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## ORIGINAL STUDIES

### ORIGINALNI NAUČNI RADOVI

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### ANTHROPOMETRIC CHARACTERISTICS AND FUNCTIONAL CAPACITY OF ELITE ROWERS AND HANDBALL PLAYERS

*ANTROPOMETRIJSKE KARAKTERISTIKE I FUNKCIONALNE SPOSOBNOSTI VRHUNSKIH VESLAČA I RUKOMETASA*

Dea KARABA JAKOVLJEVIĆ<sup>1,2</sup>, Gordana JOVANOVIĆ<sup>3</sup>, Mirela ERIC<sup>1,4</sup>, Aleksandar KLAŠNJA<sup>1,2</sup>, Danijel SLAVIĆ<sup>1</sup> and Damir LUKAČ<sup>1,2</sup>

#### Summary

**Introduction.** Anthropometric and anaerobic profile of elite athletes are fundamental for the assessment of their respective performance. The present study was designed to evaluate the anthropometric parameters, body composition and anaerobic characteristics of elite male handball players and rowers, and to compare them in relation to specific sport demands. **Material and Methods.** The study group consisted of 41 elite national level athletes: 20 handball players (aged 23.7±3.72) and 21 rowers (aged 19.7±2.84). Anthropometric characteristics (body mass, body height, skinfold thickness, body circumferences), and body fat mass were evaluated, and Wingate anaerobic test for anaerobic power assessment was applied. **Results.** The significant differences were noted in chest, upper arm, waist and hip circumferences, and supraspinal and calf skinfolds between the two investigated groups. Rowers showed higher values of fat body mass (13.2±3.76 vs. 10.7±3.76%), but lower body mass index (22.0±1.92 vs. 25.7±2.31 kg/m<sup>2</sup>) compared to handball players. When analyzing the Wingate test parameters, significantly higher values of absolute anaerobic power (786±127 vs. 691±140 W), absolute explosive power in the handball players compared to the rowers were recorded (118±26.3 vs. 105±27.8 W/s), while rowers achieved higher relative anaerobic capacity (192±31.2 vs. 177±20.8 J/kg). **Conclusion.** Specific body composition and anthropometrical assessment as a part of morphological analysis should complement physiological profile of elite athletes. The analysis of the anaerobic performance shows that the handball players have greater alactic anaerobic and explosive power component, compared to the rowers in whom the anaerobic endurance and specific training have the greatest effect on the consumption of dominant metabolic substrate during the race.

**Key words:** Anthropometry; Athletes; Anaerobic Threshold; Body Composition; Athletic Performance; Exercise Test; Body Fat Distribution; Muscle Strength

#### Sažetak

**Uvod.** Analiza antropometrijskog i anaerobnog profila vrhunskih sportista je od fundamentalnog značaja za procenu njihovih funkcionalnih sposobnosti. Cilj ovog istraživanja bio je evaluacija antropometrijskih parametara, telesne kompozicije i anaerobnih sposobnosti kod vrhunskih rukometaša i veslača i njihovo poređenje u zavisnosti od specifičnih zahteva sporta. **Materijal i metode.** Istraživanje je sprovedeno u grupi od 41 vrhunskog sportiste: 20 rukometaša starosti 23,7 ± 3,72 godina i 21 veslača starosti 19,7 ± 2,84 godina. Svim ispitanicima su izmereni antropometrijski parametri (telesna masa, telesna visina, debljine kožnih nabora i telesni dijometri), a masna masa procenjena je metodom bioelektrične impedancije. Za analizu anaerobnih sposobnosti ispitanika primenjen je Vingejt (*Wingate*) anaerobni test kojim se dobijaju sledeći parametri: anaerobna snaga, eksplozivna snaga i anaerobni kapacitet. **Rezultati.** Statistički značajne razlike zabeležene su u vrednostima obima nadlaktice, struka i kukova i grudi, kao i u vrednostima supraspinalnog i kožnog nabora potkolenice. Kod veslača su utvrđene više vrednosti masne mase tela (13,2 ± 3,76 vs. 10,7 ± 3,76%), ali niži indeks telesne mase (22 ± 1,92 vs. 25,7 ± 2,31 kg/m<sup>2</sup>) u poređenju sa rukometašima. Poredeći rezultate Vingejt testa, statistički značajno veće vrednosti apsolutne anaerobne snage (786 ± 127 vs. 691 ± 140 W) i apsolutne eksplozivne snage zabeležene su kod rukometaša (118 ± 26,3 vs. 105 ± 27,8 W/s), dok su veslači ostvarili veće vrednosti relativnog anaerobnog kapaciteta (192 ± 31,2 vs. 177 ± 20,8 J/kg). **Zaključak.** Specifična analiza telesne kompozicije i antropometrijska analiza dopunjuju fiziološki profil vrhunskih sportista. Analizirajući anaerobne sposobnosti, rukometaši poseduju izraženiju alaktatnu anaerobnu i eksplozivnu snagu u poređenju sa veslačima, kod kojih anaerobna izdržljivost i specifični trening najviše doprinose utrošku dominantnog metaboličkog supstrata tokom trke.

**Gljučne reči:** antropometrija; sportisti; anaerobni prag; sastav tela; sportski učinak; vežbe, testovi; distribucija masnog tkiva; mišićna snaga

**Abbreviations**

AC	– anaerobic capacity
AP	– anaerobic power
BMI	– body mass index
EP	– explosive power
BF (%)	– body fat percent

**Introduction**

Specific physiological and morphological parameters are important components of performance in many sports. It has been confirmed that certain physical characteristics such as body composition (body fat, body mass, muscle mass) and physique (somatotype) can significantly influence sport results [1]. Numerous studies have revealed that optimal body composition in athletes is associated with enhancements in aerobic and anaerobic performance [2, 3] and muscular strength [4–6]. It is generally accepted that lower relative body fat is desirable for successful competition in most sports. The term “morphological optimization” [7] refers to the selection of specific body structure and morphological characteristics needed for particular sport. Anthropometric measurements are of great importance for the assessment of body structure since the large amount of data can be collected with non-invasive methodology and inexpensive equipments [8, 9].

Studies on individuals with different levels of physical activity have confirmed that athletes tend to have different anthropometric parameters and energetic capacities compared to non athletes [10, 11]. In elite sports, different sport disciplines require optimal physiological and morphological attributes needed for top level performance. Optimal anthropometric profile in these disciplines may be considered as an important factor to the athlete’s success, together with the technique and experience. Several studies have shown that anthropometric characteristics influence sport performance [12–14] and they should be determined and continuously monitored during the training process [15].

Alongside with morphological measures, it is fundamental to analyze energetic capacities of athlete as well. Although aerobic capacity has been more extensively evaluated in literature, corresponding data for anaerobic performance are still scarce, particularly in elite sports. For instance, handball is physically demanding intermittent sport, with substantial aerobic component, but also with high intensity periods with anaerobic energy release. In addition, competitive rowing is a sport discipline based on highly developed both energetic capacities (aerobic and anaerobic). Since rowing and handball rely on anaerobic metabolism to some level, we wanted to explore if there were differences in specific anaerobic components (alactic and anaerobic endurance) between these athletes. There is a great number of tests that can be used to evaluate anaerobic abilities; among them is the Wingate Test, a valid and highly reproducible tool, which is easy to be administered.

The Wingate test is a 30-second supramaximal pedaling test in which the power output can be computed every 5 s [16]. Besides this, it has a meaningful correlation with anaerobic parameters such as maximum lactate concentration and oxygen deficit [17–20]. These characteristics make this test very suitable for the analysis of anaerobic performance of individuals at different levels of physical activity and sport disciplines [21, 22]. The Wingate test provides basic parameters of anaerobic performance: anaerobic power (AP) is the maximal value one achieves in the first few seconds of the test and represents the phospho-creatine energetic pathway of power development; the mean power is a unit of anaerobic capacity (AC) that includes glycolytic energy release as well; the explosive power (EP) is the speed at which maximal power is achieved and reflects transformation of chemical energy into mechanical work.

The present study was aimed at evaluating the anthropometric parameters, body composition and anaerobic performance of elite male handball players and rowers, and comparing them in relation to specific physiological demands of sport disciplines.

**Table 1.** Basic anthropometric characteristics of handball players and rowers**Tabela 1.** Osnovne antropometrijske karakteristike rukometaša i veslača

Subjects/ <i>Ispitanici</i>	Height (cm) <i>Visina (cm)</i>	Body mass (kg) <i>Telesna masa (kg)</i>	Age (years) <i>Starost (god)</i>	Sport experience (years) <i>Sportsko iskustvo (god)</i>
<b>Handball players/<i>Rukometaši</i> (n = 20)</b>				
X	189	91.6*	23.7*	9.55*
SD	4.15	8.14	3.72	3.93
MIN	181	79.0	19.0	2.00
MAX	198	112	32.0	20.0
<b>Rowers/<i>Veslači</i> (n = 21)</b>				
X	185	79.3	19.7	4.58
SD	3.58	6.13	2.84	2.14
MIN	174	68	16	1.00
MAX	191	90	25	10.0

\*p&lt;0.05

**Table 2.** Body fat mass, skinfold thickness and girds of handball players and rowers  
**Tabela 2.** Masna masa tela, debljina kožnih nabora i telesni obimi rukometaša i veslača

	Handball players/Rukometaši	Rowers/Veslači
	$\bar{X} \pm SD$	$\bar{X} \pm SD$
BF (%)	10.7 ± 3.76	13.2±3.28
BMI (kg/m <sup>2</sup> )	25.7 ± 2.31	22.0 ± 1.92
Skinfold thickness (mm)/Debljina kožnih nabora (mm)		
Chest/Grudni	8.51 ± 2.4.09	6.89± 63.37
Subscapular/Supskapularni	13.1 ± 3.95	11.2± 5.29
Midaxillary/Srednji aksilarni	10.5* ± 4.92	7.81± 3.35
Biceps/Biceps	5.13 ± 1.76	5.66 ± 2.39
Triceps/Triceps	10.2 ± 3.52	9.70 ± 3.61
Abdominal/Abdominalni	15.9 ± 5.29	14.8 ± 7.55
Suprailiac/Suprailjačni	10.8± 5.31	9.63 ± 4.31
Supraspinal/Supraspinalni	8.64 ± 4.37	11.8*± 6.32
Front thigh/Natkolenica	16.0± 3.43	16.4 ±7.06
Medial calf/Potkolenica	9.78 ± 3.97	12.8* ± 5.65
Circumferences (cm)/Obimi (cm)		
Forearm/Podlaktica	28.9 ± 1.60	27.2 ±1.51
Upper arm relaxed/Nadlaktica opuštena	31.7* ± 2.16	28.7 ± 2.42
Upper arm flexed/ Nadlaktica savijena	35.9* ± 2.57	31.8± 2.61
Chest/Grudi	101* ± 5.48	93.2± 4.90
Waist/Struk	84.6* ± 5.10	76.4 ± 3.98
Hips/Kukovi	102* ± 4.16	96.4 ± 4.76
Mid-thigh/Natkolenica	58.1± 2.68	55.1 ± 3.61
Calf/Potkolenica	40.3 ± 2.54	37.6 ± 2.71

\*p < 0,05, BMI - indeks telesne mase; BF% - procenat telesne masti

## Material and Methods

The study group consisted of 41 elite national level athletes: 20 handball players (aged 23.7±3.72) and 21 rowers (aged 19.7±2.84). We performed anthropometric measurements (body mass, body height, skinfold thicknesses, body circumferences), body composition analysis, and the Wingate anaerobic test for anaerobic power assessment. The nutritional level was defined according to the body mass index values (BMI), obtained by dividing a person's weight in kilograms by the square of the person's height in meters.

The anthropometric data included 3 types of measurements: basic (body height, body mass, BMI), body circumferences (chest, flexed and relaxed upper arm, forearm, waist, hip, mid-thigh, calf) and skinfold thickness (chest, subscapular, midaxillary, biceps, triceps, abdominal, suprailiac, supraspinal, front thigh, medial calf) on the right side of the body according to the standard methods proposed by the International Society for the Advancement of Kinanthropometry [23].

The body height was measured by Harpenden anthropometer (Holtain Ltd, Croswell, UK), with the precision of 0.1 cm. The body fat mass (FAT%) and total body mass were measured by Tanita bioimpe-

dance analyzer TBF-310 (Tanita Corporation, Tokyo, Japan). The skinfold thicknesses were measured by means of Harpenden caliper (Holtain Ltd, Croswell, UK) with the precision of 0.2 mm. All skinfold thicknesses were measured three times and the final value was the average between the three measurements.

All participants performed the Wingate Anaerobic Test in its standard version in duration of 30s on the air brake cycle with calibrated resistance [19]. All subjects underwent a 5-minute to 10-minute intermittent warm-up prior to the test. Standard measures of anaerobic abilities were recorded: the peak power, or AP is the highest power output observed during the first few seconds of test, it indicates the energy generating capacity of the immediate energy system; AC reflects the local endurance of involved muscles; and EP reflects the explosive component of muscle contraction. All parameters were recorded by means of the software installed in PC, which was directly connected with the ergometer machine and then analyzed in absolute and relative values. After the Wingate test, the individuals performed a period of active recuperation on the cycle ergometer in duration of 2 to 3 minutes.

Data Analysis: The data were analyzed by means of the t-student test. The level of significance adopted was p < 0.05.

**Table 3.** Anaerobic characteristics of handball players and rowers  
**Tabela 3.** Anaerobne karakteristike rukometaša i veslača

Subjects <i>Ispitanici</i>	Parameter <i>Parametar</i>	Anaerobic power (W) <i>Anaerobna snaga (W)</i>	Relative anaerobic power (W/kg)/Relativna anaerobna snaga (W/kg)	Explosive power (W/s) <i>Eksplozivna snaga (W/kg/s)</i>	Relative explosive power (W/kg/s)/Relativna eksplozivna snaga (W/kg/s)	Anaerobic capacity (J) <i>Anaerobni kapacitet (J)</i>	Relative anaerobic capacity (J/kg)/Relativni anaerobni kapacitet (J/kg)
Handball players <i>Rukometaši</i>	X	786*	8.52	118*	1.28	16259	177
	SD	127	1.14	26.3	0.25	2092	20.8
	min	610	6.46	77.8	0.78	11860	124
	max	1061	11.4	175	1.84	20420	220
Rowers <i>Veslači</i>	X	691	8.69	105	1.32	15211	192*
	SD	140	1.53	27.8	0.31	2778	31.2
	min	389	5.72	42.5	0.57	8900	131
	max	958	12.2	162	1.96	20310	264

\*p<0.05

## Results

**Table 1** shows the basic anthropometric characteristics and sport experience of handball players and rowers. The handball players were taller and significantly heavier than the rowers, with longer sport experience.

**Table 2** gives body fat level, body mass index, skinfold thickness and body circumferences of handball players and rowers.

The significant differences were noted in the chest, forearm, waist and hip circumferences between the two groups. In general the rowers were found to possess more deposition of subcutaneous fat in the lower regions of body (supraspinal and calf skinfold), while the value of midaxillary skinfold was higher in the handball players. Other anthropometric variables did not show any significant differences.

The values of Wingate test parameters in investigated groups are shown in **Table 3**.

The analysis of the Wingate test parameters of athletes engaged in different sport types (handball players and rowers) has revealed significantly higher values of absolute anaerobic power and absolute explosive power in the handball players representing sports with more anaerobic characteristics compared to the rowers, who had higher values of anaerobic capacity.

## Discussion

Physiological features are of great importance for achievements in elite sports. Specific sport disciplines require different body parameters and body structure for maximal performance. It has been found that the athletes with optimal body fat level have higher performance parameters, while the excess of body fat reduces physical abilities [24]. Body composition studies have found a high, negative relationship between performance in various activities, BMI and body fat mass [25]. When comparing anthropometric and body composition profiles of handball

players and rowers, significant differences were found in the values of BMI, body fat mass, body circumferences and skinfold thickness. According to our results, handball players are taller, heavier with higher BMI and all circumferences compared to rowers. Rowers in general are found to possess more deposition of subcutaneous fat in the lower body regions compared to handball players, whereas significantly higher values of upper arm, chest, waist and hip circumferences were found in handball players. These results also indicate greater lean body mass in handball players. Measurement of circumferences may be considered as a field anthropometric tool to evaluate representation of muscle mass, when other methods are not available [26] since there are a few limitations and inaccuracies associated [27].

When comparing anthropometric characteristics to recent data on handball players, we found similar values of average height to those reported from the World Cup held in 2013 where average weight of most successful teams from 24 countries amounted to 92.37 kg, and average height was 190.10 cm [28]. The analysis of previous data on anthropometry of handball players (World Cup 2007) has suggested that there is morphological evolution in this sport, presented as an increase in certain body dimensions (body height, body weight) [28]. Optimal body structure is needed for specific demands of this type of sports, with developed lean body mass and the least possible percentage of body fat. This is in accordance with our results, which show that handball players are tall, lean people with 10.7% of fat body mass.

Rowing is the kind of sports which requires both endurance and strength, where body size and structure are performance related factors [29]. Studies of morphological parameters and physical abilities in adult rowers emphasize the importance of anthropometric measurements for rowing performance [30, 31]. **Previous and recent research studies on the anthropometric profile** [32–35] have shown that elite rowers generally have the same characteristics as our

study group. Previous studies presented a typical rower as a tall, lean and heavy athlete with developed energetic capacity. Our results are similar to more recent studies showing shorter and lighter athletes compared to the data from 2008 Olympics [36]. Despite these morphological differences, athletes showed high performance in relation to body dimensions [36]. This is probably the result of excellent technical skills, genetics factors, and specific rowing training (the large volume of aerobic training together with anaerobic type of training) leading to anaerobic endurance and metabolic efficiency [14].

Body structure assessment is of great importance for general and athletic population, but there are no adequate reference values for elite athletes [37–39], especially in certain parameters such is BMI. An interesting finding of this study is BMI value of handball players ( $25.7 \pm 2.31 \text{ kg/m}^2$ ), which is similar to the values recorded in athletes from World Cup in 2013 ( $25.53 \pm 2.09 \text{ kg/m}^2$ ), indicating the importance of body fat mass measurements. The BMI considers only height and weight of an individual, but the body composition aspects are not evaluated in this assessment [40]. The BMI depends not only on the fat content in the human body, but also on the muscles and bone mass, as well as on the water content. A high value of the BMI can be measured in athletes with greater skeletal muscles mass because training in many sports disciplines leads to an increase of muscle mass and the whole body mass as well as in body mass index [41]. A high BMI value is observed in weight lifters, body builders, rowers, professional football and handball players, etc. Results of previous research [42, 43] have shown that an increase in BMI is not necessarily an indicator of excess fat in athletes, but more likely of increased muscle mass. According to the results of present research the BMI has low level of validity when assessing body composition in athletes since it does not discriminate muscle from fat mass and could lead to misinterpretation of higher values in handball players as overweight. These findings highlight the importance of body composition assessment in athletes.

The evaluation of anaerobic profiles of the study groups has revealed differences in all Wingate parameters, with significant higher values in absolute AP and absolute EP in handball players. These higher values are expected since handball is sport characterized by short high-intensity periods, where anaerobic abilities are very relevant to maximal performance [44, 45]. Another study done on professional handball players showed higher absolute maximum power and a relative maximum power compared to our investigated athletes [22]. It is possible that the discrepancies encountered in the two studies are due to differences in anthropometric characteristics (active muscle mass) and different age range of athletes.

In our investigation, handball players are taller and heavier than rowers, with longer sport experience. These anthropometrical differences could partly explain the results of Wingate Anaerobic Test, where higher values of AP and explosive power were recorded in the handball players than in the rowers. In other words, the handball players showed more alactic AP and greater AC in relation to the rowers, in whom significantly higher values were recorded in the relative AC indicating the importance of power endurance in this sport. Rowing is considered mostly aerobic sport, but at the beginning and in the finish of the race, anaerobic component also plays an important role. Secher [46] has found that the initial spurt at start of rowing race is crucial for maximal performance and probably highly depends on AP and capacity of athlete. Previous studies have also revealed that competitive rowing is sport with highly developed both (aerobic and anaerobic) energetic capacities [14, 29]. Lower values of peak and explosive power of rowers compared to handball players could be explained by the repetitive nature of rowing, where in contrast to explosive movements such as jumping present in handball, rowers are not specifically trained to produce such AP outputs. The present results are in line with other studies, suggesting that AP and specific anthropometric characteristics are important training objectives to optimize rowing performance [14]. Data from previous studies suggest that efficiency of anaerobic processes evaluated by the Wingate test could be a predictor of rowing performance [14, 32, 47]. These findings are consistent with previous studies that have confirmed that anaerobic and morphometric characteristics of rowers are the result of the large volume of aerobic training undertaken, together with weight training, leading to specific body structure and physiological profile.

## Conclusion

Specific body composition and morphometric parameters could be considered as an important factor contributing to the athlete's respective performance in addition to the technique and sport experience. Based on our Wingate test results, it can be concluded that handball players have greater alactic anaerobic power compared to rowers in whom, most likely, the anaerobic endurance and specific training contribute to the determination of the predominant metabolic substrate during the race.

These physiological attributes may be used for talent identification and to develop more specific assessment methods in elite sports. Furthermore, it may assist the trainers or sport scientists in developing a training program that targets and improves all of the essential attributes to the levels required for success.

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## COMPARISON OF DIET IN WOMEN OF REPRODUCTIVE AGE WITH AND WITHOUT DIAGNOSED POLYCYSTIC OVARY SYNDROME – PILOT STUDY

*POREĐENJE NAČINA ISHRANE ŽENA U REPRODUKTIVNOM DOBU SA DIJAGNOSTIKOVANIM SINDROMOM POLICISTIČNIH JAJNIKA I BEZ OVE DIJAGNOZE – PILOT STUDIJA*

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### Summary

**Introduction.** This study was aimed at comparing diets, dietary patterns and lifestyle habits of women with polycystic ovary syndrome and controls in Croatia. **Material and Methods.** In this pilot, matched pair study, the participants were women of reproductive age: 12 with Polycystic Ovary Syndrome and 16 healthy (between the ages of 18 and 41 years). The following data sets were collected and analysed: nutrient intake, dietary habits and physical activity, polycystic ovary syndrome symptoms, anthropometry and biochemical records. **Results.** The analyses of dietary habits showed a significantly ( $p=0.030$ ) higher score for the controls ( $92.4 \pm 8.7$  points) compared to the women with polycystic ovary syndrome ( $83.3 \pm 12.2$  points). There was a significant correlation between the age and intake of total carbohydrates, and intake of plant protein in the women with polycystic ovary syndrome. A significant correlation was found between the age and total fats intake, as well as intake of different types of fats, and energy intake in the controls. The free time activity index showed a significant difference (t-test:  $p=0.043$ , ANOVA:  $p=0.004$ ) in favour of the control group of women who were more active. **Conclusions.** This study has shown that Croatian women with polycystic ovary syndrome compared to the controls have significantly poorer dietary habits characterised by high Glycaemic Index diets, they are less physically active during free time, and have positive significant correlation between the age and carbohydrate intake whereas the controls have positive significant correlation between the age and fat intake.

**Key words:** Polycystic Ovary Syndrome; Diet; Reproduction; Life Style; Adult; Exercise; Body Mass Index; Glycemic Index; Surveys and Questionnaires

### Introduction

Polycystic Ovary Syndrome (PCOS) affects 6% to 21% of women of reproductive age and is considered a common endocrine disorder [1–3]. This disorder is characterised by endocrine (hyperandrogenism) and biochemical abnormalities, irregular menstrual cycles, lack of ovulation, enlarged ovaries with numerous cysts and infertility [4–8]. There is a correlation between PCOS and obesity, hyper-

### Sažetak

**Uvod.** Ovo istraživanje upoređuje ishranu, navike u ishrani i životne navike žena sa sindromom policističnih jajnika i žena iz kontrolne grupe u Hrvatskoj. **Materijal i metode.** U ovoj pilot-studiji slučaja i kontrole, učesnice su bile žene reproduktivnog doba: 12 sa sindromom policističnih jajnika i 16 zdravih žena (od 18 do 41 godine). Sledeći setovi podataka sakupljeni su i analizirani: unos nutrijenata, navike u ishrani i fizička aktivnost, simptomi sindroma policističnih jajnika, antropometrija i biohemijski parametri. **Rezultati.** Analiza navika ishrane pokazala je statistički signifikantno ( $p = 0,030$ ) veći zbir poena kod kontrolne grupe ( $92,4 \pm 8,7$  poena) u poređenju sa ženama kojima je dijagnostikovao sindrom policističnih jajnika ( $83,3 \pm 12,2$  poena). Pokazala se i signifikantna korelacija između godina starosti sa unosom ukupnih ugljenih hidrata i unosom biljnih proteina kod žena sa sindromom policističnih jajnika. Pronađena je signifikantna korelacija između godina starosti sa unosom ukupnih masti, unosom različitih vrsta masti i energetske unosom kod kontrolne grupe. Indeks slobodnog vremena pokazao je signifikantnu razliku (t-test:  $p = 0,043$ , ANOVA:  $p = 0,004$ ) u „korist“ žena kontrolne grupe koja je aktivnija. **Zaključak.** Ova studija pokazuje da žene u Hrvatskoj sa sindromom policističnih jajnika poređene s kontrolnom grupom pokazuju sledeće: signifikantno lošije navike u ishrani s karakteristikama ishrane visokog glikemijskog indeksa, manju aktivnost u slobodno vreme i pozitivnu signifikantnu korelaciju između godina starosti i unosa ugljenih hidrata, dok kontrolna grupa ima pozitivnu signifikantnu korelaciju između godina starosti i unosa masti.

**Gljučne reči:** sindrom policističnih jajnika; ishrana; reprodukcija; stil života; odrasli; vežbe; indeks telesne mase; glikemijski indeks; ankete i upitnici

insulinaemia and insulin resistance [7]. Different women suffering from PCOS have different and specific combinations of symptoms [9, 10]. Approximately 65% to 70% of these women have insulin resistance [11]. Insulin resistance and PCOS symptoms are aggravated by obesity [3, 12–14]. However, not all women with PCOS and/or insulin resistance are obese [3]. Besides medications, the main treatments for PCOS are weight reduction and lifestyle management practices with equivalent

**Abbreviations**

PCOS	– polycystic ovary syndrome
FSH	– follicle stimulating hormone
LH	– luteinizing hormone
RDA	– Recommended Daily Allowance
CHO	– carbohydrates
GI	– glycaemic index
BMI	– Body mass index
WHR	– waste hip ratio

therapy for obese and non-obese patients [1, 5, 15, 16]. Nevertheless, the exact diet for managing PCOS remains controversial and literature on this topic is limited [1, 16]. Moreover, the diet and lifestyle habits of these women have not been researched extensively. Some of the performed studies show that, compared to healthy counterparts, women with PCOS consume larger quantities of high glycaemic index (GI) foods [2, 15, 17]. Moran et al. have found that PCOS itself, increased energy intake, intake of high GI foods, lower physical activity and some other variables are all independently associated with a higher BMI [4].

The objective of this pilot study was to determine whether the nutritional intake of women of reproductive age with PCOS and their healthy counterparts in Croatia differ and whether these differences could relate to the aetiology of PCOS. This is the first and only study of this kind conducted in Croatia.

**Material and Methods**

Women of reproductive age with diagnosed PCOS and their healthy counterparts (controls) were matched for anthropometry, age and socio-economic characteristics. The inclusion criteria for women with PCOS were age (18 to 41 years) and a PCOS diagnosis based on Rotterdam Criteria made by the gynaecologist (Gynaecological Office Lončar, Karlovac, Croatia) [18]. For the controls, the inclusion criteria were age (18 to 41 years), absence of PCOS and/or other diagnoses indicative of hormonal imbalance. A total of 12 women with PCOS and 20 healthy counterparts were recruited over a six-month period (October 2013 to March 2014). Pairing was done on the basis of the set criteria between 12 women with PCOS and 16 healthy women. Four of the healthy women did not fulfil the criteria and were excluded. The prevalence of PCOS among women of reproductive age in Croatia is unknown [19]. The strength of the study was determined with the power analysis method based on the number of women with PCOS recruited for the study (12 women, minimum strength 80%, significance 0.05, two-sided, minimum detectable difference 0.899 units). The study protocol was approved by the Ethical Committee for the Research on People from the University of Osijek, Faculty of Food Technology. The study participants were informed in detail about the study and written consent was obtained from all of them.

After recruitment, each woman filled in a “24-Hour Diet Recall” and a “Survey on the Basic Data,

Dietary Habits, and Physical Activity”. The women with PCOS had additional questions on their gynaecological health added to the “Survey on the Basic Data, Dietary Habits, and Physical Activity” and they also filled out a “Questionnaire on Polycystic Ovary Syndrome” (adapted according to Cronin et al.) [9]. The controls filled in a separate “Questionnaire on Gynaecological Health”.

The “Survey on the Basic Data, Dietary Habits, and Physical Activity” provided data on age, socio-economic information (work status, salary, living conditions, etc.), dietary habits (number of meals per day, place of consumption, desire to experiment with food, food preferences, eating after feeling satiety, eating breakfast, eating dinner, and the consumption of dairy products, fruits and vegetables, potatoes, meat, fish, salt, fast food, candy, water, juices, coffee, sugar, alcohol, and dietary supplements) and physical activity (physical activity at work, physical activity during free time and participation in sports). The “Questionnaire on Gynaecological Health” filled in by healthy women and questions related to gynaecological health in the “Survey on the Basic Data, Dietary Habits, and Physical Activity” filled in by the women with PCOS investigated menstrual cycle, pregnancies and general gynaecological health in both groups.

Research was conducted at the University of Osijek, Faculty of Food Technology, Department of Food and Nutrition Research laboratory. Medical documentation on the history and course of PCOS was provided by the gynaecologist (Gynaecological office Lončar, Karlovac, Croatia).

Both groups of women were measured for body weight with Tanita BC-601 (Tanita Corporation, Japan) scale ( $\pm 0.1$  kg), body height without shoes with the position of the head in the Frankfurt plane ( $\pm 0.1$  cm) with portable stadiometer Seca 123 (Seca, Germany) and waist and hip circumferences with measuring tape NCD Medical/Medical Prestige (Prestige Medical, USA). Body mass index (BMI) of participants was calculated with measured weight and height data. BMI was used to group women into the following categories: underweight (BMI < 18.5 kg/m<sup>2</sup>), normal (18.5 to 24.9), overweight (25.0 to 29.9) and obese (30.0 to > 40.0) [20].

Data on blood glucose and sex hormones (testosterone overall, estradiol - E2, follicle stimulating hormone - FSH and luteinizing hormone - LH) for women with PCOS were obtained from the patients' medical documentation. All tests (hormones and blood glucose) were performed according to the standards of the good professional practice at an authorized Croatian medical biochemical laboratory [21]. Glucose levels were determined by the standard photometry UV and the hexokinase with glucose oxidase methods [22]. For the determination of hormones (testosterone overall, estradiol (E2), FSH and LH), blood samples were collected between the third and seventh day of the menstrual cycle as recommended by the PHSVP [23]. Sex hormones were measured according to the manufac-

**Table 1.** Macronutrient and fibre intake for women with PCOS (n = 12) and controls (n=16)  
**Tabela 1.** Unos makronutrijenata i vlakana za žene s PCOS-om (n = 12) i žene iz kontrolne grupe (n = 16)

	Women with PCOS/Žene s PCOS-om	Controls/Kontrolna grupa	p values p-vrednosti
	$\bar{X} \pm SD$ (min – max)		
CHO <sup>§</sup> total (g)/CHO <sup>§</sup> ukupno (g)	209.27±100.23 (51.92-368.79)	162.08±79.30 (49.93-341.39)	0.393
CHO <sup>§</sup> simple/CHO <sup>§</sup> jednostavni (g)	57.42±28.60 (2.84-101.26)	52.997±24.86 (15.52-91.91)	0.602
CHO <sup>§</sup> complex/CHO <sup>§</sup> kompleksni (g)	140.43±80.63 (47.09-298.79)	91.49±56.998 (3.97-248.15)	0.211
Fat total (g)/Mast ukupno (g)	86.43±50.68 (35.67-218.03)	81.92±52.497 (31.85-259.92)	0.925
SF <sup>§§</sup> (g)/SF <sup>§§</sup> (g)	27.99±20.43 (6.02-78.09)	22.93±17.28 (5.12-79.84)	0.537
MUFA <sup>¶</sup> (g)/MUFA <sup>¶</sup> (g)	28.70±22.30 (8.20-87.01)	30.75±28.38 (6.66-123.56)	0.424
PUFA <sup>†</sup> (g)/PUFA <sup>†</sup> (g)	19.10±9.62 (6.50-42.05)	22.18±12.12 (8.74-57.31)	0.445
Linoleic acid (g)/Linolna kiselina (g)	16.87±8.87 (4.80-37.07)	19.74±10.27 (4.32-44.96)	0.632
Cholesterol (g)/Holesterol (g)	278.66±249.93 (11.00-765.04)	232.65±211.53 (24.36-746.93)	0.538
Protein total (g)/Protein ukupno (g)	81.72±38.76 (36.31-173.83)	64.63±20.87 (35.99-112.38)	0.028
Animal protein/Animalni protein (g)	57.29±29.99 (19.59-118.96)	45.15±15.83 (20.999-72.65)	0.024
Plant protein (g)/Biljni protein (g)	24.63±14.87 (4.93-54.87)	19.03±10.28 (7.9-41.04)	0.184
Fibre (g)/CHO <sup>§</sup> vlakna (g)	15.69 ± 7.97 g (4.41-25.77)	14.17 ± 6.52 g (7.56-30.93)	0.459

§ – carbohydrates/ugljeni hidrati; §§ – saturated fats/zasićene masti; ¶ – monounsaturated fats/mononezasićene masti; † – polyunsaturated fats/polinezasićene masti

turer's protocol [22, 24]. These data were not collected for healthy women.

The assessment of the dietary intake was performed with the "24-Hour Diet Recall". The questionnaire was completed during an interview using a multiple-pass protocol. This method was selected because it shows the smallest error in terms of underestimating or overestimating nutritional intake [25].

The nutritional intake of macro and micronutrients was calculated by processing data from the "24-Hour diet Recall" with the computer program "NutriPro" that uses Croatian tables on the composition of foods and beverages [26]. The results obtained were compared with Recommended Daily Allowance (RDA) values [27].

In the analysis of dietary habits, responses from the "Survey on the Basic data, Dietary Habits, and Physical Activity" were scored and summarized according to the currently applicable guidelines on healthy eating habits. Better eating habits received higher points on a scale of one to five, where one was given for the answer corresponding to the worst and five for the best case scenario. The minimum score achieved was 27 and the maximum was 135 points.

The degree of physical activity was calculated from the "Survey on the Basic Data, Dietary Habits, and Physical Activity" for women with PCOS and the controls, adapted for Croatian language from Baecke et al. [26]. Three separate dimensions of physical activity were assessed: working time activity, sport activity, and free time activity (details in the original reference work) and converted into indices [28].

The statistical analysis was performed with the Statistica software system (version 12.0, StatSoft Inc.,

USA) to the chosen level of significance at  $p=0.05$ . The categorical variables were presented as the absolute and relative frequencies while the numerical data were presented with the use of descriptive statistical methods (mean and standard deviation).

A Chi-square test was used to compare categorical variables within and between the groups. The differences between the two dependent groups were tested with the t-test for dependent measurements, that is, using the t-test for independent measurements in the groups and the variables. An analysis of variance was performed with ANOVA. The Pearson correlation test was used for calculating the correlation of the numerical data.

## Results and Discussion

The mean BMI was  $27.4 \pm 8.5$  kg/m<sup>2</sup> and  $23.1 \pm 3.1$  kg/m<sup>2</sup> in the women with PCOS and in the controls, respectively. The difference between these two BMI values is statistically significant ( $p = 0.046$ ). This is in accordance with the findings of a 13-year research conducted by Moran et al. [4] stating that the mean BMI in women with PCOS is higher. The mean waste hip ratio (WHR) was  $0.9 \pm 0.2$  and  $0.8 \pm 0.1$  in the women with PCOS and in the controls, respectively, which is not statistically significant.

The collected biochemical data showed the typical PCOS phenotype for the women with PCOS (41.7% high LH, 41.7% high testosterone, 16.7% elevated glucose, 16.7% glucose on the upper level, 100% polycystic ovaries on ultrasound). The women with high LH did not have high testosterone and vice versa. Pavičić Baldani has shown that Croatian women with PCOS have poly-

**Table 2.** Correlation of selected variables with energy intake and macronutrient intake based on the “24-hour diet recall” – women with PCOS (n = 12)**Tabela 2.** Korelacija odabranih varijabli s unosom energije i unosom markonutrijenata na osnovu 24-satnog prisećanja – žene s PCOS-om (n = 12)

Selected variable Odabrane varijable	kcal kcal	Protein total Protein ukupno	Plant protein Biljni protein	Animal protein Ani- malni protein	Fat total Mast ukupno	SF <sup>§§</sup> SF <sup>§§</sup>	MUFA <sup>§</sup> MUFA <sup>§</sup>	PUFA <sup>†</sup> PUFA <sup>†</sup>	Linoleic acid Linolna kiselina	Chol. <sup>‡</sup> Hol. <sup>‡</sup>	CHO <sup>¶</sup> CHO <sup>¶</sup> total	CHO <sup>¶</sup> CHO <sup>¶</sup> simple	CHO <sup>¶</sup> CHO <sup>¶</sup> complex	CHO <sup>¶</sup> CHO <sup>¶</sup> fibre
Age/Godine	0.56	0.50	0.61*	0.43	0.44	0.44	0.38	0.42	0.46	0.43	0.61*	0.49	0.51	0.55
Household members/Ukućani	-0.26	-0.19	-0.35	-0.13	-0.13	-0.23	-0.12	-0.23	-0.25	-0.45	-0.41	-0.56	-0.33	-0.49
Smoking/Pušenje	-0.47	-0.48	-0.42	-0.41	-0.38	-0.43	-0.38	-0.34	-0.34	-0.29	-0.49	-0.47	-0.44	-0.52
BMI <sup>¶¶</sup> /ITM	0.44	0.17	0.43	-0.00	0.50	0.36	0.39	0.28	0.28	-0.17	0.37	0.28	0.29	0.30
Waist/Struk (W)	0.55	0.24	0.51	0.05	0.62*	0.49	0.50	0.42	0.42	-0.12	0.46	0.36	0.37	0.39
Hips/Kukovi (H)	0.42	0.16	0.40	0.01	0.49	0.37	0.39	0.35	0.35	-0.08	0.33	0.26	0.24	0.29
W/H ratio/W/H	0.53	0.21	0.49	0.00	0.59*	0.47	0.47	0.39	0.38	-0.17	0.46	0.38	0.39	0.38
Blood glucose Šećer u krvi	0.13	-0.22	0.17	-0.38	0.21	0.11	0.08	0.09	0.10	-0.26	0.14	0.33	0.07	0.13
Sum points Suma poena	0.33	0.51	0.24	0.56	0.29	0.33	0.36	0.39	0.40	0.56	0.26	0.31	0.25	0.52
Work index Indeks posla	0.50	0.56	0.64*	0.41	0.34	0.39	0.40	0.47	0.47	0.01	0.57	0.04	0.68*	0.57
Sport index Indeks sporta	-0.44	-0.33	-0.61*	-0.22	-0.31	-0.30	-0.26	-0.34	-0.35	-0.29	-0.55	-0.48	-0.53	-0.70*
Free time index Indeks slobodnog vremena	0.03	-0.03	0.12	-0.15	-0.14	-0.02	-0.14	0.13	0.20	-0.02	0.26	0.26	0.27	0.21

\* statistical significance at  $p < 0.05$ , the Pearson correlation test/statistička signifikantnost pri  $p < 0.05$ , Pirsonov test korelacije; §§ – saturated fats/zasićene masti; § – monounsaturated fats/mononezasićene masti; † – polyunsaturated fats/polinezasićene masti; ‡ – cholesterol/holesterol; ¶ – carbohydrates/ugljeni hidrati; ¶¶ – Body Mass Index/indeks telesne mase

cystic ovaries on ultrasound, elevated LH, elevated total and free testosterone, elevated insulin, low sex hormone-binding globulin (SHGB) and FSH [19]. Radulović et al. [29] in their retrospective study on 39 women with PCOS found that 43% of overweight/obese in comparison to 18.2% of normal weighted women had increased insulin. Also, for women diagnosed with PCOS undergoing fertilization treatment reduction of body weight prior to the procedure is highly recommended [14].

The analyses of dietary habits showed a significantly higher score ( $p=0.030$ ) for the controls (92.4±8.7 points) compared to the women with PCOS (83.3±12.2 points). However, Graff et al. found that the women with the typical PCOS phenotype had eating habits similar to those of healthy women except that the women with the typical PCOS phenotype ate foods with a higher GI [2]. After further analysis of the responses to the “Survey on the Basic Data, Dietary Habits, and Physical Activity” it was evident that the analysed women with PCOS showed a tendency towards higher GI foods (e.g., 33.3% of the women with PCOS vs 0% of the controls ate cakes/sweets every day, 33.3% of the women with PCOS vs 18.8% of the

controls ate bakery products for dinner, 16.6% of the women with PCOS vs 31.3% of controls never put additional sugar in their food/beverage), which contributed to their lower score on dietary habits.

The total energy intake of both groups of women was calculated as the percentage of the RDA intake based on the nutritional requirements of 2,333 kcal. The results showed that women with PCOS had a slightly higher average energy intake (82.25%±39.41%) than the controls (69.97%±26.33%). This difference did not prove to be statistically significant in multivariate analysis together with socio-economic data and anthropometry. However, Graff et al. and Moran et al. found that the women with PCOS had a higher calorie intake than the healthy ones [2, 4].

The macronutrient intake for both groups has been expressed as a percentage of total daily energy intake. The average energy intake from carbohydrates (CHO) was 43.48%±8.69% and 40.85±11.91 for the women with PCOS and for the controls, respectively. In addition, the average energy intake of protein was 17.67%±4.68% and 16.56±4.44 for the women with PCOS and for the controls, respectively, while the average energy intake from fat was

**Table 3.** Correlation of selected variables with energy intake and macronutrient intake based on the “24-hour diet recall” – controls (n = 16)**Tabela 3.** Korelacija odabranih varijabli sa unosom energije i unosom markonutrijenata na osnovu 24-satnog prisećanja – kontrola (n = 16)

Selected variable <i>Odabrane varijable</i>	kcal <i>kcal</i>	Protein <i>Protein</i>	Plant <i>Biljni</i>	Animal <i>Anima-</i>	Fat to- <i>Mast</i>	SF <sup>§§</sup> <i>SF<sup>§§</sup></i>	MUFA <sup>§</sup> <i>MUFA<sup>§</sup></i>	PUFA <sup>†</sup> <i>PUFA<sup>†</sup></i>	Linoleic <i>Linolna</i>	Chol. <sup>‡</sup> <i>Hol.<sup>‡</sup></i>	CHO <sup>¶</sup> <i>CHO<sup>¶</sup></i>	CHO <sup>¶</sup> <i>CHO<sup>¶</sup></i>	CHO <sup>¶</sup> <i>CHO<sup>¶</sup></i>	CHO <sup>¶</sup> <i>CHO<sup>¶</sup></i>
	total <i>ukupno</i>	total <i>ukupno</i>	protein <i>protein</i>	protein <i>protein</i>	total <i>ukupno</i>				acid <i>kiselina</i>		total <i>ukupno</i>	simple <i>jedno-</i>	complex <i>komple-</i>	fibre <i>vlakna</i>
			lni <i>lni</i>	pro- <i>pro-</i>							stavni <i>stavni</i>	ksni <i>ksni</i>		
Age/ <i>Godine</i>	0.63*	0.33	0.40	0.19	0.59*	0.55*	0.51*	0.53*	0.52*	0.51*	0.21	-0.04	-0.00	0.24
Household mem- bers/ <i>Ukućani</i>	-0.23	0.01	-0.01	0.01	-0.21	-0.24	-0.10	-0.26	-0.26	0.04	-0.08	-0.10	0.22	0.08
Smoking/ <i>Pušenje</i>	-0.34	-0.23	-0.38	-0.04	-0.15	-0.15	-0.16	0.04	0.11	0.02	-0.37	-0.55*	-0.17	-0.34
BMI <sup>¶¶</sup> / <i>ITM<sup>¶¶</sup></i>	0.14	0.11	0.12	0.09	0.16	0.10	0.14	0.31	0.34	-0.14	-0.01	-0.10	0.04	0.11
Waist/ <i>Struk</i> (W)	0.14	0.28	0.30	0.19	0.04	-0.00	0.05	0.12	0.13	-0.15	0.16	0.00	0.28	0.25
Hips/ <i>Kukovi</i> (H)	0.42	0.61*	0.51*	0.50	0.14	0.07	0.08	0.27	0.31	0.29	0.47	0.05	0.36	0.47
W/H/ <i>W/H</i>	-0.05	-0.02	0.09	-0.07	-0.02	-0.02	0.04	-0.02	-0.03	-0.38	-0.08	-0.01	0.13	0.02
Sum points <i>Suma poena</i>	0.04	0.03	0.08	-0.01	0.04	-0.08	0.18	-0.11	-0.16	0.02	-0.02	0.37	-0.37	0.27
Work index <i>Indeks posla</i>	0.05	0.08	0.37	-0.16	-0.09	-0.11	0.00	-0.25	-0.24	-0.15	0.27	0.10	0.47	0.33
Sport index <i>Indeks sporta</i>	-0.19	0.20	-0.19	0.40	-0.18	-0.20	-0.07	-0.21	-0.20	-0.01	-0.16	-0.26	-0.25	-0.15
Free time index <i>Indeks slobodnog vremena</i>	-0.09	0.32	0.13	0.34	-0.39	-0.44	-0.34	-0.46	-0.43	0.45	0.36	0.27	0.02	0.25

\* statistical significance at p<0.05, the Pearson correlation test/*statistička signifikantnost pri p < 0,05, Pirsonov test korelacije*; §§ – saturated fats/*zasićene masti*; § – monounsaturated fats/*mononezasićene masti*; † – polyunsaturated fats/*polinezasićene masti*; ‡ – cholesterol/*holesterol*; ¶ – carbohydrates/*ugljeni hidrati*; ¶¶ – Body Mass Index/*indeks telesne mase*

40.09%±7.70% and 43.60±11.97 for the women with PCOS and for the controls, respectively. It should be noted that one woman from the control group was on a low CHO diet and her energy intake from fat (79.6%) was high; thus, it can be concluded that without her data the average energy intake from fat for the controls would be slightly lower while CHO intake would be slightly higher. The results show minor differences in macronutrient intake when the women with PCOS consume slightly more CHO and protein and slightly less fat than the controls, but these differences have not proved to be statistically significant after the multivariate analysis with the socio-economic data and anthropometry (**Table 1**). Altieri et al. also found that the women with PCOS consume less energy from fats and eat more cheese, desserts high in GI, fibre and oil [17]. In addition, Altieri et al. have not determined the difference in intakes of macronutrients and energy between the healthy women and the women with PCOS, while Douglas et al. found similar macronutrient intake in the women with PCOS and those who did not have PCOS, noting that women with PCOS consumed large amounts of high GI foods [15, 17]. Douglas et al. concluded that this difference should be explored together with all the factors affecting glycaemic characteristics of the diet consumed by the women with PCOS [15].

Intake of fibre proved to be slightly higher in the women with PCOS compared to the controls (**Table 1**), which corresponds to the findings of Altieri et al. [17].

The correlation analysis results for variables from the questionnaires for the women with PCOS (**Table 2**) show statistically significant positive correlations between work index and intake of polysaccharides (p=0.68) and plant protein (p=0.64). A higher sport index has a statistically significant negative correlation with CHO intake from fibre (p=-0.70) and plant protein (p=-0.61). Due to the small number of women with PCOS who reported practicing sports, these results should be taken with caution. There is a statistically significant positive correlation between the total fat intakes and waist circumference (p=0.62) and WHR (p=0.59). In addition, a statistically significant correlation was found between the age and the intake of total CHO (p=0.61) and plant proteins (p=0.61).

For the women with PCOS, the number of household occupants, smoking and sports are negatively correlated with the intake of macronutrients, although not statistically significant (**Table 2**). Inclusion of a larger number of women with PCOS might have resulted in a statistical significance for some or all of the identified parameters. For the controls, this negative correlation (without statistical significance) was established only for some macronutrients.

**Table 4.** Physical activity indices for women with PCOS (n = 12) and controls (n = 16)  
**Tabela 4.** Indeksi fizičke aktivnosti žena s PCOS-om (n = 12) i kontrole (n = 16)

	Women with PCOS/Žene s PCOS-om	Controls/Kontrola	p*
Work Index/Indeks posla	2.7	2.5	0.201
Sport Index/Indeks sporta	2.5	3.7	0.134
Free time Index/Indeks slobodnog vremena	2.3	3.2	0.043*

\*statistical significance at  $p < 0.050$ , t-test

The correlation analysis for the controls showed a statistically significant correlation between the following variables (**Table 3**): age and energy ( $p=0.63$ ), age and total fat ( $p=0.59$ ), age and saturated fats (SF) ( $p=0.55$ ), age and monounsaturated fats (MUFA) ( $p=0.51$ ), age and polyunsaturated fats (PUFA) ( $p=0.53$ ), age and linoleic acid ( $p=0.52$ ), age and cholesterol ( $p=0.51$ ), smoking and monosaccharides ( $p=-0.55$ ), hips and total protein ( $p=0.61$ ), and hip and plant protein ( $p=0.51$ ).

The correlations in the controls for the age and nutrient intake were similar in the women with PCOS. However, as they aged, the women from the control group increased fat intake and total energy intake while the women with PCOS increased intake of total CHO and plant protein. These results suggest that as they get older women with PCOS should focus on reducing total CHO and plant protein when trying to lose weight in an attempt to manage PCOS symptoms.

The "Questionnaire on the Polycystic Ovary Syndrome" showed that the patients with PCOS exhibit all the relevant PCOS symptoms (excessive body weight, growth of visible body hair, visible facial hair, upper lip hair, beard, irregular menstrual periods, delayed menstruation, menstrual cramps, abdominal bloating and headaches during menstruation) [9]. The responses to the "Questionnaire on the Gynaecological Health" showed that the controls generally reported regular and mostly regular menstrual periods that were not very painful with pain lasting one to three days and periods with low or medium bleeding.

Physical activity levels showed a statistically significant difference (t-test:  $p=0.043$  and ANOVA:  $p=0.004$ ) only for the index of free time in favour of the controls who were more active (**Table 4**). This corresponds with the results obtained by Moran et al. who found that the women with PCOS spent more time sitting and had a lower degree of physical activity [4].

### Conclusion

This study has shown that in Croatia the women with polycystic ovary syndrome compared to the controls have significantly poorer dietary habits with characteristics of a diet high in glycaemic index; statistically non-significant higher energy intake from carbohydrates and protein with lower energy intake from fat; positive significant correlation between age and carbohydrates intake (the controls have a positive significant correlation between age and fat intake); statistically non-significant higher average energy intake; as well as more problems with irregular menstrual cycles and other polycystic ovary syndrome symptoms and they are significantly less physical active during free time.

A weakness of the study is the small sample size. However, the strength of the study was sufficient to identify potentially relevant differences in dietary and lifestyle habits of women with polycystic ovary syndrome as compared to controls.

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## SUN PROTECTION BEHAVIOR AMONG ADOLESCENTS – A COMPARATIVE STUDY CONDUCTED IN 2008 AND 2012

*PONAŠANJE ADOLESCENATA NA SUNCU – UPOREDNA STUDIJA U 2008. I 2012. GODINI*

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### Summary

**Introduction.** Adolescents should limit their exposure to sun and apply sun protection measures. The purpose of this study was to establish changes in adolescents' behavior regarding sun protection between years 2008 and 2012, as well as to assess the impact of sex and skin photo-type on behavior in order to suggest positive sun protection behavior practised in other countries and to improve educational program. **Material and Methods.** An original, tailor-made questionnaire (about the skin types, exposure to sun and the use of sunbed) was distributed among 16 and 17-year-old students in high school in Belgrade, Serbia to be fulfilled within the framework of the educational project in 2008 and 2012. Data were analyzed by the Pearson's chi square test and logistic regression analyses. **Results.** The total number of questionnaires completed in 2008 and in 2012 was 1138 and 583, respectively. In 2012, the students spent less time outdoors. According to the 2008 survey, the girls used more sun protection measures, but reported more sunburns and the use of sunbed than the boys. In 2012 more sunburns were reported by the boys as well as the increased use of the sunglasses, wearing a hat/cap and staying in the shade. **Conclusion.** There were statistically significant changes in behavior of adolescents regarding exposure to sun between 2008 and 2012, and between male and female gender. It is recommended to organize regular educational interventions at schools which should emphasize the following: the importance of sun protection measures, limited sunbathing and outdoor physical activities as well.

**Key words:** Surveys and Questionnaires; Sunburn; Health Knowledge, Attitudes, Practice; Adolescent Behavior; Skin Pigmentation; Ultraviolet Rays; Sunbathing; Sex Factors; Primary Prevention; Sun Protection Factor

### Introduction

In the western societies, the past several decades were dedicated to beauty, well-being and pleasure - a

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### Sažetak

**Uvod.** Adolescenti treba da ograniče vreme izlaganja suncu i primenjuju mere zaštite od sunca. Cilj ovog ispitivanja bio je da se utvrde promene ponašanja adolescenata na suncu između 2008 i 2012. godine, kao i da se proceni uticaj pola i fototipa kože na ponašanje, kako bi se predložili pozitivni modeli ponašanja na suncu iz prakse drugih zemalja i poboljšao program edukacije. **Materijal i metode.** U okviru projekta edukacije 2008. i 2012. godine, 16-godišnji i 17-godišnji učenici srednjih škola u Beogradu (Srbija) popunjavali su originalni, namenski pripremljen upitnik (o tipu kože, ponašanju na suncu i u solarijumu). Podaci su analizirani Pirsonovim  $\chi^2$ -testom i logističkom regresionom analizom. **Rezultati.** U 2008. godini popunjeno je 1138 upitnika, a u 2012. ukupno 583 upitnika. U 2012. godini, učenici su proveli manje vremena napolju/u prirodi. Rezultati iz 2008. pokazuju da su devojke više koristile mere zaštite od sunca, ali su prijavile i veći broj opekotina i poseta solarijumu od momaka. U 2012., muškarci su prijavili više opekotina, ali i veću upotrebu naočara za sunce, šešira/kapa i više vremena provedenog u hladu. **Zaključak.** Uočene su statistički značajne promene ponašanja adolescenata na suncu između 2008. i 2012. godine, kao i između muškog i ženskog pola. U buduću, potrebno je redovno organizovati edukacije u školama, a posebno treba naglasiti sledeće: značaj primene mera zaštite od sunca, ograničenog izlaganja suncu, ali i fizičkih aktivnosti na otvorenom/u prirodi.

**Ključne reči:** ankete i upitnici; opekotine od sunca; znanje o zdravlju, stavovi, praksa; adolescentsko ponašanje; pigmentacija kože; ultravioletni zraci; sunčanje; polni faktori; primarna prevencija; zaštitni faktor

reflection of that kind of life was, among other things, a tanned, sun kissed look. Although it has been well known for decades that too much exposure to sunlight and sunbathing can be harmful for the skin and the overall health, this fashion trend is still dominant in many societies. In addition to negative cultural trends, an increased number of skin cancers all over the world results from the environmental changes as well.

### Abbreviations

UV	– ultraviolet sun rays
SPF	– sun protection factor

Sun exposure is the major environmental risk factor for the development of both melanoma and non-melanoma skin cancers [1–3]. This risk depends on the individual's characteristics - skin photo-type, genetics, age, sex, occupation, intermittent but not gradual exposure to sunlight, previous history of sunburns, total amount of time spent exposed to sunlight during life, especially during childhood and adolescence, etc. During recent decades, artificial sources of ultraviolet sun rays (UV) have become an important factor contributing to the total exposure of the skin, and the number of visits and time spent in sunbeds must also be taken into account when calculating the total risk of getting skin cancers.

Adolescents, as well as other subgroups under 18 years of age, are very susceptible to UV rays regardless of the source of emission (sunlight or sunbed) [4–7]. It is well known that children and adolescents spend more time outdoors than adults. About one fourth of total lifetime exposure to sun occurs at that time. Due to the cumulative effect of the sun, it is very important to limit sun exposure during the early period of life. This measure of sun protection could reduce the lifetime risk of developing skin cancers by as much as 78% [1, 8–11].

Unfortunately, adolescents are very receptive to negative cultural trends, media and peer influences related to sun exposure and tan as well [12]. They quite unconsciously adopt fashion trends as emanated by their idols and take practices of their elders in sun behavior. They find sun kissed look very attractive and healthy, which motivates them to go sunbathing and/or use sunbed mostly in springtime. With regard to sun protective measures, adolescents want to use them in their own way, respecting no rules or recommendations of the elders. When compared with younger children, adolescents use half amount of sunscreens, and incidence of sunburns is doubled. They deliberately delay the use of sunscreens, use low SPF sunscreens or expose themselves without protection, to get a tan [8, 13]. Some studies have demonstrated that sunbathing (outdoor or in sunbed) can provoke addiction, especially among girls in adolescent period [11, 12]. Aesthetic appearance, but not the health risks could be a reason for them to change the attitude and behavior toward the UV exposure and the tan [4, 14, 15].

It is rather difficult to make the adolescent population change their behavior patterns and thus it is a challenge for this kind of projects. Their attitudes toward tan, sunbathing and sun protection is difficult to change. Public health campaigns and educational interventions for under 18-year-olds in changing the level of knowledge and attitudes about skin cancer risk factors and sun protection have much better results among younger children than in the adolescents. It is difficult to transform the acquired

knowledge and attitudes to sun smart behavior and to keep these changes for a longer period [5, 12].

Our first educational intervention “Sunbathing: Yes or No?” was held among first and second grade high-school students (16 and 17-year old) in Belgrade, Serbia in 2007 and 2008 [16]. At the beginning of the program, we applied original, tailor-made self-report multiple-choice questionnaire (“behavior test”) to make the assessment of adolescent population characteristics, attitudes and sun protection practices (skin photo-type, sun protection habits, use of sunscreens and sunbeds, etc.). To describe skin characteristics in the questionnaire, we used The Fitzpatrick Skin Type classification system (first developed in 1975 by Thomas Fitzpatrick), for skin photo-type category 1–3, and separate description of skin with many nevi for category 4.

In spring 2012 we carried out the same educational program for 16 and 17-year old students in high schools in Belgrade included in 2008 as well. We used the same questionnaires as in 2008 to investigate their attitudes and sun protection practices and behavior. This study compares the results of the 2008 and 2012 surveys.

The purposes of this study were to establish differences in students' attitudes, sun protection practices and behavior in the 4-year period (2008 – 2012) and to assess the relation between sex and skin photo-type (hair and eye color and skin characteristics) and students' sun protection behavior. This study was also aimed at finding out what corrections, if necessary, were to be made in our current educational programme for the students in high schools.

### Material and Methods

The sun protection health promotion project “Sunbathing: Yes or No?” was implemented in Belgrade high schools by the Health&Beauty Care Center, Belgrade and Serbian Society for Fight against Cancer and under the patronage of the Ministry of Health of the Republic of Serbia [17] and the Ministry of Education and Sport of the Republic of Serbia [18].

The survey included the whole classes or even the whole generation (all classes in the same generation, depending on the organizational possibilities) of the first and second grade students in the selected schools in region of Belgrade. The same schools were included in the program in 2008 and in 2012.

The original, tailor-made, self-report multiple-choice questionnaires (about the skin types, behavior regarding the exposure to the sun and the use of sunbed) were distributed to 16 and 17-year-old students in the high-schools in Belgrade, Serbia.

After data collection, the results were entered into the database and analyzed, comparing answers in 2008 and in 2012 in order to establish the changes. Data from these tests for both years were analyzed by the Pearson's chi square test and logistic regression analyses. We took into account the different number of the students in two cohorts. To

compare, analyze and present the 2008 and 2012 survey data, we used the statistical analysis similar to the method used by Gavin A, et al. [19].

**Results**

All P-values less than  $\alpha=0.05$  will be presented in boldface font (in the tables).

In this study, 1138 behavior tests were completed in 2008, and 583 in 2012.

In the 2008 sample, 65.2% were female respondents, and 34.8% were males. In the second survey sample, 49.56% were female respondents, and 50.44% were males. The majority of respondents in the 2008 sample were born in 1992 (45.9%) and 1991 (32.6%); whereas in the 2012 sample the majority of respondents were born in 1996 (52.3%) and 1995 (41.3%). Brown hair color and brown eyes were reported by the majority of respondents (55.98% in 2008 and 50.09% in 2012), and (47.1% in 2008, and 46.6% in 2012), respectively.

More than the half of the respondents in the 2008 sample (52.3%), mostly girls ( $P<0.001$ ), spent “30% - 50% of their free time outdoors”. In 2012 the number of students who chose this answer declined (38.7%), and more students spent only “10% to 30% of their free time outdoors” (23% in 2008 and 35.7% in 2012,  $P<0.001$ ) (**Table 1**). In 2012 there were no differences between males and females ( $P=0.323$ ), but the comparison of the results for 2008 and 2012 showed that females spent more time outdoors ( $P<0.001$ ), mostly 30 to 50% of their free time (34.64% females, and 16.06% males). The amount of free time spent outdoors reported in 2008 as compared with those from 2012 is related to the skin photo-type. The tendency to change the percentage

of time spent outside is affected by skin characteristics, but not hair or eye colour ( $P<0.001$ ) (**Table 1**).

In 2012, respondents were less likely to report “preparing the skin for the summer and gradual sunbathing” (41.51%) than in 2008 (57.93%), ( $P<0.001$ ), but for “avoiding midday activities” differences were not statistically significant ( $P=0.404$ ) and stayed at a low level – only 29.36% of students in 2008 and 27.67% in 2012 used this method of sun protection. Although participants in both years reported almost the same and fortunately small number of cases of “skin cancer in family history” (1.16% in 2008, and 0.88% in 2012,  $P=0.543$ ), the problem is a statistically significant increase ( $P=0.009$ ) in “occurrence of sunburns”, from 44.11% in 2008 to 49.91% in 2012. From 2008 to 2012, the respondents were more likely to wear a hat ( $P=0.002$ ), use sunglasses ( $P<0.001$ ), or stay in the shade ( $P<0.001$ ). No differences were found in the items “using sunscreens” ( $P=0.274$ ) and “clothes to cover up the skin” ( $P=0.573$ ), as measures of sun protection, between 2008 and 2012 survey. In addition, the number of sunbed uses remained at the similar level for 2008 (15.75%) and 2012 (14.01%),  $P=0.281$ .

In the 2008 survey, the female respondents were more likely to “avoid midday sun” (20.98% of females, and 8.39% of males,  $P<0.001$ ), “gradually sunbathe” (43.81% of females and 14.12% of males,  $P<0.001$ ), “wear a hat/cap” (19.70% of females and 12.50% of males,  $P<0.001$ ), “use sunglasses” (31.45% of females and 12.64% of males,  $P<0.001$ ), use “clothes to cover the skin” (1.05% of females and 0.88% of males,  $P=0.034$ ), apply “sunscreens” (51.06% of females and 13.52% of males,  $P<0.001$ ), and “stay in the shade” (21.95% of females and 20.51% of males). They reported more sunbed uses (14.91% of females and 0.4% of males,  $P<0.001$ ), and

**Table 1.** Percentage of free time spent outside, adjusted for students’ gender, hair and eye color and skin characteristics, 2008/2012

**Tabela 1.** Vreme koje učenici provode napolju/u prirodi (%), prema polu, boji kose i očiju i karakteristikama kože, 2008/2012.

Percentage of time spent outside (%), Vreme koje učenici provode napolju/u prirodi (%)	2008/2012															
	Gender/Pol			Hair colour/Boja kose				Eye colour/Boja očiju			Skin Characteristics Karakteristike kože					
	Female Ženski	Male Muški	P-value p-vrednost	Light Svetla	Brown Smeđa	Dark Tamna	P-value p-vrednost	Light Svetla	Brown Smeđa	Dark Tamna	P-value p-vrednost	Cat. 1 Kat. 1	Cat. 2 Kat. 2	Cat. 3 Kat. 3	Cat. 4 Kat. 4	P-value p-vrednost
Up to 10%, Do 10%	1.50	0.88		0.47	1.29	0.62		0.84	0.96	0.57		0.39	1.21	0.72	0.06	
10–30%	13.72	8.41	<b>&lt;0.001</b>	2.99	12.04	7.10	0.241	5.87	10.15	6.11	0.356	1.97	11.98	7.98	0.21	<b>&lt;0.001</b>
30–50%	34.64	16.06		7.08	28.67	14.95		13.80	24.08	12.82		2.67	25.72	21.80	0.51	
More than 50% Više od 50%	13.52	11.28		3.57	13.29	7.94		6.67	11.87	6.26		0.90	10.89	12.80	0.21	

Legend - Skin characteristics (for all Tables):

Cat. 1 - light, sensitive skin, with freckles, easily burns but never tans; Cat. 2 - skin that moderately burns and moderately tans; Cat. 3 - skin that rarely burns and easily tans; Cat. 4 – skin with many nevi, new nevi and freckles appear after the summer season

Legenda – karakteristike kože (za sve tabele):

Kat. 1 – svetla, osetljiva koža, sa pegama, lako gori nikada ne tamni; Kat. 2 – koža koja umereno gori i umereno tamni; Kat. 3 – koža koja retko gori, a lako tamni; Kat. 4 – koža sa puno mladeža, posle sezone sunčanja (leto), pojavljuju se novi mladeži i pege

**Table 2.** Sun protection practice and behavior (%), adjusted for gender, hair and eye color and skin characteristics, 2008/2012**Tabela 2.** Navike i ponašanje na suncu (%), prema polu, boji kose i očiju i karakteristikama kože, 2008/2012.

Question (%) Pitanje (%)	2008/2012															
	Gender/Pol			Hair color/Boja kose				Eye color/Boja očiju				Skin Characteristics Karakteristike kože				
	Female Ženski	Male Muški	P-value p-vrednost	Light Svetla	Brown Smeđa	Dark Tamna	P-value p-vrednost	Light Brown Svetla	Dark Smeđa	Tanna Tamna	P-value p-vrednost	Cat. 1 Kat. 1	Cat. 2 Kat. 2	Cat. 3 Kat. 3	Cat. 4 Kat. 4	P-value p-vrednost
Avoiding mid-day activities/Iz-begavanje aktivnosti oko podneva	20.14	9.02	<0.001	4.02	16.69	8.45	0.195	8.41	13.23	7.53	0.194	2.30	14.38	12.14	0.35	0.002
Gradual sunbathing/Postepeno sunčanje	41.65	14.36	<0.001	8.41	32.61	14.99	<0.001	16.45	26.56	13.00	<0.001	3.28	28.28	23.75	0.70	0.108
Occurrence of sunburns/Učestalost opekotina	25.62	19.18	<0.001	7.69	24.59	12.51	<0.001	13.60	20.63	10.56	<0.001	4.18	27.34	12.51	0.76	<0.001
Using sunbeds Korišćenje solarijuma	14.60	0.94	<0.001	2.83	8.45	4.27	0.001	4.18	7.34	4.02	0.985	0.55	7.08	7.75	0.16	<0.001
Skin cancer in family history/Rak kože u porodici	0.72	0.41	0.967	0.27	0.51	0.35	0.103	0.29	0.41	0.43	0.093	0.16	0.53	0.35	0.08	<0.001
Sun protection/Mere zaštite od sunca																
Hat/cap Šešir/kapa	19.05	13.90	<0.001	4.00	19.30	9.66	0.002	9.06	15.61	8.29	0.781	2.36	17.45	12.84	0.31	<0.001
Sunglasses/Naočare za sunce	32.28	14.48	<0.001	6.77	26.13	13.86	0.381	12.67	22.31	11.77	0.619	2.32	22.70	21.45	0.29	<0.001
Clothes/Odeća	0.96	1.00	0.011	0.27	0.92	0.78	0.145	0.57	0.62	0.78	0.002	0.35	0.86	0.68	0.08	<0.001
Sunscreen/Preparati za zaštitu od sunca	49.57	15.28	<0.001	9.54	36.81	18.50	<0.001	18.42	30.09	16.35	0.032	3.86	32.03	28.22	0.74	0.464
Stay in the shade Boravak u hladu	22.76	22.81	<0.001	6.54	24.02	15.01	0.002	12.31	21.49	11.77	0.970	2.95	24.71	17.47	0.43	<0.001

more frequent "occurrence of sunburns" (26.13% of females and 17.98% of males,  $P<0.001$ ), but for "number of skin cancer in family history", there were no significant differences between females and males, i.e. (0.74% and 0.42%, respectively,  $P=0.857$ ).

In the 2012 survey, there were no significant differences ( $P=0.897$ ) between the answers of the female and male responses (13.84% and 13.84%, respectively) regarding avoiding of midday sun, and this behavior changed significantly compared with the data from 2008 ( $P<0.001$ ), after adjustment for gender, hair and eye colour and skin characteristics (Table 2). Sunburns were more often reported by the male respondents (28.20%) than by females (21.72%)  $P=0.004$ , as well as wearing a hat/cap (males 24.52%, females 14.19%),  $P<0.001$  in 2012, this was significantly different from the 2008 ( $P<0.001$ ). There were differences ( $P<0.001$ ) in sunscreen use between the female and male respondents. In 2012, the females reported less sunscreen use than in 2008 (38.35% in 2012 and 51.06% in 2008), and the males increased the use of sunscreens as a measure of sun protection (28.55% in 2012 and 13.52% in 2008). In 2012,

40.11% of males and 28.9% of females,  $P<0.001$ ) reported staying in the shade, which was statistically different compared to 2008,  $P<0.001$ . Skin characteristics affect the occurrence of sunburns. In the 2008 survey the sunburns occurred in 26.99% of respondents with the "skin that moderately burns, moderately tans" (category 2), in comparison to 12.96% of those with "the skin that rarely burns, easily tans" (category 3) (OR 0.437,  $P<0.001$ ). Similar results were observed in the 2012 survey: sunburns occurred in nearly one third of respondents with the "skin that moderately burns, moderately tans" (category 2) (29.95%), that being twice more than in those with "skin that rarely burns, easily tans" (category 3) (12.96%) (OR 0.360,  $P<0.001$ ). After adjustment for gender, hair and eye colour and skin characteristics, the results for the 2008/2012 survey show significant differences (OR=0.428 and  $P<0.001$ ).

The majority of respondents who used sunscreens chose sun protection factor (SPF) = 15-30. Of respondents who reported using sunscreens, in both years, those who chose SPF=15-30 (57.7% in 2008 and 51.34% in 2012) prevailed. In 2012 the percentage of

**Table 3.** Annual number of uses of sunbed (%), adjusted for gender, hair and eye color and skin characteristics, 2008/2012**Tabela 3.** Broj poseta solarijumu godišnje (%), prema polu, boji kose i očiju i karakteristikama kože, 2008/2012.

Annual number of sunbed uses (%) Broj poseta solarijumu godišnje (%)	2008/2012															
	Gender/Pol			Hair color/Boja kose				Eye color/Boja očiju				Skin Characteristics Karakteristike kože				
	Female Ženski	Male Muški	P-value p-vrednost	Light Svetla	Female Ženski	Male Muški	P-value p-vrednost	Light Svetla	Female Ženski	Male Muški	P-value p-vrednost	Light Svetla	Female Ženski	Male Muški	P-value p-vrednost	Light Svetla
Up to 10/ <i>Do 10</i>	41.04	2.27		7.35	24.33	11.63		11.63	22.06	9.63		1.20	20.19	21.66	0.27	
10-20	35.03	0.80	<0.001	6.02	19.65	10.16	0.456	9.49	15.91	10.43	0.259	1.07	17.65	16.84	0.27	0.032
More than 20 <i>Više od 20</i>	17.91	2.94		4.81	10.29	5.75		6.02	8.96	5.88		1.34	7.49	11.50	0.53	

respondents who opted for SPF>30 rose (from 32.84% in 2008 to 38.77% in 2012), but with no statistical significance ( $P=0.054$ ). There were significant differences between the male and female users ( $P<0.001$  in 2008 and  $P=0.008$  in 2012) and between the years of survey ( $P<0.001$ ). Sunscreens with SPF=15-30 were used by 46.98% of female respondents and 10.71% of males in 2008 and by 29.41% of females and 21.93% of males in 2012. In 2012, the percentage of girls using SPF > 30 was lower than in 2008, being 20.59% and 24.63%, respectively.

On the contrary, the boys used more sunscreens with SPF>30 in 2012 than in 2008 (18.8% and 8.21%, respectively). According to the skin characteristics, the majority of those who used sunscreens were the respondents with category 2 skin, and they used mostly SPF=15-in both years (28.39% in 2008 and 28.88% in 2012).

As for the number of sunbed uses, there were some differences between the male and female respondents in the two surveys. In 2008, 14.91% of girls and 0.84% of boys used sunbeds ( $P<0.001$ ), and there were no significant differences concerning the data from 2012 ( $P=0.281$ ): 12.26% of girls and 1.75% of boys ( $P<0.001$ ). In 2008, 43.83% of those who reported using sunbeds, went there up to 10 times that year, whereas 48% used sunbed 10-20 times in 2012, thus  $P=0.047$  for 2008/2012. The number of sunbed uses depended on the skin characteristics as well ( $P=0.032$ ) (**Table 3**).

## Discussion

During the past decades, the Serbian population received a lot of information about sun protection and skin cancer prevention through the media, which greatly influenced public knowledge and behavior. As well as in many countries in the world, the key messages for the population in Serbia were to avoid mid-day sun, to prepare the skin before summer by gradual sunbathing and to use sun protection measures – to wear a hat/cap, use sunscreens, cover the skin by clothes, use sunglasses and stay in the shade [19–21].

In Serbia, there were no broad campaigns or educational programs focused on sun protection

among adolescents, so information distributed by media was very important for young people in adolescent period, too. Although the adolescents were very interested in fashion trends and sun-kissed look, they were also receptive to information and open to changes in attitude and behavior towards the sun, like their peers in other countries [22]. However, during the past several years, mass media in Serbia paid much more attention to many different health care topics, and sun protection promotion was pushed back. In addition, since 2008, media attention has been focused mostly on global economic crisis and its consequences at the local level, so the public health campaigns have become less prominent. The lack of information probably had an influence on behavior and sun protection practice among students', as shown by this investigation, the first one dealing with these issues in Serbia.

In 2012, the students spent less time outdoors than in 2008. This seems positive in relation to the sun protection and sun burns prevention, but it also raises concerns if they spent less time in the sports activities, in the fresh air, and (probably) among peers and friends. Besides, this change in the behavior could provoke a new problem – vitamin D deficiency, so in our future program the students should be informed about the importance of vitamin D for health, and sunbathing time optimal to produce enough vitamin D without getting sunburns. The participants have recently shown the tendency to spoil their previous positive practice to prepare the skin for summer by gradual sunbathing, and this should be the subject for the future educational interventions among adolescents and/or public health campaigns. It is also necessary to stress the importance of avoiding midday sun and increased use of all sun protection measures since it is a way to prevent sun burns and skin cancer development. Creating the school curricula and sports activities schedule early in the morning or later in the afternoon could become regular schools' practice since this measure has given good results elsewhere [23, 24].

In our first survey, the girls were more conscientious than the boys in adopting and applying sun protection measures, but they used sunbed much more frequently than the boys and got sunburns more often.

In 2012, the boys reported more sunburns. In spite of all activities aimed at raising the awareness of young people regarding the dangerous effects of exposure to sun, the sunburn prevalence among adolescents was higher in the recent years, which is very worrying. Long-term health risks associated with the sunburn in the childhood should be strongly emphasized in future educational interventions in schools, as well as in the media [8, 19, 20, 25].

It is encouraging that participants, particularly boys, have recently increased the use of some sun protection measures, such as wearing hat/cap, using sunglasses and staying in shade (that became the most common method of sun protection in recent years, particularly among boys). In future campaigns, more attention should be paid to using clothes to cover up and protect the skin from UV rays. In accordance with other findings [8, 9], the sunscreens have been one of the most common methods of sun protection among adolescents despite the recommendations that it should be only adjunct supplement to other forms of protection. SPF 15-30 was the dominant choice in sunscreens use in these surveys, that being similar to other studies [26]. Anyway, sun protection products with SPF>30 gradually gained the position in sun care practice of adolescents. Although some previous studies have found that adolescents deliberately use sunscreens with low SPF, it seems that in Serbia advertising campaigns of cosmetic companies which produce the sunscreens and recommend sunscreens with higher SPF, are very influential and/or that perceived social norms within the peer group have changed [8].

Obviously, the adolescents, particularly girls are still interested in using sunbeds, as shown in other

studies [9, 27], which is a serious problem in Serbia. Because of the absence of any relevant legislation or regular inspection of the equipment performances, or application of supposedly mandatory preventive measures whenever the use of sunbed is concerned, the health promotion regarding sun protection and using sunbed is going to be a burning issue that so far has failed to draw appropriate attention of either medical or general public in Serbia.

Limitations of the study are the results based on the students' self-reports.

### Conclusion

Due to the absence of appropriate educational programs in schools, the sun protection attitude and behavior among the high school students are affected and created by information distributed by media, fashion trends and peer influences. In order to keep positive trends in behavior regarding sun protection, our future educational interventions for the adolescents should be regular and focused on highlighting the following: the importance of limited exposure to sun, avoiding midday sun outdoor activities and the adoption and application of all sun protection measures. In addition, it should be emphasized that avoidance of the midday sun outdoor activities does not exclude outdoor activities but just that the regular physical activities outdoors should be planned before 10 a.m. and after 4 p.m., especially because the exposure to sun is important, particularly for children and young people, for the synthesis of vitamin D in the skin, which is necessary for the growth and development.

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## RELATIONSHIP BETWEEN HEAD POSTURE AND PARAMETERS OF SAGITTAL POSITION AND LENGTH OF JAWS

POVEZANOST POLOŽAJA GLAVE I PARAMETARA SAGITALNOG POLOŽAJA I DUŽINE VILICA

Vladanka VUKIĆEVIĆ<sup>1</sup> and Đorđe PETROVIĆ<sup>2</sup>

### Summary

**Introduction.** Head posture in relation to the cervical spine is correlated with the morphology of the face and jaw, the position and the mutual relationship of the maxilla and mandible, their length and inclination. The aim of this study is to examine the relationship between the head posture and parameters of the sagittal position and length of the jaws. **Material and Methods.** The study included 90 subjects (30 for I, II and III skeletal class each) between the ages of 8 and 14 years, who were examined at the Department of Dentistry of Vojvodina in Novi Sad. Each subject had the lateral cephalogram made, and the analysis was performed by means of the computer program "Onyx Ceph." The following parameters were analyzed: craniocervical angle, angle of maxillary prognathism, angle of mandibular prognathism, the difference angles of maxillary and mandibular prognathism, length of maxillae, and length of mandible. **Results.** The angle of maxillary prognathism was in positive correlation with the craniocervical angle in the patients with class I and II, and they were negatively correlated in the patients with class III. The angle of mandibular prognathism was in positive correlation with the craniocervical angle in the patients with class I and III, but they were negatively correlated in the patients with class II. The patients with class II had a statistically significant positive correlation between the craniocervical angle and length of the maxilla, and a significant, but negative correlation between the craniocervical angle and length of the mandible. **Conclusion.** Increased extension of the head in relation to the cervical spine can be a contributing factor to the formation of class II malocclusion.

**Key words:** Head; Posture; Jaw; Child; Adolescent; Prognathism; Malocclusion; Image Processing, Computer-Assisted; Cephalometry

### Introduction

There are many studies in orthodontic literature that have examined the relationship between the head posture and craniofacial morphology [1–18]. The head position is estimated on the basis of the craniocervical angle, which is formed by the basic anterior cranial base (NS), and odontoid process tangent (OPT) which passes through the lower end last point on the body of the second cervical vertebra [2]. The first study of the head position was published by Solow B. and A. Tallgren in 1976 [3],

### Sažetak

**Uvod.** Položaj glave u odnosu na vratnu kičmu dovodi se u vezu sa morfologijom lica i vilica, položajem i međusobnim odnosom maksile i mandibule, njihovom dužinom i inklinacijom. Cilj ovog istraživanja jeste da se analizira povezanost položaja glave i parametara sagitalnog položaja i dužine vilica. **Materijal i metode.** Ispitivanjem je obuhvaćeno 90 ispitanika (po 30 za I, II i III skeletnu klasu) starosti 8–14 godina, koji su bili pregledani na Klinici za stomatologiju Vojvodine u Novom Sadu. Za svakog ispitanika napravljen je profilni telerendgenski snimak i urađena analiza primenom kompjuterskog programa *Onix Ceph*. Analizirani su sledeći parametri: kraniocervikalni ugao, ugao maksilarnog prognatizma, mandibularnog prognatizma, razlika uglova maksilarnog mandibularnog prognatizma, dužina maksile i dužina mandibule. **Rezultati.** Ugao maksilarnog prognatizma je u pozitivnoj korelaciji sa kraniocervikalnim uglom kod ispitanika sa I i II, a u negativnoj kod ispitanika sa III klasom. Ugao mandibularnog prognatizma je u pozitivnoj korelaciji sa kraniocervikalnim uglom kod ispitanika sa I i III klasom, a u negativnoj kod ispitanika sa II klasom. Kod ispitanika sa II klasom postoji statistički značajna pozitivna korelacija kraniocervikalnog ugla i dužine maksile i značajna, ali negativna, korelacija kraniocervikalnog ugla i dužine mandibule. **Zaključak.** Povećana ekstenzija glave u odnosu na vratnu kičmu može biti faktor koji doprinosi nastanku malokluzija II klase.

**Cljučne reči:** glava; položaj; vilica; dete; adolescent; prognatizam; malokluzija; kompjuterska obrada slike; cefalometrija

who analyzed variables defining craniofacial morphology and defining head posture, on the cephalometric radiographs of 120 subject between the ages of 20 and 30 years. The results have shown that the extension of the head in relation to the cervical spine, i.e. an increased craniocervical angle, is connected with a large anterior and small posterior facial height, reduced sagittal craniofacial dimensions, large inclination of the mandible compared to the anterior cranial base and nasal plane, facial retrognathism, large angle of the cranial base and reduced nasopharyngeal space. There is a reduced

**Abbreviations**

NS	– anterior cranial base
OPT	– odontal process tangent
ANB angle	– an indication of sagittal jaws relations
SNA	– angle of maxillary prognathism
SNB	– angle of mandibulary prognathism
NS/OPT	– craniocervical angle

anterior and increased posterior facial height, increased sagittal craniofacial dimensions, reduced inclination of the mandible, facial prognathism, decreased angle of the cranial base and increased nasopharyngeal space in the flexion of the head (reduced craniocervical angle). By examining the head position in children with skeletal class I, II and III, whose average age was 9.5 years, D'Attilio M, et al. [5] found that children with skeletal class III showed a significantly lower angle of cervical lordosis than those with class I and II. A significantly higher extension of the head was found in children with skeletal class II compared to those with skeletal class I and III. There is a significant difference between these three classes in the inclination of the maxillary and mandibular plane compared to the cervical spine.

The size and position of the mandible are the characteristics that are strongly connected with the position of the head and neck [5]. Solow B. and Siersbæk N. [15] found a reduced craniocervical angle in cases where a face grew with rotation forward and an increased one in cases where a face grew with rotation backwards.

Kim Phong et al. [16] have found a connection between the extension of the head in relation to the cervical spine, with an increased angle of the cranial base, increased vertical dimensions of the face and jaws retrognathism.

By examining the sagittal jaws position in persons with skeletal class I authors found that the angle of maxillary prognathism (SNA) and angle of mandibulary prognathism (SNB) are significantly lower than the standard values, which indicates the posterior position of jaws and retrognathic facial type [19].

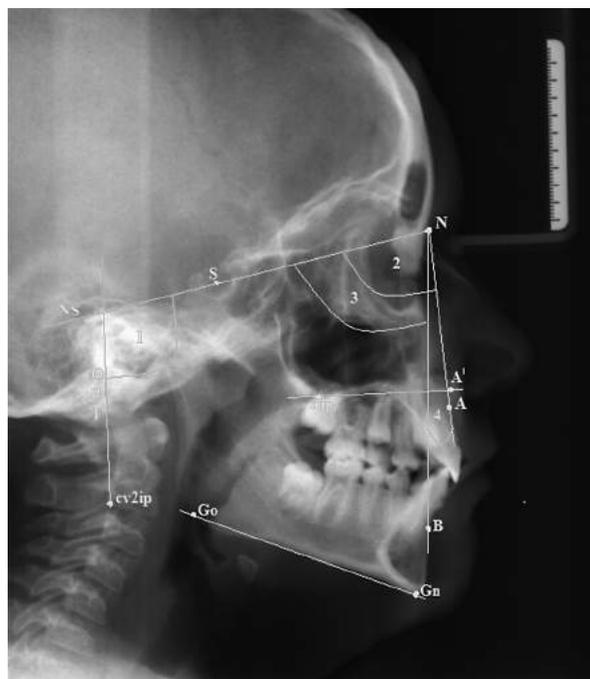
The aim of this study is to analyze the connection between head posture and parameters of the sagittal position and length of the jaws in people with different sagittal skeletal jaw relations.

**Material and Methods**

This study included 90 subjects between the ages of 8 and 14 years, who were examined at the Department of Dentistry, Faculty of Medicine in Novi Sad.

The selection of the test sample was carried out according to the following criteria:

- they had not been treated orthodontically previously;
- sagittal skeletal relation in class I, II and III;
- absence of congenital disorders of craniofacial complex, diseases of muscles and temporomandibular joint;
- absence of any upper airway obstruction;



**Figure 1.** Points, lines and angles used to assess the craniocervical angulation, sagittal position and length of jaws: N - nasion; S - sella; A - subspinale; B - supramentale; Me - menton; Gn - gnathion; A' - projection of the point A on the base plane of the maxilla; snp - spina nasalis posterior; cv2ip - most inferior and posterior point on the second cervical vertebra corpus; OPT - odontoid process tangent through cv2ip point; NS - the anterior cranial base plane; 1. NS/OPT - craniocervical angle; 2. SNA - angle of maxillary prognathism; 3. SNB - angle of mandibulary prognathism; 4. ANB angle - an indicator of sagittal jaws relations; A'-snp - length of maxilla; Gn-Go - length of mandible

**Slika 1.** Tačke, linije i uglovi korišćeni za procenu kranio-cervikalne angulacije, sagitalnog položaja i dužine vilica: N - Nasion; S - Sella; A - subspinale; B - supramentale; Me - menton; Gn - gnathion; A' - projekcija tačke A na osnovnu ravan maksile; snp - spina nasalis posterior; cv2ip - krajnja zadnja donja tačka na telu drugog vratnog pršljena; OPT - tangenta odontoidnog procesusa koja prolazi kroz tačku cv2ip; NS - osnovna ravan prednje kranijalne baze; 1. NS/OPT - kranio-cervikalni ugao; 2. SNA - ugao maksilarnog prognatizma; 3. SNB - ugao mandibularnog prognatizma; 4. ANB ugao - pokazatelj sagitalnog odnosa vilica; A'-snp - dužina maksile; Gn-Go - dužina mandibule

The subjects were divided into three groups consisting of 30 subjects with I, II and III class of sagittal intermaxillary relations based on the values of angle ANB (indicator of sagittal jaws relations) according to the following criteria:

- ANB = 2 - 4° - skeletal class I
- ANB > 4° - skeletal class II
- ANB < 2° - skeletal class III.

Lateral cephalometric radiograph was done for each subject according to the standard recording con-

**Table 1.** Craniocervical angle (NS/OPT) values as compared to skeletal class  
**Tabela 1.** Vrednosti kraniocervikalnog ugla (NS/OPT) u odnosu na skeletnu klasu

	Skeletal class/Skeletna klasa			Total/Ukupno
	I	II	III	
Number of patients/Broj pacijenata	30	30	30	90
Min	77	79.20	72.20	72.20
Max	115.20	126.30	120	126.30
Mean/Srednja vrednost	94.06	100.80	94.59	96.49
SD	1.81	11.10	1.80	10.64
ANOVA	F = 3.97; p < 0.05			
t- test (I i II)	t = -2.48			p < 0.05
t- test (I i III)	t = -0.21			p > 0.05
t-test (II i III)	t = 2.29			p < 0.05

ditions and cephalometric analysis was done by means of the computer program "Onyx Ceph". The craniocervical angle (NS/OPT) was analyzed as an indicator of the head posture in relation to the cervical spine. The following parameters were analyzed as the indicators of the sagittal position and length of jaws: the angle of maxillary prognathism, the angle of mandibular prognathism, ANB angle as an indicator of sagittal jaw relations, maxillary length (A'-snp), and the length of the mandible (Gn - Go). All the parameters are shown in **Figure 1**.

The values of the angles are expressed in degrees, and the values of jaw length in millimeters.

After completion of the analysis, the obtained data were statistically analyzed by means of methods taken from descriptive statistics methods: methods of data sorting (grouping and tabulation), arithmetic mean and standard deviation. Parametric tests for large and small independent samples (ANOVA and Student's t test) and non-parametric tests for large and small independent samples were used in this study and they were taken from differential statistical methods (Pearson  $\chi^2$  test, Mann-Whitney test and Kruskal Wallis test). In order to measure the form and degree of dependence, the correlation and regression analysis was used: linear regression, correlation coefficient and coefficient of determination.

## Results

The results obtained by the comparative analysis of the value of the angle NS/OPT in relation to the skeletal class are given in **Table 1**.

By testing the significance of differences based on ANOVA test, the difference in the value of the craniocervical angle between the analyzed groups was found to be statistically significant (F = 3.97; p < 0.05), and their comparison showed that there was a statistically significant difference between the patients with class I and II (t = 2.48; p < 0.05), and among those with class II and III (t = 2.29; p < 0.05).

The results of the comparative analysis of the value of the angle of maxillary prognathism SNA and mandibular prognathism SNB are shown in **Table 2**. ANOVA test results show a statistically significant difference in average values of SNA angle (F = 9.88; p < 0.001) between the analyzed groups of patients, and their mutual comparison led to the conclusion that there is a statistically significant difference between the patients with class I and II (t = 4.15; p < 0.01), and between those with class II and III (t = 4.09; p < 0.01). After a statistically significant difference in the values of the angle SNB between skeletal class (F = 15.82; p < 0.001) had been established, their comparison showed a statistically significant differ-

**Table 2.** SNA and SNB angle values as compared to skeletal class  
**Tabela 2.** Vrednosti ugla maksilarnog (SNA) i mandibularnog prognatizma (SNB) u odnosu na skeletnu klasu

	SNA			SNB		
	I	II	III	I	II	III
Number of patients/Broj pacijenata	30	30	30	30	30	30
Min	74.50	78	67	71.90	73.10	71
Max	85.30	85.90	86	82	79	87
Mean/Srednja vrednost	78.96	82.70	78.38	75.98	75.87	79.56
SD	0.54	0.37	0.72	0.52	0.31	0.69
ANOVA	F = 9.88; p < 0.001			F = 15.82; p < 0.001		
t-test (I i II)	t = -4.15	p < 0.001		t = 0.18	p > 0.05	
t-test (I i III)	t = 0.34	p > 0.05		t = -4.16	p < 0.001	
t-test (II i III)	t = 4.09	p < 0.001		t = -4.90	p < 0.001	

**Table 3.** Craniocervical angle correlation – parameters of jaw position  
**Tabela 3.** Korelacija kraniocervikalni ugao (NS/OPT) parametri položaja vilica

	Correlation (r)/Korelacija (r) Probability (p)/Verovatnoća (p)	NS/OPT			
		I	II	III	Total/Ukupno
SNA	r	0.103	0.112	-0.002	0.123
	p	n.s.	n.s.	n.s.	n.s.
SNB	r	0.044	-0.005	0.179	-0.066
	p	n.s.	n.s.	n.s.	n.s.
ANB	r	0.311	0.156	0.075	0.177
	p	0.05	n.s.	n.s.	0.05

n.s. – not significant/nije statistički značajno; ANB - pokazatelj sagitalnog odnosa vilica; SNB - ugao mandibularnog prognatizma, SNA - ugao maksilarnog prognatizma

ence in the value of the angle between the patients with I and III ( $t = -4.16$ ;  $p < 0.01$ ), as well as between those with class II and III ( $t = -4.90$ ;  $p < 0.01$ ).

The results of correlation analysis between the craniocervical angle and parameters of the jaw position are shown in **Table 3**. A positive correlation between the angle of NS/OPT and SNA angle was found ( $r = 0.103$ ;  $r = 0.112$ ) in the patients with I and II class, however, the degree of this dependence was not statistically significant. In the class III a negative correlation was established, but it was not statistically significant either ( $r = -0.002$ ). The coefficient of determination for all three classes was very low (less than 0.1) which indicates that the impact of variability NS/OPT angle on the value of SNA angle was a very small percentage. In the patients with class I and III a positive correlation between angles NS/OPT and SNB was found, which was not statistically significant ( $r = 0.044$ ;  $r = 0.179$   $p > 0.05$ ). In those with class II, a negative correlation was found, which was also statistically insignificant ( $r = -0.005$ ;  $p > 0.05$ ).

By analyzing the shape and degree of dependence of the ANB angle in relation to the angle of NS/OPT it was found that the forms of dependence were linear, and that the dependence degree was statistically significant ( $r = 0.311$ ,  $p < 0.05$ ) in the patients with class I. The coefficient of determination was  $R^2 = 0.2018$ ,

which indicated that 20% of the variability of ANB angle could be explained by the variability of NS/OPT angle, and that 80% was attributed to other factors. The degree of dependence was not statistically significant in the patients with class II and III ( $r = 0.156$ ;  $r = -0.075$   $p > 0.05$ ), which means that the variability of craniocervical angle had little influence on the variability of ANB angle ( $R^2$  less than 0.1 or 10%).

In the total sample consisting of the patients with I, II and III class, the angle NS/OPT was in positive correlation with the angles SNA and ANB, and in negative correlation with the angle of SNB. This would practically mean that the increase in the angle NS/OPT led to an increase in SNA angle and a decrease in the SNB angle, which led to an increase in ANB angle.

**Table 4** shows the results of the descriptive analysis of the upper and lower jaw length values in all three groups of patients. There was a significant difference in the average values of the upper jaw length between the patients with class II and III ( $t = 2.84$ ;  $p < 0.05$ ). The highest average value of the lower jaw length was observed in the patients with class III, and this value was significantly different from the average value of this parameter in those with class II ( $t = -2.83$ ;  $p < 0.01$ ).

The results of correlation analysis between the craniocervical angle and the length of the upper and lower jaw are shown in **Table 5**. Craniocervical angle in the

**Table 4.** Maxillary ( $A'-snp$ ) and mandible length (Gn-Go) as compared to skeletal class  
**Tabela 4.** Dužine maksile ( $A' - snp$ ) i mandibule (Gn-Go) u odnosu na skeletnu klasu

	$A' - snp$			Gn-Go		
	I	II	III	I	II	III
Number of patients/Broj pacijenata	30	30	30	30	30	30
Min	36.40	35.80	32.90	53.90	58.20	60.30
Max	51.50	51.10	50.30	84.20	77	87.50
Mean/Srednja vrednost	43.75	46.67	42.86	67.57	65.08	70.14
SD	0.65	0.61	0.75	1.22	0.83	1.17
ANOVA	F = 3.53; $p > 0.05$			F = 3.58; $p < 0.05$		
t-test (I i II)	t = 0.08	$p > 0.05$		t = 1.01	$p > 0.05$	
t-test (I i III)	t = 0.89	$p > 0.05$		t = -1.52	$p > 0.05$	
t-test (II i III)	t = 2.84	$p < 0.05$		t = -2.83	$p < 0.01$	

**Table 5.** Craniocervical angle correlation– lengths of jaws  
**Tabela 5.** Korelacija kraniocervikalni ugao (NS/OPT) dužine vilica

	Correlation (r)/Korelacija (r) Probability (p)/Verovatnoća (p)	NS/OPT			
		I	II	III	Total/Ukupno
A'-snp	r	0.028	0.318	-0.020	-0.057
	p	n.s.	0.05	n.s.	n.s.
Gn-Go	r	-0.107	-0.220	0.006	-0.105
	p	n.s.	0.05	n.s.	n.s.

A'-snp - dužina maksile; Gn-Go - dužina mandibule

patients with class I was in positive correlation with the length of the upper jaw and in negative correlation with the length of the lower jaw, but this correlation had no statistical significance. In the patients with class II, we found a statistically significant positive correlation of craniocervical angle and the upper jaw length ( $r = 0.318$ ;  $p < 0.05$ ), as well as a significant negative correlation of craniocervical angle and the lower jaw length ( $r = -0.220$ ;  $p < 0.05$ ). In the patients with class III a negative correlation of craniocervical angle and length of the upper jaw was found, and a positive correlation of craniocervical angle and the lower jaw length.

## Discussion

The analysis of linear and angular parameters on the lateral cephalometric radiographs of patients with malocclusions class I, II and III revealed the difference in the value of the craniocervical angle between the groups, as well as the correlation between craniocervical angulation and parameters of the sagittal position and length of the jaws.

In the patients with class I malocclusion the average value of the craniocervical angle was  $94.06^\circ$ , which is in line with the results of previous study [6] which revealed that the value of the craniocervical angle was  $94.6^\circ$  in children between the ages of 7 and 13 years, without craniofacial anomalies, diseases of the muscles and joints and without obstruction of the upper airways. A statistically significant difference of the angle values was established between the patients with class I and II, and II and III.

The highest value of the craniocervical angle ( $100.8^\circ$ ) was observed in the patients with class II, while the values for class I and III were similar. This corresponds to the findings of D'Attilio M. [5], who found that children 9.5 years old on average, with class II division showed significantly greater craniocervical angle compared with children of the same age who had class I and III. Capruso et al. [7] found a connection between skeletal class II and increased craniocervical angle. Arntsen and Sonnesen [8] also found an increased head extension in the patients with class II malocclusion. Gonzalez and Manns [9] and Festa et al. [10] found similar results. In contrast to this Hedayat et al. [11] found no significant difference in the head position between the patients with class I and II.

These results are opposed to the findings obtained by Hugare J. and Harkiness E. [12] who found that

the distal occlusion was combined with flexion of the head, and did not agree with the results of Solow and Sonnesen [6] who found that subjects with mutual distal molar relationship had angles NS/OPT and cervical spine angulation (OPT/CVT),  $3 - 4^\circ$  less than the subjects without this malocclusion.

The correlation analysis showed that the sagittal position of the maxilla was in positive correlation with the craniocervical angle in the patients with class I and II, and the correlation was negative in the patients with class III. Although it is proved that this influence of craniocervical angle on the level of the maxillary prognathism is very small (less than 10%), such correlations may contribute to an increase in the angle of maxillary prognathism in class II and to its decrease in class III, and this leads to a deterioration of basic anomaly. In addition, Marcotte M. [13] found a high correlation between the sagittal position of the maxilla and the head position. When it comes to the angle of mandibular prognathism SNB, it is in positive correlation with the craniocervical angle in subjects with class I and III, but the correlation is negative in subjects with class II. This can also be a mechanism that can lead to a deterioration of basic anomaly by increasing the angle of mandibular prognathism in class III, and by its reduction in class II. Marcotte M. [13] found a negative correlation between the craniocervical angle and the angle of the mandibular prognathism.

The craniocervical angle has a much greater effect on ANB angle, rather than individually at angles whose difference is ANB angle. This is a result of various influences on the angles of the maxillary and mandibular prognathism. By the analysis of the total test sample, regardless of the class, we obtained the result that the angle ANB was in a positive correlation with the angle NS/OPT. This again means that an increase in the angle NS/OPT favors the formation of class II, which is characterized by an increased value in ANB angle.

A statistically significant positive correlation was found between the craniocervical angle and the length of the maxilla, which disagrees with the findings of the study published by the Festa et al. [10] and which brings into connection the maxillary length only with the length of the anterior cranial base.

The lowest average value of the mandibular length was found in the subjects with class II. Given that the largest craniocervical angle was found in this

class of malocclusion, the finding which relates to the length of the mandible is in line with previous findings [14] which claim that the subjects with the extension of the head in relation to the cervical spine have reduced length of the mandible. In the subjects with class II a statistically significant positive correlation was found between the craniocervical angle and the upper jaw length, as well as a significant but negative correlation between the craniocervical angle and the lower jaw length.

The results of correlation analysis of craniocervical angle and the maxilla and mandible length in class II, as well as the previously established positive correlation between craniocervical angle and SNA angle, and the negative correlation between craniocervical angle and SNB angle indicate that an increased craniocervical angle may be one, but certainly not the only factor in the mechanism of the occurrence of class II malocclusion. This is in line with the results obtained by Arntsen and Sonnesen [8] in their analysis, which are indicative of

the correlation between the head position, the morphology of the cervical spine and craniofacial morphology in subjects with class II malocclusion.

### Conclusion

Persons with class II malocclusion have the highest value of the craniocervical angle, i.e. the greatest head extension in relation to the cervical spine. High levels of craniocervical angle in persons with class II may be a contributing factor that deteriorates the basic anomaly of class II due to their acting in terms of increasing the maxillary prognathism angle and reducing the mandibular prognathism angle.

The positive correlation between the value of the craniocervical angle and the upper jaw length and a significant negative correlation between the value of the craniocervical angle and the lower jaw length can also contribute to the occurrence of class II malocclusion.

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## CASE REPORTS

### *PRIKAZI SLUČAJEVA*

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Case report  
*Prikaz slučaja*  
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## ANAESTHESIA FOR AWAKE BRAIN TUMOUR SURGERY: CASE REPORT

### *ANESTEZIJA ZA OPERACIJE TUMORA NA MOZGU U BUDNOM STANJU: PRIKAZ SLUČAJA*

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Mladen KARAN<sup>4</sup> and Petar VULEKOVIĆ<sup>2,4</sup>

#### Summary

**Introduction.** There is an increasing trend towards performing awake craniotomy procedures. The method is indicated for surgical treatment of brain changes located in functional regions. This technique poses a unique challenge for the anaesthesiologist in view of providing adequate sedation, analgesia, hemodynamic and respiratory stability yet to keep the patient awake and cooperative during the procedure. **Case Report.** After the adequate preoperative preparation of the patient, the surgical procedure on tumorous change in the left frontoparietal area (Broca's area) was performed. Due to the tumour localization, the surgical treatment was performed in awake condition under intraoperative neurophysiological monitoring of the patient. Analgosedation (Ramsay score 2-3) was provided via continuous infusion of propofol and remifentanyl. Local infiltration anaesthesia (scalp block) was performed with levobupivacaine. The surgical procedure proceeded without any major incidents and complications. **Conclusion.** A propofol/remifentanyl combination provided safe and effective analgosedation of the patient.

**Key words:** Anesthesia; Brain Neoplasms; Neurosurgical Procedures; Wakefulness; Craniotomy; Neurophysiological Monitoring; Conscious Sedation

#### Introduction

The awake craniotomy technique is well established for surgical treatment of epilepsy, and only recently it has become more popular for surgical management of supratentorial tumours, arteriovenous malformations and mycotic aneurysms near critical regions of the brain [1]. Awake craniotomy for tumour resection presents many challenges for the neurosurgeon and the anaesthesiologist [2]. The challenge for the anaesthesiologist is to find a technique that provides adequate sedation, analgesia, and assures cardiorespiratory stability, as well as an awake and cooperative patient, without interfering with electrophysiological monitoring and cognitive tests.

#### Sažetak

**Uvod.** Izvođenje kraniotomija u budnom stanju je trend koji je sve više u porastu. Metoda je indikovana za hirurško zbrinjavanje promena na mozgu lociranih u funkcionalnim regijama mozga. Ova tehnika predstavlja jedinstven izazov za anesteziologa zato što treba da obezbedi adekvatnu sedaciju, analgeziju, hemodinamičku i respiratornu stabilnost, a da pacijent tokom izvođenja procedure bude budan i kooperativan. **Prikaz slučaja.** Nakon adekvatne preoperativne pripreme pacijentkinje, izvedena je planirana hirurška procedura na tumorskoj promeni u levoj frontoparijetalnoj regiji (Brokina zona). S obzirom na lokalizaciju tumora, hirurška procedura je sprovedena u budnom stanju, uz upotrebu neurofiziološkog monitoringa. Analgosedacija (Remzijev skor 2-3) obezbedena je kontinuiranom infuzijom propofola i remifentanila. Lokalna infiltrativna anestezija (skalp blok) izvedena je levobupivakainom. Hirurška procedura je protekla bez većih incidenata i komplikacija. **Zaključak.** Propofol/remifentanal kombinacija omogućava sigurnu i efikasnu analgosedaciju pacijenata tokom izvođenja operacija tumora na mozgu u budnom stanju.

**Ključne reči:** anestezija; tumori mozga; neurohirurške procedure; budnost; kraniotomija; neurofiziološki monitoring; svesna sedacija

Scalp block performed by the neurosurgeon allows reducing the dose of drugs used for analgosedation and thus reduces adverse effects of these drugs. It also results in lower pain scores and less need for analgesics in the first 48 hours after supratentorial craniotomy.

Few anaesthetic methods can be used for awake craniotomy. Monitored anaesthesia care (MAC) is a procedure during which the patient is analgosedated and remains spontaneously breathing throughout the entire procedure. Asleep-awake-asleep (AAA) technique is the method where patient is anaesthetized during the first and third phase and laryngeal mask (LM) or an endotracheal tube (ET) is used for ventilation. During the second phase when mapping is performed,

### Abbreviations

MAC	– monitored anesthesia care
LM	– laryngeal mask
ET	– endotracheal tube
CT	– computed tomography
MRI	– magnetic resonance imaging
BIS	– bispectral index
TCI	– target controlled infusion
SpO <sub>2</sub>	– pulse oximetry

the patient is allowed to be fully awake and the LM or the ET is removed. Asleep-awake (AA) method is similar to the previous one, yet without the third phase [3].

The aim of this case report was to present MAC, the technique involving propofol and remifentanyl combined with levobupivacaine for scalp block in neurosurgical procedure of tumour resection in the awake patient.

### Case Report

A female patient visited the neurologist reporting episodes of forgetfulness (forgetting what she was trying to say or do) and intermittent speaking inability. According to the obtained anamnestic data, clinical and neurological examination (motor dysphasia), computed tomography, magnetic resonance imaging and functional magnetic resonance of the endocranium, a multicentric infiltrative tumorous change was diagnosed in the left frontoparietal region. Approximate dimensions of the tumour were 5.5 X 4.0 X 5.2 cm. Electroencephalography revealed irritative dysrhythmia and slow activity over the central-parietal regions. Since the tumour was in the Broca's area, the neurosurgeon indicated surgical treatment in awake condition under intraoperative neurophysiological monitoring of the patient.

During the preoperative preparation period, the patient was administered dexamethasone and phenobarbitone. The patient had history of hypertension, thus she had been receiving triple antihypertensive therapy (fosinopril, metoprolol, amlodipine). The preoperative laboratory and biochemistry findings were within the reference range. Immediately before entering the operation room, the patient was administered cefuroxime 1.5 g i.v., ranitidin 50 mg i.v., metoclopramide 10 mg i.v., dexamethasone 4 mg i.v.

Upon entering the operation room, two peripheral venous lines were placed (17G, 18G), as well as an arterial cannula (a. radialis), urinary catheter and a body heater. The patient's position was semi-lateral on the right side. The patient manifested moderate hypertension (150/90 mmHg), normocardia (68/min), pulse oximetry (SpO<sub>2</sub>) 96%. The following parameters were monitored and recorded: bispectral index (BIS), electrocardiogram, invasive measurement of arterial blood pressure, pulse oximetry, arterial blood gas analysis, and hourly diuresis. Before MAC started, preoxygenation therapy via the face mask (7 L/min) was performed along with slow infusion of Ringer's solution, and midazolam 2 mg i.v. and

fentanyl 50 µg i.v. were administered. Anaesthesia was started with propofol (target controlled infusion, plasma-target 1 µg/ml). When the desired propofol concentration was reached, continuous infusion of remifentanyl was induced at a dose of 0.025 µg/kg/min, while reducing the p-target concentration of propofol to 0.7 µg/ml. After 10 minutes, scalp infiltration (scalp block) with levobupivacaine (0.5%) was performed at a total dose of 150 mg with adrenaline 5 µg/ml. The patient's head was positioned into the Mayfield skull clamp. Immediately before placing the Mayfield immobilizer, paracetamol 1g i.v. was administered, and remifentanyl dose increased to 0.05 µg/kg/min. During positioning of the skull clamp and craniotomy, the patient was completely calm, hemodynamically stable and without pain sensation. When the dura mater was opened, the dose of p-target propofol was reduced to 0.1 µg/ml, and the remifentanyl dose was decreased to 0.01 µg/kg/min. Direct cortical stimulation with bipolar electrode in the region of anticipated Broca's area, i.e. the tumour lower margin, resulted in anomia and "speech arrest". The motor response in the upper limb and face, which defined the posteroinferior resection margin, was provided by direct cortical stimulation with monopolar electrode.

Intraoperative *ex tempore* diagnosis revealed glioblastoma multiforme. After successful neurophysiological monitoring and mapping, the tumour was reduced. The doses of p-target propofol and remifentanyl were increased to 0.5 µg/ml and 0.05 µg/kg/min, respectively. The aforementioned doses remained unchanged until the end of surgical procedure. Hypertension and tachycardia episodes occurring during the neurophysiological monitoring were managed by means of urapidil and metoprolol, respectively. Throughout anaesthesia, the SpO<sub>2</sub> values ranged from 96 to 100%, whereas partial pressure of CO<sub>2</sub> in arterial blood ranged from 34.0 to 46.6 mmHg. During anaesthesia and surgical procedure, the patient did not experience any respiratory arrest. BIS values ranged within the interval of 85-95.

Postoperatively, the patient was transferred to intensive care unit and she was awake, conscious, oriented and communicative, without major neurological episodes and satisfied.

### Discussion

Awake craniotomy for tumour surgery has recently become more popular [4]. It allows cortical mapping, which is crucial during brain tumour resection in order to prevent neurological injury.

The safest way to do resection of a tumour close to the eloquent areas of the cortex is in an awake patient, who can thus provide continuous feedback to the neurosurgeon on the integrity of neurological function [5].

The role of the anaesthesiologist is to provide analgesedation and cardiorespiratory stability without interfering with electrophysiological monitoring and cognitive tests, so optimal anaesthetic management remains a challenge [6].

There are several anaesthetic methods that can be used for awake craniotomy, and our decision was to use MAC. When providing MAC as a method, the patient is sedated and remains able of spontaneous breathing throughout the entire procedure. We wanted to establish control of pain during the entire period of surgery, and this method allowed the main surgical steps to be carried out without major complications (such as psychomotor agitation, respiratory depression, hemodynamic changes, and excessive sleepiness) and airway manipulation. It did not affect the patient's cognitive evaluation [7].

Not all patients can tolerate an awake craniotomy. Our patient was conscious, highly motivated, without communication difficulties and extreme anxiety. It is necessary to make psychological evaluation. People with mental disorders cannot be included in this procedure.

To prevent complications of awake craniotomy, such as seizures, cerebral oedema, nausea and vomiting, the patient was perioperatively given anti-convulsion therapy and dexamethasone as well as antiemetic medication.

All preparations had been completed before the patient arrived in the room including extra pillows, soft mattress and warming system to ensure maximum comfort for the patient during positioning. In addition to the routine monitoring of non-invasive blood pressure, electrocardiogram and pulse oximetry, which is essential, BIS was also monitored, which is routinely used in neurosurgical procedures, invasive blood pressure and hourly diuresis. BIS is standard practice in anesthetic care [8].

A bolus of fentanyl and midazolam for anxiolysis and anterograde amnesia was used as our premedication.

We used the combination of remifentanyl and propofol because it promotes synergistic analgesia, ensu-

res acceptable sedation, and decreases the incidence of nausea and vomiting [9, 10]. Manninen et al compared the combination of fentanyl and propofol with the combination of remifentanyl and propofol. They have found that the use of remifentanyl infusion in conjunction with propofol is a good alternative to fentanyl and propofol, but they reported a higher number of respiratory complications when using fentanyl [11].

Propofol infusion was carefully titrated to keep the patient comfortably sedated and to avoid hypoventilation, with hypercapnia, cerebral hyperaemia and the tense brain.

One of the major concerns during the intraoperative period is to ensure spontaneous breathing in the patients and their being oriented and cooperative. This problem primarily arises in the most painful phase where heavy sedation is often necessary [11]. This problem did not occur in our case because we titrated intensity of analgesia with infusion of remifentanyl and we used scalp block as well. Remifentanyl has a rapid action onset, and short duration, which makes titration relatively easy with minimal effects on hemodynamic profile.

Except for hypertension, which is a relatively common complication during the procedure, we did not have any complications and the patient manifested early mobilization and was discharged uneventfully.

## Conclusion

Our experience is in accordance with literature data, which report that awake craniotomy is practicable and safe anaesthetic technique. The successful outcome depends on the anaesthesiologist's skill in the pharmacological titration, as well as his/her capability to maintain the close psychological contact with the patient throughout the surgery.

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## THE LIGATION OF THE INTERSPHINCTERIC TRACT PROCEDURE OF THE PERIANAL FISTULA: CASE REPORT

*INTRASFINKTERIČNO LIGIRANJE PERIANALNE FISTULE: PRIKAZ SLUČAJA*

Momčilo STOŠIĆ, Igor STOJANOVIĆ and Svetlana MIHAJLOVIĆ

### Summary

**Introduction.** Perianal fistula is usually of cryptoglandular origin, namely it results from inflammation of the anal glands. The main challenge in its management is how to resolve a fistula but avoid its recurrence as well as incontinence, which is even a bigger problem. Several treatment methods have been described and they all focus on cutting the anal sphincter and "opening" the fistula, placing the seton, plug technique, creating a mucosal advancement flap, injecting medical occlusive agents or using a combination of methods. In 2007 a method of managing a fistula by ligation of the intersphincteric fistula tract was described. The procedure is still getting a wider application. **Case Report.** A 60-year old male patient had had a fistula for 30 years. He underwent incision of perianal abscess on multiple occasions resulting in multiple scars in the gluteus area. The diagnosis revealed a high transsphincteric fistula. The inner ostium was diagnosed by injecting hydrogen-peroxide and by probing. The patient's general condition was satisfactory. For the first time the ligation of intersphincteric fistula tract procedure was applied in our regional hospital. Under general anesthesia, in a lithotomy position, the ligation of intersphincteric fistula tract procedure was successfully performed in approximately 30 minutes. The external opening of the fistula and the scars were widely excised. The postoperative course was uneventful. After 6 months there was no recurrence. **Conclusion.** The ligation of intersphincteric fistula tract procedure for transsphincteric fistulae can be a treatment of choice in all hospitals treating colorectal patients because the incontinence risk is low and the disease is curable at a high percentage.

**Key words:** Rectal Fistula; Anus Diseases; Reconstructive Surgical Procedures; Fecal Incontinence; Treatment Outcome

### Introduction

Perianal fistulae develop in 90% of the cases as a result of the anal gland inflammation (cryptoglandular theory). Other causes are Crohn's disease, tuberculosis, trauma, and post radiation effects [1]. According to Parks, 1976, they are classified as: intersphincteric (60–75%), transsphincteric, low and high level (15–20%), and suprasphincteric (5%) [2]. Extrasphincteric fistulae (1–3%) are not of cryptoglandular origin. Furthermore, fistulae can be simple

### Sažetak

**Uvod.** Perianalna fistula je najčešće kriptoglandularnog porekla, tj. posledica zapaljenja analne žlezde. Izazov pri lečenju bolesti je rešiti fistulu bez pojave recidiva a da pritom ne dođe do većeg problema – inkontinencije. Opisano je više metoda lečenja: presecanje analnog sfinktera i „otvaranje“ fistule, plasiranje seton trake, plasiranje čepova (*plug* tehnike), kreiranje mukoznog reznja, ubrizgavanje medicinskih okluzivnih sredstava ili kombinacijom metoda. U 2007. godini opisana je metoda rešavanja fistule podvezivanjem fistuloznog kanala u intrasfinkteričnom prostoru. Ova operacija tek počinje šire da se primenjuje. **Prikaz slučaja.** Prikazujemo muškarca starog 60 godina koji boluje od fistule oko 30 godina. Više puta je imao perianalni apsces koji je incidiran, tako da je u tom delu gluteusa imao više ožiljaka. Dijagnostikom je utvrđena visoka transsfinkterična fistula. Unutrašnji otvor je dijagnostikovao ubrizgavanjem vodonik-peroksida i sondiranjem. Opšte stanje bolesnika je bilo zadovoljavajuće. Prvi put u našoj bolnici primenjena je procedura podvezivanja fistuloznog kanala u intrasfinkteričnom prostoru. U opštoj anesteziji, u ginekološkom položaju, uspešno je urađena operacija za oko tridesetak minuta. Spoljašnji otvor fistule i ožiljci su široko ekscidirani. Postoperativni tok je protekao uredno. Posle šest meseci nema recidiva. **Zaključak.** U svim bolnicama koje leče bolesnika sa kolorektalnim problemima podvezivanje fistuloznog kanala u intersfinkteričnom prostoru može da bude operacija izbora za lečenje transsfinkterične fistule. Rizik inkontinencije je nizak a bolest je izlečiva u visokom procentu.

**Gljučne reči:** rektalna fistula; bolesti anusa; rekonstruktivne hirurške procedure; fekalna inkontinencija; ishod lečenja

and complex. It is believed that ligation of intersphincteric fistula tract (LIFT procedure) is the method of choice for some complex fistulae [3].

According to some sources, the method was first described in 2006, but the work of Matos and associates was mentioned as early as 1993 as the initial stage in introducing this method [4]. Nowadays the original work of the Thai surgeon Royanasakul has been accepted since he popularized this method in his works in 2007 [5] and 2009 [6]; it is still considered a novel method and its evaluation is under way. The purpose of this

**Abbreviations**

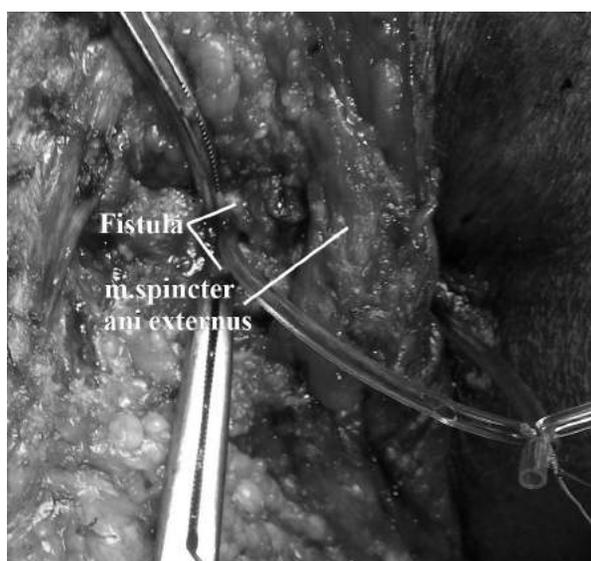
LIFT	– ligation of intersphincteric fistula tract
CRP	– C-reactive protein (test)
MRI	– magnetic resonance imaging

work is to demonstrate that the procedure can be performed with safety even in secondary hospital centers.

**Case Report**

A 60-year old male patient was admitted for a more detailed examination of the change in the left perianal region due to the inflammatory scarring change suggesting that the inflammation resulted from a high level fistula. Before admission to hospital, the patient was actively treated for almost 3 years by a dermatologist and conservatively by 2 surgeons, with antibiotics and once surgically. The total treatment lasted for about 30 years with occasional inflammatory exacerbation and incisions.

The diagnosis was made by means of magnetic resonance imaging (MRI), X-ray of the lungs, abdominal ultrasound, injecting hydrogen-peroxide, probing the fistula, the fistula cannulation with a rubber band and colonoscopy with biopsy. Fistulography was not used due to a low success rate, which is about 30% [7]. All laboratory test results (blood tests, albumins, proteins, hepatogram, electrolytes) were within normal values, including the C-reactive protein (CRP) which was less than 1 mg/L after the gluteus scar and pseudotumor excision. The MRI clearly indicated a fistula characterized as high trans-sphincteric without any tumor mass. The inner ostium was identified following the injection of hydrogen-peroxide into the external opening of the fistula. Probing had been done and the



**Figure 1.** Looped high fistula, clamps on the thickened wall, external excision

**Slika 1.** Zaočena visoka fistula; peanom uhvaćen zid fistule; spoljna ekscizija



**Figure 2.** Entrance to intersphincteric area  
**Slika 2.** Ulazak u intersfinkterični sloj



**Figure 3.** Open intersphincteric tract, looped fistula with blue sutures

**Slika 3.** Otvoren intersfinkterični prostor, zaočena fistula plavim koncem

rubber band was placed there until the surgery (**Figure 1**). Systemic examinations showed normal limits.

The patient was admitted for surgery the day before and was prepared by having his colon cleansed with a factory solution of sodium picosulfate, magnesium oxide, and anhydrous citric acid. An hour prior to the surgery, the patient was administered 1 g metronidazole and 2 g cephalosporin. The patient was in the lithotomy position. The operation was performed per technique of Rojanasakula et al. There was no combination using a bio-flap, with the plug implantation in the external part of the tract and without partial fistulotomy.

During the surgery, we probed the fistula with a metal probe again (**Figure 2**). Then the mucosa between the external and the internal sphincter was cut with a semicircular incision of 2–3 cm. Intersphincteric area was slowly entered to the depth of the fistula through which a metal probe had been inserted (**Figure 3**). The fistula with a probe was looped with a seton and



**Figure 4.** Ligation of the inner opening of the external area with non-resorbable sutures

**Slika 4.** Prešiveni unutrašnji otvor spoljašnjeg dela fistule neresorptivnim koncem

the metal probe removed. Two smaller straight clamps were placed to both ends of the fistula in the intersphincteric area and the fistula was cut. Then both ends were ligated with a transfixation suture and the area was washed (**Figure 4**). We did not suture the area of the entrance in the intersphincteric tract. The external part of the tract was curetted and the internal opening of the rectum (anal gland) was excised. The patient was on a liquid diet for three days to avoid having a stool throughout his hospital stay. The checks were carried out every 3 days during the first 15 days, then once a month. After 3 months the patient had no discharge on the external opening of the fistula which was excised.

## Discussion

The purpose of perianal surgery is to achieve treatment without further discharge, without the risk of incontinence or any other adverse consequences. All treatment methods, including surgeries, compare the healing percentage, the recurrence percentage, incon-

tinence and/or other side effects, together with the total cost of the treatment. The possibility of performing the surgery in as many hospitals as possible is also a relevant factor [8]. This procedure is still not widespread in Serbia.

All methods that use medical preparations (botulinum toxin preparations, fibrin glue, cyanoacrylate glue, collagen substance) are not financially accessible to most of our hospitals, and on the other hand some of these treatment methods have disappointing results. The success rate of fibrin glue and collagen paste (Permacol®) is 16–25% [9] and up to 54% [10], respectively in the multi-center study, but the total number of studies is still insufficient and financially costly for a complete treatment.

The success rate of isolated anal-plug technique ranges from 29 to 87%, as cited by Sirikurnpiboon et al, 2015 [11]. Mucosa-advancement flap has a high success rate but is considered the most complex surgical procedure [2]. Fistulotomy and fistulectomy are best known to solve the problem radically up to 90% [12]; however, they also have the highest percentage of different degrees of incontinence. The risk of incontinence is correlated with the treatment in a wide range of 10–57% [13]. Placing seton which cuts the sphincter slowly but without losing the function is a good method but the treatment can last from 3 to 9 months.

The LIFT procedure is performed without cutting the sphincter muscles and the success of the operation is remarkably high. In 2007, Rojanasakul reported the success rate of 94% [5]. Over time, other studies have shown the real success of the procedure of 40–95% with a recurrence rate of 6–28% [14].

## Conclusion

Compared to other methods, the ligation of intersphincteric fistula tract procedure is safe and inexpensive, it does not require special equipment, there is hardly any incontinence (with the muscles not being cut), the postoperative pain is of low intensity and the success rate is high. Its wider application is encouraged by this patient's report.

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Case report  
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## INTERMITTENT EXOTROPIA COURSE IN FRONTAL NASAL DYSPLASIA AND SEVERE ORBITAL HYPERTELORISM: CASE REPORT

*TOK INTERMITENTNE EGZOTROPIJE KOD FRONTALNAZALNE DISPLAZIJE SA IZRAŽENIM ORBITALNIM HIPERTELORIZMOM: PRIKAZ SLUČAJA*

Zorana B. PAVLOVIĆ<sup>1</sup> and Branislav R. STANKOVIĆ<sup>2,3</sup>

### Summary

**Introduction.** Frontonasal dysplasia is a rare condition of congenital structure malformations of the midface. Ophthalmologic abnormalities have been estimated to occur in 87% of cases of frontonasal dysplasia. **Case Report.** We report a case of type I frontonasal dysplasia in a 15-year old boy after the correction of severe hypertelorism, median nasal cleft with a broad nasal root and associated decompensated intermittent exotropia with overaction of the inferior oblique muscles and V pattern. He underwent bilateral lateral rectus recessions of 6.0 mm for intermittent exotropia when he was six years old. The correction of hypertelorism was performed with orbital rotation surgery when he was thirteen years old. For some time after strabismus surgery, the ocular alignment improved, but it deteriorated gradually. The ocular alignment improved after the hypertelorism correction; however, intermittent exotropia deteriorated gradually again six to seven months later. On the last ophthalmologic examination, he had the ocular alignment on the level of small angle exotropia and associated hypertropia and occasionally even small angle esotropia at near. There was bilateral overelevation in adduction and V pattern, which remained unchanged after extensive facial bones surgical procedures. **Conclusion.** The high incidence of ocular abnormalities, particularly exodeviations, indicates that the early assessment by an ophthalmologist should be a part of the initial evaluation of patients with frontonasal dysplasia to detect treatable visual or ocular problems.

**Key words:** Exotropia; Craniofacial Dysostosis; Hypertelorism; Oculomotor Muscles; Ophthalmologic Surgical Procedures; Eye Abnormalities; Strabismus

### Introduction

Frontonasal dysplasia (FND), firstly described in 1967 as the median cleft face syndrome by De Myer, is presented by congenital structure malformations of the midface [1, 2]. FND is a rare condition and only about 100 cases have been reported in the scientific literature [3, 4]. The etiology of the condition remains unknown, but seems to be linked to defective embryologic development [5]. During the critical period between 4 and 8 weeks of human fetal development, the cell proliferation and tissue fusion to form the orbital, nasal, and oral structures were stopped. A disturbance

### Sažetak

**Uvod.** Frontonalna displazija je retka urođena malformacija struktura srednjeg dela lica. Procenjeno je da se očne anomalije javljaju kod 87% slučajeva frontonalne displazije. **Prikaz slučaja.** Prikazan je slučaj frontonalne displazije tip I kod dečaka starosti 15 godina nakon korekcije izraženog hipertelorizma, središnjeg rasepa sa širokim korenom nosa i udruženom dekompenzovanom intermitentnom egzotropijom sa hiperfunkcijom donjih kosih mišića i „V“ sindromom. Urađena je obostrana retropozicija spoljašnjih pravih mišića 6 mm radi korekcije intermitentne egzotropije, u šestoj godini života. Kada je imao trinaest godina, urađena je orbitorotacija sa ciljem korekcije hipertelorizma. Posle operacije strabizma, izvesno vreme je okulomotorna ravnoteža bila bolja, ali se postepeno pogoršavala. Nakon korekcije hipertelorizma, okulomotorna ravnoteža se poboljšala, ali se nakon šest-sedam meseci intermitentna egzotropija ponovo pogoršala. Na poslednjem oftalmološkom pregledu, imao je egzotropiju na nivou malog ugla i udruženu hipertropiju, a povremeno čak egzotropiju malog ugla na blizinu. Postojala je naglašena elevacija u adukciji obostrano i „V“ sindrom, koji je ostao nepromenjen posle obimnih hirurških zahvata na kostima lica. **Zaključak.** Visoka učestalost očnih anomalija, posebno egzodevijacija, ukazuje da oftalmološki pregled treba da bude sastavni deo početnog ispitivanja pacijenata sa frontonalnom displazijom kako bi se na vreme otkrili i lečili udruženi očni poremećaji.

**Cljučne reči:** egzotropija; kraniofacijalne disostoze; hipertelorizam; očni mišići; oftalmološke hirurške procedure; anomalije oka; strabizam

to this developmental sequence causes FND, a very heterogeneous group of disorders [6, 7].

Most cases of FND are sporadic, but a few familial cases have been reported [8]. There are at least three types of frontonasal dysplasia that are distinguished by their genetic causes and their signs and symptoms [9].

The clinical picture is highly variable, but the major characteristics include hypertelorism, primary telecanthus, median nasal cleft with a broad nasal root, and a widow's peak hairline [4, 10]. Occasional abnormalities include median cleft lip and palate, basal encephalocele, and agenesis of the corpus callosum [11].

**Abbreviations**

FND – frontonasal dysplasia  
 ORH – orbital hypertelorism

Ophthalmologic abnormalities have been estimated to occur in 87% of cases of FND and include optic nerve anomalies, ptosis, exophthalmos, orbital asymmetry, microphthalmia, cataract, dermoid, nystagmus, coloboma of iris, choroidea and optic disk, refractive errors, amblyopia, and strabismus [12].

Orbital hypertelorism (ORH) is a congenital anomaly of the skull characterized by an increased distance between the medial orbital walls. The ORH can occur in a variety of conditions such as craniofacial dysplasia, craniofacial clefts and some craniosynostosis syndromes [13]. It has been reported that amblyopia and strabismus appeared in 58.3% of patients with ORH, exotropias being the most common [14].

We report a case of frontonasal dysplasia with severe hypertelorism and associated strabismus pattern.

**Case Report**

A 15-year old boy presented with features characteristic of FND type I caused by ALX3 gene mutation, after the correction of severe hypertelorism, median

nasal cleft with a broad nasal root and associated decompensated intermittent exotropia with overaction of the inferior oblique muscles with V pattern. The pregnancy, delivery, and birth weight were normal. Family history revealed no ocular defects or any similar developmental defects.

Over the years various surgical procedures were performed to correct the physical deformities typical of FND. He underwent two skin procedures at the age of 2 years to close the nose defect as well as bilateral lateral rectus recessions of 6.0 mm for intermittent exotropia when he was six years old. The correction of hypertelorism was performed with orbital “box osteotomy” technique when he was thirteen years old, and a year later, he underwent the corrective surgery for telecanthus and eyebrows transfer.

The ocular alignment improved for some time after strabismus surgery, but it deteriorated gradually. After the orbital rotation surgery aimed at correcting hypertelorism, the ocular alignment improved; however, intermittent exotropia deteriorated again after six to seven months.

On the last ophthalmologic examination, he had ocular alignment on the level of small angle exotropia and associated hypertropia and occasionally even small angle esotropia at near. Ductions and versions were full, with bilateral overaction in adduction and V pat-



**Figure 1.** Facial appearance before orbital rotation surgery. Severe hypertelorism

*Slika 1. Izgled lica pre orbitorotacije. Izražen hipertelorizam*



**Figure 2.** Facial appearance after orbital rotation surgery

*Slika 2. Izgled lica posle orbitorotacije*

tern, which remained unchanged after extensive facial bones surgical procedures. Randot forms, Lang I as well as Wirth stereo tests were negative.

He wore prescription glasses to correct mild compound myopic astigmatism. The best corrected visual acuity was 1.0 and 0.8 in the right and in the left eye, respectively. The interpupillary distance after orbital rotation surgery was 65 mm.

His overall facial appearance was significantly improved and acceptable (**Figures 1 and 2**).

### Discussion

Our case is consistent with earlier findings that hypertelorism is frequently associated with exodeviations [14, 15].

The larger interpupillary distance to a certain extent, the greater is the angle of visual disparity and the greater is the stereoscopic potential [16].

Improving of intermittent exotropia after reduction of severe hypertelorism with orbital rotation surgery indicates that interpupillary distance within normal limits facilitates the ocular alignment.

Early start and long duration of manifest deviation resulted in the absence of normal binocular vision in our patient. Associated overelevation in adduction with V pattern prevented a better horizontal alignment and binocular vision at the level of small angle devia-

tion. Bilateral inferior oblique weakening procedure is planned to enable fusional amplitudes and improve horizontal alignment.

Many theories have been suggested to clarify the etiology of patterns consisting of orbital factors such as craniofacial anomalies or heterotopia of muscle pulleys, anomalies of extraocular muscles, and disruption of fusion [17]. Some previous studies have reported a significant association between V-pattern strabismus and excyclorotation of the muscle cone due to orbital malformations [17, 18]. When a vertical deviation is greatest in adduction (overelevation in adduction), the primary oblique muscle overaction could be the commonest cause [19].

### Conclusion

Our case with frontonasal dysplasia shows that severe hypertelorism is frequently associated with exodeviations. It seems that a smaller interpupillary distance after the reduction of hypertelorism, leads to an improved ocular alignment. An associated vertical deviation contributes to the dissociation of horizontal deviation. The high incidence of ocular abnormalities indicates that the early assessment by an ophthalmologist should be a part of the initial evaluation of patients with frontonasal dysplasia to detect treatable visual or ocular problems.

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## SEMINAR FOR PHYSICIANS *SEMINAR ZA LEKARE U PRAKSI*

Institute for Pulmonary Disease of Vojvodina, Sremska Kamenica

Seminar for physicians  
*Seminar za lekare u praksi*  
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### SPECIFIC FEATURES OF ANESTHESIA IN PATIENTS WITH MYASTHENIA GRAVIS

#### *SPECIFIČNOST ANESTEZIJE KOD PACIJENATA SA MIASTENIJOM GRAVIS*

**Ivana SPASOJEVIĆ, Danica HAJDUKOVIĆ, Milena KOMARČEVIĆ, Stanislava PETROVIĆ,  
Jelena JOVANOVIĆ and Aleksandra ĆIRIĆ**

#### Summary

**Introduction.** Myasthenia gravis is an autoimmune disease caused by antibodies leading to the destruction of nicotinic acetylcholine receptors on the neuromuscular junction. It is characterized by muscle weakness that gets aggravated with physical activity and improves at rest. Myasthenia Gravis Foundation of America made the clinical classification of Myasthenia gravis which is still in use today. "Tensilon test" is still the gold standard for the diagnosis of Myasthenia gravis. In addition to this test repeated muscular stimulation can be used as well as the analysis of specific autoantibodies. **Treatment of Myasthenia Gravis.** In conservative treatment of Myasthenia gravis anticholinesterases, immunosuppressants and plasmapheresis can be used. If conservative treatment does not lead to the desired remission, surgical treatment is indicated. The most accepted indication for thymectomy is the presence of thymoma with generalized form of Myasthenia gravis in adults. **How to Distinguish Myasthenic From Cholinergic Crisis.** The following is important to make a difference between these two crises: knowledge of the events that preceded the crisis, the size of pupils as well as the presence of muscarinic signs and tensilon test. **Specific Features of Anesthesia in Patients with Myasthenia Gravis.** Mechanism of the disease development is the reason for the increased sensitivity or resistance of these patients to certain types of drugs used in anesthesia. **Protocol of Perioperative Anesthesia in Patients with Myasthenia Gravis.** Based on 35 years of experience in the surgical treatment of patients with Myasthenia gravis anesthesiologists at the Department of Thoracic Surgery, Institute for Pulmonary Diseases of Vojvodina, made the protocol of anesthesia and perioperative treatment for these patients. **Conclusion.** Anesthesiologists may have to deal with a patient with myasthenia gravis in different types of surgical interventions. The protocol for anesthesia and perioperative management of these patients herewith presented may greatly help them in their clinical practice.

**Key words:** Myasthenia Gravis; Anesthesia; Thymectomy; Perioperative Care; Signs and Symptoms; Clinical Protocols

#### Sažetak

**Uvod.** Miasthenia gravis je autoimuno oboljenje uzrokovano antitelima koja dovode do destrukcije nikotinskih acetilholinskih receptora na neuromišičnoj spojnici. Kliničku sliku karakteriše slabost mišića koja se pogoršava sa fizičkom aktivnošću, a poboljšava u mirovanju. Američka fondacija za miasteniju je napravila kliničku klasifikaciju ove bolesti koja se i danas koristi. Zlatni standard za postavljanje dijagnoze ove bolesti predstavlja tensilonski test. Pored toga koriste se i ponavljana mišićna stimulacija, kao i analiza specifičnih autoantitela. **Lečenje miastenije gravis.** U svrhu konzervativnog lečenja miastenije gravis koriste se antiholinesterazni lekovi, imunosupresivi i plazmafereza. Ukoliko konzervativno lečenje ne dovede do željene remisije bolesti pristupa se hirurškom lečenju. Najprihvaćenija indikacija za timektomiju danas jeste postojanje timoma sa generalizovanim oblikom miastenije gravis kod odraslih. **Kako razlikovati miasteničnu od holinergične krize.** U razlikovanju ove dve pojave od značaja su poznavanje događaja koji su prethodili krizi, veličina zenica, kao i pojava muskarinskih znakova i tensilonski test. **Specifičnosti primene anestezije kod bolesnika sa miastenijskom gravis.** Patofiziološke promene koje uzrokuju ovo oboljenje predstavljaju i razlog povećane osetljivosti ili rezistencije ovih bolesnika na pojedine vrste lekova koji se primenjuju u anesteziji. **Protokol perioperativne anestezije kod bolesnika sa miastenijskom gravis.** Na osnovu tridesetpetogodišnjeg iskustva u hirurškom lečenju bolesnika sa miastenijskom gravis na Klinici za grudnu hirurgiju Instituta za plućne bolesti Vojvodine, proistekao je protokol anestezije i perioperativnog tretmana kod ovih bolesnika. **Zaključak.** Anesteziozolozi svih hirurških grana se mogu susresti sa bolesnikom obolelim od miastenije gravis prilikom različitih vrsta hirurških intervencija. Navedeni protokol za anesteziju i perioperativni tretman ovih bolesnika može im biti veoma koristan.

**Ključne reči:** mijastenija gravis; anestezija; timektomija; perioperativna nega; znaci i simptomi; klinički protokoli

**Abbreviations**

MG	– Myasthenia gravis
TIVA	– total intravenous anesthesia
NDMR	– nondepolarizing muscle relaxants
PO	– per os
IV	– intravenous
IM	– intramuscular
MGFA	– Myasthenia Gravis Foundation of America
VATS	– video-assisted thoracoscopy
KS	– corticosteroids

**Introduction***History*

Myasthenia gravis (MG) was first described in the seventeenth century, but as an entity it was recognized only 200 years later when Dr Friedrich Jolly described it and named it as “Myasthenia gravis pseudoparalytica”. At that time the disease led to death as a rule within one or two years from onset its due to respiratory failure [1].

*Pathophysiology*

MG is an autoimmune disease caused by antibodies leading to the destruction of nicotinic acetylcholine receptors on the neuromuscular junction. This destruction results in a reduced number of acetylcholine re-

ceptors and reduced number and depth of wrinkles on the postsynaptic membrane on neuromuscular junction of all muscles, including those which are not clinically manifested. Autoantibodies can be detected in most cases (“seropositive patients”), but it is also known that 10–20% of “seronegative patients” also have autoantibodies. The cause of autoimmune reactions leading to MG is still unknown, but it is known that there is a very strong connection between MG and pathology of thymus. In 70–80% of patients with MG there is a thymus hyperplasia and thymoma is present in the 10–15%. The most commonly affected are women between the ages of 20 and 30 years, but in males the disease usually occurs after the age of 60 years [2].

*Clinical Signs*

Myasthenia gravis is characterized by muscle weakness that gets aggravated with physical activity and improves at rest. In most patients the disease begins with ocular symptomatology (diplopia and ptosis of the eyelids), followed by bulbar symptoms (difficulty swallowing and speech), weakness of neck and extremity muscles and at the end dyspnea may develop due to the weakness of respiratory muscles. MG can also affect the cardiac muscle resulting in palpitations, hypertension, AV block of first degree, atrial fibrillation and myocarditis [3].

**Table 1:** Modified Osserman grades**Tabela 1.** Modifikovana Ossermanova klasifikacija

	Disease localized to ocular muscles
Type I <i>Tip I</i>	Tends not to progress if remains confined to ocular muscles for first 2 years <i>Zahvaćeni samo okularni mišići.</i> <i>Nema tendencije progresije ako su zahvaćeni samo ovi mišići u prve dve godine.</i>
Type IIa <i>Tip IIa</i>	Mild generalized myasthenia Slowly progressive often from ocular muscles to skeletal and bulbar muscles; however, muscles of respiration are spared Good response to drug therapy and low mortality <i>Blaga generalizovana miastenija.</i> <i>Spora progresija na skeletne i bulbarne mišiće, pošteđeni su respiratorni mišići.</i> <i>Dobar odgovor na terapiju, nizak mortalitet.</i>
Type IIb <i>Tip IIb</i>	Moderate generalized myasthenia Gradual onset, usually ocular, progressing to more generalized, bulbar and skeletal muscles involvement Respiratory muscles are not involved More bulbar symptoms than IIa Less responsive to medical therapy than IIa <i>Srednja generalizovana miastenija.</i> <i>Veća je zahvaćenost skeletnih i bulbarnih mišića nego kod tipa IIa.</i> <i>Nisu zahvaćeni respiratorni mišići.</i> <i>Slabiji odgovor na terapiju od tipa IIa.</i>
Type III <i>Tip III</i>	Severe disease/ Progression may be gradual or sudden deterioration Poor response to drug therapy High mortality <i>Teška miastenija.</i> <i>Progresija postepena ili iznenadno pogoršanje.</i> <i>Slab odgovor na terapiju, visok mortalitet.</i>
Type IV <i>Tip IV</i>	Myasthenic crisis with respiratory failure Require intubation <i>Miastenična kriza sa respiratornom insuficijencijom.</i> <i>Zahteva intubaciju.</i>

**Table 2.** MGFA clinical classification**Tabela 2.** Myasthenia Gravis Foundation of America (MGFA) klinička klasifikacija

Class	Description/ <i>Opis klase</i>	Sub-classification/ <i>Potklasa</i>
I	Isolated ocular weakness <i>Izolovana okularna slabost</i>	No sub-classification
II	Mild weakness of extra-ocular muscles <i>Blaga slabost ekstraokularnih mišića</i>	Predominantly affecting limb, axial muscles, or both Predominantly affecting oropharyngeal, respiratory muscles, or both <i>većinom zahvaćeni ekstremiteti, ramena ili oba</i> <i>većinom zahvaćeni orofaringealni, respiratorni mišići ili oba</i>
III	Moderate weakness of extra-ocular muscles <i>Srednja slabost ekstraokularnih mišića</i>	Predominantly affecting limb, axial muscles, or both Predominantly affecting oropharyngeal, respiratory muscles, or both <i>a) većinom zahvaćeni ekstremiteti, ramena ili oba</i> <i>b) većinom zahvaćeni orofaringealni, respiratorni mišići ili oba</i>
IV	Severe weakness of extra-ocular muscles <i>Teška slabost ekstraokularnih mišića</i>	IVb Use of feeding tube without intubation <i>Upotreba nazogastrične sonde bez intubacije</i>
V	Intubation/ <i>Intubacija</i>	No subclassification

### Classification

The first classification of MG was made by Dr Osserman in 1971. The division was made according to the affected muscle groups [4] (**Table 1**).

It was the basis for the American Foundation for MG (Myasthenia Gravis Foundation of America-MGFA) to make the clinical classification of MG, which is still in use today [5] (**Table 2**).

### Diagnosis

Since 1952 “Tensilon test” has been the gold standard for the diagnosis of MG. This test is carried out by intravenous (IV) injection of edrophonium (Tensilon) and then by following the development of muscle weakness in the next 30–90 seconds. In addition to this test repeated muscular stimulation can be used as well as the analysis of specific autoantibodies according to which patients are divided into “seropositive” and “seronegative” patients [6].

### Treatment of Myasthenia Gravis

#### Conservative Treatment

In conservative treatment of MG anticholinesterases (pyridostigmine), immunosuppressants and plasmapheresis can be used:

1. Pyridostigmine (Mestinon) is the anticholinesterase of choice for MG. The action of this drug starts 30 minutes after its oral administration and the effect lasts for 3 to 6 hours. It can also be crushed and applied through a nasogastric tube or intravenously in an adjusted dose 30: 1, i.e. 30 mg of pyridostigmine given orally (PO) equals 1 mg of neostigmine given intravenously.

2. When the anticholinesterase is not enough for symptomatic disease control then immunosuppressive therapy is indicated. The most commonly used immunosuppressants are corticosteroids (CS). An alternative immunosuppressant is an azathioprine (Imuran). It takes this drug as many as 24 months to achieve the desired effect, but it may reduce the dose of corticoste-

roids to a minimum. Another available drug from this group is Cyclosporine, which is a very potent immunosuppressant, but with many toxic effects.

3. Plasmapheresis has also been in use since 1976 in the treatment of MG. The aim of plasmapheresis is to reduce titer of acetylcholine receptor antibodies in seropositive patients. Indications for plasmapheresis are: bulbar symptoms of disease, myasthenic crisis and optimization of preoperative status of the patient. It is administered in a series of 3-5 plasma exchanges in one to two weeks. Improvement after plasmapheresis may last for 2 weeks to 2 months [7].

#### Surgical Treatment

If conservative treatment does not lead to the desired remission, surgical treatment is indicated. First thymectomy for treatment of MG resulting in remission of the disease was performed by Dr Blalock in 1939. There are still controversies regarding the indication of time of surgical intervention and surgical approaches. The most accepted indication for thymectomy is the presence of thymoma with generalized form of MG in adults. Today, thymectomy can be performed with equal efficiency either transsternally or with video-assisted thoracoscopy (VATS), that being the minimum invasive approach [7, 8].

#### How to Distinguish Myasthenic from Cholinergic Crisis

In the perioperative period the greatest danger is the possibility of development of myasthenic and cholinergic crisis. The major challenge is to distinguish myasthenic from cholinergic crisis because both are characterized by muscle weakness and respiratory distress. The following is important to make a difference between these two crises: knowledge of the events that preceded the crisis, the size of pupils (in myasthenic crisis pupils are wide due to sympathetic activation, while they are narrow in cholinergic crisis), as well as the presence of muscarinic signs and tensilon test [9].

**Table 3.** Suggested preoperative investigations for the patient with myasthenia gravis  
**Tabela 3.** Preporučene preoperativne pretrage kod bolesnika sa MG

Complete blood count <i>Kompletna krvna slika</i>	May have pernicious anemia, red cell aplasia, bone marrow suppression from immunosuppressants/ <i>Perniciozna anemija, supresija koštane srži imunosupresivima</i>
Electrolytes <i>Elektrolitski status</i>	Optimized for neuromuscular function <i>Optimizovati zbog neuromišićne funkcije</i>
Creatinine, liver function <i>Kreatinin, funkcija jetre</i>	As required based on use of immunosuppressants <i>Zbog imunosupresiva</i>
TSH	Commonly have thyroid dysfunction/ <i>Često postoji tiroidna disfunkcija</i>
Chest X-ray <i>RTG grudnog koša</i>	Rule out thymoma/mediastinal mass, pneumonia (particular aspiration if bulbar symptoms) <i>Timom/mediastinalne mase; pneumonija (aspiraciona pneumonija kod bulbarnih simptoma)</i>
ECG	Arrhythmias, atrial fibrillation/ <i>Aritmije, atrijalna fibrilacija</i>
Echo <i>EHO srca</i>	If signs or symptoms of cardiac fibrillation <i>Kod postojanja simptoma zahvaćenosti srčanog mišića</i>
Pulmonary function tests <i>Plućna funkcija</i>	Useful to compare to previous for baseline <i>Procena inicijalne plućne funkcije</i>

*Myasthenic crisis* represents a rapidly progressive decrease in the muscle strength which leads to respiratory failure and life-threatening conditions. The most common causes of myasthenic crisis are: stress, surgery, infection, high body temperature and the use of certain drugs (aminoglycosides, quinolones, macrolides, beta blockers, calcium channel blockers, magnesium salts, iodine contrast, phenytoin, procainamide). When treated for myasthenic crisis the patient should be intubated promptly, then mechanical ventilation support should follow and the dose of anticholinesterase should be increased to achieve the desired effect. It is also necessary to eliminate the potential causes of the crisis and possibly consult a neurologist in order to introduce plasmapheresis or intravenous immunoglobulin (IVIG).

*Cholinergic crisis* develops due to too much acetylcholine on the cholinergic receptors. Cholinergic crisis is usually caused by anticholinesterase overdose. Its features are fasciculations, muscle weakness and positive muscarinic signs (bradycardia, bronchorexia, miosis, salivation, nausea, vomiting, diarrhea, colics, pallor, etc). Once the signs of cholinergic crisis are recognized, it is necessary to suspend further implementation of anticholinesterases, and their further application should be reconsidered depending on the general condition of the patient. The treatment is mostly symptomatic, including 0.5 mg atropine given IV if necessary, and in the case

of respiratory insufficiency the patients should be intubated and mechanically ventilated.

### Specific Features of Anesthesia in Patients with Myasthenia Gravis

Application of anesthesia in patients with MG is based on pathophysiological changes that cause the underlying disease. This mechanism of the disease development is the reason for the increased sensitivity or resistance of these patients to certain types of drugs used in anesthesia. According to the current recommendations, the following drugs can be administered in anesthesia for patients with MG:

– *Intravenous anesthetics* which are safe to be used in anesthesia are propofol, ketamine and etomidate because of their minimal effect on neuromuscular transmission. Either total intravenous anesthesia (TIVA) or inhaled anesthesia can be safely used to maintain anesthesia. TIVA and inhaled anesthesia have been proved to be equally efficient and safe to be applied both for the introduction of anesthesia and its maintenance and to create a good condition for rapid extubation, especially if combined with remifentanyl [10];

– *Opioids* should be used very carefully. Remifentanyl, sufentanyl and fentanyl can be applied. They should be titrated very carefully and given at the

**Table 4.** Prediction of myasthenia gravis patients at high risk of prolonged ventilator support  
**Tabela 4.** Bolesnici sa MG sa visokim rizikom za prolongiranu postoperativnu mehaničku ventilaciju

Advanced disease/ <i>Uznepredovala bolest</i>
Myasthenia gravis foundation class II or higher/ <i>MG klase &gt; II</i>
Myasthenia gravis > 6 years/ <i>MG &gt; 6 godina</i>
History of steroids requirements for myasthenia gravis/ <i>Upotreba kortikosteroida u terapiji MG</i>
History of myasthenia gravis-induced respiratory insufficiency/ <i>Respiratorna insuficijencija uzrokovana MG</i>
Vital capacity < 2,9 l/ <i>Vitalni kapacitet &lt; 2,9l</i>
Pyridostigmine dose > 750 mg/day/ <i>Doza Pyridostigmina &gt; 750 mg/dan</i>
Maximum expiratory force < 40-50 cmH <sub>2</sub> O/ <i>Maximum expiratory force (MEF) &lt; 40–50 cmH<sub>2</sub>O</i>

**Table 5.** Prediction of myasthenia gravis patients at high risk of prolonged ventilator support  
**Tabela 5.** Bolesnici sa MG sa visokim rizikom za prolongiranu postoperativnu mehaničku ventilaciju

Drug and formulation <i>Lek i način davanja</i>	Dose equivalent <i>Ekvivalentna doza</i>	Onset <i>Početak dejstva</i>	Time to maximum response <i>Vreme do maksimalnog odgovora</i>
Pyridostigmine oral (Mestinon)	60 mg PO	40 min.	1 h
Neostigmine oral (Prostigmine)	15 mg PO	1 h	1.5 h
Neostigmine IM	1.5 mg	30 min.	1 h
Neostigmine IV	0.5 mg	Immediate/ <i>Trenutno</i>	20 min.

lowest possible dose because of their depressive effects on the respiratory center. Opioids should not be administered in premedication! Perioperatively, priority is given to short-acting opioids (remifentanyl). Opioids should be avoided postoperatively, priority is given to regional or multimodal analgesia. If necessary, opioids should be given with careful titration [11];

– *Volatile anesthetics* – sevoflurane and isoflurane can be used safely. Volatile anesthetics can be administered to induce anesthesia and/or maintain it. The good side of volatile anesthetics is that they reduce neuromuscular transmission which reduces the need for neuromuscular relaxants, but therefore they must be carefully titrated so as not to lead to prolonged awakening and extubation. They combine with with regional analgesia and remifentanyl [12];

– When *neuromuscular relaxants* are administered, special attention should be paid to the following issues:  
– Depolarizing muscle relaxants (succinylcholine) *should not be used!* Patients with MG are resistant to succinylcholine because of the loss of nicotinic receptors. Besides, they are much more likely to develop phase II of the dual block.

b) Short-acting and intermediate-acting nondepolarizing muscle relaxants (NDMR) can be used but very cautiously and at minimal doses. Pancuronium SHO-ULD NOT BE USED! Patients with MG have increased

sensitivity to NDMR and it is recommended to avoid their use. In case that they have to be administered, it should be at a dose of 1/5–1/2 of the recommended dose. The safest recommendation is to choose a minimal dose of short-acting NDMR and allow the effect to terminate spontaneously [13]. When they must be administered, monitoring of neuromuscular strength is mandatory.

*Thoracic epidural analgesia* can be safely used for perioperative and postoperative analgesia [3].

### Protocol of Perioperative Anesthesia in Patients with Myasthenia Gravis

#### Perioperative Investigations

a) Due to the pathophysiology of MG and its impact on the function of various organs and organ systems, the following preoperative investigations are recommended [9] (**Table 3**).

b) Despite many efforts to determine the exact risk factors that could represent predictive factors for prolonged postoperative mechanical ventilation, they have not been precisely defined yet. However, it is believed that there are certain predictive conditions that represent a high risk for prolonged postoperative mechanical ventilation [9] (**Table 4**).

c) There are different opinions about preoperative doses of anticholinesterases. One of them is that antic-

**Table 6.** Thymectomies performed in treatment of myasthenia gravis at the Department of Thoracic surgery, Institute for Pulmonary Diseases of Vojvodina from 2004 to 2014**Tabela 6.** Prikaz timektomija urađenih u svrhu lečenja miastenije gravis na Klinici za grudnu hirurgiju, Institutu za plućne bolesti Vojvodine u periodu 2004–2014. godine.

Total number of patients/ <i>Ukupan broj pacijenata</i>	48
Sex <i>Pol</i>	Women – 33 (68.75%)/ <i>Žene</i> – 33 (68.75%) Men – 15 (31.25%)/ <i>Muškarci</i> – 15 (31.25%)
Average age <i>Prosečna starost</i>	Women – 37.48 years/ <i>Žene</i> – 37.48 godina Men – 52 years/ <i>Muškarci</i> – 52 godine $\Sigma = 42.02$ years/ <i>godine</i>
Class of MGFA clinical classification <i>Klasa MGFA kliničke klasifikacije</i>	I – 7 (14.5%) IIa – 6 (12.5%) IIb – 8 (16.7%) IIIa – 9 (18.75%) IIIb – 16 (33.33%) IV – 0 V – 1 (2.08%)
Surgical approach/ <i>Hirurški pristup</i>	Sternotomy – 37 (77.03%) VATS – 11 (22.92%)
Complications/ <i>Komplikacije</i>	1 (2,08%)

holinesterases should be suspended on the day of surgery to reduce the need for muscle relaxants [14]; another one is that patients with class I and II should take half of dose and with higher class full dose of the anticholinesterases [15]; it is also believed that everyone should take the full dose 1 hour before surgery since the aim is to achieve optimal muscle strength for extubation [13]. We, as well as Slinger, believe that everyone should take the full dose of Mestinon 1 h before surgery because the goal is to achieve the optimum condition of patient for extubation [9] (**Table 5**).

#### *Protocol for Perioperative Anesthesia*

Based on 35 years of experience in the surgical treatment of patients with MG anesthesiologists at the Department of Thoracic Surgery, Institute for Pulmonary Diseases of Vojvodina, made the protocol of anesthesia and perioperative treatment for these patients.

#### *Premedication:*

- Atropine 0.5 mg IM
- WITHOUT sedatives and opioids
- cephalosporine of 2nd or 3rd generation IV

#### *Induction:*

- propofol/inhaled induction (Sevoflurane)
- WITHOUT muscle relaxant
- methylprednisolone 125 mg (if the patient received corticosteroids preoperatively)

#### *Maintenance of Anesthesia*

- TIVA/inhaled anesthesia (Sevoflurane)
- opioids - the minimal dose of short-acting opioids (remifentanyl)
- nondepolarizing relaxant - if necessary, 1/5- 1/2 dose
- monitoring of muscle relaxation

#### *Postoperative Treatment*

##### *Day 0:*

- cephalosporine 2nd or 3rd generation IV
- nonsteroid antiinflammatory drugs (diclofenac, ketorolac) and/or Tramadol IM
- and/or Paracetamol IV

- and/or opioids with careful titration
- blocker of proton pump
- (neostigmine 2.5 mg + 1 mg atropine + 0.9% NaCl up to 5 ml) - 1 ml IV/4h + pp. 1 ml, if there is muscle weakness

##### *Day 1:*

- (neostigmine 2.5 mg + 1 mg atropine + 0.9% NaCl up to 5 ml) - 1 ml/6h IM
- Tbl. Mestinon 60 mg 0 + 1 + 1 PO

##### *Day 2:*

- (neostigmine 2.5 mg + 1mg atropine + 0.9% NaCl up to 5 ml) - 1 ml/8 h IM
- Tbl. Mestinon a 60 mg 3x1

##### *Day 3:*

- Tbl. Mestinon a 60 mg 3x1

### **Thymectomies Performed to Treat Myasthenia Gravis at the Department of Thoracic Surgery, Institute for Pulmonary Disease of Vojvodina from 2004 to 2014**

The first thymectomy for surgical treatment of MG at the Department of Thoracic Surgery, Institute for Pulmonary Diseases of Vojvodina in Sremska Kamenica, was performed by Prim. Jozef Jašo in 1982, via trans-sternal approach. First video-assisted thoracoscopic thymectomy at the Department of Thoracic Surgery was done in 2010 (**Table 6**).

### **Conclusion**

Myasthenia gravis is a rare autoimmune disease that has been surgically treated at the Department of Thoracic Surgery, Institute for Pulmonary Diseases of Vojvodina successfully in past 35 years. In their everyday clinical practice anesthesiologists may have to deal with a patient with myasthenia gravis in different types of surgical interventions. The protocol for anesthesia and perioperative management of these patients herewith presented may greatly help them in their clinical practice.

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# HISTORY OF MEDICINE

## ISTORIJA MEDICINE

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### NIKOLA TESLA AND MEDICINE: 160<sup>TH</sup> ANNIVERSARY OF THE BIRTH OF THE GENIUS WHO GAVE LIGHT TO THE WORLD - PART I

*NIKOLA TESLA I MEDICINA – 160 GODINA OD ROĐENJA GENIJA KOJI JE SVETU PODARIO SVETLOST – I DEO*

Danijela VUČEVIĆ, Drago ĐORĐEVIĆ and Tatjana RADOSAVLJEVIĆ

#### Summary

**Introduction.** The interest in Nikola Tesla, a scientist, physicist, engineer and inventor, is *constantly growing*. In the millennium-long history of human civilization, it is almost impossible to find another person whose life and work has been under so much scrutiny of such a wide range of researchers, medical professionals included. Although Tesla was not primarily dedicated to biomedical research, his work significantly contributed to the development of radiology, and high frequency electrotherapy. This paper deals with the impact of Tesla's work on the development of a new medical branch - radiology. **Nikola Tesla and the Discovery of X-ray radiation.** Tesla *pioneered the use of X-rays for medical purposes*, practically laying the foundations of radiology. Namely, since 1887, Tesla periodically *experimented with X-rays*, at that time still *unknown and unnamed*, which he called "shadowgraphs". Moreover, at the end of 1894, he *conducted extensive research* focusing on X-rays, but *unfortunately it was interrupted after the fire burning down his laboratory* in 1895. In 1896 and 1897, Tesla published ten papers on the biologic effects of X-ray radiation. All his studies on X-rays were experimental. During 1896 and 1897, Tesla continued improving X-ray devices. Apart from this, Tesla was the first to *point out the harmful effects of exposure to X-ray radiation on human body*. **Conclusion.** Nikola Tesla was a visionary genius of the future. *Tesla's pioneer steps*, made more than a century ago in the domain of radiology, are still being *used today*.

**Key words:** History of Medicine; Famous Persons; Portraits as Topic; Radiology; X-Rays; Radiography; Radiation Effects

#### Sažetak

**Uvod.** Interesovanje za Nikolu Teslu, naučnika, fizičara, inženjera i pronalazača, neprestano raste. Na milenijumskoj skali postojanja ljudske civilizacije, danas je gotovo nemoguće naći neku drugu ličnost čiji život i delo pobuđuju tako širok spektar zanimanja najrazličitijih istraživača, uključujući i pripadnike medicinske struke. Mada Tesla nije primarno bio posvećen biomedicinskim istraživanjima, njegov rad je značajno doprineo radiologiji i visokofrekventnoj elektroterapiji. U ovom članku je prikazan uticaj Teslinih istraživanja na razvoj radiologije kao nove grane u medicini. **Nikola Tesla i otkriće X-zračenja.** Tesla je prvi primenio X-zračenje u medicinske svrhe i time praktično postavio temelje radiologije. Naime, **Tesla je povremeno eksperimentisao sa X-zračenjem još od 1887. godine.** Ovo nepoznato zračenje on je nazvao „grafici senki“. Štaviše, Tesla je preduzeo opsežno istraživanje ove teme krajem 1894. godine koje je, nažalost, prekinuto zbog požara koji je izbio u njegovoj laboratoriji 1895. godine. Tesla je zatim 1896. i 1897. godine publikovao deset radova u kojima je opisao biološke efekte X-zračenja. Svi Teslini radovi o X-zračenju bili su eksperimentalni. U toku 1896. i 1897. godine, Tesla je nastavio da unapređuje rad rendgenskih uređaja. Uz to, Nikola Tesla je prvi ukazao na postojanje štetnog dejstva X-zračenja na ljudski organizam. **Zaključak.** Nikola Tesla je bio nenadmašni vizionar budućnosti. Njegovi pionirski koraci, koje je pre više od jednog veka načinio u domenu radiologije, u današnje vreme takođe imaju svoju punu primenu.

**Ključne reči:** istorija medicine; poznate ličnosti; portreti; radiologija; x-zraci; radiografija; efekti radijacije

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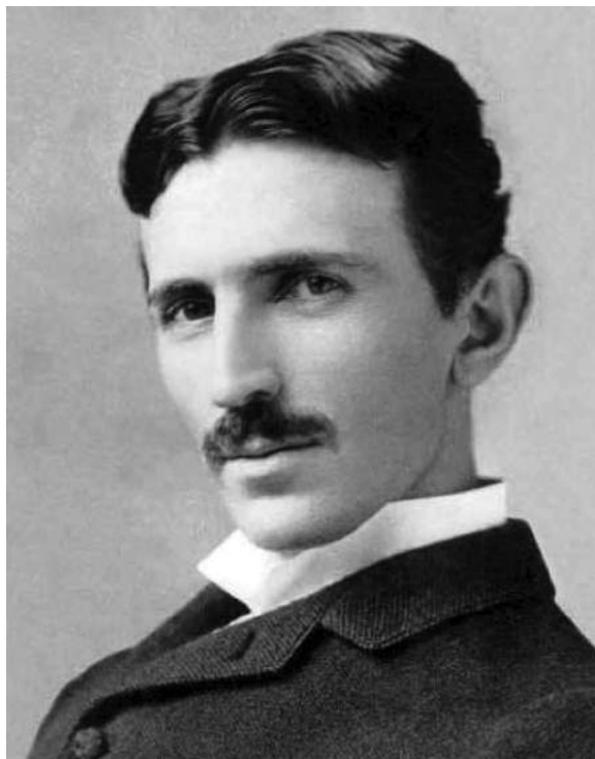
– We would like to express our deepest gratitude to Branislav Slavnić, laboratory technician, for his generous and friendly assistance in collecting references used in writing this paper

#### Introduction

*The nature and the laws of nature lay hidden in the darkness.*

*And God said: "Let there be Tesla", and there was light.*

*Bernard A. Behrend*



**Figure 1.** Nikola Tesla, 1894 - 1895  
Source: The Nikola Tesla Museum, document no. MNT, VI/V, 10.

**Slika 1.** Nikola Tesla, 1894–1895.  
Izvor: Muzej Nikole Tesle, dokument br. MNT, VI/V, 10.

It has been estimated that in the history of civilization, from 3.500 B. C. to the late 20<sup>th</sup> century, there were about 15,000 inventions in the field of natural sciences [1]. In the vast treasury of discoveries, about 200 inventions, so-called “lightning spirits of ingenious people“, are in the category of epochal inventions due to their significance [1–3]. The epochal inventions of Nikola Tesla include polyphase alternating current system of generators, undoubtedly the greatest invention in the history of electrical technology, and the discovery of high-frequency alternating current [1, 4–7].

Nikola Tesla, born in Smiljan on July 10, 1856, died in New York on January 7, 1943, (**Figure 1**) is a unique figure in the scientific history of civilization. His brilliant mind was proclaimed one of the seven wonders of the intellectual world [8]. According to *Life Magazine's* special issue in 1997, Tesla was among the 100 most famous people in the world [4]. A survey conducted by publicists promoting world science (*Explorer*, 2002), based on the applicability of inventions, Nikola Tesla took the first place [9]. In 2013, the *Wall Street Journal* presented Nikola Tesla as one of the greatest scientists ever [10]. Similarly, a national technology news website, the *GeekWire*, organized a Geek Madness Championship in 2013: Who is the greatest geek of all time? Among the world famous sci-

entists and inventors, Tesla was announced the greatest geek ever [4].

An unequalled genius, Tesla dedicated his life to inventions and science - the “noble, bright, enormous, faithful goddess that tolerates no liars” [11]. Nikola Tesla published 73 articles in various scientific journals [12, 13], devoted solely to the welfare of mankind. Unlike his countrymen, also world famous scientists, Milutin Milanković and Mihajlo Pupin, whose scientific papers are still cited, Nikola Tesla has been much less cited as an author [14]. The main reason lies in the fact that inventions were Tesla's greatest achievements, and they were described and incorporated into his patents, not in scientific papers [14–22]. Nikola Tesla was granted 116 basic patents, of which 109 in the United States of America, and 7 in the United Kingdom of Great Britain. In addition, he patented 181 analog or repeated patents in countries around the world, so that according to the latest research of the *Office of Intellectual Property* of the Republic of Serbia, the total number of registered Tesla's patents is 297. However, the exact number of applications and inventions he intended to patent is unknown [23].

Apart from diligent scientific and experimental laboratory work, Nikola Tesla also promoted his achievements, giving spectacular lectures in the most prestigious scientific institutions in the United States, United Kingdom and France [2, 4, 5, 23]. His outstanding results were recognized and rewarded. For decades of persistent, hard work in the field of technical and natural sciences, Nikola Tesla was awarded numerous honorary doctoral degrees from a number of universities including: *Columbia University*, 1894, *Vienna University of Technology (K.K. Technische Hochschule in Wien)*, 1908, *Technical University of Belgrade*, 1926, *University of Zagreb*, 1926, *Czech Technical University in Prague (Česka Visoka Učeni technice)*, 1936, *Paris Sorbonne University (Universite de Paris)*, 1937, *University of Poitiers (Universite de Poitiers)*, 1937, *Polytechnic Institute in Graz (Technische und Montanistische Hochschule in Graz)*, 1937, *University of Technology of Dr. Edvard Beneš in Brno (Vysoka Škola Technicka dr Edvard Beneš)*, 1937, *Polytechnic School in Bucharest King Carol II (Scoală Politehnica Regele Carol II)*, 1937, *University of Grenoble*, 1938, *Sofia University St. Kliment Ohridski (Universitet Sv. Kliment Ohridski)*, 1939, [13, 24, 25] and *Yale University*, 1894. In 1896, this erudite, polyglot and cosmopolitan became an honorary member of the *Yugoslav Academy of Arts and Sciences* (current *Croatian Academy of Sciences and Arts*, HAZU) and the *American Philosophical Society* in Philadelphia. Nikola Tesla was also a long-term associate of the *New York Academy of Sciences*, and in 1907 was elected an active member. In 1894, he became a corresponding member of the *Serbian Royal Academy (SRA)*, (current *Serbian Academy of Sciences and Arts*, SANU); the famous scientist Milutin Milanković proposed him for full

membership and he was elected a full member of SRA in 1937 [13, 24].

During six decades of continuous work in the field of electrical engineering, mechanical engineering and physics, Nikola Tesla initiated the second technological revolution in the second half of the 19th century, and marked the early 20<sup>th</sup> century by numerous technological inventions [24]. In 1893, Tesla was awarded the *Elliott Cresson Gold Medal* of the *Benjamin Franklin Institute of Technology*, Philadelphia, the *Thomas A. Edison Gold Medal* in 1917, handed to him by his colleagues, members of AIEE (*American Institute of Electrical Engineers*), as well as the *John Scott Medal* in 1934 [13, 25]. He was also nominated for the Nobel Prize for physics in 1937 [25, 26]. However, the Nobel Committee rejected the nomination on the grounds that, although Tesla's inventions of high frequency currents and rotating magnetic field were ingenious, they had been accomplished forty years before [26].

Tesla's greatest inventions were made in the 19th century [27–29]. The use of these inventions marked the 20<sup>th</sup> century, and Tesla's visionary solutions and pioneering steps, which were made a century ago in the field of remote control, radio technology, high-frequency electricity and wireless technologies, have not reached full implementation till the present time [29]. Among other things, Nikola Tesla was a visionary inventor in the field of charged particles, electromagnetic radiation and conductors, as well as the *forerunner* in the discovery of electrons, X-rays, radar, electronic microscope, cosmic radiation and induced radioactivity [2-8, 12, 13, 23, 25, 27-34] (**Table 1**).

So far, this fact has not been adequately evaluated in the world of scientific history [27], and Tesla himself commented on it in his way: *"The present is yours, but the future is mine. I don't care that they stole my ideas... I care that they don't have any of their own!"* [10]. *"In a thousand years there will be many Nobel Prize winners. And I have four dozen papers which bear my name in technical literature... These honors real and permanent which are bestowed not by a few who are apt to err, but by the whole world which seldom makes a mistake, and for any one of them I would give all the Nobel Prizes that will be awarded during the next several thousand years..."* [26].

Were we to eliminate the results of Tesla's work, the wheels of industry would cease to turn [35]. There is no area of human activity where products of Tesla's mind are not involved in the progress, restoration, prosperity, knowledge, preservation of youth and longevity, happy and glorious future of humanity [30]. Hence, no wonder that interest in Nikola Tesla is constantly growing [9, 10, 29]. Today, it is almost impossible to find another figure whose life and work have attracted so much attention of a wide range of researchers: from historians of science, electrical, mechanical and information technology engineers, experts in the fields of tele-

communication, aviation, military science to medical experts, ecologists, psychologists and philosophers [29]. In addition, Nikola Tesla has become an icon of popular culture and constant inspiration for artists and their work [11, 36–50]. The man who invented the 20<sup>th</sup> century, "inventist" ("inventor plus artist" a word coined by Laza Kostić for Nikola Tesla, bearing in mind that the Tesla's perception of art was built into his work), inventor, master-inventor of dreams, visionary, humanist, idealist, man out of time, colossus of science, divine lightning in the darkness of time, creator of the modern era, one of the most useful men ever, master of lightning, modern Prometheus, the only thunder-man who lived among people, wizard of electricity, poet of electricity, genius of light and spirit, time traveler, keeper of the last cosmic secrets, are just some of the poetic metaphors used by his numerous admirers used to express their admiration and gratitude [36, 51–54].

### Nikola Tesla and the Discovery of X-ray Radiation

It is almost impossible to exclude Tesla's inventions that are only partly related to medicine from those specific for medicine [32]. Current diagnosis and therapy are unimaginable without his numerous inventions [2–7, 12, 13, 23, 27, 28, 30, 32, 33].

The sensational discovery of X-ray radiation (a form of electromagnetic radiation that occurs when high velocity electrons collide with a metal target within a glass vacuum tube), officially attributed to Wilhelm Conrad Roentgen, a German physicist and professor at several universities in Germany, led to increased interweaving between physics and medicine and gave impetus to further research in these scientific fields [12, 25, 28, 31]. *Roentgen* was already working on the effects of *cathode rays* during 1895; he wrapped some black cardboard around a Crookes tube and *noticed* a fluorescent effect on a small paper screen painted with barium platino-cyanide [28, 55]. Roentgen concluded that the tube was producing invisible radiation of an unknown nature, which he called X-rays [28]. Exploring this new phenomenon, Roentgen *found* that the new rays passed *through* most *substances*, and that photographic plates were also sensitive to X-rays [27, 28]. Because of the apparent connection between X-rays and fluorescence, he made a radiograph of his wife's hand [28]. In November 1895, Roentgen read about his discovery before the *Würzburg Physical and Medical Society*, and on the 28<sup>th</sup> of December he submitted his manuscript "On a New Kind of Ray" to the *Bulletin of the Berlin Academy* [13, 28, 56, 57]. On January 6, 1896, the *New York Sun* reported that Roentgen discovered "the *light that never was*", which can take images of hidden things such as *bones* inside a *body* [28, 58–60]. Shortly after this event, the whole world heard about Roentgen's work, and X-rays were named after him – Roentgen rays, whereas a few years later, in

**Table 1.** Nikola Tesla as a forerunner of relevant discoveries  
**Tabela 1.** Nikola Tesla kao preteča značajnih otkrića

Discovery forerunner <i>Preteča otkrića</i>	Discovery <i>Otkriće</i>	Scientific award winners <i>Dobitnici naučnih priznanja</i>
Nikola Tesla, in 1891. <i>Nikola Tesla, 1891. godine.</i>	Accelerator for increasing the kinetic energies of charged particles <i>Akcelerator čestica</i> Cyclotron <i>Čiklotron</i>	Ernest Orlando Lawrence, in 1931; Nobel Prize, in 1939. <i>Ernest Orlando Lorens, 1931. godine; Nobelova nagrada 1939. godine.</i> Sir John Douglas Cockroft and Ernest Thomas Sinton Walton, in 1932; Nobel Prize, in 1951./ <i>Džon Kokroft i Ernest Volton, 1932. godine; Nobelova nagrada 1951. godine.</i>
Nikola Tesla, in 1891. <i>Nikola Tesla, 1891. godine.</i>	Electron microscope <i>Elektronski mikroskop</i> Scanning tunnelling microscope (STM) <i>Skenirajući tunelski mikroskop (STM)</i>	Ernst August Friedrich Ruska, in 1931; Nobel Prize, in 1986./ <i>Ernst Ruska, 1931. godine; Nobelova nagrada 1986. godine.</i> Heinrich Rohrer and Gerd Binnig, in 1981; Nobel Prize, in 1986./ <i>Hajnrh Rorer i Gerd Binig, 1981. godine; Nobelova nagrada 1986. godine.</i>
Nikola Tesla, in 1891. <i>Nikola Tesla, 1891. godine.</i>	Electron <i>Elektron</i>	Sir Joseph John Thomson, in 1897; Nobel Prize, in 1906. <i>Džozef Džon Tomson, 1897. godine; Nobelova nagrada 1906. godine.</i>
Nikola Tesla, in 1893. <i>Nikola Tesla, 1893. godine.</i>	Laser (light amplification by stimulated emission of radiation) <i>Laser</i>	Charles Hard Townes, Nicolay Gennadiyevich Basov, and Aleksandr Prokhorov, in 1952; Nobel Prize, in 1964. <i>Čarls Tauns, Aleksandar Mihailovič Prohorov i Nikolaj Genadijevič Basov 1952. godine; Nobelova nagrada 1964. godine.</i>
Nikola Tesla, in 1894. <i>Nikola Tesla, 1894. godine.</i>	X- rays <i>X-zračenje</i>	Wilhelm Conrad Röntgen, in 1895; Nobel Prize, in 1901. <i>Vilhelm Konrad Rendgen, 1895. godine; Nobelova nagrada 1901. godine.</i>
Nikola Tesla, in 1897. <i>Nikola Tesla, 1897. godine.</i>	Cosmic rays <i>Kosmičko zračenje</i> Positrons <i>Pozitroni</i>	Victor Franz Hess, in 1912; Nobel Prize, in 1936. <i>Viktor Hes, 1912. godine; Nobelova nagrada 1936. godine.</i> Carl David Anderson, in 1932; Nobel Prize, in 1936. <i>Karl Anderson, 1932. godine; Nobelova nagrada 1936. godine.</i>
Nikola Tesla, in 1898. <i>Nikola Tesla, 1898. godine.</i>	Radio <i>Radio</i>	Guglielmo Marchese Marconi, in 1901; Nobel Prize, in 1909./ <i>Guljelmo Markoni, 1901. godine; Nobelova nagrada 1909. godine.</i> Karl Ferdinand Braun, Nobel Prize, in 1909./ <i>Karl Ferdinand Braun, Nobelova nagrada 1909. godine.</i>
Nikola Tesla, in 1899. <i>Nikola Tesla, 1899. godine.</i>	Artificial radioactivity <i>Indukovana radioaktivnost</i>	Irene Joliot-Curie, in 1934; Nobel Prize, in 1935./ <i>Irena Žolio-Kiri, 1934. godine; Nobelova nagrada 1935. godine.</i>
Nikola Tesla, in 1903. <i>Nikola Tesla, 1903. godine.</i>	Radar (radio detection and ranging)/ <i>Radar</i>	Émile Girardeau, in 1934. <i>Emil Zirardo, 1934. godine.</i>

1901, he was awarded the first-ever *Nobel Prize in Physics* [55].

Nikola Tesla experimented with X-ray radiation since 1887 [25, 31, 57]. According to many sources, he was the first to discover *Roentgen radiation*, and named it “*special radiation*” [2, 4, 6, 12, 13, 23, 27, 28, 30, 32, 55, 57, 61–63], since a few years before the discovery of X-rays he investigated the phenomenon of glowing tubes with diluted gas in order to obtain low cost lighting [55]. Tesla’s light bulbs without wires are well known - single-wire tubes with high vacuum and a molten metal ball of poorly soluble metal, as well as wireless vacuum tubes shining in strong field of high-frequency waves [30, 55, 57]. In this regard, in his *lectures* at the *Royal Society* of Great Britain in London in 1892, Tesla noticed that his oscillators emitted “*ordinary visible and two types of invisible waves and these are*

*ordinary dark waves of all lengths, and, in addition, waves of a well defined character*” [23]. That same year, Tesla made an X-ray of his hand [30]. However, due to lack of equipment and resources, as well as involvement in other projects, at this point Tesla stopped his studies of “*special radiation*” [23, 28, 30]. A thorough study of this phenomenon started in late 1894 when Tesla conducted experiments with phosphorescent and fluorescent substances and their use in producing light bulbs [23, 28]. Using one of his high-frequency oscillators, he charged Crookes tubes and tubes he designed himself with one electrode or without electrodes [23]. He realized that these tubes exerted different effects on photographic plates in the laboratory, placed aside, with blurred shadows and stains, probably originating from some unknown radiation from the tubes [23, 28, 30]. Unfortunately, he did not describe “*special*



**Figure 2.** Mark Twain and Nikola Tesla in Tesla's New York lab in 1894 Source: T.C.M., "Tesla's Oscillator and Other Inventions", *The Century Magazine* 49:916-33. (April 1895), photograph no. 13.

**Slika 2.** Mark Tven i Nikola Tesla u Teslinoj laboratoriji u Njujorku 1894. godine. Izvor: T.C.M., *Tesla's Oscillator and Other Inventions*, *The Century Magazine* 49:916-33. (april 1895), slika br. 13.

radiation" in any articles he published in this period [2]. In the early 1895, Tesla continued his work on this phenomenon with great enthusiasm, but due to the fire in his laboratory at Houston Street New York, on March 13, 1895, he was forced to stop his work again [30]. If there had been no fire to burn down his lab at this critical moment, it is almost certain that X-rays would be called Tesla-rays, and Tesla would probably have been the first Nobel Prize winner in physics [27].

Interestingly, although Tesla was well known for his extraordinary intuition, when it comes to initial investigations of X-ray radiation, he succeeded only after two missed opportunities [23, 28]. This is vividly described by Bernard Carlson in his book "Tesla: Inventor of the Electrical Age": "At the end of 1894, Tesla decided to investigate whether his lamps affected photographic plates in the same way as light coming from the sun or other sources of illumination. To do so, he sought the assistance of a photographer employed by Tonnele & Company. Over a period of several months they tried a great variety of phosphorescent lamps, Crookes tubes, and vacuum bulbs with different kinds of electrodes. Since this was not a major project, Tesla and Alley worked on it periodically, and Alley stored spare glass photographic plates in a corner of the laboratory. However, they noticed that the unexposed plates had "uncountable marks and defects" indicating that they had somehow been spoiled. Tesla wondered, in passing, if the plates might have been affected by cathodic rays, which were a stream of charged particles that passed between the electrodes in some of his vacuum tubes when a voltage was

applied across the electrodes. Tesla had recently read reports about how a Hungarian student of Heinrich Hertz, Philipp Lenard, was getting interesting results using tubes with an aluminium window that allowed the rays to pass out of the tube. However, before he could follow up on this hunch, the laboratory fire occurred and depression kept Tesla from working" [28].

"The second missed opportunity came a few months later. In 1895, Tesla was discussing these photographic experiments with Edward Ringrose Hewitt, who was the son of the mayor of New York, Abraham Hewitt, and brother of Peter Cooper Hewitt, who would invent the mercury vapor lamp in 1902. Through his brother's research, Edward was familiar with Crookes tubes, and in the course of conversation Tesla and Edward decided to try taking some photographs using these tubes as the light source. Perhaps knowing that Mark Twain had posed for a similar photograph (Figure 2), Hewitt arranged for Twain to come to the lab. Because the light coming from Crookes tube was weak, Twain had to sit still for fifteen-minute exposure with his head supported by a headrest. A few days later, Hewitt checked to see how the portrait had turned out, and Tesla reported that the experiment failed as the glass photographic plate had somehow been spoiled" [28].

"Hewitt let the matter drop until he heard a few months later about the discovery of X-rays. Upon reading about Roentgen's discovery, Hewitt rushed to Tesla's laboratory and begged to see the photographic plate taken a few months earlier" [28]. This is how Hewitt remembered those moments: "Tesla brought it out of the dark room and held it up to the light. There I saw the picture of the circle of the lens, with the adjusting screw at the side – also round dots, which represented the metal wood screws in front of the wooden camera. Tesla gave one look. Then he slammed the plate on the floor, breaking it into thousand pieces, exclaiming: "Damned fool! I never saw it" [28, 63].

"What Tesla and Hewitt had missed was that the Geissler tube had produced not only visible light, but also invisible radiation – X-rays – that had spoiled the plate before the cap had even been taken off the lens and the exposure begun." "Too late", Tesla lamented, "I realized that my guiding spirit had again prompted me and that I failed to comprehend his mysterious signs" [28].

Although the lab fire in South Fifth Avenue, as mentioned before, may have distracted Tesla from discovering X-rays before Roentgen, Tesla gave Roentgen full credit for the finding [2, 23, 27, 30, 32] and was fascinated by this mysterious radiation: "Roentgen advanced modestly his results, warning against too much hope. Fortunately his apprehensions were groundless, for, although we have to all appearance to deal with mere shadow projections, the possibilities of the application of his discovery are vast. These discoveries of Roentgen, exactly of the order of the telescope and microscope, his seeing

through a great thickness of an opaque substance, his recording on a sensitive plate of objects otherwise invisible, were so beautiful and fascinating, so full of promise, that all restraint was put aside, and every one abandoned himself to the pleasures of speculation and experiment. Would but every new and worthy idea find such an echo! I am happy to have contributed to the development of the great art he has created [56, 57, 61].

When he found out about the discovery of X-ray radiation, Tesla decided to make up for lost time and immediately undertook a series of experiments to examine the nature of this radiation [2, 23, 27, 28, 30, 32]. A few weeks later he told the *New York Times* that he had begun his experiments “half an hour after the news of Prof. Roentgen’s discovery was cabled to this country” [28]. Tesla was using high-frequency waves of highest power at the time, and he was convinced that his radiation and X-ray radiation were very similar, although his X-ray radiation was obtained in a different way [57]. In fact, from the beginning of January 1896, in his experiments Tesla used his own transformer (coil), which would later be named after him “Tesla coil” [23, 30, 57, 64] (**Figure 3**).

Tesla was using an oscillating transformer, which he transformed during 1895 and 1896 into a compact device, which could be supplied from existing electrical networks and raise the voltage and current frequency [28]. Tesla then used this improved oscillating transformer to power a *new vacuum tube lamp*, which he claimed gave out more light [2, 13, 23, 32, 36, 56, 57, 61]. To demonstrate the power of his new lamp, Tesla posed for a portrait, but the exposition took only two seconds [28] (**Figure 4**).

Having checked the experiments of Professor Roentgen, Tesla wrote: “I’ve dedicated all my energy to research the nature of radiation and to perfecting the means of its production” [61]. After new experiments, Tesla sent Professor Roentgen shadowgraphs obtained by using “special radiation”. Professor Roentgen replied with enthusiasm: “The pictures are very interesting. Would you be so kind as to disclose the manner in which you obtained them?” [2, 6, 32, 57].

The advantage of Nikola Tesla in the study of the nature of the X-ray radiation was that at that time only he produced this radiation in the tube with alternating current power, while others used direct current [56, 57, 61]. Having this in mind, Roentgen also used Tesla’s coil and alternating currents in order to obtain clear shadows on the radiograph [23, 61]. Thus, in the article “On a New Form of Radiation”, published on April 24, 1896, in the journal *Electrician*, Roentgen wrote: “In many cases, it is useful to insert a Tesla coil between the X-ray generator and Ruhmkorff coil” [23, 30].

In 1896, Tesla published a series of articles on new radiation in the American journal *Electrical Review*, and by August 11, 1897, he had published a total of ten papers all in this field [4, 6, 13, 28, 32, 56, 57, 65–74]. All Tesla’s papers on X-ray radiation were experimental [57, 65–74]. The articles described in detail



**Figure 3.** Tesla transformer (Tesla coil) Source: [www.tesla-museum.org](http://www.tesla-museum.org)

**Slika 3.** Teslin transformator (Teslin kalem) Izvor: [www.tesla-museum.org](http://www.tesla-museum.org)

the technique of making radiographs and included X-rays that he himself made [32, 62]. Images of human body parts made by means of his mighty apparatus, Tesla called “shadowgraphs”, effectively laying the foundations of radiology and radiography [28, 57].

One of the first images showed a man’s right shoulder, his ribs, shoulder bone and upper arm bones [28]. On the application and beauty of the resulting X-ray, Nikola Tesla wrote: “Through the body of the experimenter the shadows of small buttons and alike objects are quickly obtained, while with an exposure from one hour and a half the ribs, shoulder bones and the bones of the upper arm appear clearly on the sensitized plate. It is now demonstrated beyond any doubt that small metallic objects or bony or chalky deposits can be infallibly detected in any part of the body” [30, 56, 57]. “Clear shadows of the bones of human limbs are obtained by exposures ranging from a quarter of an hour, and some plates have shown such an amount of detail that it is almost impossible to believe that we have to deal with shadows only” [28, 57].

When analyzing another image of a foot with a shoe, Nikola Tesla stated the following: “A picture of a foot with a shoe on shows every fold of the leather, trousers, stocking, etc., while the flesh and bones stand out sharply” [25, 28, 31, 56, 57, 61] (**Figure 5**).



**Figure 4.** Nikola Tesla in his New York lab in 1896, reading Ruder Bošković's book "Theory of Natural Philosophy", seated in front of the spiral coil of his high-frequency transformer. Source: The Nikola Tesla Museum, document no. MNT, VI/V, 14.

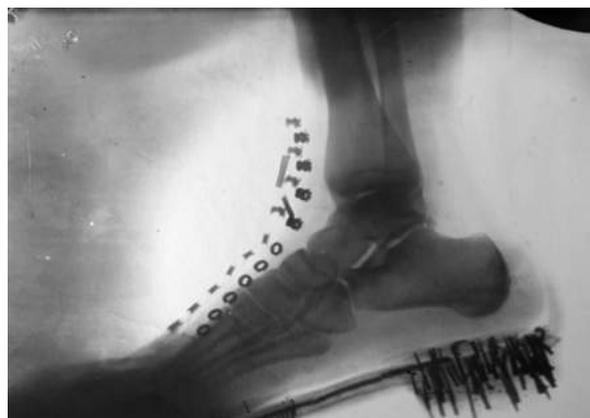
**Slika 4.** Nikola Tesla čita knjigu Rudera Boškovića „Teorija prirodne filozofije“ u svojoj laboratoriji u Njujorku 1896. godine. U pozadini je njegov visokofrekventni transformator sa spiralnom zavojnicom. Izvor: Muzej Nikole Tesle, dokument br. MNT, VI/V, 14.

Undoubtedly aware of the fact that *Edison had seen only “curvilinear murkiness”* when he X-rayed the brain for *New York Journal*, Tesla has made clear outlines of the skull exposing his own head to radiation between twenty and forty minutes [28]. In this regard Tesla wrote: *“An outline of the skull is easily obtained with an exposure of twenty to forty minutes. In an instance an exposure gave clearly not only the outline, but the cavity of the eye, the chin and the cheek and nasal bones, the lower jaw and connections to the upper one, the vertebral column and connections to the skull, the flesh and even the hair”* [30].

Another area related to medicine was the focus of Tesla's research - X-ray tubes different from those used by Roentgen [75]. Tesla experimented with Crookes tube and designed his own vacuum tube for producing X-ray radiation [13]. As mentioned earlier, Tesla immediately noticed that other researchers were limited by the use of weak Ruhmkorff coils or electrostatic generators, so he started using his new compact oscillating transformer (Tesla transformer) [28]. In his published papers, Tesla explained how his tube worked using alternating current power. Thus, during each *alternating current half-cycle*, cathode and anode operate normally (cathode is negative and anode

is positive), but in the next half-cycle it all changes (anode becomes negative, and cathode positive), and this process is alternately repeated [61, 65–74]. Using the advantages of higher voltage and frequency of his apparatus, Tesla was able to create far more powerful X-ray radiation than most of his contemporaries [28, 30]: *“I make shots from a distance of 13 meters. I repeat, 13 meters and more”*, reported Tesla in March of 1896 [28, 30, 66]. In the following few months, Tesla hired a glassblower, as he experimented with dozens of different tubes, and corresponded with Hewitt on the methods of their testing [28]. In his article, published in April 1896, Tesla explained, for the first time, the technical details based on which he improved X-ray devices, with special emphasis on the maintenance and regulation of the vacuum in the X-ray tubes [13, 23, 30, 32, 68]. In addition, Tesla designed a cooling system for X-ray tubes [13].

On April 6, 1897, Tesla gave a lecture before the *New York Academy of Sciences* and presented his X-ray devices [23, 30]. After that, in the same year, he published a paper dealing with the sources of X-ray radiation and wrote the following: *“I have for some time felt that a few indications in regard to the practical construction of Lenard tubes of improved designs, a great number of which I have recently exhibited before the New York Academy of Sciences, would be useful and timely, particularly as by their proper construction and use much of the danger attending the experimentation with the rays may be avoided... My efforts were directed to finding answers to the following questions: First, is it necessary that the impact body should be within the tube? Second, is it required that the obstacle in the*



**Figure 5.** A shadowgraph of a human foot with a shoe on. Tesla made this image in 1896 with X-rays generated by his own vacuum tube, at a distance of 2.5 meters. Source: The Nikola Tesla Museum, document no. MNT, VI/II, 122. <http://radiographics.rsna.org/content/28/4/1189.full>

**Slika 5.** Snimak ljudskog stopala u cipeli napravljen u Teslinoj laboratoriji 1896. godine. Zračenje je generisano pomoću vakuumske cevi na rastojanju od oko 2,5 metara. Izvor: Muzej Nikole Tesle, dokument br. MNT, VI/II, 122. <http://radiographics.rsna.org/content/28/4/1189.full>

*path of the cathodic stream should be a solid or liquid? And, third, to what extent is the velocity of the stream necessary for the generation of and influence upon the character of the rays emitted... In the hollow aluminum cap A of a tube, I placed a half-dollar silver piece, supporting it at a small distance from and parallel to the window or bottom of the cap by strips of mica in such a manner that it was not touching the metal of the tube, an air space being left all around it” [30, 74].*

Tesla was investigating how different conditions (length of exposition and distance) affected the quality of X-rays [13]. Like other researchers, in the beginning he considered X-radiation harmless [28], and he proposed its use in the detection of lung disease and foreign bodies in the body [13]. However, he and his assistants soon experienced eyestrain, headaches, and burns on the hands [13, 28]. Moreover, in the spring of 1897, Nikola Tesla was sick for several weeks and said that his disease was caused by X-radiation [57]. At first Tesla attributed these injuries to the ozone produced when running the tubes at high voltages, but he came to realize that the rays themselves were causing damage [28]. Tesla was particularly upset when “a dear and zealous assistant” suffered severe burns on his abdomen after being exposed for five minutes to an X-ray tube positioned thirty centimeters from his body [28, 73]. “Fortunately”, he wrote, “frequent warm baths, free application of Vaseline, cleaning and general bodily care soon repaired the ravages of the destructive agent, and I breathed again freely” [28]. Soon after that, Nikola Tesla was the first to point out the harmful effects of X-radiation on the human body [13, 23, 28, 30, 57, 64, 73]: “The use of X-rays should not be avoided, but one needs to be cautious, because the knowledge about these rays is still incomplete. However, ignoring the danger is also not recommended, now that we know that under certain circumstances, it really exists. In my opinion, it is much more necessary to be aware of these dangers, as I presume new devices will be developed, capable to create radiation of unpredictably higher power. In scientific laboratories these instruments are usually handled by persons who are trained to do so, capable to roughly estimate the effects, so at the present state of our knowledge we need not be afraid, even without necessary precautions” [30, 57].

Tesla had carefully noted the visible effects of X-radiation on the body: “When the head is exposed to strong radiation, some unusual effects occur. For example, I feel drowsy and it seems as if time passes quickly. There is a general soothing effect, and I have felt a sensation of warmth in the upper part of the head” [28, 30, 57]. The feeling of somnolence, registered by Tesla, is called “radiological hangover” [57].

In his following papers on X-ray radiation, Tesla was the first to recommend using a grounded aluminum shield around the X-ray tube to protect doctors from X-ray radiation, as well as avoiding getting too close to the tube, and limiting the exposure time [13, 23, 28, 30, 57, 64, 73, 74]. In order to provide radiation protection, he was also the first to point to the importance of the square law (it states that the further the point source of radiation, the intensity is reduced by four times (two squared) [57]. In addition, Tesla had experimentally proved that high energy natural radiations also produce X-radiation [23, 30, 64]. Tesla also experimented with reflected x-rays, using different materials [13]. Apart from direct reflection of X-rays, Tesla had produced a secondary effect, today known as Back Scattering Electrons (BSE) [27]. He believed that the produced rays were minute particles, and he put a lot of effort to obtain experimental evidence; this hypothesis was found partially justified only after the acceptance of the concept of dual (corpuscular and wave) nature of radiation in 1923 [23, 64].

## Conclusion

Nikola Tesla was a visionary genius of the future. His pioneer steps, made more than a century ago, especially in the domain of radiology, are still being used today.

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## 120 YEARS SINCE THE DISCOVERY OF X-RAYS

### 120. GODINA OD OTKRIĆA X-ZRAKA

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#### Summary

This paper is intended to celebrate the 120th anniversary of the discovery of X-rays. X-rays (Roentgen-rays) were discovered on the 8th of November, 1895 by the German physicist Wilhelm Conrad Roentgen. Fifty days after the discovery of X-ray, on December 28, 1895, Wilhelm Conrad Roentgen published a paper about the discovery of X-rays - "On a new kind of rays" (Wilhelm Conrad Roentgen: Über eine neue Art von Strahlen. In: Sitzungsberichte der Würzburger Physik.-Medic.-Gesellschaft. 1895.). Therefore, the date of 28th of December, 1895 was taken as the date of X-rays discovery. This paper describes the work of Wilhelm Conrad Roentgen, Nikola Tesla, Mihajlo Pupin and Maria Sklodowska-Curie about the nature of X-rays. The fantastic four - Wilhelm Conrad Roentgen, Nikola Tesla, Mihajlo Idivorski Pupin and Maria Sklodowska-Curie set the foundation of radiology with their discovery and study of X-rays. Five years after the discovery of X-rays, in 1900, Dr Avram Vinaver had the first X-ray machine installed in Šabac, in Serbia at the time when many developed countries did not have an X-ray machine and thus set the foundation of radiology in Serbia.

**Key words:** X-Rays; History of Medicine; Famous Persons; Radiology; Portraits as Topic; Radiation

#### Introduction

The 120th anniversary of the discovery of X-rays, which are called roentgen rays in the honor of Wilhelm Roentgen, was celebrated on the 28<sup>th</sup> of December 2015. The nature of X-rays itself (roentgen rays) speaks about what kind of discovery it is. They are the electromagnetic waves of a wavelength ( $\lambda$ ) ranging from 0.01 - 10 nanometers, which are in the spectrum of electromagnetic radiation between the ultraviolet and gamma ( $\gamma$ -) radiation; they carry a lot of energy and have power to ionize atoms which makes it a type of ionizing radiation [1–26].

The application of X-rays for medical purposes made revolutionary advances in medicine, the approach of doctors to patients has changed since the doctors

#### Sažetak

Rad je posvećen 120-godišnjici od otkrića X-zraka. Rendgenske zrake (X-zraci) je 8. novembra 1895. godine otkrio nemački fizičar Vilhelm Konrad Rendgen. Pedeset dana od otkrića X-zraka, 28. decembra 1895., Vilhelm Konrad Rendgen objavljuje rad o otkriću X-zraka – *O novoj vrsti zraka (Wilhelm Conrad Röntgen: Über eine neue Art von Strahlen. In: Sitzungsberichte der Würzburger Physik.-Medic.-Gesellschaft. 1895.)*. Ovaj datum – 28. decembar 1895. godine je datum otkrića X-zraka.

U radu se opisuje rad Vilhelma Konrada Rendgena, Nikole Tesle, Mihajla Idivorskog Pupina i Marije Sklodovske Kiri (*Marie Sklodowska-Curie*) na izučavanju prirode X-zraka. Fantastična četvorica – Vilhelm Konrad Rendgen, Nikola Tesla, Mihajlo Idivorski Pupin i Marija Sklodovska Kiri, otkrićem i proučavanjem X-zraka, postavili su temelj radiologije. Pet godina od otkrića X-zraka, 1900. godine, dr Avram Vinaver instalira u Šapcu, u Srbiji, prvi rendgen-apat, u vreme kada mnoge razvijene zemlje sveta nisu imale rendgen-apat i postavlja temelj radiologije u Srbiji.

**Ključne reči:** x-zraci; istorija medicine; poznate ličnosti; radiologija; portreti; radijacija

could visualize the inside of the patient's body for the first time without surgical opening. Radiology today, along with the energy of X-ray (X-ray diagnosis and computed tomography) uses the energy of radioisotopes (nuclear medicine), ultrasound (ultrasonography) and color Doppler) and electromagnetic field (magnetic resonance imaging).

The fantastic four - Wilhelm Conrad Roentgen (1845-1923), Nikola Tesla (1856-1943), Pupin (1854 - 1935) and Maria Sklodowska-Curie (1867-1934), who had worked independently of each other, did not know that their work on the nature of X-rays would set the foundation of the new branch of medicine - radiology and contribute to its evolution, without which the modern medicine cannot even be imagined [1–27].

**Abbreviations**

AC	– alternating current
Mx	– maxwell
T	– tesla
N	– newton
Gs	– gauss

Nikola Tesla thought that Roentgen's discovery of X-rays was as important as the invention of the telescope and microscope because it enabled seeing through an opaque substance of great thickness and making an image of objects otherwise invisible on a sensitive plate, which were so beautiful and fascinating and promising at the same time that everybody was delighted to think

about them and make experiments. He only wished that every new idea would have such an echo.

**Wilhelm Roentgen - Discovery of X-rays**

Wilhelm Roentgen (German: Wilhelm Conrad Roentgen, 27 March 1845, Lenepa, Prussia – 10 February 1923, Munich, Germany; **Figure 1a**) was a German physicist who discovered X-rays, on the 8<sup>th</sup> of November, 1895. He studied mechanical engineering at the University of Utrecht (Utrecht, Netherlands) and the Technical University of Zurich (Eidgenössische Technische Hochschule Zürich, Switzerland), from which

**Table 1.** Pupin's patents released in the United States**Tabela 1.** Patenti Mihajla Pupina ostvareni u Sjedinjenim Američkim Državama

Patent Number <i>Broj patenta</i>	Title/Naziv patenta	Publication date <i>Datum objave patenta</i>
519346	Apparatus for telegraphic or telephonic transmission <i>Aparat za telegrafске i telefonske prenose</i>	08.05.1894.
519347	Transformer for telegraphic, telephonic or other electrical systems <i>Transformator za telegrafске, telefonske ili druge električne sisteme</i>	08.05.1894.
640515	Art of distributing electrical energy by alternating currents <i>Tehnika razvođenja električne energije pomoću naizmjenične struje</i>	02.01.1900.
640516	Electrical transmission by resonance circuits <i>Električni prenos pomoću rezonantnih strujnih kola</i>	02.01.1900.
652230	Art of reducing attenuation of electrical waves and apparatus therefore <i>Tehnika smanjenja slabljenja električnih talasa i aparati za to</i>	19.06.1900.
652231	Method of reducing attenuation of electrical waves and apparatus therefore <i>Metod smanjenja slabljenja električnih talasa i aparati za to</i>	19.06.1900.
697660	Winding - machine/ <i>Mašina za namotavanje</i>	15.04.1902
707007	Multiple telegraphy/ <i>Višestruka telegrafija</i>	12.08.1902
707008	Multiple telegraphy/ <i>Višestruka telegrafija</i>	12.08.1902.
713044	Producing asymmetrical currents from symmetrical alternating electro-motive process/ <i>Proizvođenje asimetričnih struja pomoću simetričnog elektromotornog procesa</i>	04.11.1902
768301	Wireless electrical signaling/ <i>Bežično prenošenje električnih signala</i>	23.08.1904.
761995	Apparatus for reducing attenuation of electric waves <i>Aparat za smanjenje električnih talasa</i>	07.06.1904
1334165	Electric wave transmission/ <i>Prenošenje električnih talasa</i>	16.03.1920.
1336378	Antenna with distributed positive resistance <i>Antena sa raspodeljenim pozitivnim otporom</i>	06.04.1920.
1388877	Sound generator/ <i>Zvučni generator</i>	03.12.1921.
1415845	Multiple antenna for electrical wave transmission <i>Višestruka antena za prenošenje električnih talasa</i>	23.12.1921.
1388441	Selective opposing impedance to received electrical oscillation/ <i>Selektivna impedancija koja se suprotavlja primljenim električnim oscilacijama</i>	09.05.1922.
1416061	Radio receiving system having high selectivity <i>Radioprijemni sistem visoke selektivnosti</i>	10.05.1922.
1456909	Wave conductor/ <i>Talasni provodnik</i>	29.05.1922.
1452833	Selective amplifying apparatus/ <i>Aparat za selektivno pojačavanje</i>	24.04.1923.
1446769	Aperiodic pilot conductor/ <i>Aperiodični pilotni provodnik</i>	23.02.1923.
1488514	Selective amplifying apparatus/ <i>Selektivni aparat za pojačavanje</i>	01.04.1923.
1494803	Electrical tuning/ <i>Električno podešavanje</i>	29.05.1923.
1503875	Tone producing radio receiver/ <i>Radiofonski prijemnik</i>	29.04.1923



**Figure 1.** a) Wilhelm Conrad Roentgen (born March 27, 1845, Lennep, Prussia – died February 10, 1923, Munich, Germany); b) Wilhelm Conrad Röntgen: *Über eine neue Art von Strahlen*. In: *Sitzungsberichte der Würzburger Physik.-Medic.-Gesellschaft*. 1895; c) a radiograph of the hand of the Swiss anatomist and psychologist Albert von Kelikera, one of the first radiographs made by Wilhelm Conrad Roentgen

**Slika 1.** a) *Vilhelm Konrad Rendgen* (nemački: *Wilhelm Conrad Röntgen*; 27. mart 1845. g., Lenep, Pruska – 10. februar 1923. g., Minhen, Nemačka); b) *Wilhelm Conrad Röntgen: Über eine neue Art von Strahlen*. In: *Sitzungsberichte der Würzburger Physik.-Medic.-Gesellschaft*. 1895.; c) *Rendgenogram šake švajcarskog anatoma i psihologa Alberta fon Kelikera, jedan od prvih rendgenograma koje je Vilhelm Konrad Rendgen načinio*

he graduated. He received his Ph.D. at the University of Zurich in 1869 [1, 2].

During 1895 Roentgen was investigating the effects of high voltage on electrical discharge in diluted gases in vacuum tubes. There was a bag with barium platinocyanide on the desk where he worked. In the dark, one meter from the apparatus, Roentgen noticed some sort of faint shimmering on the desk whenever he turned on the camera (the 8<sup>th</sup> of November, 1895). The shimmering came from the bag containing the barium platinocyanide prepared for one of his experiments. Roentgen did not come out from his laboratory in the following weeks. He worked in his laboratory day and night on experiments, eating and sleeping there. He speculated that this was a new kind of radiation. Since he did not know what kind of radiation it was, he called it X-rays.

In one of his repeated experiments while investigating the ability of various materials to stop the rays, Roentgen brought his hand incidentally to the shield and saw his own bones. This picture made a strong impression on him and he decided to continue his experiments in secrecy.

Fifty days after the discovery of X-rays, on the 28<sup>th</sup> of December, 1895 Roentgen published a paper on the X-rays - "On a new kind of rays" (Wilhelm Conrad Roentgen: *Über eine neue Art von Strahlen*. In: *Sitzungsberichte der Würzburger Physik.-Medic.-Gesellschaft*. 1895.; **Figure 1b**) [2]. This date – the 28<sup>th</sup> of December 1895 was to be taken as the date of the discovery of X-rays.

One of the first X-ray images that Wilhelm Roentgen made was a radiograph of the hands of the Swiss

anatomist and psychologist Albert von Kelikera (German: Albert Von Kölliker, 6 July 1817 – 2 November 1905, **Figure 1c**).

In 1901 Roentgen was awarded the first Nobel Prize in Physics and he donated the money he received to his university where he worked. He refused to patent his invention for moral reasons. X-rays are called after his name – Roentgen rays. In November 2004 the International Union of Pure and Applied Chemistry named 111<sup>th</sup> elementary element of the Periodic System roentgenium (Rg).

### Nikola Tesla – about the X-rays

Nikola Tesla (10 July 1856, Smiljan, the Austro-Hungarian Empire - January 7 1943, New York, USA; **Figure 2a**), was a Serbian Orthodox, inventor and scientist with over 1,000 inventions and patents, such as asynchronous motor and transmission of electricity (the 12<sup>th</sup> of October, 1887), generator and transformer of polyphase current, induction motor with short circuit and contact rings (the 30<sup>th</sup> of November, 1887), high-frequency transformer (1891). He announced the basic concept of radio techniques in lectures in London and Paris (on the 3<sup>rd</sup> and 19<sup>th</sup> of February, 1891).

Nikola Tesla studied the X-rays as well and laid the basic principles of radiology, later to be introduced into everyday use by radiologists and manufacturers of X-ray apparatus.

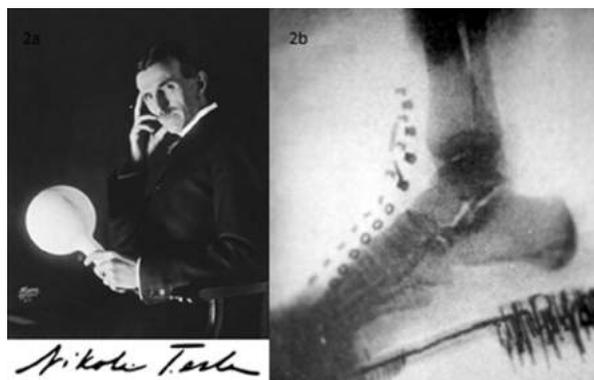
Tesla made only experiments with X-rays, that being specific to his work. His advantage when studying the nature of X-rays was that he used the alternating current (AC) to make his tubes function. At that time, it was only Tesla who worked on the production of X-rays in tubes with AC while the rest of the world worked with direct current. Nikola Tesla was the only one who could invent that.

In 1892, Nikola Tesla observed the "visible light, the black light, and a special kind of radiation" in his bulb for molecular bombardment [8]. Tesla did not explain the nature of that radiation until the discovery of X-rays by Wilhelm Konrad Roentgen (December 1895).

Nikola Tesla first tested the experiment of Prof. Roentgen and got the same results as Roentgen. Having finished the experiments, Tesla sent the images of shadows he had obtained by means of this radiation to prof Wilhelm Roentgen who responded that the pictures were very interesting and asked Tesla to explain how he got them [8]. In 1896 Roentgen emphasized the importance of Tesla's transformer and AC power as a relevant means for obtaining the clear shadows.

On the 11<sup>th</sup> of March, 1896 Nikola Tesla published the first paper on X-rays, to be followed by ten papers in this area by the 11<sup>th</sup> of August 1897:

- On Roentgen rays (1) *Electrical Review*, March 11, 1896;
- On Roentgen rays (2) *Electrical Review*, March 18, 1896;
- On reflected Roentgen rays, *Electrical Review* April 1, 1896;



**Figure 2.** a) Nikola Tesla (born - July 10, 1856 Smiljan Austro-Hungarian Empire – died January 7, 1943, New York, USA), b) one of the radiographs made by Nikola Tesla and his comment: “the image of a foot with the shoe revealing every fold of skin, pants, socks, etc., while the muscles and bones are sharply shown”

**Slika 2.** a) Nikola Tesla (10. jul 1856. g., Smiljan, Austro-ugarska Carevina – 7. januar 1943. g., Njujork, USA); b) jedan od rendgenograma koje je načinio Nikola Tesla komentarišući “...sнимак jedne noge sa cipelom, pa se vidi svaki nabor na koži, pantalonama, čarapi itd., dok se mišići i kosti oštro ističu”

- On Roentgen radiations, Electrical Review, April 8, 1896.;
- Roentgen ray investigations, Electrical Review, April 22, 1896.;
- An interesting feature of X-ray radiations, Electrical Review, July 8, 1896.;
- Roentgen rays or streams, Electrical Review, August 12, 1896.;
- On the Roentgen streams, Electrical Review, December 1, 1896.;
- On the hurtful actions of Lenard and Roentgen tubes, Electrical Review, May 5, 1897.;
- On the source of Roentgen rays and the practical construction and safe operation of Lenard tubes, Electrical Review, August 11, 1897.

Tesla’s experimental work in the field of X-ray was aimed at explaining what the X-rays were, what their nature was, whether they were particles or waves. Tesla was convinced that the X-rays were particles. However, later research in the field of quantum mechanics confirmed that X-rays had corpuscular-wave dualism, i.e. they had at the same time the property of corpuscular particle and of electromagnetic wave, suggesting the question - what to say about Tesla’s understanding of the nature of X-rays (X-ray material particle), who claimed that the X-rays were particles many years before Compton!?

Tesla was delighted with the nature of X-rays because Roentgen’s discovery had enabled seeing through an opaque material by means of fluorescent screen and visualising metal objects, bones and calcareous shadows in every part of the body [7].

Speaking of the value and beauty of radiographs (**Figure 2b**), Nikola Tesla wrote that the clear shad-

ows of human limb bones had been obtained by exposing them for 15 to 60 minutes and some of the images showed such an amount of details that was almost impossible to believe they were only shadows. For example, the image of a foot with the shoe revealed every fold of skin, pants, socks, etc., while the muscles and bones were sharply shown [7, 9].

Nikola Tesla was the first who recognized harmful effects of X-ray on the living cell. He carefully recorded the visible effects of X-rays on the human body and tried to give an explanation of the harmful effects of X-rays. Nikola Tesla wrote that some strange effects had been observed when the head was exposed to strong radiation such as feeling sleepy and having the impression of time passing quickly. The general effect was the one of calmness and the sensation of warmth in the upper part of the head [7].

In the spring of 1897 Tesla mysteriously got ill and was ill for several weeks, and claimed that X-rays had caused a shock to his eyes and that they made him ill [8]. He thought that dangers resulting from this radiation should not be ignored. In order to get protection against harmful effects of X-ray, Nikola Tesla tried to find a protection shield. He suggested the use of aluminum plate placed between the person exposed to the X-rays and X-ray tubes and pointed to the importance of inverse square law.

In honor of Nikola Tesla the term “tesla” was introduced as the unit measure for magnetic field strength (T). Tesla is an SI derived unit. Tesla is magnetic induction of homogeneous magnetic field with acting force of 1 N (Newton) on the line conductor 1 meter long, placed perpendicularly to the field when the conductor current is 1 A (ampere) or  $1 \text{ T} = 1 \text{ N}/1 \text{ m} \cdot 1 \text{ A}$ . A smaller unit for magnetic induction is Gauss (Gs), where  $1 \text{ Gs} = 10^{-4} \text{ T}$ .

Tesla can be displayed via Weber. Weber (Wb) is a unit of magnetic flux. This is a SI derived unit. Weber is magnetic flux through the flat surface of  $1 \text{ m}^2$  (square meter), which is perpendicular to the direction of the homogeneous magnetic field induction of 1 T (tesla) or  $1 \text{ Wb} = 1 \text{ T} \cdot 1 \text{ m}^2$ . A smaller unit of Weber is maxwell (Mx) where  $1 \text{ Wb} = 10^8 \text{ Mx}$ . Using the analogy of Tesla, it is easy to conclude that  $1 \text{ Mx} = \text{Gs} \cdot \text{cm}^2$ .

Today, the power of magnetic resonance apparatus (MR) is expressed in units of tesla (T), so there are magnetic resonance apparatus of 0.5 T, 1.0 T, 1.5 T.

In honor of Nikola Tesla, a banknote of 100 dinars, blue colored, with his portrait was issued by the National Bank of Yugoslavia in 2000. It is still in use; although this one was issued by the National Bank of Serbia [26].

### Pupin - invention of fast recording by means of X-ray

Pupin (October 9, 1854, Idvor, the Austro-Hungarian Empire - March 12, 1935, New York, USA; **Figure 3a**) was a Serbian Orthodox, inventor, scientist, professor at Columbia University (Columbia University in the city of New York, USA), holder of

the Yugoslav Order of the White eagle - first class, winner of the Pulitzer Prize (1924 for autobiography - From Immigrant to Inventor), member of the American Academy of Sciences, the royal Serbian Academy, honorable doctor of science at 18 universities and honorable consul of Serbia in the United States [12–16]. He patented 34 inventions (**Table 1**).

Immediately after the discovery of X-rays in February 1896, Pupin began his research on X-rays, X-fluoroscopy and shortening of the exposure time. During this research Pupin discovered the secondary X-rays, calling them “H-rays” and informed the Academy of Sciences (the 6<sup>th</sup> of April, 1896) about them [12–16].

The secondary X-rays are widely applied in medicine and nuclear physics. Each chemical element irradiated by X-rays reflects electromagnetic waves of a certain wavelength with characteristic spectrum which corresponds only to that chemical element. Today, this Pupin’s discovery is applied in space research as well as in radiology. The film used nowadays in rentgenography emit the light of a certain wavelength, i.e. the brightness of a specific color to which the film is sensitive. This enables the transfer of latent X-ray image as the brightness from the film to X-ray film, thus making it visible [10–13].

During the X-ray illumination of the body of patients Pupin managed to shorten the exposure time, calling it “the invention of fast recording by means of X-ray”. Pupin made this discovery by placing a photographic plate behind the fluorescent screen, thereby reducing the exposure time from about an hour to a few seconds.

In his autobiography, “From Immigrant to Inventor” [16] Pupin disclosed details about his contribution to the development of radiology, which was a new branch of medicine at that time, in the section “My invention of fast recording by means of X-rays.” Pupin says: “On the 7<sup>th</sup> of February 1896, the famous surgeon Dr. Bull sent me a patient with almost hundred lead balls in his hand. His and my friends asked me to obtain an X-ray image so Dr. Bull could find and take out all of the lead balls. The first attempt failed because the patient was too weak to stand still for nearly an hour which is the time it took to get an X-ray photo at the time. My good friend Thomas Edison sent me a few extraordinary fluorescent cardboard (screens), and using their fluorescent light we could see the numerous small balls. On first sight it was clear that the combination of fluorescent cardboard and eyes is more sensitive than photographic plate. That is why I tried to combine Edison’s fluorescent screen with photographic plate. I put the fluorescent screen on the photographic plate and the patient’s hand on the screen. X-rays passed through the patients hand and caused the screen to fluoresce, which then exposed the photographic plate. It turned out much better than I expected. A fairly good image was obtained with an exposure of only a few seconds. On photographic plate appeared many balls, as if drawn with pen and ink” [15, 16]. This Pupin’s invention of fast recording using X-ray, which shortened

the exposure time from an hour to a few seconds, was both ingenious and simple and is widely used today. Pupin invented “fast recording by means of X-rays” 40 days after Roentgen had discovered X-rays. Pupin did not patent this invention.

The 7<sup>th</sup> of February, 1896, the day when Pupin took the radiograph of the hand of a patient referred to him by Dr. Bull is considered as the date when the first radiograph was taken in the United States of America (**Figure 3b**). At the same time, it is also the date when the first surgery using the radiographs was performed in United States. Therefore, Pupin is considered the father of American Radiology [12].

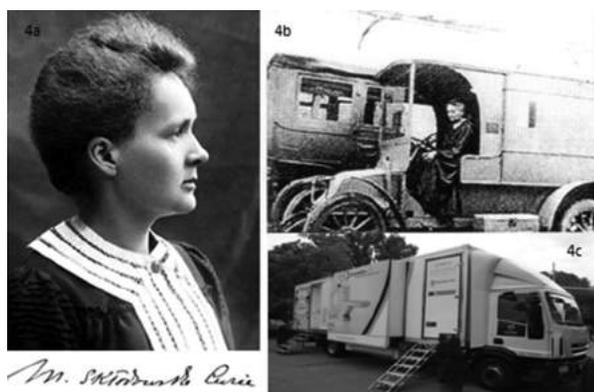
### Marie Sklodowska Curie - the mobile hall with X-rays

Marie Sklodowska Curie (Polish: Maria Sklodowska-Curie, November 7, 1867 Warsaw, Poland - 4 July 1934 Salans, France; **Figure 4a**) is a famous Polish and naturalized-French who studied the physical and chemical properties of radioactive elements, radioactivity and discovered radioactive elements - polonium ( $^{84}\text{Po}^{210}$ ), thorium ( $^{90}\text{Th}^{232}$ ) and radium ( $^{88}\text{Ra}^{226}$ ). She spent most of her life in France, where she started a scientific career. She was the first woman in France who acquired a scientific degree of Doctor of Science, the first woman to become a professor at the University of Paris, Sorbonne (1908), the first and only woman in the world who won the Nobel Prize twice- in 1903 Marie Sklodowska Curie shared the Nobel Prize in Physics with Pierre Curie and Henri Becquerel for research on the radiation. In 1911



**Figure 3.** a) Mihajlo Idvorski Pupin (born October 1854, Idvor, Austro-Hungarian Empire – died March 12, 1935, New York, USA), b) a radiograph of a hand of a patients made by means of the Pupin’s invention “X-ray fast recording” on February 7, 1896, that being the date of the very first radiograph made in the USA

*Slika 3. a) Mihajlo Idvorski Pupin (9. oktobar 1854. g., Idvor, Austrougarska Carevina – 12. mart 1935. g., Njujork, USA); b) rendgenogram šake bolesnika sa mnogobrojnim dramlijama učinjen Pupinovim pronalaskom “brzog snimanja pomoću X-zraka” 7. februara 1896. godine – to je datum prvog načinjenog rendgenograma u USA*



**Figure 4.** a) Marie Skłodowska Curie (born November 7, 1867, Warsaw Poland – died July 4, 1934, Sancellemoz, France); b) Maria Skłodowska Kiri behind the wheel of a “mobile room with X-rays” c) a modern “mobile room with X-rays”

*Slika 4. a) Maria Skłodowska Kiri (poljski: Maria Skłodowska-Curie; 7. novembar 1867. g. Varšava, Poljska – 4. jul 1934. g. Salanš, Francuska); b) Maria Skłodowska Kiri za volanom “mobilne sale sa X-zracima” c) savremena “mobilna sala sa X-zracima”*

she won her second Nobel Prize, this time in Chemistry for the discovery of the chemical elements radium ( $^{88}\text{Ra}^{226}$ ) and polonium ( $^{84}\text{Po}^{210}$ ).

By discovering the radioactive elements Marie Skłodowska Curie introduced a new medical discipline in medicine - radiotherapy, and with her work in the field of X-ray (a radiology car) she gave the medicine something completely new - a mobile X-ray diagnostic tool. During the First World War, Marie Skłodowska Curie worked on the creation of “mobile X-ray station” (**Figure 4b**) (17-19). Alliance of French women provided the funds for the creation of a mobile hall with X-rays. Thus, in 1914 the first mobile “radiology car” was produced, which was later called “little Curie”. Marie Skłodowska Curie showed the world how to install X-ray machine into the car and how to use the dynamo, which sets a car into motion, to produce electricity to operate X-ray machines.

At the request of Marie Curie many rich Frenchwomen donated their cars to be equipped with an X-ray machine during the First World War. It was their contribution to the defense of France and the rescue of French soldiers. Thus, Marie Curie had 20 vehicles equipped with a mobile radiological laboratory and trained 150 people to operate them. She kept one vehicle for her personal use to be able to reach the war zone and to train medical staff to operate them and to take radiograms of wounded soldiers in outpatient conditions.

This ingenious work of Mari Curie made it possible to diagnose injuries of wounded soldiers on the front line on the basis of X-rays, to detect the presence and localization of residual parts of shells in the body, and to diagnose broken bones. Marie Curie introduced something completely new in medicine - mobile radiology diagnostics and war radiology [18, 19].

Today, many armies of the world have modern mobile radiological services. For example, the army of the former USSR had a truck with X-ray machines and mini-labs, which were made in our Electronic Industry in Nis (SFR Yugoslavia, today: the Republic of Serbia).

Nowadays, manufacturers of X-ray machines produce and install the standard X-ray machines, computed tomography apparatus, magnetic resonance imaging machine in truck trailers (**Figure 4c**) with or without echo apparatus, making them mobile and available to all communities, in all weather conditions, during war or peacetime. Well, are not the buses with fluorographic apparatus, which were used to examine the population in the prevention of tuberculosis, what Marie Skłodowska Curie imagined, created and implemented in practice [17–19]?

#### Dr. Avram Josif Vinaver - a pioneer of radiology in Serbia

Dr. Avram Josif Vinaver (1862, Warsaw, Poland - August 24, 1915, Gevgelija, Serbia, Macedonia today; **Figure 5a**) was a Polish Jew, Serbian pioneer in radiology, who contributed to the development of health services in Serbia, especially in Sabac, Macva district in peacetime and in war [20–25]. He finished primary and secondary school in his hometown, where he graduated from the Faculty of Medicine in 1887. After acquiring his academic title, Dr. Avram J. Vinaver settled in Sabac (1890), in the former Kingdom of Serbia, where he worked and lived. Dr. Avram Vinaver spoke Hebrew, German, French, Polish, Russian and Serbian. He participated in the Balkan wars and the First World War. After the victory of the Serbian army in the Battle of Cer and Kolubara, Dr. Avram Josif Vinaver arrived with his unit in Gevgelija (Serbia, Macedonia today). Exhausted from myocardial typhus, he suffered from malaria and died in 1915. He was buried in a common grave at his own request.

Dr. Avram Vinaver set the foundation of today's radiology in Serbia. In 1900, Dr. Avram Vinaver brought the first X-ray machine in Sabac, just five years after the discovery of X-rays, at the time when many developed countries of the world did not have an X-ray machine. It was an X-ray machine with gas (ion) tube, bought in Vienna, placed in a building which was next to the apartment of Dr. Abraham Vinaver. Thus, Sabac became the first city in the Kingdom of Serbia which had an X-ray machine. However, it should be emphasized that an X-ray machine had already been purchased for the Military Hospital in Belgrade by the Serbian Army in 1897. However, that X-ray machine was used only for the purposes of army, while the X-ray machine, which was owned by Dr. Avram Vinaver was the first X-ray machine in Serbia used in diagnostics and development of health care of the civilian population of Serbia, and therefore the date of purchasing the X-ray machine in 1900 by Dr. Abraham Vinaver is taken to be the date of the first X-ray machine in Serbia.

Dr. Vinaver wrote about his experience with X-rays, diagnostic and therapeutic possibilities of X-rays in the first published papers, which he presented at the "First Congress of Serbian physicians and naturalists under the highest protection of His Majesty King Peter I", held in Belgrade from the 5<sup>th</sup> to the 7<sup>th</sup> of September 1904. The papers from the Congress were published in the Proceedings of the "First Congress of Serbian physicians and naturalists under the highest protection of his Majesty King Peter I in Belgrade, held on the 5<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> of September 1904, printed in the state printing house of the Kingdom of Serbia 1905".

The following papers were presented: "Diagnostic importance of X-ray beams in diseases of the lungs, especially in the initial tuberculosis", "Five years of treatment with Roentgen rays" and "Several contributions to solving the question whether the father's syphilis is hereditary" [22–24].

Dr. Vinaver's papers of "Diagnostic importance of X-ray beams in diseases of the lungs, especially in the initial tuberculosis" [22] and "Five years of treatment with Roentgen rays" [23] were the first studies within radiology in Serbia, and among the first publications of this type in the world.

In "Diagnostic importance of X-ray beams in diseases of the lungs, especially in the initial tuberculosis" [22]. Dr. Avram Vinaver wrote that X-rays were meant to make a breakthrough in this field as well but they had not yet become available to the general population in spite of being a valuable diagnostic tool.

Dr. Avram Vinaver gave the axiom of the overall radiological diagnostics: "It is not the X-rays but the intellect of a doctor that establishes a diagnosis."

Dr. Avram Vinaver prophesied that X-rays and X-ray diagnostic application were the method of future. In his study "Five years of treatment with Roentgen rays" [23] Dr. Avram Vinaver presented therapeutic options of X-ray used on 62 treated patients where he quoted Prof. Holzknacht from Vienna who was one of the eminent radiologist of the world at that time. Dr. Avram Vinaver concluded that it would be an unforgivable sin against our patients to remain indifferent to the Roentgen-therapy and not make it possible for them to be treated and cured by means of X-rays.



**Figure 5.** a) Dr Avram Josif Vinaver (born 1862, Warsaw, Poland – died August 24, 1915, Gevgelija Serbia, today Macedonia); b) a stamp featuring Dr Avram Josif Vinaver *Slika 5. a) Dr Avram Josif Vinaver (1862., Varšava, Poljska - 24. avgust 1915., Đevđelija, Srbija, danas Makedonija); b) Doplatna poštanska marka sa likom dr Avrama Josifa Vinavera*

## Conclusion

This paper is dedicated to the 120th anniversary of the discovery of X-rays. Wilhelm Roentgen (1845-1923) discovered the X-rays (Roentgen rays) on the 28<sup>th</sup> of December, 1895. The nature of the X-ray was studied by Nikola Tesla (1856-1943), Pupin (1854 - 1935.g) and Maria Sklodowska Curie (1867-1934). The Fantastic Four - Wilhelm Conrad Roentgen, Nikola Tesla, Pupin and Maria Sklodowska Curie set the foundation of a new branch of medicine - radiology. Five years after the discovery of X-rays, in 1900, Dr. Avram Vinaver (1862-1915) had the first X-ray machine installed in Sabac, in Serbia, at the time when many developed countries of the world did not have an X-ray machine and thus set the foundation of radiology in Serbia. The papers of Dr. Vinaver "Diagnostic importance of X-ray beams in diseases of the lungs, especially in the initial tuberculosis" and "Five years of treatment with Roentgen rays" were the first studies within radiology in Serbia, and among the first publications of this type in the world.

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Tekst rada treba da bude napisan u programu *Microsoft Word* za *Windows*, na A4 formatu stranice (sve četiri margine 2,5 cm), proreda 1,5 (isto važi i za tabele), fontom *Times New Roman*, veličinom slova 12 pt. Neophodno je koristiti međunarodni sistem mernih jedinica (*SI*), uz izuzetak temperature (°C) i krvnog pritiska (*mmHg*).

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#### 1. Naslovna strana

Naslovna strana treba da sadrži: kratak i sažet naslov rada, bez skraćenica, skraćeni naslov rada (do 40 karaktera), imena i prezimena autora (ne više od 6) i afilijacije svih autora. Na dnu strane treba da piše ime, prezime i titula autora zaduženog za korespondenciju, njena/njegova adresa, elektronska adresa, broj telefona i faksa.

#### 2. Sažetak

Sažetak ne može da sadrži više od 250 reči niti skraćenice. Treba da bude strukturisan, kratak i sažet, sa jasnim pregledom problema istraživanja, ciljevima, metodama, značajnim rezultatima i zaključcima.

Sažetak originalnih i stručnih članaka treba da sadrži uvod (sa ciljevima istraživanja), materijale i metode, rezultate i zaključak.

Sažetak prikaza slučaja treba da sadrži uvod, prikaz slučaja i zaključak.

Sažetak preglednih članaka treba da sadrži Uvod, podnaslove koji odgovaraju istima u tekstu i Zaključak.

Navesti do 10 ključnih reči ispod sažetka. One su pomoć prilikom indeksiranja, ali autorove ključne reči mogu biti izmenjene u skladu sa odgovarajućim deskriptorima, odnosno terminima iz *Medical Subject Headings, MeSH*.

Sažetak treba da bude napisan na srpskom i engleskom jeziku. Sažetak na srpskom jeziku trebalo bi da predstavlja prevod sažetka na engleskom, što podrazumeva da sadrži jednake delove.

#### 3. Tekst članka

Originalni rad treba da sadrži sledeća poglavlja: Uvod (sa jasno definisanim ciljevima istraživanja), Materijal i metode, Rezultati, Diskusija, Zaključak, spisak skraćenica (ukoliko su

korišćene u tekstu). Nije neophodno da se u posebnom poglavlju rada napiše zahvalnica onima koji su pomogli da se istraživanje uradi, kao i da se rad napiše.

Prikaz slučaja treba da sadrži sledeća poglavlja: Uvod (sa jasno definisanim ciljevima), Prikaz slučaja, Diskusija i Zaključak.

#### **Uvod**

U poglavlju Uvod potrebno je jasno definisati predmet istraživanja (prirodu i značaj istraživanja), navesti značajne navode literature i jasno definisati ciljeve istraživanja i hipoteze.

#### **Materijal i metode**

Materijal i metode rada treba da sadrže podatke o vrsti studije (prospektivna/retrospektivna, uslove za uključivanje i ograničenja studije, trajanje istraživanja, demografske podatke, period praćenja). Detaljno treba opisati statističke metode da bi čitaoci rada mogli da provere iznesene rezultate.

#### **Rezultati**

Rezultati predstavljaju detaljan prikaz podataka koji su dobijeni istraživanjem. Sve tabele, grafikoni, sheme i slike moraju biti citirani u tekstu rada i označeni brojevima po redosledu njihovog navođenja.

#### **Diskusija**

Diskusija treba da bude koncizna, jasna i da predstavlja tumačenje i poređenje rezultata studije sa relevantnim studijama koje su objavljene u domaćoj i međunarodnoj literaturi. U poglavlju Diskusija potrebno je naglasiti da li su postavljene hipoteze potvrđene ili nisu, kao i istaknuti značaj i nedostatke istraživanja.

#### **Zaključak**

Zaključci moraju proisteći isključivo iz rezultata istraživanja rada; treba izbegavati uopštene i nepotrebne zaključke. Zaključci koji su navedeni u tekstu rada moraju biti u saglasnosti sa zaključcima iz Sažetka.

### **4. Literatura**

Potrebno je da se literatura numeriče arapskim brojevima redosledom kojim je u tekstu navedena u parentezama; izbegavati nepotrebno velik broj navoda literature. Časopise bi trebalo navoditi u skraćenom obliku koji se koristi u *Index Medicus* (<http://www.nlm.nih.gov/tsd/serials/lji.html>). Pri citiranju literature koristiti Vankuverski sistem. Potrebno je da se navedu svi autori rada, osim ukoliko je broj autora veći od šest. U tom slučaju napisati imena prvih šest autora praćeno sa *et al.*

Primeri pravilnog navođenja literature nalaze se u nastavku.

#### **Radovi u časopisima**

##### **\* Standardni rad**

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. *J Thromb Haemost* 2003;1:1435-42.

##### **\* Organizacija kao autor**

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002;40(5):679-86.

##### **\* Bez autora**

21st century heart solution may have a sting in the tail. *BMJ*. 2002;325(7357):184.

##### **\* Volumen sa suplementom**

Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxis. *Pharmacol Res Commun* 1988;20 Suppl 5:75-8.

##### **\* Sveska sa suplementom**

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. *J Clin Psychopharmacol* 1988;8(4 Suppl):31S-37S.

##### **\* Sažetak u časopisu**

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by *Toxoplasma gondi* [abstract]. *Clin Res* 1987;35:475A.

#### **Knjige i druge monografije**

##### **\* Jedan ili više autora**

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical microbiology*. 4th ed. St. Louis: Mosby; 2002.

##### **\* Urednik (urednici) kao autor (autori)**

Danset J, Colombani J, eds. *Histocompatibility testing 1972*. Copenhagen: Munksgaard, 1973:12-8.

##### **\* Poglavlje u knjizi**

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: Saunders; 1974. p. 457-72.

##### **\* Zbornik radova sa kongresa**

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. *Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland*. Berlin: Springer; 2002. p. 182-91.

##### **\* Disertacija**

Borkowski MM. *Infant sleep and feeding: a telephone survey of Hispanic Americans* [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

#### **Elektronski materijal**

##### **\* Članak iz časopisa u elektronskom formatu**

Aboud S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

##### **\* Monografija u elektronskom formatu**

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

##### **\* Kompjuterska datoteka**

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

### **5. Prilozi (tabele, grafikoni, sheme i slike)**

#### **BROJ PRILOGA NE SME BITI VEĆI OD ŠEST!**

Tabele, grafikoni, sheme i slike se postavljaju kao posebni dokumenti.

– Tabele i grafikone bi trebalo pripremiti u formatu koji je kompatibilan programu u kojem je napisan tekst rada. Slike bi trebalo poslati u jednom od sledećih oblika: *JPG, GIF, TIFF, EPS*.

– Svaki prilog mora biti obeležen arapskim brojem prema redosledu po kojem se navodi u tekstu rada.

– Naslovi, tekst u tabelama, grafikonima, shemama i legendi slika bi trebalo da budu napisani na srpskom i engleskom jeziku.

– Nestandardne priloge označiti u fusnoti uz korišćenje sledećih simbola: \*, †, ‡, §, ||, ¶, \*\*, † †, ‡ ‡.

– U legendi slika trebalo bi napisati korišćeno uveličanje okulara i objektivna mikroskopa. Svaka fotografija treba da ima vidljivu skalu.

– Ako su tabele, grafikoni, sheme ili slike već objavljene, navesti originalni izvor i priložiti pisano odobrenje autora za njihovo korišćenje.

– Svi prilozi će biti štampani kao crno-bele slike. Ukoliko autori žele da se prilozi štampaju u boji, obavezno treba da plate dodatne troškove.

### **6. Dodatne obaveze**

**AUTORI I SVI KOAUTORI RADA OBAVEZNO TREBA DA PLATE GODIŠNJU PRETPLATU ZA ČASOPIS *MEDICINSKI PREGLED*. U PROTIVNOM, RAD NEĆE BITI ŠTAMPAN U ČASOPISU.**

## INFORMATION FOR AUTHORS

**Medical Review** publishes papers (previously neither published in nor submitted to any other journals) from various fields of biomedicine intended for broad circles of doctors.

Since January 1<sup>st</sup>, 2013 the Medical Review has been using the service e-Ur: Electronic Journal Editing. All users of the Registration system, i.e. authors, reviewers, and editors have to be registered users with only one e-mail address. Registration should be made on the web address:

<http://aseestant.ceon.rs/index.php/medpreg/user/register>.

Manuscript submission should be made on the web address:

<http://aseestant.ceon.rs/index.php/medpreg/>

A SUPPLEMENTARY FILE, WITH THE STATEMENT THAT THE PAPER HAS NOT BEEN SUBMITTED OR ACCEPTED FOR PUBLICATION ELSEWHERE AND A CONSENT SIGNED BY ALL AUTHORS, HAVE TO BE ENCLOSED WITH THE MANUSCRIPT.

Authors may not send the same manuscript to more than one journal concurrently. If this occurs, the Editor may return the paper without reviewing it, reject the paper, contact the Editor of the other journal(s) in question and/or contact the author's employers.

Papers should be written in English language, with an abstract and title page in English, as well as in Serbian language.

All papers submitted to **Medical Review** are seen by one or more members of the Editorial Board. Suitable articles are sent to at least two experts to be reviewed, their reports are returned to the assigned member of the Editorial Board and the Editor. Revision of an article gives no guarantee of acceptance and in some cases revised articles are rejected if the improvements are not sufficient or new issues have arisen. Material submitted to *the Journal* remains confidential while being reviewed and peer-reviewers' identities are protected unless they elect to lose anonymity.

**Medical Review** publishes the following types of articles: editorials, original studies, preliminary reports, review articles, professional articles, case reports, articles from history of medicine and other types of publications.

**1. Editorials** – up to 5 pages – convey opinions or discussions on a subject relevant for the Journal. Editorials are commonly written by one author by invitation.

**2. Original studies** – up to 12 pages – present the authors' own investigations and their interpretations. They should contain data which could be the basis to check the obtained results and reproduce the investigative procedure.

**3. Review articles** – up to 10 pages – provide a condensed, comprehensive and critical review of a problem on the basis of the published material being analyzed and discussed, reflecting the current situation in one area of research. Papers of this type will be accepted for publication provided that the authors confirm their expertise in the relevant area by citing at least 5 self-citations.

**4. Preliminary reports** – up to 4 pages – contain scientific results of significant importance requiring urgent publishing; however, it need not provide detailed description for repeating the obtained results. It presents new scientific data without a detailed explanation of methods and results. It contains all parts of an original study in an abridged form.

**5. Professional articles** – up to 10 pages – examine or reproduce previous investigation and represent a valuable source of knowledge and adaption of original investigations for the needs of current science and practice.

**6. Case reports** – up to 6 pages – deal with rare casuistry from practice important for doctors in direct charge of patients and are similar to professional articles. They emphasize unusual characteristics and course of a disease, unexpected reactions to a therapy, application of new diagnostic procedures and describe a rare or new disease.

**7. History of medicine** – up to 10 pages – deals with history with the aim of providing continuity of medical and health care culture. They have the character of professional articles.

**8. Other types of publications** – The journal also publishes feuilletons, book reviews, extracts from foreign literature, reports from congresses and professional meetings, communications on activities of certain medical institutions, branches and sections, announcements of the Editorial Board, letters to the Editorial Board, novelties in medicine, questions and answers, professional and vocational news and In memoriam.

### Preparation of the manuscript

The complete manuscript, including the text, all supplementary material and covering letter, is to be sent to the web address above.

### The covering letter:

– It must contain the proof given by the author that the paper represents an original work that it has neither been previously published in other journals nor is under consideration to be published in other journals.

– It must confirm that all the authors meet criteria set for the authorship of the paper, that they agree completely with the text and that there is no conflict of interest.

– It must state the type of the paper submitted (an original study, a review article, a preliminary report, a professional article, a case report, history of medicine).

### The manuscript:

#### General instructions.

Use Microsoft Word for Windows to type the text. The text must be typed in font *Times New Roman*, page format A4, space 1.5 (for tables as well), margins set to 2.5 cm and font size 12pt. All measurements should be reported in the metric system of the International System of Units – SI. Temperature should be expressed in Celsius degrees (°C) and pressure in mmHg.

The manuscript should contain the following elements:

#### 1. The title page.

The title page should contain a concise and clear title of the paper, without abbreviations, then a short title (up to 40 characters), full names and surnames of the authors (not more than 6) indexed by numbers corresponding to those given in the heading along with the full name and place of the institutions they work for. Contact information including the academic degree(s), full address, e-mail and number of phone or fax of the corresponding author (the author responsible for correspondence) are to be given at the bottom of this page.

#### 2. Summary.

The summary should contain up to 250 words, without abbreviations, with the precise review of problems, objectives, methods, important results and conclusions. It should be structured into the paragraphs as follows:

– Original and professional papers should have the introduction (with the objective of the paper), materials and methods, results and conclusion

– Case reports should have the introduction, case report and conclusion

– Review papers should have the introduction, subtitles corresponding to those in the paper and conclusion.

The authors should provide up to 10 keywords below the summary. These keywords will assist indexers in cross-indexing the article and will be published with the summary, but the authors' keywords could be changed in accordance with the list of Medical Subject Headings, MeSH of the American National Medical Library.

The summary should be written in both languages, English as well as Serbian. The summary in Serbian language should be the translation of the summary in English; therefore, it has to contain the same paragraphs.

### 3. The text of the paper.

The text of original studies must contain the following: introduction (with the clearly defined objective of the study), materials and methods, results, discussion, conclusion, list of abbreviations (if used in the text) and not necessarily, the acknowledgment mentioning those who have helped in the investigation and preparation of the paper.

The text of a case report should contain the following: introduction (with clearly defined objective of the study), case report, discussion and conclusion.

**Introduction** contains clearly defined problem dealt with in the study (its nature and importance), with the relevant references and clearly defined objective of the investigation and hypothesis.

**Materials and methods** should contain data on design of the study (prospective/retrospective, eligibility and exclusion criteria, duration, demographic data, follow-up period). Statistical methods applied should be clear and described in details.

**Results** give a detailed review of data obtained during the study. All tables, graphs, schemes and figures must be cited in the text and numbered consecutively in the order of their first citation in the text.

**Discussion** should be concise and clear, interpreting the basic findings of the study in comparison with the results of relevant studies published in international and national literature. It should be stated whether the hypothesis has been confirmed or denied. Merits and demerits of the study should be mentioned.

**Conclusion** must deny or confirm the attitude towards the Obased solely on the author's own results, corroborating them. Avoid generalized and unnecessary conclusions. Conclusions in the text must be in accordance with those given in the summary.

**4. References** are to be given in the text under Arabic numerals in parentheses consecutively in the order of their first citation. Avoid a large number of citations in the text. The title of journals should be abbreviated according to the style used in Index Medicus (<http://www.nlm.nih.gov/tsd/serials/lji.html>). Apply Vancouver Group's Criteria, which define the order of data and punctuation marks separating them. Examples of correct forms of references are given below. List all authors, but if the number exceeds six, give the names of six authors followed by 'et al'.

#### Articles in journals

##### *\* A standard article*

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. *J Thromb Haemost* 2003;1:1435-42.

##### *\* An organization as the author*

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002;40(5):679-86.

##### *\* No author given*

21st century heart solution may have a sting in the tail. *BMJ*. 2002;325(7357):184.

##### *\* A volume with supplement*

Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxis. *Pharmacol Res Commun* 1988;20 Suppl 5:75-8.

##### *\* An issue with supplement*

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. *J Clin Psychopharmacol* 1988;8(4 Suppl):31S-37S.

##### *\* A summary in a journal*

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by *Toxoplasma gondii* [abstract]. *Clin Res* 1987;35:475A.

#### Books and other monographs

##### *\* One or more authors*

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical microbiology*. 4th ed. St. Louis: Mosby; 2002.

##### *\* Editor(s) as author(s)*

Danet J, Colombani J, eds. *Histocompatibility testing 1972*. Copenhagen: Munksgaard, 1973:12-8.

##### *\* A chapter in a book*

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: Saunders; 1974. p. 457-72.

##### *\* A conference paper*

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. *Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming*; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

##### *\* A dissertation and theses*

Borkowski MM. *Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]*. Mount Pleasant (MI): Central Michigan University; 2002.

#### Electronic material

##### *\* A journal article in electronic format*

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

##### *\* Monographs in electronic format*

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

##### *\* A computer file*

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

### 5. Attachments (tables, graphs, schemes and photographs).

THE MAXIMUM NUMBER OF ATTACHMENTS ALLOWED IS SIX!

– Tables, graphs, schemes and photographs are to be submitted as separate documents, on separate pages.

– Tables and graphs are to be prepared in the format compatible with Microsoft Word for Windows programme. Photographs are to be prepared in JPG, GIF, TIFF, EPS or similar format.

– Each attachment must be numbered by Arabic numerals consecutively in the order of their appearance in the text

– The title, text in tables, graphs, schemes and legends must be given in both Serbian and English languages.

– Explain all non-standard abbreviations in footnotes using the following symbols \*, †, ‡, §, ||, ¶, \*\*, † †, ‡ ‡.

– State the type of color used and microscope magnification in the legends of photomicrographs. Photomicrographs should have internal scale markers.

– If a table, graph, scheme or figure has been previously published, acknowledge the original source and submit written permission from the copyright holder to reproduce it.

– All attachments will be printed in black and white. If the authors wish to have the attachments in color, they will have to pay additional cost.

### 6. Additional requirements

SHOULD THE AUTHOR AND ALL CO-AUTHORS FAIL TO PAY THE SUBSCRIPTION FOR MEDICAL REVIEW, THEIR PAPER WILL NOT BE PUBLISHED.