Rīgas Stradiņa universitāte

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HEAD AND NECK BASAL CELL CARCINOMA TREATMENT

Summary of the Doctoral Thesis
for obtaining the degree of a Doctor of Medicine

Specialty – Oncology

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The present Doctoral Thesis has been conducted at the Riga East University Hospital, Latvian Oncology Centre. It has been approved by the Ethics Committee of RSU, 23 September 2010.

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The Doctoral Thesis is available at the RSU library and on the RSU web page: www.rsu.lv

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INTRODUCTION

Skin cancer is one of the most common cancer forms [1–5] .

Basal cell carcinoma (BCC) is the most common malignant tumor in Latvia and all over the world [6, 7]. BCC is slow-growing, locally invasive malignant epidermal skin tumor, with very limited capacity to metastasize [7, 8]. Death is caused by wide areas of defective tissue on head and neck, that impact functionality of vital organs and vessels [9, 10].

In the past years, there has been an increasing incidence of BCC – this type of tumor amounts to 5–10% among skin cancer patients [7]. Until now, BCC was considered a disease of the elderly. However, in the past few years, there has been a significant increase in middle - aged patients diagnosed with BCC. For these patients, not only is it important to treat the tumor, but so is the cosmetic outcome that can impact the social rehabilitation of the patient [4, 11–13].

The main peculiarities of BCC are: its frequent recurrence, long development process, localization in such cosmetically important places as nose, lips, forehead, cheeks, eyelids, ears, scalp and neck. Preceding localizations are common in 80–90% of cases [7, 14]. Frequent recurrence is one of the most common problems in treatment of BCC patients. Most often, recurrence develops in 0.5–3 year period after the end of treatment [15, 16]. Although, in some cases recurrence is detected after 5–10 years [3, 17, 18]. The recurrence rate of primary tumors depends on the treatment method and is present in 1–28% of all cases, repeated recurrenece in the same place is detected in 4.8–42.8% cases [2, 3, 9, 17–24]. The difficulty in choosing a treatment method lies in the inability of any treatment method to guarantee non-recurrence. According to various authors, the recurrence rate differs according to chosen treatment method [25–30].

During the last 10 years, the quality of life has become very important for skin cancer patients. It has been proven that all head and neck BCCs can create a different level cosmetics defect, independent of the treatment method. These visual defects impact the quality of life of the patient, causing deep impact on the physical state of the patient and can cause psychopatological reactions [31]. Psychological borderline is detected in 82% among basal cell carcinoma patients [32]. Changes in psychological state significantly impact the treatment process of the malignant tumor, social rehabilitation, employment and quality of life in general [31–33].

Therefore, the frequent incidence, frequent recurrence and localization on head and neck, and the cosmetict defects that reduce the quality of life, create the necessity to choose the most effective and cosmetically appropriate treatment method [3, 34–36].

Complicated and up-to-date question is in the choice of the most optimal treatment method, in order to achieve satisfactory cosmetic result, and taking into account the necessity to divest new tumors and reach resistant clinical effect.

Aim of the work

To determine the efficacy of different head and neck basal cell carcinoma treatment methods, taking into consideration clinical and histological types, size and exact anatomic localization, as well as compare these treatment methods with respect to cosmetic results.

Tasks

Task fulfilment is based on the follow up data for more than 5 years.

1. Analyze head and neck basal cell carcinoma clinical picture and recurrence rate.

2. Compare four treatment methods (surgery, radiotherapy, laser surgery and cryosurgery) efficacy with respect to development of recurrence.
3. Analyze recurrence rates after surgery, radiotherapy, laser surgery and cryosurgery with respect to primary head and neck basal cell carcinoma clinical and histological type, size and exact anatomic localization.
4. Determine factors that reduce the possibility of surgery, radiotherapy, laser surgery and cryosurgery for head and neck basal cell carcinoma treatment.
5. Evaluate and compare efficacy of different treatment methods in more than 5 year non-recurrence cases, taking into account cosmetic results.
6. Develop recommendations for the choice of head and neck basal cell carcinoma treatment methods, depending on clinical and histological type, size, exact anatomic localization, gender, age and cosmetic results.

Scientific innovation

First time performed:

1. Complex head and neck basal cell carcinoma treatment method comparative analysis after more that 5 year follow up period.
2. Complex comparative analysis of different head and neck basal cell carcinoma treatment methods with respect to clinical and histological types with exact anatomic localisation and sizes.
3. Comparative analysis of cosmetic results after head and neck basal cell carcinoma treatment with more than 5 years non recurrence follow up.

Practical novelty

Research results enable to develop treatment algorithm, depending on clinical and histological types, size and exact anatomic localization. Developed treatment algorithm and “Unified skin cancer patient clinical card” can be

recommended for the use by dermatologists, surgeons and oncologists in outpatient practice.

Proposed hypothesis

In case of specific clinical and histological types, sizes and exact localization of head and neck basal cell carcinoma, such alternative treatment methods as radiotherapy, laser surgery, cryosurgery are as efficient as traditional treatment method – surgery. Moreover, alternative treatment methods have good cosmetic results.

Research time and place

Research was performed from November, 2010 until September, 2013 in Latvian Oncology Center of Riga Eastern Clinical University Hospital.

Personal investment

Analysis of available literature, development of research design and coordination in the Ethics Committee of RSU, selection of patient medical documentation, systematisation of medical data with respect to chosen criteria, patient's routine health analysis, research summary, development of practical recommendations, writing of articles and Doctoral thesis.

Research amount and structure

Research is written in Latvian. It consists of following parts: introduction, literature review, methods and materials, results, discussion, conclusions and used literature sources. Research consists of 138 pages. There are 39 tables, 13 figures and 5 Appendices. There are 235 headings in the footnotes.

Ethics Committee permit

Research is accepted by Rīga Stradiņš university Ethics Committee on 23th of September 2010.

1. METHODS AND MATERIALS

1.1. Research type, permission of Ethics Committee

Research type – retrospective. Research is accepted by Rīga Stradinš University Ethics Committee decision on 23 September 2010.

1.2. Research structure

Research consists of 2 parts: **1 part** – efficacy analysis of different head and neck basal cell carcinoma treatment methods, taking into account development of recurrence (observation performed more than 5 years after the treatment) (futher in the text "recurrence analysis"); **2 part** – efficacy analysis of head and neck basal cell carcinoma treatment methods, taking into account the cosmetic results (futher in the text "scar analysis"), if during more than 5 year follow up period there was no recurrence.

1st stage of research: Construction of research sample: selection of medical documentation according to particular criteria in the time period from 1st of January of 2010 until 30th of December 2005.

2nd stage of research: work with selected medical documentation: systematisation of medical data, according to chosen criteria.

3rd stage of research: recurrence analysis – comparative analysis and different treatment method efficacy detection, taking into account clinical and histological types, size and exact anatomic localisation.

4th stage of research: comparative analysis of different treatment methods, taking into account the cosmetic results. This stage has several substages: 1) analysis of cases if there was no BCC recurrence during the follow up in more than 5 years; 2) meetings with patients, execution of informative agreement, performing patient routine health check, questionnairing and taking photography of the scar; 3) cosmetic results evaluation by experts; 4) comparative analysis of obtained data.

5th stage of research: Development of head and neck BCC treatment algorithm. Establishment of treatment calculator.

Figure 1.1. shows the structure of the research which consists of five connected stages.

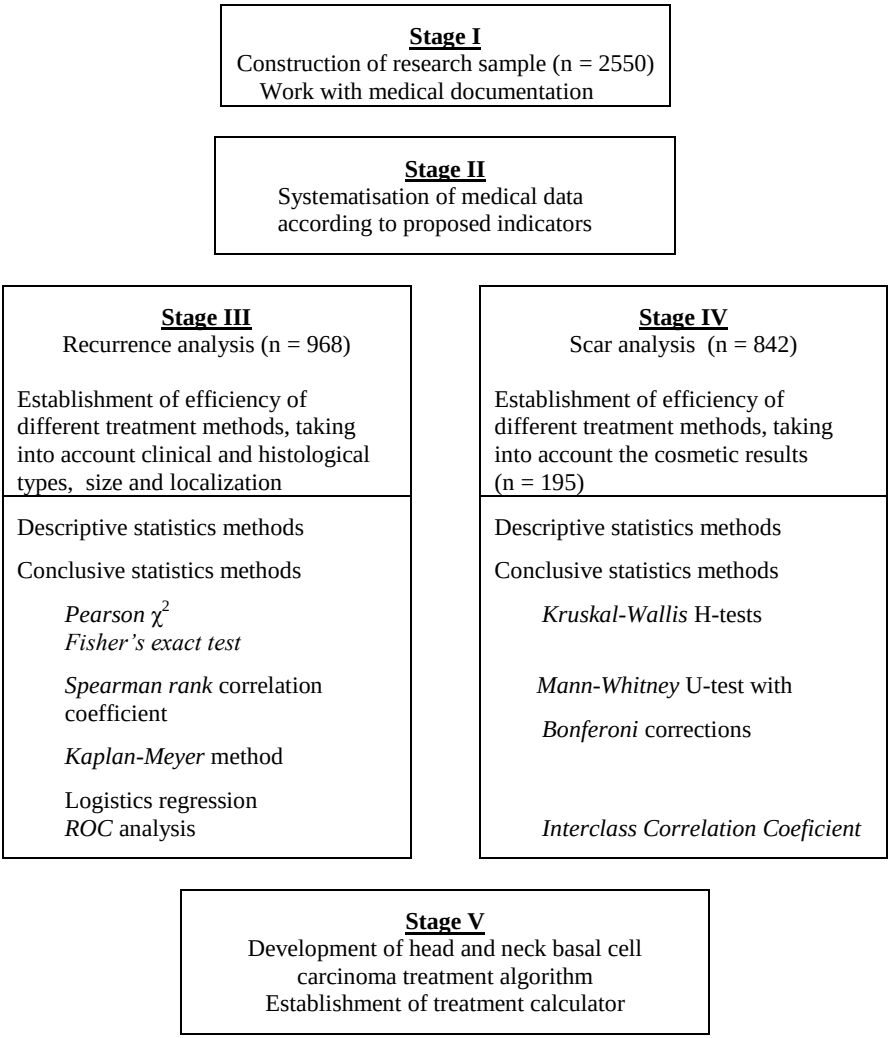

Figure 1.1. **Research structure**

1.3. Development of research sample

Patients who were treated in LOC from January 1, 2000 until December 31, 2005 were selected for the research [6]. For patient selection, medical documentation data was used (outpatient medical card – form Nr. 025/u).

Criteria for patient selection into the research: 1) morphologically (histologically or cytologically**)** verified diagnosis – primary BCC with T1-T2N0M0 (according to UICC 2009 TNM classification, 7th edition); 2) over 18 years of age; 3) BCC localisation on head and neck with International statistical illness and health problem codes C44.0 – skin of lip, C44.1 – skin of eyelid, C44.2 – external ear, C44.3 – skin of other and unspecified parts of the face, C44.4 – skin of scalp and neck; 4) patients are alive and consult in LOC for more than 5 years from the beginning of treatment; 5) doctors who performed treatment have worked in oncology for no less than 10 years.

Criteria for not selecting patients for the research: 1) patients who received combined treatment; 2) patients who declined treatment; 3) patients who did not show up for the control for more than 5 years; 4) patients whose ambulatory cards were not found.

In the first part of the research, 968 patients were included. In the following work with medical documentation, all patients were divided into four groups, according to the treatment methods. Second part of the research consisted of patients in whom the recurrence was not monitored for more than 5 years – it consisted of 842 patients. There were 195 patient photographs selected for expert evaluation.

1.4. Description of research methods

For the first part of the research, it was necessary to systematize research data and further systematic analysis, therefore the author created "indication classificator". In this classificator following information was included:

1) patient identification data (script of medical cards), 2) patient demographic data (age, gender), 3) localisation of tumor according to UICC 2009 TNM classification, 4) exact anatomic localization (lip, eyelid, ear, nose, cheek, neck, forehead, scalp and chin; 5) tumor size in milimeters (mm) – according to NCCN recommendation division of face, head and neck skin into H and M zones, there were 4 research groups constructed and analysed, where tumor sizes were < 6 mm, 6–10 mm, 11–20 mm and > 20 mm [7]; 6) Clinical forms of BCC (superficial, nodular, infiltrative) and tumor histological type;
7) treatment date, 8) chosen treatment type, 9) presence of recurrence; date when primary recurrence was diagnosed; 10) duration of patient observation.

In the second part of the research, cosmetic results were evaluated – independent exprets performed evaluation according to Visual Analogue Scale *(VAS)* [37].

1.5. Statistical analysis procedure

1 part: comperative efficiency analysis of different BCC treatment methods.

Comparative analysis of recurrence rate was performed, taking into account clinical and histological form, exact anatomic localization, size, patients' age and gender. For primary data description, descriptive statistics were used to determine statistically significant differences between surgery and other treatment methods. Time until recurrence and overall follow up time was analyzed using *Kaplan-Meier* method. For analysis of non-parametric data *Pearson $\chi 2$* and *Fisher's Exact test* was performed (in case if in any table the number of expected values is less than 5 [38]. It was agreed that results are statistically significant if $p < 0.05$. In order to detect relationship between treatment result and tumor characterizing values, as well as demographic data, multifunctional binary logistics regression analysis and *ROC* (*Receiver Operating Charateristic*) were used. In order to evaluate correlation between

BCC recurrence rate and size, as well as patient demographic data (age, gender), *Spearman's rank* correlation coefficient was performed.

2 part: comparative efficacy analysis of head and neck basal cell carcinoma treatment methods, taking into account the cosmetic results, is based on the expert evaluation. For general description of obtained data, descriptive statistics were used. Prior to using conclusive statistics elements, consensus of expert responses has to be checked. In order to perform this analysis, *Intraclass Correlation Coefficient* (ICC) is used in each group. Furhtermore, data were analyzed using *Kruskal-Wallis* H-test criteria, in order to determine statistically significant differences in evaluation of cosmetic results. In order to determine statistically significant differences between treatment methods, *Mann-Whitney* U-test with *Bonferroni adjustment* was used for *p* value significance, which enabled the comparision of groups in pairs [38].

Statistical data analysis was performed using IBM SPSS v.20.0 software.

2. RESULTS

2.1. Sample description

Ambulatory patient cards were used in the research for 968 patients – 634 women (65.5%) and 334 men (34.5%). Data on patients who were assigned one of the four treatments are analysed separately in table 2.1.

Table 2.1.

Demographic data of the sample

	Patients, n	Men, n (%)	Women, n (%)	Average age, M	Standart deviation SD	Min	Max	Age mode
Surgery	273	107 (39.2%)	166 (60.8%)	62.14	13.61	20	87	60
Radiotherapy	223	109 (48.9%)	114 (51.1%)	69.33	12.02	28	87	77
Laser surgery	341	66 (19.4%)	275 (80.6%)	63.74	12.97	26	92	75
Cryosurgery	131	52 (39.7%)	79 (60.3%)	67.58	7.94	42	86	70
Total	968	334 (34.5%)	634 (65.5%)	65.10	12.68	20	92	70

2.2. Analysis of BCC recurrence peculiarities

BCC recurrence peculiarities are displayed in Tables 2.2., 2.3., 2.4. and Figure 2.1., 2.2.

Table 2.2.

Recurrence distribution by clinical and histological types

BCC types	n	R	R, %
Superficial	388	42	10.82
Nodular	536	57	10.64
Infiltrative	44	27	61.36
Total	968	126	13.02

n – total number of cases in the group; R – number of recurrence; R, % – recurrence rate

Table 2.3.

Distribution of BCC recurrence by tumor size

Tumor size, mm	n	R	R, %
< 6 mm	184	11	5.98
6 – 10 mm	626	84	13.42
11 – 20 mm	117	24	20.51
> 20 mm	41	7	17.07

n – total number of cases in the group; R – number of recurrence; R, % – recurrence rate

After performing correlation analysis, it was concluded that there is positive statistically significant correlation between tumor size and recurrence rate – *Spearman's rank* correlation coefficient $p = 0.01$.

Reccurrence rate with exact anatomic localization of tumor is presented in Figure 2.1.

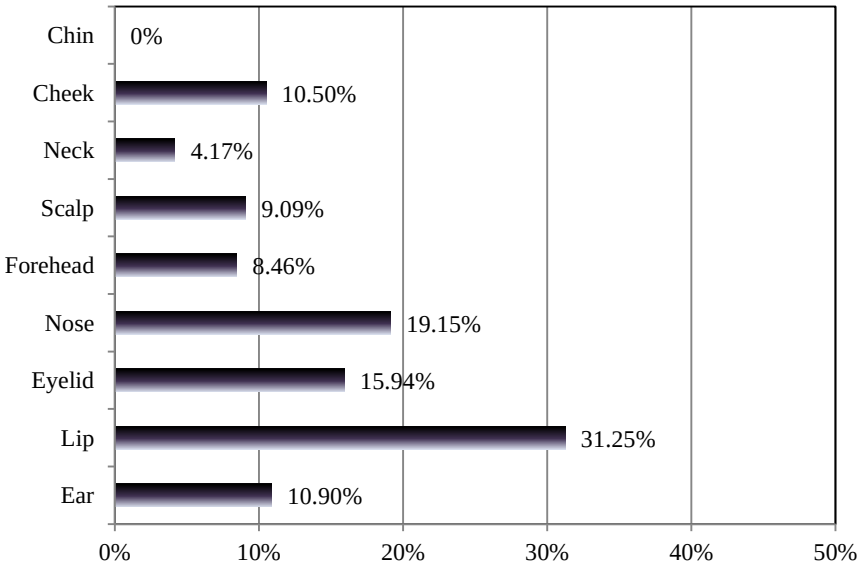

Figure 2.1. **Distribution of BCC recurrence (%) by exact anatomic localization**

Statistically significant differences were not present when tested against gender: recurrence among women was present in 13.41% cases, among men – 12.27%. Performing *Spearman's rank* analysis, it was concluded that there is no statistically significant correlation between gender and recurrence rate.

BCC recurrence rate (%) by patients' age is presented in Figure 2.2.

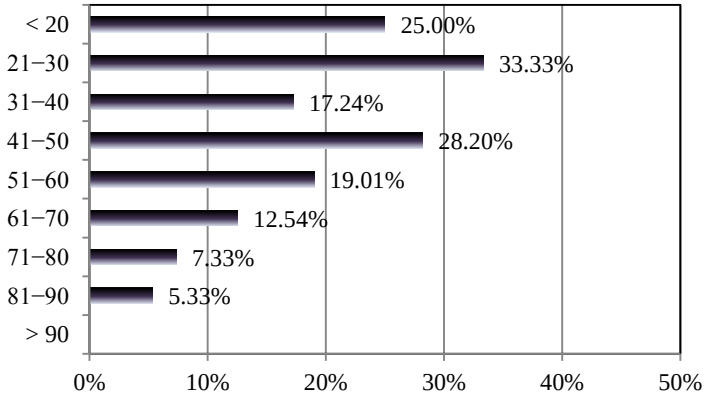

Figure 2.2. **BCC recurrence rate (%) by age**

Correlation analysis showed that there is statistically significant negative correlation between age and recurrence rate – *Spearman's rank* correlation coefficient $p = 0.01$.

Kaplan-Meyer method showed that median time of recurrence is 22.0 months (Table 2.4).

Table 2.4.

Time (months) until BCC recurrence: arithmetic average and median

Treatment method	Arithmetic average time until recurrence (M), months				Time until recurrence median, months			
	Cal-culated	Standard deviation	95% Confidence interval (TI)		Cal-culated	Standard deviation	95% Confidence interval (TI)	
			Lover level	Upper level			Lover level	Higher level
Surgery	36.0	5.9	24.4	47.6	24.0	8.4	7.5	40.5
Radiotherapy	42.1	7.1	28.2	55.9	36.0	4.2	27.8	44.2
Laser surgery	22.4	2.3	18.0	26.8	19.0	2.7	13.6	24.4
Cryosurgery	30.0	4.7	20.8	39.1	20.0	3.5	13.0	26.9
Total	30.2	2.3	25.7	34.7	22.0	1.8	18.5	25.5

2.3. Efficacy analysis of different head and neck BCC treatment methods

The main efficacy criteria of BCC treatment method is lack of recurrence [3, 7]. Therefore, it is necessary to compare recurrence rate after surgery and after other treatment methods (radiotherapy, laser surgery and cryosurgery). Moreover, the factor that promotes recurrence is not only the chosen treatment method, but also the clinical and histological form, size as well as exact anatomic localization.

2.3.1. Regularity of BCC recurrence rate depending on treatment method and relationship between different tumor characterizing factors

Descriptive statistics of recurrence rate in relationship with treatment method are presented in Table 2.5., 2.6., 2.7., 2.8. and Figure 2.3.

Table 2.5.

BCC recurrence rate distribution by treatment method

Treatment method	n	R	R, %
Surgery	273	25	9.2
Radiotherapy	223	19	8.5
Laser surgery	341	47	13.8
Cryosurgery	131	35	26.7
Total	968	126	13.02

n – total number of cases in the group; R – number of recurrence; R, % – recurrence rate

Table 2.6.

BCC recurrence rate distribution by clinical and histological form and treatment method

BCC types	Surgery			Radiotherapy			Laser surgery			Cryosurgery		
	n	R	R,%	n	R	R,%	n	R	R,%	n	R	R,%
Superficial	70	4	5.7	100	5	5.0	137	14	10.2	81	19	23.5
Nodular	184	17	9.2	116	8	6.9	188	18	9.6	48	14	29.2
Infiltrative	19	4	21.1	7	6	86.0	16	15	93.8	2	2	100.0

n – total number of cases in the group; R – number of recurrence; R, % – recurrence rate

Table 2.7.

Distribution of BCC recurrence by tumor size and treatment method

Tumor size, mm	Surgery			Radiotherapy			Laser surgery			Cryosurgery		
	n	R	R,%	n	R	R,%	n	R	R,%	n	R	R,%
< 6	55	1	2.0	25	2	8.0	73	5	6.8	31	3	9.7
6−10	159	13	8.2	145	9	6.2	232	34	14.7	90	28	31.1
11−20	38	8	21.1	39	6	15.4	30	6	20.0	10	4	40.0
> 20	21	3	14.3	14	2	14.3	6	2	33.3	–	–	–

n – total number of cases in the group; R – number of recurrence; R, % – recurrence rate

Table 2.8.

BCC recurrence rate distritbution by exact anatomic localization and treatment method

Exact anatomic localisation	Surgery			Radiotherapy			Laser surgery			Cryosurgery		
	n	R	R,%	n	R	R,%	n	R	R,%	n	R	R,%
Ear	28	1	3.6	14	1	7.0	8	2	25.0	5	2	40.0
Lip	5	0	0	2	0	0	7	3	42.9	2	2	100.0
Eyelid	31	5	16.1	17	3	18.0	19	3	15.8	2	0	0
Nose	68	8	12.0	60	9	15.0	129	22	17.1	51	20	39.2
Forehead	38	1	2.6	45	1	2.2	77	8	10.4	29	6	20.7
Scalp	30	4	13.3	38	2	5	10	0	0	10	2	20.0
Neck	17	1	6.0	4	0	0	14	1	7.1	13	0	0
Cheek	51	5	9.8	41	3	7.3	70	8	11.4	19	3	15.8
Chin	5	0	0	2	0	0	7	0	0	5	0	0

n – total number of cases in the group; R – number of recurrence; R, % – recurrence rate

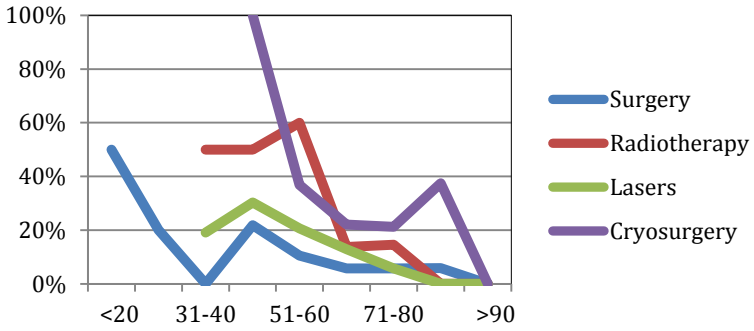

Figure 2.3. **BCC recurrence rate (%) by age and treatment method**

2.3.2. Comparative analysis of BCC recurrence rate, taking into account the clinical and histological form, size and exact anatomic localization

Comparison of BCC recurrence rate by clinical and histological form, size and exact anatomic localization is presented in Tables 2.9., 2.10. and 2.11.

Table 2.9.

Comparison of BCC recurrence rate by clinical and histological form and treatment method

BCC types	Radiotherapy, *p*	Laser surgery, *p*	Cryosurgery, *p*
Superficial	1.000 ns	0.227 ns	0.002 **
Nodular	0.475 ns	0.912 ns	<0.001 ***
Infiltrative	0.005 **	<0.001 ***	<0.001 ***

p – Pearson χ^2 vai *Fisher's exact test*, ns – not significant difference

Table 2.10.

Comparison of BCC recurrence rate by tumor size and treatment method

Tumor size, mm	Radiotherapy, *p*	Laser surgery, *p*	Cryosurgery, *p*
< 6	0.229 ns	0.236 ns	0.131 ns
6 – 10	0.508 ns	0.053	<0.001 ***
11 – 20	0.519 ns	0.915 ns	<0.001 ***
> 20	1.000 ns	0.303 ns	–

p – Pearson χ^2 or *Fisher's exact test* ; "–" – no patients with recurrence

Table 2.11.

Comparison of BCC recurrence by exact anatomic localisation and treatment method

Exact anatomic localization	Radiotherapy, *p*	Laser surgery, *p*	Cryosurgery, *p*
Ear	1.000 ns	<0.001 ***	0.053 *
Lip	–	<0.001 ***	0.048 *
Eyelid	1.000 ns	1.000 ns	1.000 ns
Nose	0.590 ns	0.326 ns	<0.001 ***
Forehead	1.000 ns	0.268 ns	0.037 *
Scalp	0.394 ns	0.556 ns	0.629 ns
Neck	1.000 ns	1.000 ns	1.000 ns
Cheeck	0.728 ns	0.776 ns	0.678 ns
Chin	–	–	–

p – Pearson χ^2 or *Fisher's exact test* ; "–" – no patients with recurrence

2.3.3. The prognosis of BCC recurrence peculiarities in connection with treatment method, clinical and histological form, size, exact anatomic localization and sample demographic data

Multifunctional binary logistics regression was used for each treatment method separately. Logistics regression model is used for five non related variables: clinical and histological form, size, exact anatomic localization, gender and age.

Surgery: overall model is statistically significant at the $p < 0.001$ level. Binary logistics regression on probability of recurrence after surgery is:
logit (probability of recurrence after surgery) = – 1.293 – 0.482 × age + 0.721 × BCC size.

Radiotherapy: overall model is statistically significant at the $p < 0.001$ level. Binary logistics regression on probability of recurrence after radiotherapy is: *logit (probability of recurrence after radiotherapy) = – 3.226 – 0.361 × age + 1.699 × clinical and histological form.*

Laser surgery: overall model is statistically significant at the $p<0.001$ level. Binary logistics regression on probability of recurrence after laser surgery is: *logit (probability after laser surgery) = – 1.655 – 0.184 × localization – 0.502 × age + 0.694 × size + 1.182 ×* clinical and histological form.

Cryosurgery: overall model is statistically significant at the $p<0.001$ level. Binary logistics regression on probability of recurrence after cryosurgery is: *logit (probability of recurrence after cryosurgery) = – 1.185 – 0.453 × localization + 1.2450 × size.*

2.3.4. Summary analysis of different BCC treatment methods

Results analysis of different BCC treatment methods is summarised in Table 2.12.

Table 2.12.

BCC recurrence rate after different treatment methods

BCC	Surgery		Radiotherapy			Laser surgery			Cryosurgery		
	R,%	Log R	R,%	χ^2	Log R	R,%	χ^2	Log. R	R,%	χ^2	Log R
Superficial	5.7		5.0	–	0.001 ***	10.2	–	<0.001 ***	23.5	0.002 **	
Nodular	9.2		6.9	–		9.6	–		29.2	<0.001 ***	
Infiltrative	21.1		86.0	0.005 **		93.8	<0,001 ***		100.0	<0.001 ***	
< 6 mm	2.0	0.002 **	8.0	–		6.8	–	0.02 *	9.7	–	0.004 **
6–10 mm	8.2		6.2	–		14.7	0,053		31.1	<0.001 ***	
11–20 mm	21.1		15.4	–		20.0	–		40.0	<0.001 ***	
> 20 mm	14.3		14.3	–		33.3	–		No	No	
Ear	3.6		7.0	–		25.0	<0,001 ***	0.049 *	40.0	0.053	0.001 ***
Lip	0		0	–		42.9	<0,001 ***		100.0	0.048 *	
Eyelid	16.1		18.0	–		15.8	–		0	–	
Nose	12.0		15.0	–		17.1	–		39.2	<0.001 ***	
Forehead	2.6		2.2	–		10.4	–		20.7	0.037 *	
Scalp	13.3		5.0	–		0	–		20.0	–	
Neck	6.0		0	–		7.1	–		0	–	
Cheeck	9.8		7.3	–		11.4	–		15.8	–	
Chin	0		0	–		0	–		No	No	
Age		0.002 **			0.033 **			<0.0 01 ***			

BCC – basal cell carcinoma; R, % – recurrence rate; χ^2 – *Pearson* χ^2 (only significant results are presented in the table, "—" result is not statistically significant); Log.R – logistics regression; table displays only those variables that have statistically significant impact on recurrence; No – no cases

2.4. Comparative analysis of different treatment methods in relationship with cosmetic results

For this research part, 195 photographs were selected on random basis. Descriptive statistics on expert evaluation of cosmetic results by treatment method are presented in Table 2.13. and 2.14.

Table 2.13.

Cosmetic results evaluation by doctors and patients

Treatment method	Average, M (doctors)	Average, M (patients)	Average, Me (doctors)	Average, Me (patients)
Surgery	3.14	1.55	2	1
Radiotherapy	3.92	2.15	3	2
Laser surgery	2.69	1.56	2	1
Cryosurgery	3.86	1.54	3	1

The Interclass Correlation Coefficient (ICC) for the group has average of 0.65, proving average consistency in expert evaluation ($p < 0.001$***).

For revealing statistically significant differences between treatment methods in evaluation of skin cosmetic defect (scar) severity stage *Kruskal-Wallis* anaylsis of variance by ranks is used (Table 2.14 and Figure 2.4).

Table 2.14.

Cosmetic results evaluation by treatment method

Treatment method	n	*Mean rank*	*p*
Surgery	58	80.89	< 0.001***
Radiotherapy	55	131.43	
Laser surgery	43	56.16	
Cryosurgery	39	122.44	

p - Kruskal-Wallis test

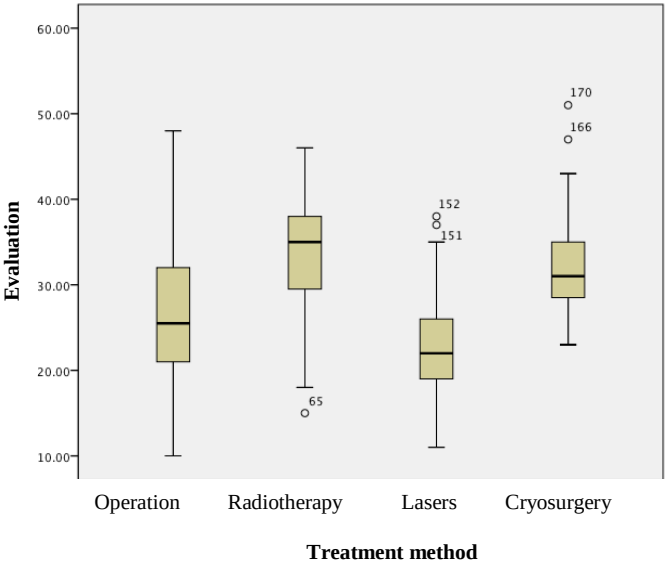

Figure 2.4. **Cosmetic results evaluation**

3. DISCUSSION

3.1. Analysis of head and neck BCC clinical picture and recurrence

Comparing results of this research on clinical picture and recurrence peculiarities of head and neck BCC with other existing researches in this field enable to conclude that overall obtained results comply with those of other researches. Although it should be noted that majority of other researches use data with 5 year follow up (in several researches – 2–3 years (*Wooldridge at al.* (1975), *Bath-Hextall et al*. (2014)). Comparing this paper's results with other researches, classical BCC recurrence peculiarities have to be taken into account, which were highlited in *Rowe et al.* (1989): around 30% of recurrence is formed within first year, 50% – during the second year, 66% – during the third year and 18% – in the following 6–10 years. The average follow up of this research amounts to 8.5 years, therefore recurrence rate is slightly higher than in the majority of other researches, where observation period is smaller. This complies with results of *McGovern et al.* (1999) and *Boztepe et al*.(2004) research results.

It is concluded that recurrence rate of head and neck BCC in follow up over 5 years amounts to 13.02% which complies with the results majority of published researches (*Rowe et al.* (1989), *Silverman et al.* (1991), *Sartore et al.* (2011), *Nakayama et al.* (2011), *Chren et al.* (2013)).

Revealed relationships between recurrence rate and clinical and histological form, tumor size and exact localization overall comply with the results of other researches (*Silverman et al.* (1991), *Zagrodnik et al.* (2003), *Caccialanza et al*. (2013)). Recurrence is mostly present in cases of infiltrative BCC form: in this research – 61.36%, other researches – from 27% (*Blixt et al.* (2013)) until 61,8% patients (*Peres et al.* (2012)). It was not been proven that there is a difference in recurrence rate in case of nodular (10.82%) or superficial (10.64%) clinical and histological BCC form – these results comply

with *Sexton et al.* (1990), *Emmett et al* (1990) researches, however contrasts to *Dandurand et al.* (2006), where it was concluded that patients with nodular clinical and histological BCC form have recurrence more frequent than those with superficial form.

In order to determine precise clinical and histological form it is better to use non-invasive methods – dermascopy (*Altamura et al.* (2010) [39]), skin photobleaching (*Ferulova et. al*. (2012) [40]), multispectral imaging (*Diebele et al.* (2012) [41]) and confocal laser microscopy (*Ulrich et al.* (2012) [42]). Moreover, it is necessary to perform tumor morphological verification **before treatment**, if infiltrative BCC form is suspected (*Mosterd et al.* (2009)).

Within this research, tumors have been classified not only according to TNM classification, as it is common in majority of countries, but also according to tumor size in accordance with suggestions from *Silverman et al.* (1991) and *NCCN* (2014) recommendations, where following tumor size groups are mentioned: tumor < 6 mm, 6–10 mm, 11–20 mm, tumor > 20 mm [3, 7].

Research has proven the necessity to group tumors according to above mentioned size parameters, as statistically significant ($p < 0.05$) increase in the recurrence rate was observed in each ascending tumor size group. This relationship proves necessity to choose the most optimal treatment method, especially when thinking about alternative treatment methods.

The largest group in the number of presented cases is tumors in the size group 6–10 mm (64.67%), second – tumors < 6 mm (19.01%), third place – tumors in the size 11-20 mm and tumors > 20 mm amount to 16.32%. This tendency is in line with results obtained in *Avril et al.* (1997) (n = 347: tumors sized 6–10 mm – 50%, <6 mm – 11%, tumors sized 11–20 mm – 33%, >20 mm – 6%). On the contrary, in *Moskalik et al.* (2010) (n = 2743) research tumors <10 mm amounted to 34.67%, tumors sized 11–20 mm – 57.45%, tumors > 20 mm – 7.87% of cases. It can be thought that large number of

tumors sized 6–10 mm is a result of prophylactic work and can be a sign that patients have turned to doctors in the early stage of changes in their skin.

Division of BCC according to exact anatomic localization is more precise as it is proven in the research. For example, localization with ICD-10 code C44.3 (nose, forehead, cheek, chin) proved to have statistically significant differences with resepct to recurrence rate – from 19.15% on the nose to 0% on the chin. This should be taken into account when deciding about the treatment method. Overal, in descending order the recurrence rate on the face, neck and head regions is as following: lip – 31.25%, nose – 19.15%, eyelid – 15.94%, ear – 10.9%, cheek – 10.5%, scalp – 9.09%, forehead – 8.46%, neck – 4.17% and chin – 0%. These results comply with similar researches by *Mosterd et al.* (2009), *Pazdrowski et al.* (2012) and *Goto et al.* (2012).

In several Western European researches (*Silverman et al.* (1991), *Zak-Prelich et al.* (2004), *de Vries et al.* (2012)) it was concluded that head and neck BCC is present more often among men, whereas in Latvia there is an opposite tendency – 65.6% of cases were presented by women and only 34.4% – by men. Moreover, in research performed in several Eastern European countries (*Trakatelli et al.* (2007)) and in Russia (*Снарская et al.* (2005)) it was concluded that BCC of head and neck is more common in women than men. This tendency is also supported in *Birch-Johansen et al (2010)* research with 30 year follow up. This tendency highlights the need for new prophylactic innovations as to diagnose the disease faster and apply the most appropriate treatment method.

Some authors (*Silverman et al.* (1991), *Veronese et al* (2012), *Cognetta et al.* (2012)) are sure that there is a relationship between BCC recurrence rate and patient's gender – according to their data, men have higher recurrence rate than women, however in particular research this relationship did not prove to be statistically significant – recurrence rate among women was present in 13.4%, where as for men – 12.3%.

Presence of BCC in different age groups in Latvia shows general tendencies that were highlighted in other researches – the older the patient, the more likely is presence of BCC. Results are statistically significant (*Silverman et al.* (1991), *Bath-Hextall et al*. (2007), *Telfer et al.* (2008) and others). Significant question about BCC recurrence tendencies is in connection with the age – younger people have higher risk of recurrence, whereas older people have less – as person becomes older, the probability of BCC is lower. The largest recurrence rate was observed in the age group 41–60 – which is in line with similar researche results by *Betti et al* (2009), *Skellett et al.* (2012)), however contradict with *Roudier-Pujol et al.* (1999) research, where it was not proven that there is statistically significant difference between recurrence rate in the age group until 35 yeras versus age age group above 35 years.

3.2. Head and neck BCC treatment methods

The number of various head and neck BCC treatment methods is large, as well as the large variety of researches in this field, however, the optimal treatment method for BCC is still a source for discussion. The difficulty in the choice of appropriate treatment method lies in the fact that although from oncological point of view the disease does not cause death, it has quite high recurrence rate. After recurrence tumor is more aggressive, therefore there is vicious cycle – recurrence – treatment – new recurrence – new treatment. It can cause disruption in organ functionality, the scar looks worse, creating additional problems for the patient and reducing the quality of life. According to *Holfeld et al.* (1990), *Essers et al.* (2007), *Fagundes et al.* (2012), cosmetic defect on the scalp, especially on the face, can cause psychoemotional stress and in some cases – severe depression.

When choosing treatment method, it is important to take into account full cancer cell removing not only to maintain maximum functionality of the organ, but also the necessity to ensure that the natural face relief is maintained.

Therefore, when choosing appropriate head and neck BCC treatment method, it is necessary to take into account not only factors that characterize tumors, age of the patient and gender, but also proposed cosmetic results.

The necessity for the "golden middle way" between efficacy (rare recurrence) and good cosmetic result opened the door for wide range of alternative treatment methods. The search for efficient alternative BCC treatment method in the recent years has become the mainstream topic for many researches (*Wang et al* (2001), *Ozolins et al.* (2010), *Amini et al.* (2010), *Attili et al.* (2012)). Although many alternative treatment methods show good cosmetic results with simple procedures, it would be necessary to evaluate the adequacy of use of these methods, taking into account recurrence rate in more than 5 years. In the majority of researches authors explain the recurrence reasons with inappropriate choice of alternative treatment methods. (*Silverman et al.* (1991), *Ko et al.* (1992), *Telfer et al.* (2008)).

In this research four different BCC treatment method (surgery, radiotherapy, laser surgery and cryosurgery) comparative analysis were performed, as well strict borders were drawn for the use of each method, revealing the risks and limitations in the use of each method, in connection with several factors that characterize the tumor – clinical and histological form, size, exact anatomic localization and proposed cosmetic result.

3.3. Possibilities of surgery for head and neck BCC treatment

The most secure BCC treatment method is considered operation (especially Mohs micrographic surgery, which is currently unavailable in Latvia). BCC recurrence in 5 year follow up after Mohs surgery is 0.7–3%, after surgery with histological control of resection line amounts to 2–14%. In this reserach the recurrence rate 9.2%: in case of superficial form BCC – 5.7%, nodular form – 9.2%, infiltrative form – 21.1%. In author's opinion, it can be connected with the sample specifics (follow up more than 5 years (on average –

8.5 years), as a result, the recurrence rate is higher), with difficulties to define such terms as clinical margins and surgical margins, as well as difficulties to determine these margins (*Telfer et al.*, 2008)). Unfortunately, information on difficulties to determine margins was not found in the patient medical records, as well as there was lack of exact surgical margins.

When analyzing recurrence rate, the distance from tumor clinical margins is crucial, in case of operation. According to Griffiths et al. (2007), Malik et al. (2010), Cecchi et al. (2011), in case of non radical operation, recurrence rate is larger – up to 41%. It is proven in the research that minimum distance has to be 4–5 mm (Kimyai-Asadi et al. (2005)), whereas in case of infiltrative tumor – up to 10–15 mm (Breuninger H. and Dietz K. (1991). During histological verification analysis in LOC no information was obtained about exact distance from tumor clinical margins. According to Royal College of Pathologists (2012) expert opinion, it is important that after opreation margins are controlled in the following distance from tumor margins: < 1 mm, 1–5 mm, > 5 mm. It is possible that relatively high recurrence for tumors sized 11–20 mm can be explained with lack of control on the tumor margin distance – in present research recurrenece after operation amounts to 21.1%, whereas for tumors with size < 6 mm – 2.0%, 6–10 mm large tumors – 8.2%. If tumor is large, surgeons have to find the optimal way between efficacy (low recurrence rate), maintenance of organ fuctionality and necessity to perform as harmless incision as possible, especially when localization is on eyelid, lip, nose or ear. Most recurrence after surgery is seen on eyelid (16.1%), scalp (13.3%) and nose (12.0% cases). From surgical point of view, these localizations are considered difficult and reconstructive surgery is necessary in many cases. In this research classically considered “difficult” locations have following recurrence – on ear – 3.6% cases and on lip – 0%.

3.4. Possibility of radiotherapy for head and neck BCC treatment

Comparative analysis of different head and neck BCC treatment methods reveal the existing problems in the scientific world. One such contrary question which made NCCN expert opinion up to date after publication in the last years (2010) is the question on comparison of efficacy of surgery and radiotherapy. Majority of authors (*Avril et al,, Rowe et al., Zagrodnik et al. and others)* consider operation as "golden standard", namely more efficient treatment method than radiotherapy, however in some researches, it is conculded that radiotherapy can be as efficient as surgery: in the *Olschewski et al*. (2006) research (n = 104) recurrence rate was 0%. In *Cognetta et al.* (2012) research (n = 712) in 5 year follow up recurrence rate amounted to 4.2%, however, in research by *Caccialanza, M. et al.* (2013) (n = 986) during 5 years follow up – 5.47%.

Recurrence rate after radiotherapy for all BCC forms (except infiltrative) was lower than after surgery: in case of superficial form – 5.0% (after operation – 5.7%), in case of nodular form – 6.9% (after surgery – 9.2%). Similar or even less recurrence rate was observed for different size tumors: if tumor was < 6 mm, recurrence rate was observed in 8.0% cases (after surgery 2.0%), 6–10 mm tumor – 6.2% cases (after surgery – 8.2%), in case of 11–20 mm tumors – 15.4% cases (after surgery – 21.1%). After performing comparative analysis of BCC recurrence rate for different tumor localizations, it was concluded that after radiotherapy in comparison with surgery, recurrence is observed in less cases on scalp – 5.0% cases (after surgery – 13.3%) and on cheek – 7.3% cases (after surgery – 9.8%). Although no statistical significant differences were observed between recurrence rate after surgery and radiotherapy (except for infiltrative BCC form), additional research should be performed in this field.

Following restricting factors were outlined for radiotherapy: age – *NCCN* and *EDF* recommend radiotherapy for patients only after they are 60 years old, as it can induce skin cancer in 15–20 years; complicated use of radiotherapy in case of “difficult" localisations - eyelid, nose, ear; radiotherapy causes different skin cosmetic defects – alopecia on the scalp, sometimes telangiectasia, radiodermatitis, radiation ulcer till radionecrosis.

However, in particular cases (patient's chosen therapy, contrindications for surgery, appropriate age) following certain rules (in fractional way, small doses (2–3 Gy)) radiotherapy can be more efficient than surgery. In author's opinion, it would be necessary to make prognosis in which cases radiotherapy is more optimal than surgery – for example, large size superficial and nodular form tumors that are located in places where it is too difficult to apply surgery. O*lschewski et al*. (2006) recommends following treatment option – 5 × 3 Gy per week until total dose is 57 Gy – as a standard therapy for head and neck BCC. Recurrence after such treatment is rare.

It was concluded that in case of infiltrative form head and neck BCC recurrence rate after surgery is (21.1%) which proves to be statistically significant different from radiotherapy (86.0%), which is in line with other similar reserach results (*Zagrodnik et al.* (2003), *Cognetta et al.* (2012)). Authors consider infiltrative clinical and histological form as additional risk factor for recurrence, whereas *Cognetta A. et al.* recommends to use electron radiotherapy for head and neck BCC treatment in case of infiltrative form. This proves the necessity to determine clinical and histological form **before beginning of treatment**, as well as it is necessary to perform additional diagnostic to clarify clinical and histological form and tumor infiltration depth (for example, high frequence ultrasound imading), which would allow to choose more optimal radiotherapy method.

3.5. Possibilities of lasers for head and neck BCC treatment

During last 10 years, lasers have become a well-known method for BCC treatment, due to several advantages as compared to surgery or radiotherapy: minimal blood loss, possibility to apply for patients who use anticoagulants (which can be contraindication for surgery), protective and local application area, good cosmetic result and the method's cost effectiveness (*Moskalik et al.* (2009), *Tran et al.* (2012)).

Results obtained in the reserach prove that despite advantages of the method, there are several disadvantages. Recurrence rate after lasers is 13.8%, which is higher than after surgery (9.2%) and radiotherapy (8.5%). This difference is not statistically significant, however, comparing recurrence rate with respect to clinical form, size and exact anatomic localization, statistically significant difference was observed comparing surgery versus lasers.

Statistically significant differences in recurrence rate between lasers and surgery were present in case of infiltrative form – 93.8% after lasers, 21.1% - after surgery. Statistically significant differences between lasers and surgery were not observed in case of superficial and nodular form BCC (superficial: after lasers – 10.2%, after surgery – 5.7%; nodular form: after lasers – 9.6% cases, after surgery – 9.2%). High recurrence rate after lasers was observed when tumor size was 11–20 mm (20.0%) and more than 20 mm (33.3%). Differences in recurrence rate for tumors sized 11–20 mm were not statistically significant, as after surgery recurrence was 21.1%. However, recurrence rate in case of BCC located on lip and ear showed statistically significant differences – on lip 42.9%, on ear – 25%.

Obtained results prove that the use of lasers has limitation; therefore this method is efficient for superficial and nodular form tumors, if tumor size is < 10 mm (question about tumors sized 11–20 mm is debateable), if tumor is located on nose, forehead, scalp, neck, sheek and chin. The use of lasers is

limited to application on infiltrative form BCC, larger than 20 mm, with localization on lip and ear.

Overall obtained research results comply with other similar researches. The only difference is on the use of lasers, for example *Moskalik et al.* (2010) in the research states that lasers can be used for T1N0M0 and T2N0M0 BCC treatment, however, even in this research it is stated that the use of lasers is significantly limited when tumor depth is larger than 5 mm. On the other hand, in reserach performed in Korea (*Jung et al.* (2011)) it was concluded that in case of lasers recurrence develops "invisibly" (tumor development period is longer before it is diagnosed), the histological form is more aggressive and several Mohs micrographic surgery cycles are necessary for recurrence treatment. Yet it is not quite accurate to compare newly occured BCC with recurred, as recurred form can be more agressive (*Boulinguez et al.* (2004)). Moreover, it is stated that there was lack of oncological experience for doctors who performed lasers, therefore they could misjudge the tumor and classify it as benign tumor (ceratosis or nevus) – this could highlight that there is necessity for detailed diagnostics and experience of doctors, rather than prove inefficiency of the method.

The largest disadvantage in the use of lasers is the impossibility to make tumor morphological verification after treatment is applied, as well as lack of standartized methodics in application of this treatment method and ingorance of the factors that limit the use of this method (described above).

3.6. Possibilites of cryosurgery for head and neck BCC treatment

As BCC is mostly diagnosed among elderly people (in this research – 71% participants were older than 61 year), who have somatic problems often, it is advised to use methods that are less harmful for head and neck BCC treatment. Such method is cryosurgery.

However, research results prove that recurrence develops very often exactly after cryosurgery – in 26.7% cases – and this result is statistically significant when compared to surgery (9.2%), radiotherapy (8.5%) and lasers (13.8%). Moreover, contrary to lasers, in case of cryosurgery BCC recurrence was present in all clinical and histological forms (for superficial form – 23.5% cases, nodular – 29.2%, infiltrative – 100% cases) and for all tumors that are larger than 6 mm. Obtained reserach results comply with international research results, for example, in *Hall et al.* (1986) after cryosurgery recurrence rate amounted to 39%, in *Thissen et al.* (2000) – 8.2%. In this research, cryosurgery has the smallest use possibilities – these results comply with other research results: *Thissen et al.* (2000) recommended cryosurgery for patients who are unable to have surgery and only in cases of superficial and nodular clinical and histological forms, if tumor size is small (until 10 mm). In this reserach statistically significant differences were observed for exact anatomic localization and size, comparing surgery and cryosurgery. Detailed analysis revealed that after cryosurgery on lip BCC recurrence was in 2 cases out of 2 (100%), on ear – in 2 out of 5 (40%), on nose – in 20 cases out of 51 (39.2%); 6–10 mm large tumors showed recurrence rate of 31.1%, 11–20 mm - 40.0%, and all these results were statistically significantly different from surgery.

In some research the prognosis of the use of cryosurgery for head and neck BCC treatment is quite optimistic. In *Kuflik and G.Gage* (1991), *Kuflik, E.* (2004) researches, analyzing 30 year experience of the use of cryosurgery for BCC treatment it was concluded that recurrence rate during 5 year follow up amounts to 1–2% and no proof was found that there is any connection with exact anatomic localization and the outcome. However, when analyzing the sample, it can be concluded that positive research outcome is linked to the sample choice: only those patients who “comply with criteria for treatment with cryosurgery" [43] were selected for the research and had tumors with easy to determine clinical margins.

In author's opinion, which is based on this reserach and 30 year experience in oncology, as well as on other research done all over the world, efficacy of each treatment method depends not only on technical possibilities of the method, but also on **precise patient selection** for particular treatment method. This means that:1) it is necessary to know the risk factors and limitations of each treatment method, exact instructions and contraindications of particular treatment method; 2) It is important exact tumor diagnosics before treatnet method is chosen: correct diagnosis of clinical and histological form, precise tumor margin, if necessary additional diagnostics procedure (dermoscopy, high frequency ultrasound imading, confocal laser mikroscopy) and mandatory is tumor morphological verification; 3) it is necessary to understand relationships between different factors: socially demographic factors (age and gender of the patient), time of illness (possible comorbidities), clinical peculiarities of tumor and results of diagnostics. Selecting suitable patients for each treatment method can reduce recurrence rate until minimum.

3.7. Cosmetic result

80–90% basal cell carcinoma (BCC) is located on face, head and neck, therefore it is important to choose treatment method, which can completely eliminate tumor and ensure good cosmetic result, maintainting functions of organs and face individual relief. According to *Shah et al.* (2011) and *Fagundes et al* (2012) research results, all face and neck BCC can cause different degree skin cosmetic defect. These visual defects can have negative impact on patients' life quality, have impact on psychological state and even cause psychopatalogical reactions (*Pragnell J.* and *Neilson J.* (2010)). During last 10 years, not only efficacy of treatment method is important, but also good cosmetic result. Reaching these aims and mainainting functionality of organs are tasks for which the doctor is responsible, when choosing treatment method (*Maize et al.* (2005)).

Facial skin relief is very difficult and therefore it is complicated to make wide operations. All BCC treatment methods in any way cause the skin cosmetic defect and each treatment method has its own weaknesses. For **surgery**, at least 5 mm wide derogation is necessary from visible tumor margins, however in case of infiltrative form, wider margin is necessary (at least 10–15 mm). When surgery is performed on scalp, lip or ear after malignant tumor correction of defects caused by surgery can cause problems for plastic surgeons and oncological surgeons. According to *Norman et al* (2009) research results, surgery performed on nose can also be technically difficult and cause cosmetic defects and functionality disruptions. Whereas, according to *Paoli et al.* (2011) research, anatomic peculiarities of this area, possible aesthetic problems and functional disruptions create necessity to have very high accuracy during plastic surgery. **Radiotherapy** causes different skin cosmetic defects – radiodermatitis, skin atrophy and hipo- hiperpigmenatation. It is observed that good cosmetic result at first can worsen later. According to *Paavilainen et al.* (2007), while performing theraphy on eyelid, complications are quite frequent – radiodermatitis, conjunctivitis and cataract. After application of **lasers** there is area not covered with skin, which during healing process becomes a scar, which is different from other part of the skin (*Trelles et al.* (1996)). Imperfection of **cryosurgery** is cryonecrosis and long epithelisation time, yet in case of lip and eyelid BCC after scar is formed, there is deformation of skin (*Kuijpers et al.* (2007)).

Separate aim of the research was to perform comparative analysis of skin cosmetic defect (scar) severity stage, using expert evaluation (experts were both – patients and doctors). As a result, it was concluded that every treatment method results in different skin cosmetic defect (scar) severity stage and these differences are statistically significant ($p < 0.05$). According to expert opinion, smallest skin cosmetic defect (scar) severity stage is in case of lasers (comparing arithmetic average: M = 2.69), in second place – surgery

(M = 3.14), third place – cryosurgery (M = 3.89) and in the last place with the highest severity stage of skin cosmetic defect – radiotherapy (M = 3.92), which is in line with other researches.

Petit et al. (1999) (n = 347) compared cosmetic result after 48 months post surgery and radiotherapy. It is concluded in the research that cosmetic result after surgery is better than after radiotherapy, according to expert evauation, which is in line with results of this research. On the contrary, *Caccialanza et al.* (2009), when analysing results of radiotherapy (n = 671), concluded that cosmetic result after radiotherapy is "good" or "acceptable" (in 3 point scale) in 96,84% after radiotherapy. However, research results were not compared to other treatment methods and experts were the same doctors who previously performed radiotherapy, therefore subjectivity factor was not excluded. During this research, cosmetic result evaluation was performed by independent experts. All possible scar photographs after BCC treatment were presented for expert evaluation, which, in author's opinion, is more methodologically correct as it allows to eliminate subjective expert evaluation and provides wide possibilities for comparison. *Moskalik et al.* (2009) (n = 3346) found "acceptable" cosmetic result after lasers. However, also in this research there was no comperative analysis of other treatment methods and evaluation was performed by the same doctors who performed treatment. *Thissen et al* (2000) (n = 96) compared cosmetic results after surgery and radiotherapy after 12 months from beginning of treatment and concluded that cosmetic results after surgery is better than after cryosurgery.

Patients who participated in the research evaluated cosmetic result better than doctors-experts: evaluation of surgery M_{pat} = 1.55; M_{eksp} = 3.14; radiotherapy M_{pat} = 2.15; M_{eksp} = 3.92; lasers M_{pat} = 1.56; M_{eksp} = 2.69; cryosurgery M_{pat} = 1.54; M_{eksp} = 3.86, which is in line with other research results (*Rhee et al* (2004), *Steinbauer et al.* (2011)). Yet, tendencies in

patient-expert and doctor-expert evauations comply (lasers and surgery are evaluated better than cryosurgery and radiotherapy).

3.8. Possible result extrapolation on other BCC treatment methods

Within the research, four head and neck BCC treatment methods were compared – surgery, radiotherapy, lasers and cryosurgery (leaving out such treatment methods as Mohs micrographic surgery, photodynamic therapy, topical therapy with *Imiquimod*). Taking into account overall tendencies it is possible to make result extrapolation on other treatment methods. For example, after tumor treatment possibility of recurrence is larger, when (1) more complicated is tumor clinically morphological form (superficial – nodular – infiltrative), (2) tumor size is larger, (3) there are specific localizations – lips, ear, eye, nose BCC cases. This testifies necessity to choose less "cosmetic" and economic, though more efficient treatment method – such traditional treatment method as surgery (and in some cases – radiotherapy).

When choosing appropriate treatment method in each particular case, it is necessary to evaluate possibility of using more considered alternative treatment method. The most crucial thing is to determine clinically morphological form of BCC before treatment, as it enables to evaluate risk facors adequately and prognose possible outcome of each treatment method.

3.9. Development perspectives and possibilities for further researches

During this research criteria for chosing particular treatment method were clinically morphological form of face and neck BCC, tumors size, exact anatomic localization, as well as socially demographic data of patients (age and gender) and skin cosmetic defect (scar) severity stage (cosmetic result after treatment). According to *Griffiths et al.* (2007), *Malik et al.* (2010), *Cecchi et al.* (2011), it would be beneficial to supplement these factors with "clinical and surgical margins", as exact difficulties to determine clinical margins together

with other factors can be important, when choosing treatment method. However, adding another variable to the research would cause the necessity to analyze additional impact of this variable.

Additional investment could be research on combined BCC treatment method possibilities, where traditional treatment methods are combined with alternative – for example, lasers and surgery, lasers and therapy with Imiquimod, Imiquimod and cryosurgery, photodynamic therapy in combination with surgery or lasers. It could be especially important if BCC is located in anatomically complicated areas such as lip, eyelid, ear and nose.

3.10. Research limitations

About some lip, chin, eyelid BCC treatment methods it was possible to make conclusions only on tendency level, as (1) total number of cases was not big enough to determine statistically significant differences and (2) in order to prove these tendencies it would be necessary to do additional research.

4. CONCLUSIONS

1. BCC recurrence is mostly presented in infiltrative clinically morphological form for tumors sized 11–20 mm, located on lip, nose and eyelid; BCC recurrence is least presented for tumor size less than 6 mm (< 6 mm), with location on neck or chin area. There is no connection between BCC recurrence and patient's gender, however, there is relationship between the ages: the older the patient is, the less likely the recurrence is.

2. Radiotherapy and laser surgery are as efficient as operation for BCC treatment. Cryosurgery is the least efficient treatment method.

3. For superficial and nodular BCC treatment, the most efficient treatment methods are surgery, radiotherapy and laser surgery. For infiltrative form BCC operation proves to be more efficient. Any treatment method described in this research can be used for tumors sized less than 6 mm. It is better to use surgery or radiotherapy for larger size tumors (6–10 mm, 11–20 mm and more than 20 mm), though laser surgery and cryosurgery are efficient only in particular localisation for this size tumors.

4. Factors that restrict (or prohibit) use of particular treatment method for head and neck BCC: **radiotherapy**: any size and localization infiltrative from BCC; **laser surgery**: any size and localization infiltrative from BCC; any size and clinically morphological BCC located on ear or lip; **cryosurgery**: any size and localization infiltrative form BCC; any clinically morphological form for BCC located on ear, lip, nose, forehead or eyelid.

5. According to expert evaluation, the best cosmetic result can be achieved if laser surgery or surgery is used; worst cosmetic result is considered after radiotherapy and cryosurgery.

6. Research hypothesis is accepted partly. Part of the hypothesis that is connected to comparison of treatment methods (specific clinical and

histological forms, sizes and exact localization of head and neck basal cell carcinoma such alternative treatment methods as radiotherapy, laser surgery, cryosurgery are as efficient as traditional treatment method – surgery) is accepted. However, the part of the hypothesis on cosmetic results is rejected: better cosmetic result is after laser surgery and operation; worst – after radiotherapy and cryosurgery.

5. PRACTICAL RECOMMENDATIONS

1. When filling in pateint's medical documentation for the first time head and neck BCC, it it necessary to note following: clinical and histological form, size and exact anatomical localization.
2. For easier description of abovementioned indications, it is suggested to use author's created "Unified primary skin cancer pateient clinical card".
3. When choosing most appropriate treatement method, following tumor characterizing variables should be taken into account: clinical and histological form, size and exact anatomical localization, patient's gender, age, comorbidities and wish.
4. For optimal treatment method choosing precise and adequate tumor diagnostics before treatment is crucial: it is important to determine clinical and histological form (paying special attention to infiltrative form).
5. Expected cosmetic result is an important criteria, though secondary, when comparing to efficacy of the treatment method. It is important to explain this to patient if he/she chooses less efficient treatment method.
6. It is suggested to use author's developed "Algorithm for the choice of treatment method" and "Treatment calculator", when choosing more optimal treatment method, taking into account such variables as clinical and histological form, size, exact tumor localization and expected cosmetic result.

6. PUBLICATION, ABSTRACTS, PRESENTATIONS ON THE RESEARCH TOPIC

Publications (scientific articles) on the study research topic

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