokuda on 160 patients, who were surgically treated with anterolateral approach. Of these, by means of extended lateral orbital approach by microscopic and endoscopic-assisted technique were operated 42 patients, and the remaining 116 were a control group.

For reliable statistical analysis, the group of patients operated on with extended lateral orbital approach was divided into two main subgroups according to the pathology: patients treated for a ruptured aneurysm and patients operated for meningioma of the anterior and middle cranial fossa. These subgroups were compared with the control group of patients operated on in the clinic during the same period, on the occasion of the same pathology, but with other approaches.

In 19 patients with vascular pathology, criteria for operative treatment with extended lateral orbitotomy included pathology of the internal carotid, anterior, and middle cerebral arteries. During the same time period, the clinic operated on 65 patients for ruptured anterior circulation aneurysms through other anterolateral approaches.

In 15 patients with tumor pathology, criteria for operative treatment with extended lateral orbitotomy were: extra or intraaxial pathology of the front and middle cranial fossa (meningioma of the sphenoid wing, sphenoorbital meningioma, meningioma of the anterior sphenoid process, meningioma of the tuberculum sellae). During the same period, 53 patients were operated on for meningiomas with the same location through other anterolateral approaches,

In each patient, a computed tomography or nuclear magnetic resonance-based 3D reconstruction was performed preoperatively, using the OsiriX software. In the course of the clinical study, the following parameters were monitored: adequacy of intraoperative exposure to achieve the goals of the operative intervention, duration of the operative intervention, intraoperative problems, duration of the operative intervention, postoperative clinical course and postoperative hospital stay, cosmetic result and postoperative complications were compared with control groups. Patients were followed up clinically and with imaging studies for a period of six months to three years with follow-up examinations and imaging studies. The statistical analysis of the data was carried out using the Microsoft Office Excel software package. The cosmetic aspect of approach was evaluated at control clinical examinations and recorded with photographic material. The quantitative evaluation of this subjective result was carried out with a point system adapted to the study.

## V. Results

The results of anatomical dissections, with microscopic and endoscopic instruments, have a mainly descriptive purpose. They build on the knowledge from published studies and systematize the steps and anatomic markers for performing an extended lateral orbital approach, the options to reach the anterior cranial fossa, the posterior part of the lateral wall of the cavernous sinus, the posterior cranial fossa, and the pterygoid fossa.

In the clinical study, all patients operated on for vascular pathology are with successfully clipped aneurysms. In this group, 95% (excluding deceased patient number 20 - 5%) were discharged in good general condition, without gross neurological deficit, and had a good quality of life. In the group of patients operated on for an intracranial space occupying lesions, the postoperative improvement in symptoms was 100% for headache, exophthalmos, and

epileptic seizures for the postoperative follow-up period. Regarding the visual status of the patients, no improvement was observed, but no deterioration was observed during the follow-up. Oculomotor nerve paresis and diplopia were observed in three patients (7% of the total group), in whom the anatomical integrity of the nerve was preserved, but postoperative improvement in its function was not reported for a period of up to 12 months. Regarding hypoesthesia as a symptom, postoperative dynamics were also not observed. In the patients operated with extended lateral orbitotomy because of intracranial tumor pathology, there were no cases of postoperative recurrence due to approach -limited resection and surgical freedom. To reduce the risk of complications and to improve the cosmetic result, bone defects were reconstructed in 40 patients (95% of the total group) with a low-profile titanium mesh. It restores the original anatomy. In all patients, the goal of the operative intervention was achieved, without switching intraoperatively to another approach and without related incidents compromising the outcome of the treatment.

For the group of patients with complete orbital lesions, in the postoperative period, improvement in vision and correction of exophthalmos was reported in all.

Statistical analysis, conducted with the Student T test did not show a significant difference in intraoperative time between the group with the lateral orbital approach and with the other approaches used.

The protocol for postoperative imaging examinations as a standard included a control scan in patients with tumor pathology and a control CT angiography in cases with vascular pathology on the 1st postoperative day, or earlier in case of deterioration of the general and neurological status.

The postoperative hospital stay of patients who underwent operative treatment with extended lateral orbitotomy was 9 days on average.

Based on an in-depth discussion of the study results, Dr. Laleva draws the following conclusions:

1. The extended lateral orbital approach is a minimally invasive and direct approach that can be used as an alternative for a large part of neurosurgical pathology, that is routinely treated with pterional approach and its variations after selection of patients according to established criteria.
2. The extended lateral orbitotomy adapted for the purposes of intracranial pathology includes part of the frontal bone and the pterion area. This approach allows for four targeted endoscopic corridors.
3. The choice of this approach does not compromise the radicality of the tumor resection, the possibilities of clipping the aneurysm and applying technically more complex manipulations such as anterior clinoidectomy and control of intraoperative rupture
4. Compared with other conventional frontolateral neurosurgical approaches, the extended lateral orbitotomy is associated with less dissection of soft tissues and bony structures, with a smaller craniotomy area, resulting in a lower risk of complications such as epidural hemorrhage, dysfunction of the temporomandibular joint, temporal recess, postoperative epilepsy.
5. Compared to the most common minimally invasive anterolateral approaches, there is no statistically significant difference in operative time, postoperative complications and postoperative hospital stay.
6. The approach can be conducted with microscopic, endoscopic and combined operative techniques. The endoscopic technique has indisputable advantages for atraumatic approach in depth in the conditions of anatomical dissection and is of key importance in accessing those

areas of tumor pathology, outside the conic field of the microscope. In clinical settings, when treating vascular pathology and a large part of tumor pathology, the microscopic technique combined with endoscopic examination gives good results.

7. In clinical settings, the approach is not associated with serious complications and is well tolerated by patients.

8. When a transpalpebral skin incision is used, followed by staged reconstruction and surgical closure of the tissues, the approach has good cosmetic results.

On the basis of the conducted research and the conclusions drawn, the contributions for science and practice have been formulated as follows:

Of a scientific-theoretical nature

1. A literature analysis of the historical and anatomical factors predisposing to the introduction of lateral orbitotomy in neurosurgical practice

2. An anatomical study was performed, followed by a focused description of the approach - specific anatomy. Possible surgical corridors are also classified

Methodical in nature

1. An approach classically used in orbital surgery for the treatment of intracranial vascular and tumor pathology was applied

2. The indications, benefits, and risks of approach implementation are described. They are compared with the known and used in practice alternative approach for the same type of pathology

Of a scientific and applied nature

1. Patient selection criteria for extended lateral orbitotomy were formulated

2. Detailed description of the steps for approach during an operational intervention

3. Detailed description of the specific stages and technical nuances in the implementation of approach

4. Description and analysis of the postoperative period in terms of clinical course, complications and cosmetic result.

## VI. Characteristics and evaluation of the dissertation work

The present scientific study examines properly selected literature sources and own results of anatomical and clinical research on the application of lateral orbital approach adapted for the treatment of intracranial pathology. The freely movable endoscopic technique with specialized instrumentation allows targeted dissection through narrow and minimally invasive corridors.

Anatomical studies allows for detailed study and comparison of different approaches, as well as their quantitative assessment. The performed dissections lay a theoretical basis on which the clinical application of minimally invasive lateral orbital approach in vascular and tumor intracranial pathology can be performed in a maximally safe manner. They provide the surgeon with confidence, spatial orientation and dexterity before starting to apply a new technique.

Clinical results demonstrate that extended lateral orbitotomy is an adequate surgical approach for the treatment of orbital, intracranial vascular and tumor pathology. With proper patient selection, minimal invasiveness does not compromise the goal of surgical treatment. Extended lateral orbitotomy has specific characteristics that do not prolong operative time and is comparable to other approaches applied in daily practice. It has been shown to have a good clinical and cosmetic effect, with a low rate of complications. Based on the anatomical and clinical study, the indications and contraindications for the use of the extended lateral

orbitotomy in the surgical treatment of tumor and vascular intracranial pathology have been formulated.

Dr. Laleva's dissertation is structured according to accepted standards, contains all elements of scientific development and meets the requirements of Z.R.A.S.R.B. The results are reliably described. Discussions on them are comprehensively reflected and cover all aspects of the set tasks, which allows the achievement of the goal. I consider the developed dissertation work to be the author's personal work. The abstract contains and illustrates all parts of the dissertation work. Dr. Laleva has presented 7 printed publications in scientific journals and 5 participations in scientific congresses and conferences.

## VII. Conclusion

The dissertation work of Dr. Lily Laleva contains scientific and scientifically applied results that represent a contribution to Bulgarian medical science and practice. She confirms that the author has in-depth theoretical and professional qualities, as well as skills for conducting scientific research, which meets all the requirements of ZRASRB and the rules for the development of the academic staff in Acibadem City Clinic UMBAL Tokuda - Sofia.

All of the above gives me the reason to positively evaluate the dissertation work "Minimally invasive extended lateral orbital approach for intraorbital and intracranial pathology" and to vote "YES" for awarding the educational and scientific degree "DOCTOR OF PHILOSOPHY" to Dr. Lili Naskova Laleva in professional direction 7.1 Medicine, Scientific specialty Neurosurgery.

Sofia,  
21.12.2022

Reviewer:  
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