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DOCTORAL FIELD MEDICINE

DOCTORAL THESIS ABSTRACT

EVALUATION OF AESTHETIC RESULTS OF RECONSTRUCTION METHODS AFTER EXCISION OF CUTANEOUS CARCINOMAS FROM THE MIDDLE THIRD OF THE FACE

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List of abbreviations

cm: centimeter
mm: millimeter
nr : number
HPV: Human Papilloma Virus
FGF: fibroblast growth factor
EGF: epidermal growth factor
PDGF: platelet derived growth factor
TGF: transforming growth factor
TNF: tumor necrosis factor
VEGF: vascular endothelial growth factor
PMN: polymorphonuclears (leucocytes)
NO: nitric oxide
MSH: melanocyte-stimulating hormones
GM-CSF: Granulocyte-macrophage colony-stimulating factor
GAG: Glycoaminoglycans
UV: ultra-violets (rays)
APUD: amine precursor uptake decarboxylation
IL: interleukins
SMAS: superficial muscular aponeurotic system
VSS : Vancouver Scar Scale

Contents

I. SITUATION ON NATIONAL AND INTERNATIONAL PLAN IN THE FIELD 2
Selective Bibliography 10
II. EPIDEMIOLOGICAL AND CLINICAL-HISTOPATHOLOGICAL ASPECTS OF THE FACIAL SKIN CANCER..... 13
Selective Bibliography 18
III. PHYSIOPATHOLOGY OF WOUNDS HEALING 20
Selective Bibliography 25
IV. SURGICAL RECONSTRUCTION METHODS USED AT THE MIDLE FACIAL THIRD IN RELATION TO REGIONAL ANATOMIC PARTICULARITIES 27
Selective Bibliography 38
V. MOTIVATION OF THE RESEARCH 40
VI. MATERIAL AND METHOD 43
VI.1. Population in the study 43
VI.2. Study parameters 44
VI.3. Methods of investigation 45
VI.4. Statistical Data Processing 46
VI.6. Working method 48
VI.7. Limitations of this study 53
VII. RESULTS 54
VIII. DISCUSSION 90
VIII.1 Using of Direct Suture Techniques 90
VIII.2 Local flaps (rotation and transposition flap) and skin transplants 92
VIII.3 Localization of the tumor in the middle third of the face..... 95
VIII.3.A Nasal region. 95
VIII.3.B Orbital Regions 97
VIII.3.C Infra-orbital and zigomatic regions 98
Selective Bibliography 100
IX. CLINICAL CASES 102
X. CONCLUSION 116
BIBLIOGRAPHY..... 118

KEY WORDS: Skin carcinomas, middle facial third, oncological resection, local flaps, skin transplants, aesthetic results Vancouver scar score.

INTRODUCTION. RESEARCH MOTIVATION

This study presents the aesthetic results obtained after the reconstruction of the midle sub-regions of the face after excision of cutaneous carcinomas at this level.

For the reconstruction of the resulting defects, 4 surgical methods were used. The method was choosed individually for each patient according to the size of the skin defect, the loco-regional anatomic features and the clinical condition of the patient.

The astetic results, according to the Vancouver scar score, were compared in the reconstruction method on each of the mid-section sub-regions of the face. To determine statistical relevance, the data obtained was stored in contingency tables and statistically processed using the Chi square test.

This study was structured into two parts. A first general part, in which we synthesized the main epidemiological and morphopathological aspects of cutaneous carcinomas in the regions of the face. At the same time, I rememberd the theoretical principles of wounds healing as well as the main surgical methods used for the reconstruction of skin defects.

In the second part of the paper I presented the study of the population with the inclusion and exclusion criteria, the means of investigation and the working method, as well as the parameters of the study. The results obtained were presented and discussed according to the surgical method used and the interested anatomical subregion.

At the end of the paper we presented some clinical cases that I consider it representative for this study.

Every year there are as many cases of skin carcinomas as all other cases of cancers diagnosed. Although these cancers have a relatively low mortality, the morbidity and the therapeutic costs attributed to them are significant.

The incidence of all types of skin cancer has been steep in the last thirty years. Furthermore, actinic keratosis has a variable prevalence depending on different regions and may reach up to 40% of the Caucasian population over 50 years.

Other types of malignant epithelial tumors such as keratoacanthoma, trichocholiculoma, Bowen morbus are rare in terms of incidence, and establishing the type and degree of histopathological differentiation are quite difficult, requiring extensive experience from the anatomo-pathologist.

Precise diagnosis of the tumor from a histopathological exam is very important for assessing clinical development and prognosis as well as for establishing or completing treatment.

Even though the skin cancer curability rate exceeds 97% and the risk of dissemination or metastasis is low or even absent, however, the regular oncological follow-up of these patients is absolutely necessary.

The main carcinogen for the development of epithelial skin tumors is cumulative exposure to ultraviolet rays throughout their lives. Ultraviolet rays are now considered the most important factor for the induction and promotion of epithelial cutaneous tumors.

Normally, each individual, depending on the type of skin, has a cumulative number of hours for which exposure to the sun has beneficial effects. If this number of hours is exceeded, conditions favorable to the appearance of skin cancer are created. The most common carcinogenic cofactor for skin cancer is the immunosuppressant therapy.

For the treatment of epithelial cutaneous tumors there is a wide range of conservative or surgical therapeutic options. As a rule, abrasive methods are indicated for superficial tumor processes (pure epidermal dysplasia, invasive epidermal tumors that do not penetrate deeper the papillary layer of the dermis).

Tumors that invade the middle or deep layer of the dermis benefit from surgical procedures, cryotherapy or radiotherapy with a high healing rate of over 90%.

Here, it should be noted that, especially for well-defined clinical tumors that do not invade more than the deep dermis, cryotherapy or radiotherapy can be therapeutic alternatives to surgery. However, these alternative radical methods, like any therapeutic method, require sufficient medical experience as well as a biopsy before applying it.

In most cases, surgical excision is, however, the easiest and most direct way to solve problems.

Surgical excision in skin cutaneous lesions often causes postoperative defects that require immediate reconstruction. Besides knowing the causes that can influence wound development, the surgeon has to carefully handle the tissues and avoid unnecessary additional tensions or pressures, but with a strong resonance on healing.

Due to its multiple and complex functions, the facial region is difficult to rebuild. The surgeon who deals with this pathology needs to know and follow the principles of using of skin flaps, requiring more than a simple understanding of tissue transport techniques. Knowledge of geometry, biomechanics and stratigraphy of the skin and subtle skin structures must be corroborated with the sense of aesthetics, shape and symmetry, as well as the vision of the final result.

The purpose of this paper is to evaluate and compare aesthetic results obtained after resection of cutaneous tumors from the middle-third regions of the face and their reconstruction through various surgical procedures.

MATERIAL AND METHOD

This retrospective study was performed in a group of 165 patients admitted between January 2013 and December 2016 in the County Emergency Clinical Hospital "Sf. Apostol Andrei "Constanta, in the Plastic Surgery and Reconstructive Microsurgery Clinic. All patients were diagnosed with a cutaneous carcinoma tumor in the middle third of the face. Patients enrolled in the study were 18 to 91 years old. All patients underwent surgery to remove the tumor and reconstruct the resulting defect.

To centralize the information, we have used an Excel database, in which we have completed the following information:

a) Patient data:

First, the descriptive data for each patient were recorded: name, age and gender.

b) The particularities of the tumor or the resulting post-excisional defect. The characteristics of tumor lesions have been documented. These included the anatomical location (we included the subregion within an aesthetic unit of the face), the dimensions, as well as the anatomopathological diagnosis of the tumor.

c) the incidence of cutaneous carcinomas in the middle face of the face during the study years.

d) How to cover the skin defect.

e) The results obtained after Vancouver Scar Scale Scoring (VSS) assessment of scar appearance after at least one month from reconstruction of the post-excision skin defect:

- coloration due to scar vascularisation;

- pigmentation of the scar;

- the degree of elasticity (flexibility) of the reconstructed area;

- degree of height of the scar.

Information about aesthetic results was processed and analyzed statistically, and then compared with those in the literature.

The results obtained from the patient evaluation were stored and sorted in Excel tables, for which we used the Apache OpenOffice ™ version 4.1.3. To test the statistical significance of differences in a classification system and to the relationship between two classification systems, we used the Pearson-chi^2 test.

Statistical data processing was performed using MedCalc ™ version 16.8.4. Data collected from patients was categorized into different frequency tables containing information from patients belonging simultaneously to at least two different categories.

Vancouver's quantitative score, aims to provide a standard for scar tissue analysis. It is based on the sum of four values assigned to each parameter: flexibility, denivelation, vascularization and pigmentation. Each of these four categories can score between 0 and 4.

Pigmentation
0 = Normal color
1 = Hypopigmentation
2 = Hyperpigmentation
Vascularity
0 = Normal
1 = Pink (slight increase in blood supply)
2 = Red (significant increase in blood supply)
3 = Purple (excessive local blood supply)
Pliability
0 = Normal
1 = Supple (flexible with minimal resistance)
2 = Yielding (giving way to pressure, offering moderate resistance, but does not behave as a solid scar mass)
3 = Firm (solid/inflexible unit, not easily moved, resistant to manual pressure)
4 = Banding (rope-like tissue that blanches with extension of scar, does not limit range of motion)
5 = Contracture (permanent shortening of scar producing deformity or distortion; limits range of motion)
Height
0 = Normal
1 = <2 mm
2 = ≥2 mm and <5 mm
3 = ≥5 mm

Tabel 1 - *Vancouver* scar score

RESULTS AND DISCUSSIONS

Of the 165 patients diagnosed and operated between January 2013 and December 2016, with a mid-facial skin carcinoma, the male / female ratio was 1.46 (98 males and 67 women respectively).

Almost three quarters of patients were diagnosed with basal cell carcinoma, respectively 129 patients (78.18%). Of these, 76 were men.

Spinocellular carcinomas (33 patients) and those of adjacent structures (3 patients) were identified in 36 patients (21.82%).

	Basal cell carcinoma	Squamos cell carcinoma	Adnexal skin carcinoma	Total
Male	76	20	2	98
Female	53	13	1	67

Tabel 2 - Gender distribution of forms of skin carcinoma

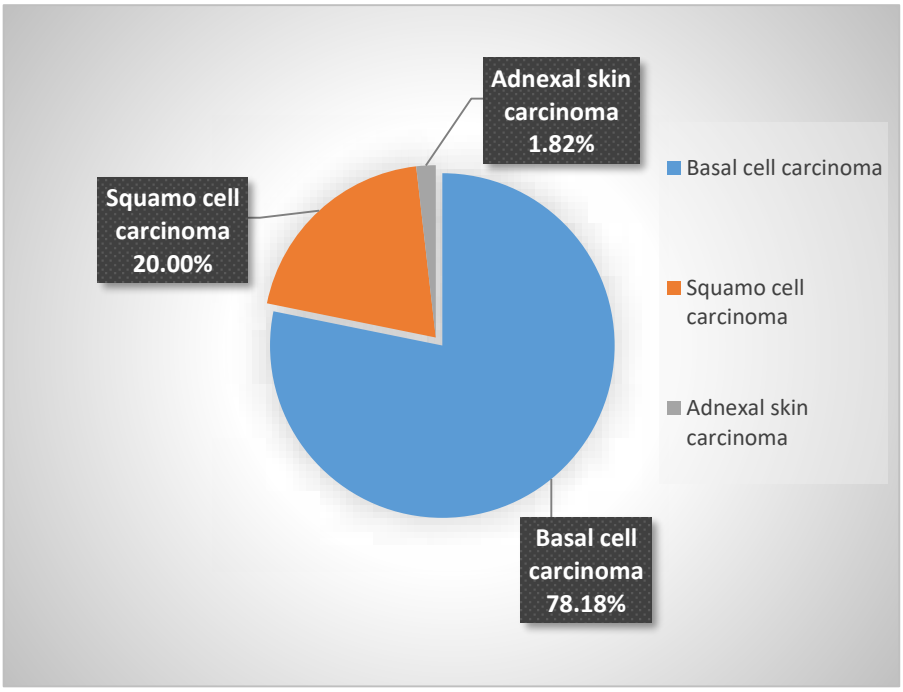

Chart 2. Distribution of patients by the anatomo-pathological form of cutaneous carcinomas.

Regarding the surgical method used for the reconstruction of post-excision skin defects in the middle face of the face, the technique of direct sutures was most used, possibly accompanied by the take-off and elongation of the margins of the skin defect after removal of the cutaneous tumor. Thus, the retrospective study included 90 cases of direct sutures, more than half of the patients.

Local flaps were used in a total of 54 patients (32.72%), of which 47 patients benefited from flap reconstruction and only 7 patients from the transplant flap.

Also, 21 patients benefited from skin defect coverage with skin transplants (split or full thickness).

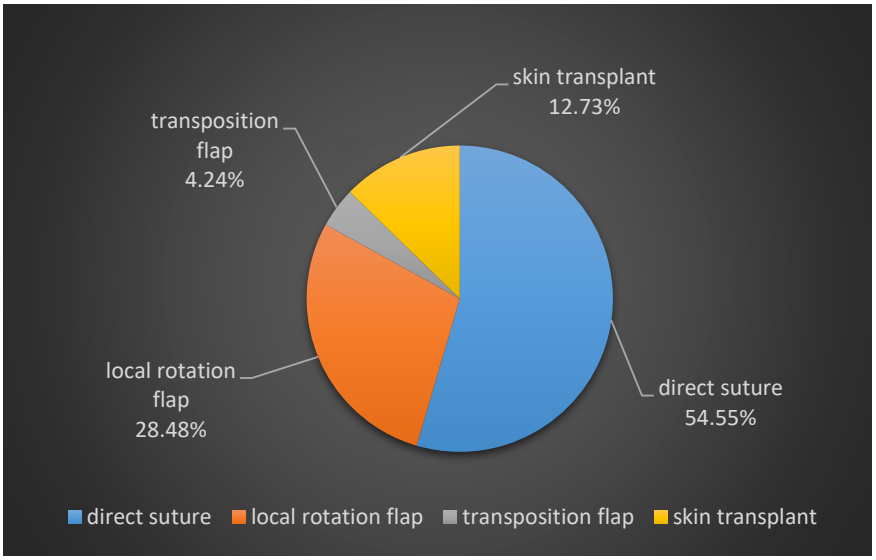

Chart 6. Distribution of surgical reconstruction methods

Because of the morpho-functional similarities and the reconstructive surgical features, we divided the middle facial region into several sub-regions.

Many of the tumor formations are located at the border between the aesthetic units of the face; Also the large tumor excision, respecting the oncological safety margins, does not always take into account the topographical limits of the consecutive subregions.

In correlation with the aesthetic units of the face, the table below shows the absolute and percentage incidence of cutaneous carcinomas in each subregion.

Subregion of the facial medial third	Number of casses	Percent
Nasal region	74	44,85%
Eyelid regions	51	30,91%
Infra-orbitar şi zygomatic regions	26	15,75%
Eyebrown region	6	3,64%
Temporal region	8	4,85%
TOTAL	165	

Tabel 5 - Sub-region distribution of the post-excisional skin defects

Nasal region

At the level of the nasal pyramid, the use of skin transplants has often resulted in less aesthetic results in terms of scar color in terms of scar tissue vascularization. The best results were obtained after using direct sutures (87%) and rotary flaps (76%).

Skin transplants used in the nasal pyramid caused the formation of hyper-pigmentation scars in 82% of cases. Thus, compared to the other surgical methods, we observed a difference with statistical significance ($p < 0.0001$) in the case of direct sutures, respectively ($p = 0.0002$) of the local flaps.

In order to cover post-excisional skin defects in the nasal pyramid, the use of direct suture techniques (97%), transposition flaps (71%), and rotation flaps (88%) led most of the time to the formation of scars with normal or almost normal flexibility.

The palpebral subregion

Patients evaluated in this study and operated at the level of the upper eyelid subregion benefited from two reconstructive surgical methods. It is the rotary flap as well as the direct stitch technique with the take-off of the edges of the post-excision skin defect. In the lower eyelid, free skin transplants (split or all thickness) were used, in addition to local flaps and direct suture techniques.

The use of skin transplants in the palpebral region (lower eyelid) resulted in scarring with a different appearance in terms of coloration due to vascularization compared to the adjacent skin in most cases (83.33%).

Rotation flaps and direct suture techniques used for the reconstruction of this region resulted in the best aesthetic results in terms of pigmentation of the scar area: 92% after using direct sutures and 83% after the use of rotating flaps.

In comparison with the results of the use of direct sutures ($p = 0.000039$) or rotation flaps ($p = 0.016827$), the use of skin transplants in the palpebral region resulted in lower aesthetic results, from the point of view of the occurrence of the height of the reconstructed area.

Infra-orbital and zigomatic subregions

At the level of infra-orbital and zigomatic regions, in addition to local flaps, direct suture techniques and free skin transplants (split or all thickness)

The use of skin transplants in the infra-orbital and zigomatic regions has resulted in discromic scars due to a degree of vascularization different from the adjacent skin in most cases.

Possible treatment methods start from direct skin suture eventually accompanied by additional take-off of the defect margins, the use of flaps that can be of variable complexity, and finally skin transplants that are commonly used to cover larger skin defects.

At the center of the discussion is the correlation between concrete aesthetic and functional results, and various surgical procedures of excision-reconstruction of cutaneous carcinomas, from the middle level of the face. At the same time, this study presents a comparison of several surgical methods used in important functional areas of the face such as the palpebral area or the nasal pyramid.

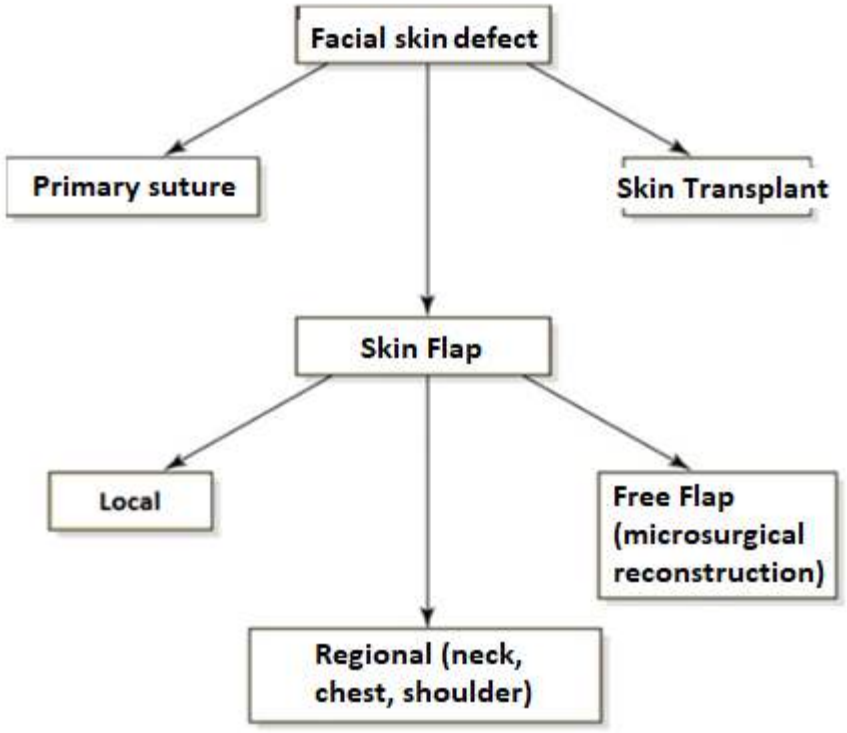

Figura 13 - Algorithm for Choosing the Surgical Method of Reconstruction of a Post-Excision Cutaneous Facial Disorder in the Middle Facial Floor

CONCLUSIONS

- Epithelial tumors are by the far the most common neoplasms, with as many cases of skin carcinomas diagnosed annually as all other cases of combined cancers; The main carcinogen is cumulative exposure to ultraviolet rays.
- Facial carcinomas are today a major medical-social problem through the psychologically major impact on the patient and his / her entourage.
- Due to its multiple and complex functions, the middle face is difficult to rebuild; Knowledge of geometry, biomechanics and stratigraphy of subregions must be

corroborated with the sense of aesthetics, shape and symmetry as well as the vision of the final result.

- The management of post-excisional skin defects should be systematized in the sense of initially approaching simple and effective methods.
- In the present study, by far, the most common are basal cell carcinomas followed by spinocellular carcinomas with a 4: 1 ratio in favor of basal-cell carcinoma.
- Skin carcinomas (basal-cellular and spinocellular) occur frequently in the head and neck regions.
- This study analyzes the postoperative results from a functional and aesthetic point of view, while recognizing the priority importance of oncological aspects.
- Direct sutures were most commonly used (54.55%); Even if it was necessary in some cases to further take off the edges of the defect, one can appreciate that simple techniques give the best cosmetic and functional results.
- The use of skin transplants has led to the formation of scars with a high degree of visibility. Moreover, the postoperative scar level differences compared to the skin surrounding it, play an important role in the good recovery of the final aesthetic appearance.
- Most of the color differences of the area in question occurred after the use of skin transplants. The use of skin transplants provides aesthetically poor results compared to local flaps (76% in the case of skin transplants compared to approximately 19% in the case of local flaps).
- Skin transplants at the tip of the nose have had aesthetic results weaker than direct sutures. However, these data should also be interpreted in terms of skin defect size and the impossibility of direct suture application for skin defects greater than 1 cm^2.
- For the temporal region, the most commonly used were direct sutures (64.28%), and in the case of larger defects the local skin flaps (explicitly the flap advanced) were preferred.
- In case of reconstruction of the palpebral regions after tumor excercise, direct suture can be achieved even if the eyelid skin was reduced to one-third. For larger defects (over 1.5 cm in cross-section), all-thickness skin transplants have been used as they provide better cosmetic results.

BIBLIOGRAPHY

1. Aasi SZ, Leffell DJ. Bilobed transposition flap. Dermatol Clin 2005; 23: 55 – 64.
2. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma: analysis of 1000 autopsied cases. Cancer 1950; 3:74-85.
3. Acarturk, T., Edington, H, „Nonmelanoma skin cancer," vol. 32, nr. 237-48, apr. 2005.
4. Ackermann PW, Hart DA: Influence of comorbidities: neuropathy, vasculopathy, and diabetes on healing response quality. Adv Wound Care (New Rochelle) 2013; 2: 410–421.
5. Alberdas JL, Shibahara T, Noma H: Histopathologic damage to vessels in head and neck microsurgery. J Oral Maxillofac Surg 2003; 61:191-196.
6. Albu I., Georgia R.: Anatomie topografică. Ediţia a II-a, Ed. ALL, Bucureşti. 1998; 1-10.
7. Almeida CA, Barry SA. Skin Cancer. In: Cancer: Basic Science and Clinical Aspects. New Jersey: Wiley- Blackwell, 2010.
8. Antohi N., Stîngu C., Stan V. - Reconstrucţia microchirurgicală a membrului pelvin. Ed. România Liberă, 2002, 91:95.
9. Amin A, Rifaat M, Civantos F, et al. Free anterolateral thigh flap for reconstruction of major craniofacial defects. J Reconstr Microsurg 2006; 22(2):97-104.
10. Arden R.L., Miguel G.S., „The subcutaneous melolabial island flap for nasal alar reconstruction: a clinical review with nuances in technique" The Laryngoscope, vol. 122, nr. 8:1685-9, august 2012.
11. Argenta LC, Watanabe MJ, Grabb WC - The use of tissue expansion in head and neck reconstruction. Ann Plast Surg 1983; 11:31.
12. Arlette, J.P. „Treatment of Bowen's disease and erythroplasia of Queyrat," British Journal of Dermatology, nr. 149:43, 2003.
13. Arlette JP, et al. Basal cell carcinoma of the periocular region. J Cutan Med Surg 1998;2(4):205.
14. Armstrong BK, Kricker A. The epidemiology of UV induced skin cancer. J Photochem Photobiol B 63:8-18, 2001
15. Bae SH, Bae YC: Analysis of frequency of use of different scar assessment scales based on the scar condition and treatment method. Arch Plast Surg 2014; 41: 111–115.
16. Bainton B.,Upton J.,Acland R., Shaw W.W., Finseth F.J..Rogers C., Pearl R., Hentz V.R. - Experience with the temporoparietal fascial free flap. Plast Recons.Surg.,2004,177-188.
17. Bakamjian, VY, Long M, Rigg B. Experience with medially based deltopectoral flap in reconstructive surgery of the head and neck. Br. J. Plast. Surg. 1971; 24: 174 – 183
18. Baker NJ, Webb AAC, Macpherson D. Surgical management of cutaneous squamous cell carcinoma of the head and neck. Br J Oral Maxillofac Surg,vol 39, issue 2, 2001, p 87-90.

19. Baker S., „Local flaps in facial reconstruction", Mosby-Elsevier, 2007, pp. 71-105.
20. Baker S. Nasal cutaneous flaps. In: Baker S. Principles of nasal reconstruction 2nd ed. Springer 2011, p 163-209.
21. Baker SR. Rotation flaps. In: Baker SR. Local Flaps in Facial Reconstruction 2nd ed. 2008 Mosby, 108-130.
22. Baker S. reconstruction of facial defects. In: Flint PW, Haughey BH, Lund VJ. Niparko JK. Richardson MA, Robbins KT, Thomas JR, editors. Cummings Otolaryngology: Head & Neck Surgery 5th ed. Mosby 2010, p 342-363.
23. Baker SR: The orbit and midface. In: Soutar DS, Tiwari R, ed. Excision and Reconstruction in Head and Neck Cancer, New York: Churchill Livingstone; 1994.
24. Bargman H, Hochman J. Topical treatment of Bowen's disease with 5-Fluorouracil. J Cutan Med Surg. Mar-Apr 2003;7(2):101-105.
25. Bath-Hextall FJ, Perkins W, Bong J, et al: Interventions for basal cell carcinoma of the skin. Cochrane Database Syst Rev 2007; 1:CD003412.
26. Bayramiçli M. A new classification system and an algorithm for the reconstruction of nasal defects. J Plast Reconstr Aesthet Surg. 2006; 59:1222–32.
27. Berger A., Hierner R., „Plastiche Chirurgie Band zwei Kopf und Hals", Springer, Berlin 2005, pp. 5-24.
28. Beausang E, Floyd H, Dunn KW, Orton CI, Ferguson MW. A new quantitative scale for clinical scar assessment. Plast Reconstr Surg 1998; 102:1954-1061.
29. Bordeianu I., Iordache I.V., Caraban B.M. – Chirurgie plastică și microchirurgie reconstructivă, Ed. Muntenia, Constanța, 2010.
30. Blondeel P.N., Morris S.F., Hallock G.G., „Perforator flaps: Anatomy, technique & clinical applications", Quality Medical Publishing, Inc; Louis, 2006.
31. Braathen LR, Szeimies RM, Basset-Seguin N, Bissonnette R, Foley P, Pariser D, et al. Guidelines on the use of photodynamic therapy for nonmelanoma skin cancer: an international consensus. International Society for Photodynamic Therapy in Dermatology, 2005. J Am Acad Dermatol. Jan 2007;56(1):125-43
32. Braverman, I.M „The cutaneous microcirculation," J Investig Dermatol Symp Proc vol. 5, nr. 3, 2000.
33. Bray R, Forrester K, Leonard C, McArthur R, Tulip J, Lindsay R. Laser Doppler imaging of burn scars: a comparison of wavelength and scanning methods. Burns 2003; 29:199-206.

34. Breidenbach WC, Trager S. -The use of quantitative cultures in determining succesful free flap closure of complex wounds. Abstracts of the Fourth Annual Meeting of the American Society for Reconstructive Microsurgery, Baltimore,1988.
35. Brewster DH, Bhatti LA, Inglis JH, Nairn ER, Doherty VR., „Recent trends in incidence of nonmelanoma skin cancers in the East of Scotland 1992-2003" British Journal of Dermatology June, nr. 156(6):1295–300, 2007.
36. Brown MD. Recognition and management of unusual cutaneous tumors. Dermatol Clin. 2000 Jul;18(3):543-52
37. Bruschi S., Marchesi Simona, Boriani F., „Forehead Flap for Lower One-Third Nasal Reconstruction", Annals of Plastic Surgery, 63:67-70, 2009.
38. Bunkis J, Mulliken JB, Upton J, Murray JE - The evolution of techniques for reconstruction of fullthickness defects. Plast reconstr Surg 70:319, 1982.
39. Burt JD, Burns AJ, Muzaffar AR, Byrd HS, Hobar PC, Beran SJ, Adan Kenkel J. - Total soft-tissue reconstruction of the middle and lower face with multiple simultaneous free flaps in a pediatric patient. Plast Reconstr Surg 2000 Jun;105(7):2440-7.
40. Chen WL, Yang ZH, Zhang DM, Huang ZQ, Fan S, Wang L. Reconstruction of majorfull cheek defects with combined extensive pedicled supraclavicular fasciocutaneous island flaps and extended vertical lower trapezius island myocutaneous flaps after ablation of advanced oral cancer. J Oral Maxillofac Surg. 2012 May;70(5):1224-31
41. Cheney M.L. – Facial Surgery Plastic and Reconstructive, Baltimore, Williams & Wilkins Company, 1997, 147-157.
42. Cheng F., Li Y., Zhang W., Zhu H., Wu H., Zhang Y., Yin S., "Reconstruction of external nose defect with local flaps," Journal of clinical otolaryngology - head and neck surgery, vol. 27, no. 23:1303-6, 2013.
43. Cherry G.W., Austad ED., Pasky K.,et al - Increased survival and vascularity of random pattern skin flaps elevated in controlled expanded skin. Plast Reconstr Surg 72:680, 1983
44. Chiotan N., Matusz P., Florescu I. „Cicatrizarea" – Naţional, București 1999
45. Chiotan N. (sub redacție) – Probleme actuale ale infecțiilor chirurgicale, Ed. Național, București, 2000, 5-67.
46. Choi Y, Lee JH, Kim YH, Lee YS, Chang HS, Park CS, et al. Impact of postthyroidectomy scar on the quality of life of thyroid cancer patients. Ann Dermatol 2014; 26:693-699.
47. Clevens R.A., Baker S.R., „Conceptual considerations in head & neck reconstruction. Defect analysis and options for reconstruction" Otolaryngologic Clinics of North America, vol. 30, nr. 4:495-517, 1997.

48. Clark CM, Furniss M, Mackay-Wiggan JM: Basal cell carcinoma: an evidence-based treatment update. Am J Clin Dermatol 2014; 15: 197–216
49. Cook TF, Fosko SW. Unusual cutaneous malignancies. Semin Cutan Med Surg. 1998 Jun;17(2):114-32
50. Cordoro L.R., Russel L. - Free flaps. Plastic Reconstructive Surgery 90:87, 2005.
51. Cormack & Lamberty. - The Arterial Anatomy of the Skin Flaps. Edinburgh Churchill Livingstone, 1986.
52. Cumberland L, Dana A, Liegeois N. Mohs micrographic surgery for the management of nonmelanoma skin cancers. Facial Plast Surg Clin North Am. 2009 Aug;17(3):325-35
53. Dessinioti C, Antoniou C, Katsambas A, et al: Basal cell carcinoma: what's new under the sun. Photochem Photobiol 2010; 86: 481–491.
54. DeVita, V., Hellman T., Rosenberg S. „Cancer: Principles & Practice of Oncology", 8th Edition, Lippincott Williams & Wilkins, Philadelphia, 2008.
55. Dubas LE, Ingraffea A. Nonmelanoma skin cancer. Facial Plast Surg Clin North Am. 2013 Feb;21(1):43-53
56. Draaijers LJ, Tempelman FR, Botman YA, Tuinebreijer WE, Middelkoop E, Kreis RW, et al. The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation. Plast Reconstr Surg 2004; 113:1960-1965.
57. Draaijers LJ, Tempelman FR, Botman YA, Kreis RW, Middelkoop E, van Zuijlen PP. Colour evaluation in scars: tristimulus colorimeter, narrow-band simple reflectance meter or subjective evaluation? Burns 2004; 30:103-107.
58. Enescu D.M., Bordeianu I. – Manual de chirurgie plastică, Ed. Ovidius University Press, Constanța, 2001.
59. Erovic. B., Lercher, P. „Manual of Head and Neck Reconstruction Using Regional and Free Flaps", Springer-Verlag, Wien, 2015.
60. Evans GR, Williams JZ, Ainslie NB. Cutaneous nasal malignancies: is primary reconstruction safe? Head Neck 1997; 19:182-187.
61. Florescu I., Bratu T., Matusz P., Chiotan N., „Tratamentul cicatricilor cutanate" – Ed. Mirton, Timişoara, 2002
62. Garner, Kyle L. et al. „Basal and squamous cell carcinoma," Primary Care: Clinics in Office Practice, vol. 27, nr. 2, 2000.
63. Giuglea Carmen, „Transferul liber microchirurgical ca modalitate de reconstrucție anatomică și funcțională a unor defecte post excizionale la nivelul capului și feței", teză de doctorat, U.M.F. Carol Davila, București, 2007.

64. Grigorescu-Sido Fr.: Anatomia omului. Generalităţi. Casa Cărţii de Ştiinţă, Cluj-Napoca. 1999; 20-25.
65. Goldman M.P., Weiss R., „Advanced Techniques in Dermatologic Surgery", Taylor & Francis Group, 2006.
66. Gonzales-Ulloa M - Reconstruction of the face covering by means of selective skin in regional aesthetic units. British Journal of Plastic Surgery 1986; 9:212.
67. Guy, G. P., Machlin, S. R., Ekwueme, D. U., & Yabroff, K. R., „Prevalence and Costs of Skin Cancer Treatment in the U.S., 2002–2006 and 2007–2011.," American Journal of Preventive Medicine, vol. 48(2), nr. 183–187, 2015.
68. Inyang M., Doerfler L., Strowd L., „Patient satisfaction with treatment of non-melanoma skin cancer," Expert Review of Quality of Life in Cancer Care, vol. 1, nr. 2, 2016.
69. Ha S.M., Back T. - Temporary arterio-venous shuting in microvascular free tissue transfer. J. West Pac. Orthop. Assoc.26:1,1999
70. Häfner, H., Schnabl, S., Breuninger, H., „Chirurgische Therapie der epithelialen Hauttumore und ihrer Vorstufen," Hautarzt, vol. 558, 2013.
71. Hafner J., Kempf W., Schmid H.M, Kurz M., Urosevic M., Dummer R., Burg G., „Epitheliale Hauttumore. Eine interdisziplinäre Aufgabe für Grundversorger und Spezialisten," Schweiz Med Forum, nr. 16, April 2002.
72. Herford A.S., Zide M.F., „Reconstruction of superficial skin cancer defects of the nose" Journal of oral and maxillofacial surgery, vol. 59, nr. 7:760-7, 2001.
73. Hicks D.L., Watson D., „Soft tissue reconstruction of the forehead and temple.," Facial Plastic Surgery Clinics North America, vol. 13, nr. 2, 2005.
74. Hilko, W. „Reconstructive facial plastic surgery – A problem-solving manual", Thieme, Stuttgart 2001, pp. 3-21.
75. Ho T, Byrne PJ. Evaluation and initial management of the patient with facial skin cancer. Facial Plast Surg Clin North Am. 2009 Aug;17(3):301-7
76. Idriss N, Maibach HI. Scar assessment scales: a dermatologic overview. Skin Res Technol 2009; 15:1-5.
77. Isac F. et al. Lambourile pediculate. Editura Mirton, Timişoara, 1995.
78. Jones N.F., Lister G.D., - Free Skin and Composite Flaps in Green's Operative Hand Surgery, Fourth Edition, 1999.
79. Kalus R, Zamora S., "Aesthetic considerations in facial reconstructive surgery: the „V-Y" flap revisited.," Aesthetic plastic surgery, vol. 20, no. 1:83-6, 1996.

80. Kraft S, Granter SR. Molecular pathology of skin neoplasms of the head and neck. Arch Pathol Lab Med. 2014 Jun;138(6):759-87
81. Kuo YR, Jeng SF, Wei FC, Su CY, Chien CY. Functional reconstruction of complexlip and cheek defect with free composite anterolateral thigh flap and vascularized fascia. Head Neck. 2008 Aug;30(8):1001-6
82. Lai Y.S., Weber R. S, „High-risk non-melanoma skin cancer of the head and neck", Current Oncology, 2005.
83. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33:159-174.
84. Lee DA, Miller SJ. Nonmelanoma skin cancer. Facial Plast Surg Clin North Am. 2009 Aug;17(3):309-24.
85. Li YY, Sun JE, Li G, Liang M. Reconstructing a full-thickness cheek defect ofelectrical burn with a folding radial forearm flap. J Oral Maxillofac Surg. 2013 Oct;71(10):1811
86. Lomas A, Leonardi-Bee J, Bath-Hextall F: A systematic review of worldwide incidence of nonmelanoma skin cancer. Br J Dermatol 2012; 166: 1069–1080.
87. Marks R., „Hauterkrankungen bei älteren Menschen", Deutscher Ärzte – Verlag, Berlin 1990.
88. Marinescu, R. „Plastia reconstructiva a defectelor faciale cu lambouri din vecinatate", Editura Didactica și Pedagogica, București 2002.
89. Mathes S.J. – Plastic Surgery 2nd Ed, Philadephia Sounders, 2006, vol. I, General Principles, 508-533.
90. Mathes S.J., Nahai F. - Reconstructive Surgery: Principles, Anatomy and Technique, New York, QMP/Churchill Livingstone, 1997
91. Mathes S.J., Nahai F. - Clinical Atlas of Muscle and Musculocutaneous Flaps. St Louis, C.V. Mosby Co, 1979.
92. McCarthy – Plastic Surgery – General Principles (vol.1), Sounders, London, 1990.
93. McCormack CJ, Kelly JW, Dorevitch AP: Differences in age and body site distribution of the histological subtypes of basal cell carcinoma. A possible indicator of differing causes. Arch Dermatol 1997; 133: 593–596.
94. McCraw J. Dibbell D. Carraway J. - Clinical definition of independent myocutaneous vascular territories. Plast Reconstr Surg. 1977;60.
95. McGregor A.D., Fundamental techniques of plastic surgery, Elsevier Limited, Tottenham, 2000.
96. Menick F.J., "Principles and Planning in Nasal and Facial Reconstruction: Making a Normal Face.," Plastic and reconstructive surgery, vol. 137, no. 6:1033e- 47e, 2016.

97. Mercandetti M. „Medscape," WebMD Health Professional Network, 3-4, 2013.Available: http://emedicine.medscape.com/article/1298129.
98. Miloro M., „Peterson's Principles of Oral and Maxillofacial Surgery", B.C. Decker Inc., Canada, 2009.
99. Mureau M., Moolenburgh Sanne, Levendag P., „Aesthetic and Functional Outcome following nasal suegery, Plastic Reconstructive Surgery, 2007.
100. Mullen J.T, Feng L., Xing Y., „Invasive Squamous Cell Carcinoma of the Skin: Defining a High-Risk Group", Annals of Surgical Oncology, 2010.
101. Naimer S.A., Biton A., Topaz M., „The subcutaneous loop: a single suture technique for skin closure after superficial and subcutaneous surgery.," Journal of drugs in dermatology, vol. 5, nr. 10: 966-8, 2006.
102. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Basal Cell Skin Cancer. Version 1.2015. 2014. http://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf.
103. Papel I., „Facial plastic and reconstructive surgery" 2nd ed., Thieme, 2002, pp. 3-61.
104. Pepper J.P., Baker S.R. „Local flaps: cheek and lip reconstruction.," JAMA Facial Plastic Surgery, vol. 15, nr. 5:374-82, 2013.
105. Pierpont YN, Dinh TP, Salas RE, et al: Obesity and surgical wound healing: a current review. ISRN Obes 2014; 2014: 1–13.
106. Piesold J., Vent S., Krüger R., Pistner H., „Operationergebnisse für Basalzellkarzinome des Kopf- und Halsbereiches nach verschiedener Rekonstruktionstechniken.," Mund Kiefer Gesichtschir., vol. 3, nr. 143-51, 2005.
107. Pribaz J.J., Caterson E.J., "Evolution and limitations of conventional autologous reconstruction of the head and neck.," The journal of cranio-facial surgery, vol. 24, no. 1:99-107, 2013.
108. Popian Șt. – chirurgia estetică și reparatoare a feței, Ed. Medicală, București, 1956, 140-145.
109. Poulsen, M., Burmeister, B., Kennedy, D., „Preservation of Form and Function in the Management of Head", World Journal Surgery, 2003.
110. Rapstine E.D., Knaus W.J., Thornton J.F., „Simplifying cheek reconstruction: a review of over 400 cases.," Plastic and reconstructive surgery, vol. 129, nr. 6:1291-9, 2012.
111. Reinstadler DR, Sinha UK. Uncommon cutaneous neoplasms of the head and neck. Facial Plast Surg Clin North Am. 2012 Nov;20(4):483-91
112. Riedel, F., Hörmann, K., „Plastische Deckung von Weichteildefekten im Gesicht," HNO - Prinzipien und Perspektiven, vol. 53:12 Springer, 2005.
113. Robinson, J. „Sun exposure, sun protection, and vitamin D," JAMA, vol. 294, nr. 1541-43, 2005.

114. Robinson JK, Anderson ER. Skin structure and surgical anatomy. In: Robinson JK, Hnke CW, Sengelmann RD, Siegel DM, editors Surgery of the skin. Philadelphia: Elsevier Mosby, 2005:6-10.
115. Rodriguez PG, Felix FN, Woodley DT, et al: The role of oxygen in wound healing: a review of the literature. Dermatol Surg 2008; 34:1159–1169.
116. Rohrich R.J., Griffin J.R., Ansari M., Beran S.J., Potter J.K. „Nasal reconstruction--beyond aesthetic subunits: a 15-year review of 1334 cases.," Plastic and reconstructive surgery, vol. 114, nr. 6:1405-16, 2004.
117. Roth JJ, Granick MS. Squamous cell and adnexal carcinomas of the skin. Clin Plast Surg. 1997 Oct;24(4):687-703.
118. Roques C, Teot L. A critical analysis of measurements used to assess and manage scars. Int J Low Extrem Wounds 2007; 6:249-253.
119. Roques C, Téot L, Frasson N, Meaume S. PRIMOS: an optical system that produces three-dimensional measurements of skin surfaces. J Wound Care 2003; 12:362-364.
120. Rustemeyer J., Bremerich A., „Outcomes after surgical treatment of facial skin basal cell carcinomas" Acta chirurgicae plasticae, vol. 48, nr. 3:89-92, 2006.
121. Sadler W.T.: Medizinsche Embryologie. Georg Thieme Verlag Stuttgart - New York. 1998: 322-376.
122. Salasche S., „Epidemiology of actinickeratoses and squamous carcarcinoma," Journal of American Dermatology, vol. 42, nr. 4-7, 2000.
123. Sheehan JM, Kingsley M, Rohrer TE. Excisional surgery and repair, flaps, and graft. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's dermatology in general medicine. 8th ed. New York: McGraw-Hill, 2012:2944-2949.
124. Siemionow Maria, Eisenmann-Klein Marita, „Plastic and Reconstructive Surgery", Springer, Hamburg 2010.
125. Skidmore R.A. Jr., Flowers F.P., „Nonmelanoma skin cancer," Med Clin North Am, vol. 82, nr. 1309-23, 1998.
126. Schöne P., „Retrospektive Untersuchung zur Epidemiologie, Ätiologie und Behandlung von Hauttumoren der Nase", Dissertation, Bochum, 2011.
127. Scrivener Y, Grosshans E, Cribier B: Variations of basal cell carcinomas according to gender, age, location and histopathological subtype. Br J Dermatol 2002; 147: 41–47.
128. Silverman N, Shinder R. What's New in Eyelid Tumors. Asia Pac J Ophthalmol (Phila). 2017 Mar-Apr;6(2):143-152

129. Sobanko JF, Sarwer DB, Zvargulis Z, Miller CJ. Importance of physical appearance in patients with skin cancer. Dermatol Surg 2015; 41:183-188.
130. Son D, Harijan A: Overview of surgical scar prevention and management. J Korean Med Sci 2014; 29: 751.
131. Slutsky JB, Jones EC. Periocular cutaneous malignancies: a review of the literature. Dermatol Surg. 2012 Apr;38(4):552-69
132. Sgonc R, Gruber J: Age-related aspects of cutaneous wound healing: a mini-review. Gerontology 2013; 59: 159–164.
133. Sullivan T, Smith J, Kermode J, McIver E, Courtemanche DJ. Rating the burn scar. J Burn Care Rehabil 1990; 11:256-260.
134. Takiwaki H. Measurement of skin color: practical application and theoretical considerations. J Med Invest 1998; 44:121-126.
135. Tan P-Y, Ek E., Su Shirley, „Incomplete Excision of Squamous Cell Carcinoma of the Skin: A Prospective", Plastic Reconstructive Surgery 120: 910, 2007
136. Taylor B, McGrouther DA, Bayat A. Use of a non-contact 3D digitiser to measure the volume of keloid scars: a useful tool for scar assessment. J Plast Reconstr Aesthet Surg 2007; 60:87-94.
137. Telfer NR, Colver GB, Morton CA; British Association of Dermatologists: Guidelines for the management of basal cell carcinoma. Br J Dermatol 2008; 159: 35–48.
138. Thomas D.J., King A. R., Peat B., „Excision Margins for Nonmelanotic Skin Cancer", Plastic Reconstructive Surgery, Jul;112(1):57-63, 2003.
139. Tost, F. "Periocular surgery and the impact of split-thickness skin grafts," Klinische Monatsblatter fur Augenheilkunde, vol. 228, no. 1:35-40, 2011.
140. Tuncel U, Aytaç S. Reconstruction of full-thickness cheek defects with using free osseocutaneous radial forearm flap. J Craniofac Surg. 2012 Jul;23(4)
141. Truong PT, Lee JC, Soer B, Gaul CA, Olivotto IA. Reliability and validity testing of the Patient and Observer Scar Assessment Scale in evaluating linear scars after breast cancer surgery. Plast Reconstr Surg 2007; 119:487-494.
142. Van de Kar AL, Corion LU, Smeulders MJ, Draaijers LJ, van der Horst CM, van Zuijlen PP. Reliable and feasible evaluation of linear scars by the Patient and Observer Scar Assessment Scale. Plast Reconstr Surg 2005; 116:514-522.
143. Velupillai I., Madan E., Tian Ee S., „Local Flaps in Facial Reconstruction", Springer International Publishing, Switzerland-Berna: 2015.

144. Viola KV, Jhaveri MB, Soulos PR, Turner RB, Tolpinrud WL, Doshi D, et al. Mohs micrographic surgery and surgical excision for nonmelanoma skin cancer treatment in the Medicare population. Arch Dermatol 2012; 148:473-477.
145. Weathers WM, Bhadkamkar M, Wolfswinkel EM, Thornton JF. Full-thickness skin grafting in nasal reconstruction. Semin Plast Surg 2013; 27:90-95.
146. Wei Y, Li-Tsang CW, Luk DC, Tan T, Zhang W, Chiu TW. A validation study of scar vascularity and pigmentation assessment using dermoscopy. Burns 2015; 41:1717-1723.
147. Wells MD, Luce EA., "Reconstruction of midfacial defects after surgical resection of malignancies.," Clinics in plastic surgery, vol. 22, no. 1:77-79, 1995.
148. Wozniak K, Sommer F., "Surgical management of entropion," Der Ophtalmologe, vol. 107, no. 10:905-10, 2010.
149. Wu, T., "Plastic surgery made easy - simple techniques for closing skin defects and improving cosmetic results," Australian family physician, vol. 35, no.7:492-6, 2006.
150. Wysong A, Aasi SZ, Tang JY: Update on metastatic basal cell carcinoma: a summary of published cases from 1981 through 2011. JAMA Dermatol 2013; 149: 615–616.
151. Zavos G, Karidis NP, Tsourouflis G, Bokos J, Diles K, Sotirchos G, Theodoropoulou E, Kostakis A. Nonmelanoma skin cancer after renal transplantation: a single-center experience in 1736 transplantations. Int J Dermatol. 2011 Dec;50(12):1496-500
152. Zeplin P.H., Schmidt K., Laske M., Ziegler U.E., „Comparison of various methods and materials for treatment of skin laceration by a 3-dimensional measuring technique in a pig experiment.," Annals of plastic surgery, vol. 58, nr. 5:566-72, 2007.
153. Zhang W., Zhang Y., Wu H., Zhu H., Cheng F., Yin S. „Reconstruction of large external nose defect with forehead flap," Journal of Otolaryngology, Head and Neck Surgery, vol. 26, nr. 23:1057-60, 2012.
154. Zhou W, He M, Liao Y, Yao Z. Reconstructing a complex central facial defect with a multiple-folding radial forearm flap. J Oral Maxillofac Surg. 2014 Apr;72(4):836