„CAROL DAVILA” UNIVERSITY OF MEDICINE AND PHARMACY
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MEDICINE

The versatility of the fibular flap customized according to its anatomical variants

ABSTRACT OF THE PhD THESIS

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General Idea Synthesis

Currently, the fibular flap remains the sole method for extensive bone defect reconstruction, enabling the safe harvesting of grafts up to 26 centimeters in length. It is considered the gold standard for total mandibular reconstruction but has also found success in reconstructing bone defects in the limbs. The free fibular flap was first used in 1975 by Taylor for lower limb bone defect reconstruction. Subsequently, various harvesting techniques have been described, allowing for the collection of the flap with a composite osteo-septo-cutaneous structure [1, 2, 3, 4]. Until 1989, this flap was exclusively used for limb bone defect reconstruction. Hidalgo deserves credit for being the first to describe the use of the fibular flap for mandibular defect reconstruction through segmental osteotomies of the bone flap [5].

Segmental bone defects continue to pose a challenge in medical practice since maintaining the integrity of the bone support is essential for the patient's quality of life. The most used methods for bone reconstruction, aside from vascularized bone grafts, include allografts, hybrid grafts, devitalized extracorporeal autografts, distraction osteogenesis, and segmental prostheses. However, these solutions come with a series of complications, including the risk of disease transmission, infection, or autoimmune rejection [6, 7]. Vascularized bone autografts represent the ideal option for bone defect reconstruction due to their histocompatibility, osteoinductive, and osteogenic properties, but using them as microsurgical free grafts is much more demanding in terms of surgical technique [6].

The fibular flap, with its multiple benefits, presents an advantageous surgical solution for complex cases requiring bone reconstructions, whether dealing with post-traumatic defects, pseudarthrosis, osteonecrosis, or post-tumor resections.

The advent of computer-aided design (CAD) and computer-aided manufacturing (CAM) in addition to their implementation in medical practice have elevated reconstructive procedures in the oro-maxillo-facial domain to new heights. This technology allows for the creation of virtual models of mandibular defects and fibular grafts, osteotomy guides necessary for fibular shaping, and estimation of the postoperative outcome. The integration of modern computer-assisted surgical planning technologies enhances the accuracy, reliability, and efficiency of fibular flap reconstructions by simplifying osteosynthesis and improving aesthetic contours, reducing surgical and ischemic times, minimizing postoperative complications through preoperative planning, and intraoperative guidance, enhancing aesthetic and functional outcomes by planning dental implant insertion in the fibula, thus restoring occlusion and temporomandibular joint function [8, 9, 10, 11].

Hypothesis and General Objectives

The fibular flap and its clinical aspects have been extensively studied internationally in recent decades, with numerous articles and studies published or currently in progress. There is a growing interest in optimizing results from both an aesthetic and functional perspective, particularly for complex defects, especially in the head and neck region.

Although anatomical studies have lost some of their appeal in the current era, analyzing anatomical variations provides a basis for advancements in various fields, representing a cost-effective and accessible study method, especially in medical training institutions where current technologies such as virtual reality and augmented reality are not yet alternatives [12, 13]. Additionally, specialized literature is limited when it comes to issuing conclusive findings on the general population [14].

The fact that a significant portion of surgical errors are attributed to difficult or abnormal anatomy, with a 2006 study describing an incidence of 13% for this type of medical mistake, underscores the importance of anatomical studies [15].

Starting from these premises and considering the increasing number of cases with complex bone and soft tissue defects requiring reconstruction using a vascularized free fibular flap, I aim to highlight the anatomical peculiarities of the fibular flap and how they influence its clinical applications.

I also aim to develop work protocols that contribute to:

- Reducing surgical intervention duration.
- Optimizing functional and aesthetic surgical outcomes.
- Streamlining interdisciplinary collaboration and teamwork, especially in head and neck reconstructions.
- Rapidly integrating the patient into the therapeutic process, reducing case analysis and surgical indication times.

- Monitoring and evaluating patients in the short and long term, analyzing therapeutic outcomes, and continuously improving work protocols.

General Research Methodology

To achieve the objectives outlined in this work, I conducted my research systematically, starting with a descriptive anatomical study on cadavers. Through the dissections performed on fresh cadavers, I aimed to highlight the anatomical characteristics of the fibular flap and how these can influence therapeutic decisions. As a secondary goal, I sought to improve surgical technique. Subsequently, with the experience gained from the first study, I initiated a prospective observational clinical study conducted on patients who underwent extensive bone reconstructions using the fibular flap. The objectives of this study were to emphasize the versatility of the fibular flap in various clinical applications. From the initial clinical study cohort, a subgroup of patients with reconstructions in the maxillofacial region was identified, for whom preoperative computerized planning and 3D printing techniques were used. For these patients, I developed a working protocol aimed at streamlining and improving communication between medical teams and the technical team. Finally, through the analysis of case studies from the clinical study and postoperative results, correlated with current data from the international literature, I proposed a therapeutic algorithm for the implementation of fibular flap usage in routine practice.

Anatomical-Surgical Study on Cadavers

Anatomical dissections on cadavers can be a useful method for surgeons seeking to expand their expertise by familiarizing themselves with anatomical structural landmarks. In the present study, my goal was to highlight the presence and type of perforating vessels and analyze the variability of the length of the peroneal vascular pedicle. These variables are crucial for the success of fibular flap reconstructions. For the study, 10 fibular flaps were harvested from 5 fresh cadavers, three males and two females, who exhibited no traumatic marks, postoperative scars, or structural deformities of the lower limbs, and the relevant anatomical elements were identified. The parameters tracked included:

- Cutaneous perforating vessels (number, type, and distribution).
- Length of the peroneal vascular pedicle.
- Distance from the proximal end of the fibula to the emergence of the peroneal pedicle.

- Length of the fibula.
- Diameter of the peroneal vessels. Results and Conclusions:

1. Most frequently, the perforators in our study were found at the junction of the middle third with the distal third of the leg, confirming findings in specialized literature. Specifically, 4 perforators (14.8%) were identified in the distal third of the leg, 20 perforators (74.1%) were identified in the middle third, and 3 perforators (11.1%) were identified in the proximal third.

2. Compared to various studies in the literature conducted to date, the number of perforators originating from the peroneal artery identified in our study was generally smaller, at only 2.7 perforators [16, 17, 18, 19]. For instance, Yoshimura et al. (1990) identified 4.8 +/- 1.4 perforators [20], Beppu et al. (1992) identified 4.7 perforators [21], Hamscha et al. (2019) identified 4.2 perforators [22], Gholami et al. (20) identified 1.7 perforators [23], and Poulet et al. (2022) identified 2.8 perforators [24]. In 2012, Iorio et al. published a detailed analysis of the specialized literature available at that time on peroneal artery perforators, from which they selected 6 cadaveric studies and 3 clinical studies for analysis. In total, they analyzed 1626 perforators from 392 dissected legs, 608 septocutaneous from 345 dissected legs, and 831 musculocutaneous from 292 dissected legs [25].

3. Regarding the type of perforators, 17 (62.96%) were septocutaneous, 7 (25.93%) were musculocutaneous, and 3 (11.11%) were septomusculocutaneous. In comparison, the table below presents data from other studies in literature, with generally significant variations in the types of perforators encountered. Nevertheless, septocutaneous perforators are most found distally, while musculocutaneous perforators predominate proximally.

4. The distance from the level of the fibular head to the emergence of the peroneal artery varied between 6 and 7.1 cm, with an average of 6.51 cm, data consistent with the specialized literature. This aspect is extremely important for preoperative planning, determining the level of proximal osteotomy.

5. The diameter of the peroneal artery at its emergence averaged 2.63 mm, ranging from 2.5 to 3 mm, while the diameter of the peroneal vein at the same level averaged 3.94 mm, with variations between 3.5 and 5 mm. If the arterial

diameter is within normal limits, allowing for anastomoses with the main arteries of the limbs and head and neck, the venous diameter is increased relative to potential recipient veins. Knowledge of the diameter of the peroneal vein is important for careful planning of the future venous anastomosis, which should be performed with a vein of at least the same diameter.

6. The length of the fibula ranged from 31 to 35.3 cm, with an average of approximately 33 cm. Thus, in our study, the available fibula for harvesting ranged from 21 to 25.3 cm, with an average of approximately 23 cm, representing another extremely important criterion in preoperative planning.

Clinical Study

In this work, I aimed to investigate the clinical applications of the fibular flap for reconstructing defects in the head and neck, upper limb, lower limb, post-traumatic cases, infections, or due to oncological pathology. Additionally, I sought to analyze, based on preoperative and intraoperative experience, aspects of the vascularization of the fibular flap that can be extremely useful in streamlining preoperative planning. I conducted a prospective study on adult patients who presented extensive bone defects and underwent surgical treatment for this pathology between 2014 and 2023. The inclusion criteria for patients in the study group were the elective use of the free fibular flap as a therapeutic method. Demographic data, including age, sex, comorbidities, etiology, and location of the bone defect, type of surgical intervention performed, and postoperative complications, were collected from these patients. Specific anatomical elements of the fibular flap, such as fibula length, dimensions of the skin island, distance between the fibular head and the emergence of the anterior tibial artery and peroneal artery, the number of perforators, and their distribution along the leg, were also studied. Postoperative complications, hospitalization duration, and the time to resumption of walking were evaluated. The variables used in this analysis were primarily quantitative parameters. They were analyzed using Microsoft Excel and the SPSS statistical program. For the parameters or variables used in this work, extreme values, mean and standard deviation, coefficient of variation, standard error, and the hypothesis of normality were checked, both through assessing symmetry using the median and using multiple normality tests (Shapiro-Wilk). The Chi-square test was used to determine whether null hypotheses were true (the p-value is statistically significant if $p < 0.05$).

Results and Conclusions:

1. By dividing the study group into subgroups based on the etiology of the defect, its location, and the type of reconstruction, reduced numbers of subjects were obtained in certain lots. For this reason, it was deemed necessary to compare the results obtained with specialized literature.

2. Globally, cancers of the oral cavity represent approximately 4% of all cancers, with the highest prevalence being squamous cell carcinoma, accounting for over 90% of all oral malignancies, and mandibular involvement is observed in 49% of cases [26, 27]. In the present sample, squamous cell carcinoma was reported with an incidence of 54.5%. Rare tumors, such as ectopic mucoepidermoid carcinoma with an extremely rare incidence in the mandible/maxilla, of only 2-4%, or giant cell granuloma, a type of non-odontogenic non-osseous tumor, had an incidence of 4.5% and 9.1%, respectively [28, 29, 30].

3. The average length of the harvested fibular segment is in line with previous studies, being of adequate size for the proposed reconstructions [31, 32]. Thus, the length of the fibula ranged from 32.4 to 43.1 cm, with an average of approximately 38.2 cm +/- 2.9 cm. The length of the utilized fibular segment ranged from 7 to 23 cm, with an average of 12.24 cm +/- 3.65 cm.

4. In a significant proportion of cases - 32 (86.5%) - the fibular osteocutaneous flap was used. This type of flap was generally used for soft tissue defect coverage, but in some cases, raising the skin island was decided as a clinical indicator for postoperative vascular perfusion monitoring.

5. Most frequently, the perforators in our study were found at the junction of the middle third with the distal third of the leg, confirming findings in specialized literature. Specifically, 30 perforators (27.78%) were identified in the distal third of the leg, near the junction with the middle third, 72 perforators (66.64%) were identified in the middle third, and 6 perforators (6.48%) were identified in the proximal third.

6. Compared to various studies in the literature conducted to date, the number of perforators originating from the peroneal artery identified in our study was generally smaller, at only 2.91 +/- 1.09 perforators. It should be noted, however,

that the identification of perforators was mixed, clinical and imaging, and imaging could not identify perforators with a diameter below 0.3 mm. Nevertheless, studies have shown that the accuracy rate in identifying perforators using angio-CT is extremely high, with very low rates of false positives and false negatives [33]. For example, Cho et al. (2001) identified an average of 3.58 +/- 0.71 perforators [34], while Yu et al. (2011) identified an average of 2.52 perforators [35]. In 2012, Iorio et al. conducted a thorough analysis of the specialized literature available at that time on peroneal artery perforators, from which they selected 6 cadaveric studies and 3 clinical studies for analysis. They thus analyzed 1626 perforators from 392 dissected legs, 608 septocutaneous from 345 dissected legs, and 831 musculocutaneous from 292 dissected legs [36]. In 2010, Ribuffo et al. conducted an imaging study in which they identified 171 perforators in 82 analyzed legs [37].

7. As for the type of perforators, 68 (62.96%) were septocutaneous, and 40 (37.04%) were musculocutaneous. Most studies show that septocutaneous perforators are most commonly found distally, while musculocutaneous perforators predominate proximally.

8. The distance from the level of the fibular head to the emergence of the anterior tibial artery varied between 2.6 and 5 cm, with an average of 3.54 cm +/- 0.65 cm, and at the emergence of the peroneal artery, it ranged from 5.28 to 8.87 cm, with an average of 6.65 cm +/- 0.81 cm, data consistent with the specialized literature. This aspect is extremely important for preoperative planning in establishing the level of proximal osteotomy for optimal dissection of the peroneal pedicle along its entire length.

9. The most used recipient vessels for anastomoses were:

9.1. In the head and neck, the facial artery (95.65%) and facial vein (54.54%), and external jugular vein (36.36%).

9.2. In the lower limb, the anterior tibial artery (50%) and anterior tibial vein (50%).

10. The success rate of the fibular flap was calculated at 97.3%, in line with the results of other studies conducted on larger patient cohorts [38, 39, 40].

11. The low rate of complications observed in our study can also be correlated with the low rate of comorbidities and the low rate of smoking among patients. Therefore, patients experienced the following complications:

11.1. Receptor site complications:

11.1.1. In the skin island of the flap, out of 32 cases, necrosis of the skin was observed in 4 cases, superficial (2), partial (1), or total (1).

11.1.2. At the level of the cutaneous flap or cervical region, when reconstructions were performed in the head and neck, there were 5 cases (13.51%) of dehiscence, mainly in irradiated and/or secondary reconstruction patients.

11.2. Donor site complications:

- Partial integration of the skin graft in 3 (17.65%) out of 17 cases where the defect was covered with a skin graft.
- 1 case (5%) of wound dehiscence, out of 20 cases where the defect was closed by direct suturing.
- 1 case (5%) of superficial necrosis at the suture line, out of 20 cases where the defect was closed by direct suturing.

11.3. Infectious complications:

11.3.1. 3 (8.1%) infections at the recipient site, in the cervical region.

11.3.2. 2 (5.4%) infections at the donor site, in the leg.

11.4. Other complications:

- 6 cases of oro-cutaneous fistulas.
- 1 case of hallux claw due to flexor hallucis longus fibrosis.

Design Protocol and Workflow in 3D Printed Surgical Guide Production

Reconstructions involving virtual planning techniques require a high-volume bidirectional exchange of information between the multidisciplinary medical team and the technical team, composed of experts in graphic software and 3D printing technicians. To prevent communication gaps in an information loop with multiple components, we have developed a working protocol that has led to much more efficient information transmission.

Protocol for Implementing the Use of the Fibular Flap in Medical Practice

By synthesizing information gathered from specialized literature, combined with clinical experience, we have developed an algorithm for using the fibular flap based on the location of the bone defect, targeting adult patients. This algorithm aims to overcome the challenges posed by the complexity of reconstructive cases involving bone defects and to provide patients with quicker and easier access to specialized treatment.

Conclusions and Personal Contributions

The fibular flap, despite representing a well-documented reconstructive method with a history spanning nearly five decades, continues to serve as the cornerstone for extensive osseous defect reconstructions. Loss of osseous support, whether concerning limb bone defects or viscerocranial defects, significantly impacts the quality of life, adversely affecting the patient's social integration.

Reconstruction of osseous defects with the fibular flap remains a contemporary, versatile, and reliable method, characterized by a low rate of postoperative complications and minimal functional deficit at the donor site.

In-depth knowledge of anatomy through cadaveric dissections familiarizes the surgeon with potential anatomical variations, preparing them for various pre- or intraoperative scenarios.

In the present study, the fibular flap has proven to be a dependable method for microsurgical reconstruction of extensive mandibular defects, with low postoperative complication rates and the achievement of a high-quality bone graft conducive to prosthetic oral rehabilitation.

Multidisciplinary collaboration is a distinctive feature of the cases presented. Throughout this study, teams of surgeons from different specialties have continually improved their approach to cases. Additionally, the involvement of a technical team that assisted in computerized planning of interventions on the mandible or maxilla decisively contributed to enhancing postoperative outcomes.

Most oncological patients included in this study (15 out of 16 - 93.75%) were staged as T4 at the time of surgical treatment initiation, with oncologic resection performed for palliative purposes and to enhance their quality of life. This underscores the necessity of facilitating patient access to specialized curative treatment.

To expedite patient access to specialized medical treatment, it is imperative to raise awareness about the issue and inform doctors in related fields (oral and maxillofacial surgery) about the available therapeutic, especially reconstructive, methods. This way, patients will have easier access to surgical treatment as a primary curative option instead of being initially recommended adjuvant treatment (chemotherapy and, especially, radiation therapy), which merely delays disease progression and severely limits subsequent therapeutic options.

Given the low rate of patient attendance at postoperative follow-up appointments, the study could not analyze long-term postoperative outcomes. This is why the inclusion of patient follow-up in the treatment algorithm was deemed necessary.

From the accumulated intraoperative experience, the following conclusions were drawn:

- Proximal osteotomy is recommended to be performed at approximately 6 cm from the upper extremity of the fibular head. This approach allows for a clear visualization of the bifurcation of the posterior tibial artery and the peroneal artery, which is typically located around 6.5 cm from the upper extremity of the fibular head. It also makes vascular pedicle dissection of the peroneal artery easier.

- Distal osteotomy is recommended to be performed at least 7 cm from the distal extremity of the fibula. Besides maintaining ankle stability, at this level, the tibiofibular syndesmosis consists of four components: the anterior-inferior tibiofibular ligament, posterior-inferior tibiofibular ligament, transverse tibiofibular ligament, and interosseous membrane. The more distal the osteotomy, the more challenging it becomes due to these structures and the proximity to the tibia.

- Primary closure of leg defects is recommended for defects with a width under 3.5 cm. For carefully selected cases, such as elderly patients with lax skin or when the donor site is situated above the midpoint of the leg, the width of defects amenable to primary closure can extend to 4-4.5 cm. In all other cases, the use of a skin graft for defect coverage is recommended.

Technical and Economic Advantages and Disadvantages

Integration of revolutionary computerized planning and 3D printing technologies into clinical practice, particularly in maxillary and mandibular reconstructions, has injected new life into anatomical and clinical studies related to this flap. The aim is to achieve rapid and near-normal restoration of form and function in the affected segment.

Regrettably, the high cost of current-generation technologies such as computerized preoperative planning and 3D printing renders them inaccessible to the Romanian healthcare system. Hence, collaborations with research institutes that make these technologies more affordable represent a domestic solution for implementing these techniques in routine medical practice.

Future Directions

The medical field is in constant pursuit of therapeutic solutions that yield increasingly better functional and aesthetic outcomes with minimal drawbacks. Any deficit, be it functional or aesthetic, in the donor site is deemed unacceptable. Thus, new horizons are emerging through the development of 3D-printed structures designed to specifically address bone defects. These structures are constructed from biocompatible materials, populated with stem cell cultures, and associated with growth factors to overcome any limitations of current bone reconstruction methods.

The implementation of artificial intelligence in medical practice is also on the horizon. Although artificial intelligence is not yet fully adapted to analyze the specific issues of a specialized or super-specialized domain, it is likely that, with the aid of databases encompassing preclinical and clinical information, super-specialized artificial intelligences tailored to a specific field will be created shortly. These will undoubtedly find utility in managing patients with complex defects, especially in cases of irradiated oncological patients or those receiving adjuvant treatment, where surgical risks and the complexity of the intervention are elevated. In these cases, medical simulations for optimal recipient vessel selection or complication anticipation algorithms may be developed. To achieve this, a sufficiently extensive database is necessary, encompassing all perioperative aspects and imaging data, to provide the groundwork for reliable algorithms.

Artificial intelligence can also potentially be employed during certain surgical procedures, such as fibular modeling osteotomies, which could be performed with extreme precision and speed in the future, with the aid of specialized robots guided by artificial intelligence.

Personal Contributions

Starting with the anatomical-surgical study on cadavers, I assessed anatomical variations of the fibular flap, simultaneously seeking to enhance the operative technique. I attempted to identify multiple parameters, including data about the peroneal vascular pedicle, perforators of the peroneal artery, and fibula length.

Through the conducted dissections:

1. I identified the distribution of perforators of the peroneal artery, which coincided with data in the specialized literature.
2. I compared the obtained data about the peroneal artery perforators with those from several literature studies.
3. I discussed the types of peroneal artery perforators and their distribution by type.
4. I calculated the distance from the fibular head to the emergence of the peroneal artery, a crucial element for determining the proximal osteotomy site.
5. I evaluated the diameters of the peroneal vessels to establish optimal recipient vessels for microvascular anastomoses.
6. I assessed fibula and fibular flap lengths, another essential reference for preoperative planning.

I conducted a clinical study on a significant patient cohort, all of whom presented complex defects that were challenging to address with other surgical methods, often accompanied by significant comorbidities and pathologies necessitating multidisciplinary approaches. I analyzed demographic data, comorbidities, involved pathologies, and data related to the use of the fibular flap for reconstructing these defects.

From the clinical study:

1. I compared data related to oncological pathology as described in the literature with clinical study data.
2. I evaluated fibula and fibular flap lengths, essential references for preoperative planning.
3. I identified the distribution of perforators of the peroneal artery, which coincided with data from specialized literature.
4. I compared data about peroneal artery perforators obtained with those from several literature studies.
5. I discussed the types of peroneal artery perforators and their distribution by type.
6. I calculated the distance from the fibular head to the emergence of the peroneal artery, a crucial element for determining the proximal osteotomy site.
7. I established the preferred recipient vessels for microvascular anastomoses in reconstructions involving the head, neck, and lower extremities.
8. I analyzed postoperative complications.

From the study group, I selected a subgroup of patients with oro-maxillofacial pathologies for whom I developed a working protocol for computer-assisted planned reconstructions using 3D printing techniques. This protocol is of utmost importance for efficient communication between the medical and technical teams.

I also followed through with the implementation of this protocol, including:

1. Obtaining DICOM images of the region of interest.
2. Post-processing DICOM images (radiological software, 3D graphics software).
3. DICOM data segmentation, resulting in a digital 3D model of the region of interest.
4. Designing and constructing mandibular and fibular guides using open-source software (Blender 3D).
5. Preparing the .stl model for 3D printing (slicing process).

6. Post-processing 3D printing.
7. Implementing the protocol into routine medical practice.

Building upon the synthesized clinical treatment of the presented cases, I proposed a protocol for implementing the use of the fibular flap into routine practice, with the primary objectives of patient safety, achieving maximal functional and aesthetic outcomes, and long-term patient follow-up.

This protocol includes:

1. Patient assessment.
2. Evaluation of osseous defects.
3. Assessment of the donor site.
4. Preoperative planning based on cadaveric and clinical anatomical studies.
5. Principles of osseous defect reconstruction in the head and neck area, using the fibular flap.
6. Principles of osseous defect reconstruction in limb bones using the fibular flap.
7. Patient follow-up.

I concluded the doctoral research work by developing three algorithms for:

1. Preoperative planning based on cadaveric and clinical anatomical studies.
2. Selecting the type of fibular flap for mandibular and maxillary defects.
3. Selecting the type of fibular flap for long bone defects in the limbs.

In conclusion, the vascularized free fibular flap is an extremely versatile flap and remains the gold standard for the reconstruction of long bone defects and extensive mandibular defects.

Bibliography

[1] G. Taylor, G. Miller și F. Ham, „The free vascularized bone graft. A clinical extension of microvascular techniques.," *Plast Reconstr Surg,* vol. 55, p. 533—44, 1975.

[2] R. G. Roger G. Graham, M. C. Swan, D. A. Hudson și J. E. van Zyl, „The fibula free flap: advantages of the muscle sparing technique," *British Journal of Plastic Surgery,* vol. 56, p. 388–394, 2003.

[3] A. Gilbert, „Vascularized transfer of fibula shaft," *Int J Microsurg,* p. 1:100, 1979.

[4] Z. Chen și W. Yan, „The study and clinical application of the osteocutaneous flap of fibula," *Microsurgery ,* vol. 4, p. 11, 1983.

[5] D. Hidalgo, „Fibula free flap: a new method of mandible reconstruction.," *Plast Reconstr Surg ,* vol. 84, p. 71—9, 1989.

[6] F. Migliorini, G. L. Padula, E. Torsiello, F. Spiezia, F. Oliva și N. Maffulli, „Strategies for large bone defect reconstruction after trauma, infections or tumour excision: a comprehensive review of the literature," *Eur J Med Res,* vol. 26, nr. 1, p. 118, 2021.

[7] C. Wee, D. Ruter, S. Schulz, G. Sisk, J. West, S. Tintle și I. Valerio, „Reconstruction of extremity long bone defects with vascularized fibula bone grafts," *Plast Aesthet Res,* p. 6:12, 2019.

[8] A. H. Sweed, A. R. Bolzoni, A. Kadubiec, G. A. Beltramini, A. Cherchi și A. Baj, „Factors influencing CAD/CAM accuracy in fibula free flap mandibular reconstruction," *Acta Otorhinolaryngol Ital,* vol. 40, nr. 2, pp. 138-143, 2020 .

[9] R. H. Schepers, G. M. Raghoebar, A. Vissink, M. W. Stenekes, J. Kraeima, J. L. Roodenburg, H. Reintsema și M. J. Witjes, „Accuracy of fibula reconstruction using patient-specific CAD/CAM reconstruction plates and dental implants: A new modality for functional reconstruction of mandibular defects," *Journal of Cranio-Maxillofacial Surgery,* vol. 43, nr. 5, pp. 649-657, June 2015.

[10] D. F. Zweifel, C. Simon, R. Hoarau, P. Pasche și M. Broome, „Are virtual planning and guided surgery for head and neck reconstruction economically viable?," *J Oral Maxillofac Surg,* vol. 73, nr. 1, pp. 170-5, 2015 .

[11] G. D. Santis, M. Pinelli și M. Starnoni, „Extended and unusual indications in jaw reconstruction with the fibula flap: An overview based on our 30-year experience," *Ann Med Surg (Lond),* vol. 62, p. 37–42, 2021.

[12] O. Habbal, „Anatomical Research-Misconceptions and opportunities," *Sultan Qaboos Univ Med J,* vol. 17, nr. 1, p. e1–e2, 2017.

[13] J. Sañudo, R. Vázquez și J. Puerta, „Meaning and clinical interest of the anatomical variations in the 21st century," *Eur J Anat,* vol. 7, pp. 1-3, 2003.

[14] B. M. Henry, K. A. Tomaszewski și J. A. Walocha, „Methods of Evidence-Based Anatomy: a guide to conducting systematic reviews and meta-analysis of anatomical studies," *Annals of Anatomy,* vol. 205, pp. 16-21, 2016.

[15] S. O. Rogers, A. A. Gawande, M. Kwaan, A. L. Puopolo, C. Yoon, T. A. Brennan și D. M. Studdert, „Analysis of surgical errors in closed malpractice claims at 4 liability insurers," *Surgery,* vol. 140, nr. 1, pp. 25-33, 2006.

[16] T. P. Whetzel, M. A. Barnard și R. B. Stokes, „Arterial fasciocutaneous vascular territories of the lower leg," *Plast Reconstr Surg,* vol. 100, nr. 5, pp. 1172-83, 1997.

[17] C. Heitmann, F. N. Khan și L. S. Levin, „Vasculature of the Peroneal Artery: An Anatomic Study Focused on the Perforator Vessels," *Journal of Reconstructive Microsurgery,* vol. 19, nr. 3, pp. 157-162, 2003.

[18] N. Q. Duc, V. N. Lam și N. P. Tien, „An anatomic study of the perforators from the peroneal artery. A new method to locate the cutaneous perforator," *Annals of Medicine and Surgery,* vol. 78, p. 103735, 2022.

[19] C. R. Lee, S. H. Kim, H. J. Kwon, M. Y. Ahn, Y. S. Nam și S.-H. Moon, „Proximal peroneal perforator flap, cadaveric study, and clinical applications for shallow defect reconstructions," *Microsurgery,* vol. 43, nr. 5, pp. 460-469, 2023.

[20] M. Yoshimura, S. T. și M. Hosokawa, „The vasculature of the peroneal tissue transfer," *Plast Reconstr Surg,* vol. 85, nr. 6, pp. 917-921, June 1990.

[21] M. Beppu, D. Hanel, G. Johnston, J. Carmo și T. Tsai, „The osteocutaneous fibula flap: an anatomic study," *J Reconstr Microsurg,* vol. 8, nr. 3, pp. 215-23, May 1992.

[22] U. Hamscha, W. Weninger, C. Freystatter, C. Tzou și C. Radke, „Anatomical Study of a Chimeric Fascio-Osteomyocutaneous Fibula Flap for Free Microvascular Tissue Transfer," *J Reconstr Microsurg,* vol. 35, nr. 6, pp. 438-444, 2019.

[23] M. Gholami, A. Hedjazi și A. Milani, „Evaluation of Anatomic Variations of Fibula Free Flap in Human Fresh Cadavers," *World J Plast Surg,* vol. 8, nr. 2, pp. 229-236, 2019.

[24] V. Poulet, A. Prevost, Z. Cavallier, S. Alshehri, F. Lauwers și R. Lopez, „Fibula free flap perforasomes: vascular anatomical study and clinical applications," *Surg Radiol Anat.,* vol. 44, nr. 5, pp. 637-644, May 2022.

[25] M. Iorio, M. Cheerharan și M. Olding, „A Systematic Review and Pooled Analysis of Peroneal Artery Perforators for Fibula Osteocutaneous and Perforator Flaps," *Plastic and Reconstructive Surgery,* vol. 130, nr. 3, pp. 600-607, September 2012.

[26] S. N. Rogers, J. Devine, L. Derek., P. Shokar, J. S. Brown și E. D. Vaugman, „Longitudinal health-related quality of life after mandibular resection for oral cancer: a comparison between rim and segment," *Head Neck,* vol. 26, nr. 1, pp. 54-62, 2004.

[27] A. K. Markopoulos, „Current aspects on oral squamous cell carcinoma. Open Dent J 2012;6:," *Open Dent J,* vol. 6, pp. 126-130, 2012.

[28] B. L. Dunfee, O. Sakai, R. Pistey și A. Gohel, „Radiologic and pathologic characteristics of benign and malignant lesions of the mandible," *Radiographics,* vol. 26, nr. 6, pp. 1751-68, 2006.

[29] L. Avril, T. Lombardi, A. Ailianou, K. Burkhardt, A. Varoquaux, P. Scolozzi și M. Becker, „Radiolucent lesions of the mandible: a pattern-based approach to diagnosis," *Insights Imaging,* vol. 5, nr. 1, pp. 85-101, 2014.

[30] D. Raut și S. Khedkar, „Primary intraosseous mucoepidermoid carcinoma of the maxilla: a case report and review of literature," *Dentomaxillofac Radiol,* vol. 38, nr. 3, pp. 163-8, 2009.

[31] N. A. Papadopulos, J. Schaff, R. Sader, L. Kovacs, H. Deppe, A. Kolk și E. Biemer, „Mandibular reconstruction with free osteofasciocutaneous fibula flap: a 10 years experience," *Injury,* vol. 39, nr. Suppl 3, pp. S75-82, 2008.

[32] H. Pototschnig, J. Schaff, L. Kovacs, E. Biemer și N. A. Papadopulos, „The free osteofasciocutaneous fibula flap: Clinical applications and surgical considerations," *Injury,* vol. 44, pp. 366-369, 2013.

[33] K. Ettinger, J. Morris, A. Alexander, J. Nathan și K. Arce, „Accuracy and Precision of the Computed Tomographic Angiography Perforator Localization Technique for Virtual Surgical Planning of Composite Osteocutaneous Fibular Free Flaps in Head and Neck Reconstruction," *J Oral Maxillofac Surg.,* vol. 80, nr. 8, pp. 1434-1444, 2022.

[34] B. Cho, S. Kim, J. Park și B. Baik, „Blood supply to osteocutaneous free fibula flap and peroneus longus muscle: prospective anatomic study and clinical applications," *Plast Reconstr Surg.,* vol. 108, nr. 7, pp. 1963-71, 2001.

[35] P. Yu, E. Chang și M. Hanasono, „Design of a reliable skin paddle for the fibula osteocutaneous flap: perforator anatomy revisited," *Plast Reconstr Surg.,* vol. 128, nr. 2, pp. 440-446, 2011.

[36] M. Iorio, M. Cheerharan și M. Olding, „A Systematic Review and Pooled Analysis of Peroneal Artery Perforators for Fibula Osteocutaneous and Perforator Flaps," *Plastic and Reconstructive Surgery,* vol. 130, nr. 3, pp. 600-607, September 2012.

[37] D. Ribuffo, M. Atzeni, L. Saba, M. Guerra, G. Mallarini, E. Proto, D. Grinsell, M. Ashton și W. M. Rozen, „Clinical study of peroneal artery perforators with computed tomographic angiography: implications for fibular flap harvest," *Surg Radiol Anat.,* vol. 32, nr. 4, pp. 329-334, 2010.

[38] M. Knitschke, S. Sonnabend, C. Bäcker, D. Schmermund și S. Böttger, „Partial and Total Flap Failure after Fibula Free Flap in Head and Neck Reconstructive Surgery: Retrospective Analysis of 180 Flaps over 19 Years," *Cancers,* vol. 13, nr. 4, p. 865, 2021.

[39] A. O. Momoh, P. Yu, R. J. Skoracki, S. Liu, L. Feng și M. Hanasono, „A Prospective Cohort Study of Fibula Free Flap Donor-Site Morbidity in 157 Consecutive Patients," *Plastic and Reconstructive Surgery,* vol. 128, nr. 3, pp. 714-720, 2011.

[40] P.-J. Verhelst, F. Dons, P.-J. V. Bever, J. Schoenaers, L. Nanhekhan și C. Politis, „Fibula Free Flap in Head and Neck Reconstruction: Identifying Risk Factors for Flap Failure and Analysis of Postoperative Complications in a Low Volume Setting," *Craniomaxillofac Trauma Reconstr,* vol. 12, nr. 3, pp. 183-192, 2019.

[41] T. W. Huntington, „Case of bone transference. Use of a segment of fibula to supply a defect in the tibia," *Ann Surg,* vol. 41, nr. 2, pp. 49-51, 1905.

[42] M. L. Urken, Atlas of Regional and Free Flaps for Head and Neck Reconstruction: Flap Harvest and Insetting, LWW, 2011.

[43] K.-D. Wolff și F. Holzle, „Fibular Flap,” în *Raising of Microvascular Flaps A Systematic Approach*, Springer, 2005, pp. 107-134.

Author's scientific publication list

1. **Iulia MURARU**, Dragoş MURARU, Bogdan M. MARINESCU, Ioana TUHAR, Ionuț GUZGANU, Paul IONESCU, Liliana MORARU, Cătălin DUMITRU, Ana CĂRUNTU, Ioan LASCĂR, Adrian GABĂRĂ, **RAMUS TO RAMUS MANDIBULAR DEFECT RECONSTRUCTION WITH OSTEOCUTANEOUS FIBULA FREE FLAP – CASE PRESENTATION**, in *MAEDICA – a Journal of Clinical Medicine, 15(3): 401-408, 2020.*

https://doi.org/10.26574/maedica.2020.15.3.401 Chapter 9, pg. 62-69 ;

2. **Iulia MURARU**, Dragoş MURARU, Dragoş ZAMFIRESCU, Ioan LASCĂR, **THE CLINICAL USE OF THE FIBULAR FLAP**, in *Romanian Journal of Medical Practice, 15(3): 297-301, 2020.*

https://doi.org/10.37897/RJMP.2020.3.7 Chapter1, pg. 8-19 ;

3. **Iulia MURARU**, Eduard LICIU, Adrian GABĂRĂ, Dragoş MURARU, Daniel CRISTEA, Mihai DRAGOMIR, Ioan LASCĂR, **DESIGN PROTOCOL AND MANUFACTURING WORKFLOW OF 3D PRINTED SURGICAL GUIDES IN MANDIBULAR RECONSTRUCTION WITH VASCULARIZED PERONEAL GRAFT AND MUSCULOCUTANEOUS FLAP,** in *Technology and Innovation in Life Sciences,2(1): 1-15, 2023.*

https://doi.org/10.56051/tils.v2i1.12 Chapter 5, pg. 37-48 ; Chapter 10, pg. 146-167 ;