MEASURING THE VOLUME OF UTERINE FIBROIDS USING 2- AND 3-DIMENSIONAL ULTRASOUND AND COMPARISON WITH HISTOPATHOLOGY

Nikica Živković[1], Krešimir Živković[2], Albert Despot[3], Josip Paić[4] and Ana Zelić[5]

[1]Department of Gynecology and Obstetrics, Šibenik-Knin County General Hospital, Šibenik; [2]Internship at Zagreb University Hospital Center, [3]University Department of Gynecology and Obstetrics, Zagreb University Hospital Center, Zagreb; [4]Polytechnic of Šibenik, Šibenik; [5]Internship at Dr Vesna Plešić General Practice Office, Zagreb, Croatia

SUMMARY – The aim of this study was clinical testing of the reliability and usability of three-dimensional (3D) and two-dimensional (2D) ultrasound (US) technology. The ultimate aim and purpose of this study was to establish ultrasound methods, standards and protocols for determining the volume of any gynecologic organ or tumor. The study included 31 women in reproductive age and postmenopause. All patients were examined with a RIC 5-9 3D-endovaginal probe (4.3-7.5 MHz) on a Voluson® 730 Pro ultrasound device. The volume of myomas was measured by using the existing 2D and 3D ultrasound methods on the above mentioned device. All patients underwent myomectomy or hysterectomy due to clinically and ultrasonographically diagnosed uterine myomas indicating operative intervention. After the operation, the pathologist determined the volume of removed myomas by measuring them in a gauge bowl containing water, i.e. using Archimedes' principle (lift), serving as the control group with histopathologic diagnosis. A total of 155 myoma volumes were processed on 2D display, 31 myoma volumes were preoperatively measured on 3D display and 31 myoma volumes were measured by the pathologist. The values of US measurements for each US method were expressed as mean value of all measurements of myoma volumes. Statistical processing of the results and Student's t-test for independent samples revealed that the 2nd examined US method (measuring of myoma by using an ellipse and the longer tumor diameter) and 4th examined US method (measuring of myoma by using the longer and shorter tumor diameters together with establishing their mean values) in 2D US technique, as well as the 6th examined US method in 3D US technique showed no significant measurement differences in comparison with control measurement in a gauge bowl containing water ($p<0.05$), indicating acceptability of the US methods for verifying tumor volumes. The standard error in determining the volume of myomas by the above US methods varied between 15% and 25%, so it is concluded that these three methods can be used in clinical practice to determine tumor volumes, in this case uterine myomas. The 3D MultiPlane method proved to be the most reliable method of determining the volume of uterine myomas.

Key words: *Fibroid uterus; Ultrasonography; 3-D imaging; Tumor volume; Histopathology*

Introduction

Uterine leiomyomas are the most common benign tumors of the female genital system. The prevalence of myomas within the female population ranges from 20% to 50%, depending on the age, parity, ethnicity and diagnostic methods with which their presence was confirmed[1]. The real prevalence of myomas during pregnancy is unknown and varies from a low percentage of 0.1% to 12.5% of all pregnant women[2]. The term 'myoma' is used more frequently, but they

Correspondence to: *Nikica Živković, MD, MS*, A. Šupuka 18/III, HR-22000 Šibenik, Croatia
E-mail: nikica.zivkovic.gin@gmail.com

Received March 12, 2012, accepted June 18, 2012

are also called fibroids. Myomas are responsible for at least one-third of admissions to gynecologic wards. They are most common in the third and fourth decades of life. Despite various scientific disputes, most researchers believe in biochemical activity of myomas. Clinical researches confirmed growth of myomas under conditions of hyperestrogenism. A positive metabolic response was established by the action of estradiol on estrogenic and progesteronic receptors in the cytosol of myometrium and leiomyoma tissues[3,4]. In the myoma tissue, there are prostaglandin E and F receptors[5], oxytocin receptors[6] and sites at which it is associated with the epidermal growth factor[7]. In menopause, myomas decrease, become fibrous, and some of them calcified. On examination of 50 women in menopause treated with a combination of 4 mg estradiol valerate and 200 mg of progesterone ethanate, an increase in the number (from 2.2 to 3.5) and diameter (from 29.4 to 35 mm) was recorded[8]. During pregnancy, myomas grow due to proliferation and hypertrophy of cells. Leiomyomas probably grow due to the activity of estrogens on the receptor system in tissue cytosol. There is no experimental evidence that estrogen causes the emergence of myomas. Leiomyomas are mostly located in the uterus body and rarely encompass uterus ligaments, the lower uterine segment or the cervix. Histopathologically, they are made of cone bundles of smooth muscle cells similar to myometrium constitution. Cell nuclei are oval and oblong; mitoses are scarce, whereas there are neither giant cells nor anaplasia.

Uterine myomas can be symptom-free and are frequently discovered only at gynecologic examination. Symptomatic patients can complain of an increased mass in the abdomen, abnormal bleeding, acute or chronic pelvic pain, and feeling of pressure in the abdomen. The precise mechanism of abnormal vaginal bleeding is unknown. Submucous myoma increases the surface of the uterus cavity, which peels off and consequently causes bleeding. Deligdish and Loewenthal describe atrophy of endometrium under a submucous myoma[9]. Cyclic endometric changes are not possible in the atrophic area. The same authors have described hyperplastic changes of endometrium resulting from hyperestrogenism in half of the patients having uterine myomas[9]. Large intramural myomas may endanger venal flow in the uterus wall, which in turn can cause repeated vaginal bleeding. Pain due to a myomatous uterus is described as a feeling of weight or dysmenorrhea. Sudden acute pain can be caused by myoma necrosis, inflammation of overlaying serosis, or myoma torsion on the stalk. Pain in the back or legs arises when an enlarged myoma presses the lumbosacral nerve plexus. Disuric pain, reduced capacity of the bladder, incontinence, hydronephrosis, constipation, and the occurrence of hemorrhoidal knots are the possible signs of pressure of an enlarged myoma on visceral structures in the small pelvis. Due to abundant bleeding, a myomatous uterus frequently causes secondary anemia and general weakness. During pregnancy, leiomyomas are usually asymptomatic. By examining the dynamics of myoma volume in 107 women who underwent two or more ultrasound examinations during pregnancy, both reduction (55.1%) and increase (44.9%) of tumor volumes were observed[10]. In very rare cases, the clinical course of pregnancy and myoma requires surgical intervention[11].

Most frequently, a myoma is discovered by bimanual palpation of an irregularly increased uterus. In 84% of cases, the myoma suspected in gynecologic office is confirmed histologically after surgical intervention; in 30% of women operated on, myomas were not diagnosed preoperatively[12]. By bimanual gynecologic examination, it is difficult to differentiate between a myoma on the stem and an ovarian tumor. Submucous, intramural or subserous myomas are diagnosed operatively by means of hysteroscopy, laparoscopy or laparotomy (hysterectomy). Ultrasound, computerized tomography and magnetic resonance are diagnostic methods with which symptomatic or asymptomatic myomas are continuously diagnosed. Due to its simplicity, noninvasiveness, reliability, and a relatively low price of examination, ultrasound is the method of choice for clinical confirmation of the existence of myomas. There are two-dimensional (2D) and three-dimensional (3D) ultrasound (US) methods combined with Doppler visualization of myoma blood vessels available. Transvaginal ultrasound is a standard diagnostic tool[13], and combined with sonohysterography, its reliability in diagnosing uterine myoma ranges from 98% to 100%[14,15]. Because of typical imaging on the ultrasound screen gray scale, sonographic tumor morphology of endometrial cyst, teratoma or leiomyoma very rarely differs from the ultimate histologic

confirmation[16]. Based on transvaginal ultrasound examinations using color Doppler, color Doppler spectrometry was employed in an attempt to differentiate malignant from benign adnexal neoplasms[17]. At the beginning, this aroused scientific dispute all over the world. Today, following many scientific verifications, medical profession has concluded that it was impossible and potentially dangerous, based on ultrasound Doppler abstraction (RI <0.42; PI <1.00), to go into the adventurism of differentially diagnosing benign and malignant tumors prior to histopathologic verification[18-22].

Small asymptomatic myomas do not need any therapy. It is necessary to closely observe the growth of myoma at 4- to 6-month intervals. In women with symptomatic myomas, sometimes it is necessary to evaluate the existence of endometrial hyperplasia and to carry out conservative hormonal therapy with previous fractional curettage and histopathologic verification of the state of endometrium. If after conservative hormonal therapy there is no improvement and symptoms persist, surgical treatment is needed, i.e. myomectomy or hysterectomy. Classic indications for myomectomy are fast myoma growth, persisting abnormal bleeding, pain during lower abdomen palpation, infertility or asymptomatic myoma bigger that 6 cm in diameter in women who did not bear children nor ended reproduction. Myomectomy as treatment of infertility is justified, according to results of some studies. This especially holds for abdominal myomectomy, since it has no limitations regarding size and number of myomas[23]. Contraindications for myomectomy are pregnancy, adnexal diseases in an advanced stage, malignant small pelvis tumors, and situations in which operations lead to reduction of endometrial surface and dysfunction of uterus. A surgical dilemma between myomectomy and hysterectomy is not easy to solve, as stated by Richard TeLinde: "All indications and counter indications in the medicine are relative, especially when it comes to deciding between a myomectomy and a hysterectomy"[24]. Indications for hysterectomy due to a myomatous uterus are somewhat simpler compared to myomectomy. A myomatous uterus that by its size corresponds to 12- to 14-week pregnancy and growth of myoma in menopause, with the mentioned contraindications for myomectomy, are the reasons for surgical removal of the uterus. Myomectomy and/or hysterectomy, apart from laparotomy, can also be carried out hysteroscopically or laparoscopically.

Some researchers showed that gestagens favored the growth of myomas[25,26]. The mitotic activity of leiomyomas is greater in an early luteal phase than in the follicular phase[27]. The RU 486 antiprogesterone slows down the growth of myomas and is an indicator of biochemical role in the emergence and growth of fibroids[28]. Due to this information, after applying GnRH agonists in conservative therapy of myomas, danazol was introduced as a synthetic steroid with antigonadotropin characteristics, with biochemical affinity for cytoplasmic receptors and influence on steroidogenesis of the ovary and suprarenal gland[29]. Administration of danazol after GnRH agonists reduced the volume of fibroids by 30% in comparison with control group[30].

Selective embolization of uterine artery represents an alternative method of treating myomas in patients in whom abundant bleeding or surgical procedure are to be avoided[31,32]. Although pregnancies after selective myoma embolization have been described[33], this method can be dangerous in women who had no children due to consequent uterine fibrosis and infertility.

The aim of this paper is to evaluate the reliability of diagnostic possibilities of ultrasound in determining myoma volumes. Determining the most reliable ultrasound method was only a temporary aim. The ultimate one, as well as the scope of this study, was to establish ultrasound methods and protocols for determining the volume of any gynecologic organ or tumor. Also, one of the aims was to clinically test the reliability and usability of 3D ultrasound technology as opposed to conventional 2D real-time ultrasound.

Patients and Methods

The study included 31 women in reproductive age and postmenopause. All patients were examined with a 4.3-7.5 MHz RIC 3D endovaginal multi frequency probe on a Voluson® 730Pro (General Electric Medical Systems Kretztechnic GmbH & Co. OHG 2003, Austria) ultrasound device. The myoma volumes were measured by using the existing 2D and 3D ultrasound methods that make up part of the software system of

Fig. 1. Measuring myoma by using three diameters.

Fig. 2. Measuring myoma volume by using a longer or shorter diameter and an ellipse.

this ultrasound device. Of ultrasound methods for myoma volumes, five 2D methods and one 3D method were used.

A. Measuring the volume of ovoid body by using three diameters: 2D ultrasound program of measuring the volume of ovoid bodies with three diameters is the most frequent one in gynecologic practice. First must be measured the D1 distance between two opposed poles in the longest transverse myoma section. Then, tumor width or D2 anterior-posterior diameter is determined through the center of tumor in vertical display compared with the preceding section. The width or D3 transverse diameter is vertical length on the anterior-posterior diameter or D2 (Fig. 1). The ultrasound device software automatically measures the volume according to the formula for the volume of ellipsoid:

$$V = \frac{\pi}{6} \times d_1 \times d_2 \times d_3$$

B. Measuring ovoid volumes by using the longer diameter and an ellipse: the volume of ellipsoid in GE Voluson 730 Pro software is determined from two mutually vertical ellipse axes and one distance (Fig. 2). The formula for determining the volume of body by using one diameter and ellipse reads as follows:

$$V = \frac{4 \times \pi \times a \times b \times c}{3}$$

whereby:

$$a = \frac{D_1}{2} \qquad b = \frac{D_2}{2} \qquad c = D_3$$

The above formula that has not been found in relevant expert literature represents an integral part of 730 Voluson Pro devices. It was supplied by the courtesy of Mr. Michael Heinziger from GE Medical Systems Kretztechnik GmbH & Co. OHG, Austria.

C. Measuring ovoid volumes by using the shorter diameter and an ellipse: on the same ultrasound display, the myoma volume is determined by using the longer diameter and an ellipse (description B) and then, by using the shorter diameter, which is vertical and passes through the center of the longer one, the volume of a myoma numerically different from the method described under section B is determined (Fig. 2). For measuring ellipsoid volumes by using the shorter diameter and ellipse, the same formula and description is valid as for measuring the volume by using the longer diameter and ellipse.

D. Measuring ovoid volumes by using the longer and shorter diameter with determination of their mean values: it is possible to calculate the volume of a spherical body if its diameter is known or using the formula:

$$V = \frac{4r^3\pi}{3}$$

The same formula represents an integral part of the software of the above mentioned ultrasound device. In our research, a methodology of determining the longer diameter of D1 ellipsoid and V1 volume and, following that, the vertical shorter diameter of D2

Fig. 3. Measuring myoma volume by using a longer and shorter diameter.

ellipsoid and V2 volume, was used (Fig. 3). Finally, both volumes were added and divided by two:

$$\frac{V_1(D_1)+V_2(D_2)}{2}$$

E. Measuring ovoid volumes by using one ellipse: ellipsoid volume in the software of the device can be determined by rotating the ellipse around an axis (on the ultrasound device display it is shown as a dotted ellipse line) (Fig. 4). The formula for determining the volume of ovoid body from one ellipse is:

$$V = (4 \times \pi a \times b \times b)$$

where $a = \frac{D_1}{2}$ and $b = \frac{D_2}{2}$

Fig. 4. Measuring myoma volume by using an ellipse.

Neither this formula was found in relevant expert literature, but it is an integral part of the mentioned ultrasound device software. It was also supplied by the courtesy of Mr. Michael Heinziger from GE Medical Systems Kretztechnik GmbH & Co. OHG, Austria.

F. Measuring ovoid volumes by using 3D presentation and 3D MultiPlane methodology: the volume of ovoid bodies can be measured by means of ultrasound technology contained in the software of this ultrasound device. For measuring the volume of ovoid body by 3D MultiPlane technology, display or storing ultrasound pictures in 3D X, Y and Z systems is necessary. The ovoid body (myoma) is shown at the intersection of the longest axis. The moving of one end (pole) of the ovoid body toward the opposite end (pole) takes place simultaneously at all three ultrasound X, Y and Z intersections. At the intersection with the longest axis of ovoid body, the motion of one end towards another one in one of the remaining two intersections of the coordinate system is controlled. By means of 'slice methodology', the outlines of the ovoid body are drawn, i.e. the surface of transverse intersection at each point of opposite ends is determined. The multiplication of all surfaces and distances between the two opposite ends of ovoid bodies gives the ellipsoid volume. Here, the principle of measuring consists of the so-called 'fan scan' with a basic demand that the 2D display is in a vivid picture as a central plane for orientation inside the volume depicted. A multisectional, multiplane 3D display is, actually, depiction of volume in three mutually vertical intersections (Figs. 5 and 6).

All patients underwent operative intervention, myomectomy or hysterectomy, due to clinically and ultrasonographically diagnosed uterine myomas that indicated the necessity of operative intervention. The myoma volume was preoperatively measured with the ultrasound techniques described. Postoperatively, the pathologist determined the volume of the same myomas, now in a test bowl using Archimedes' principle. Simultaneously, it served as the control group or histopathology group in this study. Archimedes' principle is a law of physics stating that the upward force (buoyancy) exerted on a body immersed in a fluid is equal to the weight of the amount of fluid the body displaces. In other words, an immersed object is buoyed up by a force equal to the weight of the fluid

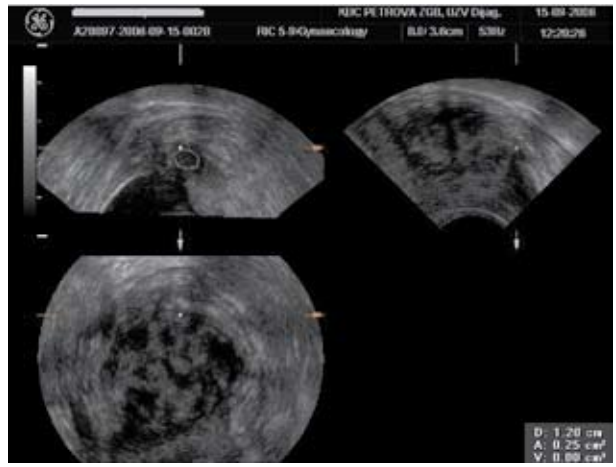

Fig. 5. and Fig. 6. Measuring myoma volume by a 3D display and 3D Multiplane methodology.

it actually displaces. The volume of body determined in a gauge bowl containing water is the most correct volume.

The values of ultrasound measurements of myomas for each ultrasound method were expressed as the mean values of all measurements of myoma volumes. The mean values of myoma volumes measured by ultrasound were compared to the real mean values of myoma volumes measured by using Archimedes' principle, which represented control histopathology group. All values acquired by measuring myoma volumes are depicted in tables and figures. On statistical data processing, Student's t-test for independent samples was used. It is one of mostly used statistical tests. It is counted as one of parametrical statistical tests and is used for comparing two sets of data on the same sample, i.e. for testing quantitative variables.

Results

The study included 31 patients of reproductive age and in postmenopause. The methods used in the study were 5 methods of determining myoma volume on 2D and one on 3D ultrasound displays. Postoperative measurements of the myoma volumes in a test bowl with water at pathology department served as control group. Reliability of determining the myoma volume by the ultrasound techniques was tested by use of diagnostics and preoperative measurements. The values measured by each ultrasound method were sorted into appropriate groups, including respective control histopathology group. In total, 155 myoma volumes in 2D ultrasound display and 31 myoma volumes in 3D ultrasound display were determined prior to operative intervention, as well as 31 determinations of the real myoma volumes by the pathologist. The values of myoma ultrasound measurements for each US method were expressed as the mean values of all measurements of myoma volumes. Ultrasonographically measured mean values of all measurements of myoma volumes were compared mutually as well as with the real mean values of myoma volumes recorded by the pathologist using Archimedes' law, which represented the control histopathology group. The values of myoma volume

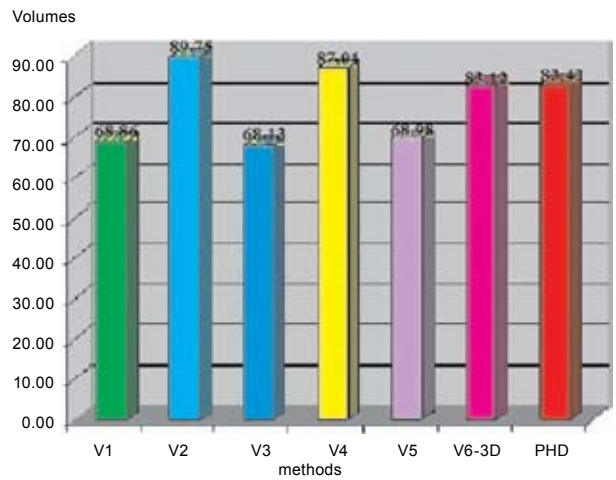

Fig. 7. Mean values of myoma volumes measured in 2D and 3D ultrasound displays, and their relation to control histopathology group.

Table 1. Numerical display of myoma volume measurements in two-dimensional and three-dimensional ultrasound displays of their mean values and comparison with control histopathology group

V_1	V_2	V_3	V_4	V_5	V_6 3D	Histopathology
131.47	156.02	117.13	151.45	121.37	221.98	160.00
262.98	354.17	272.91	338.73	216.14	275.38	360.00
140.19	158.27	131.08	153.27	142.54	176.92	120.00
22.51	34.17	24.16	32.16	24.21	30.15	30.00
21.70	26.08	25.74	25.91	24.54	27.12	24.00
62.30	80.76	59.19	79.56	60.97	77.01	80.00
93.34	136.50	106.39	115.96	124.36	117.01	90.00
133.40	212.52	154.73	198.02	182.94	115.21	100.00
289.00	339.21	258.56	337.42	258.42	297.93	300.00
13.57	14.20	9.80	17.96	13.86	13.41	18.00
31.68	56.93	31.64	59.97	33.48	32.13	30.00
50.83	57.85	36.18	57.90	41.05	57.05	80.00
40.63	52.46	41.38	51.42	43.40	55.90	80.00
31.61	40.21	26.45	36.89	27.58	35.34	43.00
23.64	27.80	21.18	22.84	24.94	33.88	40.00
8.45	8.88	6.70	8.32	8.64	7.28	10.00
94.13	109.33	91.22	113.67	98.75	130.78	110.00
119.33	155.39	132.76	146.84	136.72	119.39	150.00
45.90	48.93	39.24	54.68	47.35	40.98	55.00
16.55	23.98	18.24	22.69	17.90	19.90	30.00
42.15	92.25	58.66	96.73	56.79	90.81	70.00
54.76	82.16	52.26	81.92	54.39	67.04	85.00
32.76	34.44	34.02	33.91	35.55	42.64	40.00
57.25	76.73	53.83	74.80	59.29	82.57	72.00
50.55	69.62	49.60	64.73	45.99	60.91	55.00
114.89	149.63	121.28	141.85	121.63	151.90	160.00
10.31	25.97	10.41	24.94	10.98	20.60	20.00
54.54	61.42	49.45	60.26	53.62	72.42	78.00
32.92	39.92	31.93	37.25	32.11	37.45	31.00
29.68	34.10	29.20	33.27	33.09	34.30	35.00
21.67	22.42	16.62	22.04	16.87	31.41	30.00
68.86	89.75	68.13	87.01	69.98	83.12	83.42

measurements are shown in Table 1 and Figure 7. The mean values of deviations for each US method of volume measuring are shown in Tables 2 and 3 and Figure 8. Statistical data processing was done by use of Student's t-test for independent samples, t-value and statistical significance of difference. P-value was calculated for each US method *versus* control histopathology group (Fig. 9).

The results obtained suggested the following conclusions: 1st US method of myoma volume measurement *versus* control histopathology to be unacceptable for clinical use ($t=0.948$, $p>0.05$); 2nd ultrasound

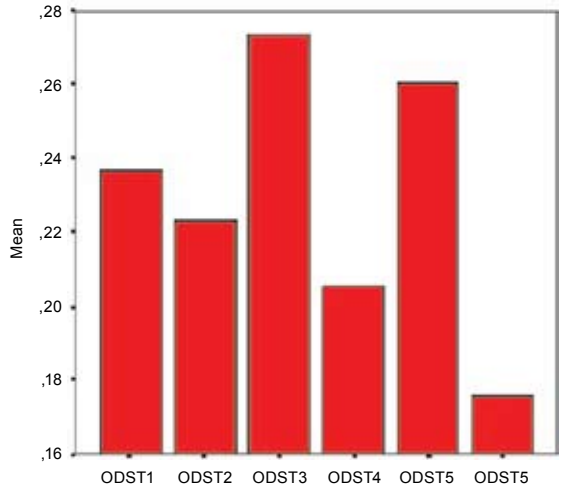

Fig 8. Numerical display of the lowest aberrations for each ultrasound method.

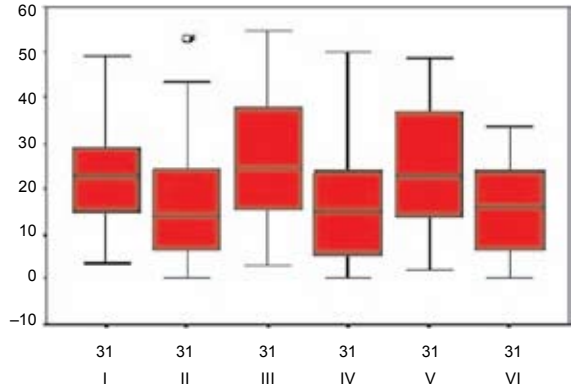

Fig. 9. Cumulative display of errors in determining volumes in 2D and 3D displays.

method of myoma volume measurement *versus* control histopathology group to be acceptable for clinical use (t=0.036, p<0.05); 3rd ultrasound method of myoma volume measurement *versus* control histopathology group to be unacceptable for clinical use (t=0.40, p>0.05); 4th ultrasound method of myoma volume measurement *versus* control histopathology group to be acceptable for clinical use (t=0.01, p<0.05); 5th ultrasound method of myoma volume measurement *versus* control histopathology group to be unacceptable for clinical use (t=0.185, p>0.05); and 6th ultrasound method of myoma volume measurement by means of 3D US presentation with 3D Multiplane method *versus* control histopathology group to be acceptable for clinical use (t=0.01, p<0.05).

Table 2. Mean values of aberrations for each ultrasound method of measurement

Vol. I	Vol. II	Vol. III	Vol. IV	Vol. V	Vol. VI
0.23688	0.22324	0.27360	0.20536	0.26054	0.17588

Table 3. Numerical display of ultrasound methods with lowest aberrations on determining myoma volume

		Frequency	Percent	Valid percent	Cumulative percent
Method	1	2	6.5	6.5	6.5
	2	5	16.1	16.1	22.6
	3	4	12.9	12.9	35.5
	4	8	25.8	25.8	61.3
	5	1	3.2	3.2	64.5
	6	11	35.5	35.5	100.0
Total		31	100.0	100.0	

Discussion

In the present study, the US possibilities of myoma volume measurement carried out by means of 2D US technology in five variations and one type of 3D US technology were assessed. In the literature, US measurement of the volume of polycystic ovaries by 2D technology is most frequently described[34-38], so this study is unique and represents significant contribution to medical profession and daily clinical routine. Measuring the volume of some organs with US methods exists and has been described in the literature. Orsini *et al.* have published one of the first studies dealing with the problem of measuring the volume of polycystic ovaries. It was concluded that there was a significant difference between healthy women with normal ovaries and women with polycystic ovary syndrome, particularly regarding the value of ovary volume, the volume of uterus, and the size of both these volumes[34]. It was a pioneer research in which US techniques of measuring the volume of female reproductive organs were defined. The development of US technology has enabled 3D measurement of the volume of ovoid

bodies. Recently, this is presented by papers on measuring the volume and weight of single structures and organs, calculated by computing methods. A study by Rovio *et al*. is important for having compared the formulas for preoperative evaluation of the weight of myomatous uterus in 12 women with symptomatic myomas[39]. It was concluded that a geometric formula that combines an ellipsoid and a cylinder in comparison with a formula combining only an ellipsoid makes possible better preoperative evaluation of the weight of myomatous uterus. Accordingly, it is clear that preoperative evaluation of the volume, but also of the weight acquired by calculating measures of 2D and 3D displays, gives significantly better information for planning the strategy of treatment. The technology used in 3D US presentations is called VOCAL (Volume Calculation or Virtual Organ Computer-aided Analysis). In our research of myoma volume measurement, VOCAL was not used as it is an integral part of Voluson 730 Pro ultrasound device. The development of medical technology brings new diagnostic and therapeutic standards. On clinical evaluation of the spread of any gynecologic malignant neoplasia, the value of the primary tumor volume is a very important factor in choosing the method of treatment.

Conclusion

The information presented makes the first step towards new diagnostic standards in the use of volumetry in daily US diagnostic practice, whether an organ or tumor is assessed. Apart from the US (study groups) and pathologic (control group) measurements, the research presented had a scientific dimension because, with statistical processing, it determined the US methods that yielded measurements closest to the real tumor volumes. The standard error in the 2nd and 4th US study groups and in the 6th 3D US study groups varied between 15% and 25% compared with the control measurement in a gauge bowl containing water. This indicates that the mentioned methods could be used in clinical practice. Only aberrations from the real values measured in the gauge bowl can define which US methods are best for measuring myoma volumes. More expensive US technologies, such as 3D US method of examination, are at the same time less accessible to patients because they are reserved for gynecologic departments and well-equipped tertiary institutions. By introducing 3D US technology in everyday clinical practice, the very top of noninvasive diagnostics might be reached. On comparing the methods of US examination to one another, it is necessary to stress that 3D US technology offers better results in case of unclear and complicated structures. To the examining physician, especially one with clinical experience with 2D ultrasound, it helps in diagnosing the smallest of neoplasms and abnormalities. 3D US has improved volumetry and made it more precise with a small percentage of errors. Everyday advances in US technology create new possibilities of diagnostic approaches and, connected with this, timely therapeutic solutions. It is known that the change in diameter of ovoid or oval bodies from 4 to 5 cm in 2D is a 100% volume difference in 3D system. These are very important data in current gynecologic practice, where various malignant tumors are found. This difference in size, even if it is only one centimeter, may mean complete healing or the loss of battle for life. Consequently, one of the long-term purposes of this study should be the use of the experiences of measuring myoma volume as well as other gynecologic tumors in the diagnosis and treatment of malignant diseases of the female reproductive system. Finally, this study proved that, in the absence of expensive and modern 3D US devices, tumor volume can be measured with high precision by using 2D US devices. The highest precision can be achieved if the 2nd or 4th method of tumor volume measurement is used, so that when measuring, the longer diameter of the tumor is measured and around the same tumor an ellipse is set; in the second option, the measured longer and shorter diameter of the myoma are taken into account.

References

1. FLETCHER MH, FREDERICK J. Abdominal myomectomy revisited. Prog Obstet Gynaecol 2005;16:277-86.
2. COOPER NP, OKOLO S. Fibroids in pregnancy – common but poorly understood. Obstet Gynecol Surv 2005;60:132-8.
3. PUUKKA MJ, KONTULA KK, KAUPPILA AJ, JANNE OA, VIHKO RK. Estrogen receptor in human myoma tissue. Mol Cell Endocrinol 1976;6:35-44.
4. POLLOW K, GEILFUSS J, BOQUOI E, POLLOW B. Estrogen and progesterone binding proteins in normal human myometrium and leiomyoma tissue. J Clin Chem Clin Biochem 1978;16:503-11.

5. HOFMANN GE, RAO CV, BARROWS GH, ROSSANO LT, SANFILIPPO JS. Prostaglandin E and F2 receptors in human uterine leiomyomas. J Clin Endocrinol Metab 1984;58:454-7.
6. DEN K, SAKAMOTO H, KIMURA S, TAKAGI S. Study of oxytocin receptor: gestational changes in oxytocin activity in human myometrium. Endocrinol Jpn 1981;28:375-9.
7. HOFMAN GE, RAO CV, BARROWS GH, SCHULTZ GS, SANFILIPPO JS. Binding sites for epidermal growth factor in human uterine tissues and leiomyomas. J Clin Endocrinol Metab 1984;58:880-4.
8. FRIGO P, EPPEL W, ASSERYANIS E, SATOR M, GOLASZEWSKI T, GRUBER D, *et al*. The effect of hormone substitution in depot form on the uterus in a group of 50 perimenopausal women – a vaginosonographic study. Maturitas 1995;21:221-5.
9. DELIGDISH L, LOEWENTHAL M. Endometrial changes associated with myomata of the uterus. J Clin Pathol 1970;23:676-80.
10. HAMMOUD AO, ASAAD R, BERMAN J, TREADWELL MC, BLACKWELL S, DIAMOND MP. Volume change of uterine myomas during pregnancy: do myomas really grow? J Minim Invasive Gynecol 2006;13:386-90.
11. SANTOS L, VICENTE L, NUNES MJ, NERY I, CAETANO M, ASSUNCAO N. Myomectomy in early pregnancy – a case report. Gynecol Surg 2006;3:228-9.
12. LEE NC, DICKER RC, RUBIN GL, ORY HW. Confirmation of preoperative diagnosis for hysterectomy. Am J Obstet Gynecol 1984;150:283-7.
13. VITELLO D, McCARTHY S. Diagnostic imaging of myomas. Obstet Gynecol Clin North Am 2006;33:85-95.
14. LASEK M, MIGDA M, PILECKI S, SERAFIN Z, JEKA S, ROSINSKA-MIGDA J. Transvaginal ultrasonography and sonohysterography in the diagnosis of benign uterine lesions in women at peri- and postmenopausal age. Pol Merkur Lekarski 2004;17:47-9.
15. LEONE FP, LANZANI C, FERRAZZI E. Use of strict sonohysterographic methods for preoperative assessment of submucous myomas. Fertil Steril 2003;79:998-1002.
16. SLADKEVICIUS P, VALENTIN L, MARSAL K. Transvaginal Doppler examination of uteri with myomas. J Clin Ultrasound 1996;24:135-40.
17. BOURNE TH, GRUBOCK K, TAILOR A. The study of ovarian tumours. In: BOURNE TH, JAUNIAUX E, JURKOVIĆ D, editors. Transvaginal colour Doppler. The scientific basis and practical application of colour Doppler in gynaecology. Berlin-Heidelberg-New York: Springer-Verlag, 1995;131-45.
18. KURJAK A, ŽALUD I, JURKOVIĆ D, ALFIREVIĆ Ž, MILJAN M. Transvaginal color Doppler for the assessment of pelvic circulation. Acta Obstet Gynecol Scand 1991;68:131-5.
19. KURJAK A, ŽALUD I, ALFIREVIĆ Ž. Evaluation of adnexal masses with transvaginal color ultrasound. J Ultrasound Med 1991;10:295-7.
20. BOURNE T, CAMPBELL S, STEER C, WHITEHEAD MI, COLLINS WP. Transvaginal colour flow imaging: a possible new screening technique for ovarian cancer. BMJ 1989;299(6712):1367-70.
21. WEINER Z, THALER I, BECK D, ROTTEM S, DEUTSCH M, BRANDES JM. Differentiating malignant from benign ovarian tumors with transvaginal color flow imaging. Obstet Gynecol 1992;79:159-62.
22. DESPOT A. Fiziološka cirkulacija kroz uterine arterije mjerena dvodimenzionalnim prikazom protoka u boji i spektrometrijom doplerskih pomaka. PhD thesis. Zagreb: School of Medicine, University of Zagreb, 1994. (in Croatian)
23. KASUM M. Fertility following myomectomy. Acta Clin Croat 2009;48:137-43.
24. DROEGEMUELLER W. Benign gynecologic lesions. Leiomyomas. In: DROEGEMUELLER W, HERBST AL, MISHELL DR, STENCHEVER MA, editors. Comprehensive gynecology. St. Louis: The C.V. Mosby Company, 1987;459-66.
25. REIN MS, BARBIERI RL, FRIDMAN AJ. Progesterone: a critical role in the pathogenesis of uterine myomas. Am J Obstet Gynecol 1995;172:14-8.
26. TAMAYA T, FUJIMOTO J, OKADA H. Comparison of cellular levels of steroid receptors in uterine leiomyomata and myometrium. Acta Obstet Gynecol Scand 1985;64:307-9.
27. BUCHI KA, KELLER PJ. Cytoplasmatic progestin receptors in myomal and myometrial tissues. Acta Obstet Gynecol Scand 1983;62:487-92.
28. MURPHY AA, KETTEL LM, MORALES AJ, ROBERTS VJ, YEN SS. Regression of uterine leiomyomata in response to the antiprogesterone RU 486. J Clin Endocrinol Metab 1993;76: 513-7.
29. BARBIERI RL, LEE H, RYAN KY. Danazol binding to rat androgen, glucocorticoid, progesterone and estrogen receptors: correlation with biologic activity. Fertil Steril 1979;31:182-6.
30. De LEO V, MORGANTE G, LANZETTA D, D'ANTONA DD, BERTIERI RS. Danazol administration after gonadotropin-releasing hormone analogue reduces rebound of uterine myomas. Hum Reprod 1997;12:357-60.
31. RAVINA JH, HERBRETEAU D, CIRARU-VIGNERON N, BOURET JM, HOUDART E, AYMARD A, *et al*. Arterial embolisation to treat uterine myomata. Lancet 1995;346:671-2.
32. ZUPI E, POCEK M, DAURI M, MARCONI D, SBRACIA M, PICCIONE E, *et al*. Selective uterine artery embolization in the management of uterine myomas. Fertil Steril 2003;79:107-11.
33. RAVINA JH, VIGNERON NC, AYMARD A, Le DREF O, MERLAND JJ. Pregnancy after embolization of uterine myoma: report of 12 cases. Fertil Steril 2000;73:1241-3.
34. ORSINI LF, VENTUROLI S, LORUSSO R, PLUCHINOTTA V, PARADISI R, BOVICELLI L. Ultrasonic find-

ings in polycystic ovarian disease. Fertil Steril 1985;43:709-14.

35. HANN LE, HALL DA, McARDLE CR, SEIBEL M. Polycystic ovarian disease: sonographic spectrum. Radiology 1984;150:531-4.
36. FULGHESU AM, CIAMPELLI M, BELOSI C, APA R, PAVONE V, LANZONE A. A new ultrasound criterion for the diagnosis of polycystic ovary syndrome: the ovarian stroma/total area ratio. Fertil Steril 2001;76:326-31.
37. NARDO LG, BUCKETT WM, KHULLAR V. Determination of the best-fitting ultrasound formulaic method for ovarian volume measurement in women with polycystic ovary syndrome. Fertil Steril 2003;79:632-3.
38. BALEN AH, LAVEN JS, TAN SL, DEWAILLY D. Ultrasound assessment of the polycystic ovary; international consensus definitions. Hum Reprod Update 2003;9:505-14.
39. ROVIO PH, LUUKKAALA T, VUENTO M, OKSA S, SUNDSTROM H, HEINONEN PK. Ultrasonographic assessment of weight of the myomatous uterus. A pilot study using a new combined geometrical formula. Eur J Obstet Gynecol Reprod Biol 2008;137:193-7.

Sažetak

MJERENJE VOLUMENA MIOMA DVODIMENZIONALNIM I TRODIMENZIONALNIM ULTRAZVUČNIM PRIKAZOM I USPOREDBA S PATOHISTOLOŠKIM NALAZOM

N. Živković, K. Živković, A. Despot, J. Paić i *A. Zelić*

Cilj ovoga istraživanja je bio klinički testirati pouzdanost i upotrebljivost trodimenzionalne (3D) i dvodimenzionalne (2D) ultrazvučne (UZ) tehnologije. Krajnji cilj i smisao ovoga istraživanja je bio ustanoviti ultrazvučne metode, standarde i protokole za određivanje volumena bilo kojeg ginekološkog organa ili tumora. Istraživanje je obuhvatilo 31 ženu u reproduktivnoj dobi i poslijemenopauzi. Sve bolesnice su pregledane 3D endovaginalnom multifrekventnom sondom (4,3-7,5 MHz) RIC 5-9 na ultrazvučnom aparatu Voluson® 730 Pro. Volumeni mioma su se mjerili upotrebljavajući 2D i 3D ultrazvučne metode koje su sastavni dio softverskog sustava navedenog ultrazvučnog aparata. Sve bolesnice su podvrgnute miomektomiji ili histerektomiji zbog klinički i ultrazvučno dijagnosticiranih mioma maternice koji su indicirali operacijski zahvat. Kod istih bolesnica poslijeoperacijski je patolog odredio volumen odstranjenih mioma mjerenjem u baždarenoj posudi s vodom, tj. primjenom Arhimedova zakona (uzgon), a to je bila kontrolna skupina ili patohistološki dijagnosticirana skupina u ovom istraživanju. Ukupno je bilo određeno 155 volumena mioma u 2D ultrazvučnom prikazu i 31 mjerenje volumena mioma u 3D ultrazvučnom prikazu prije operacijskog zahvata i 31 mjerenje stvarnog volumena mioma koje je proveo patolog. Vrijednosti UZ mjerenja volumena mioma za svaku pojedinu UZ metodu izražene su kao srednje vrijednosti svih mjerenja volumena mioma. Statističkom obradom rezultata i primjenom Studentova t-testa za nezavisne uzorke utvrđeno je da 2. ispitivana UZ metoda (mjerenje volumena mioma upotrebom elipse i duljeg promjera tumora) i 4. ispitivana UZ metoda (mjerenje volumena mioma upotrebom duljeg i kraćeg promjera tumora uz određivanje njihovih srednjih vrijednosti) u 2D UZ tehnici te 6. ispitivana UZ metoda u 3D UZ tehnici nisu pokazale značajnost razlike prikazanih mjerenja u odnosu na kontrolna mjerenja u baždarenoj posudi s vodom ($p<0,05$), što upućuje na prihvatljivost navedenih UZ metoda za procjenu volumena tumora. Veličina pogreške pri izračunu volumena mioma kod prethodno spomenutih UZ metoda varirala je između 15% i 25%, pa se zaključuje da se tri navedene UZ metode mogu rabiti u kliničkoj praksi pri pokušaju izračuna volumena tumora, u ovom slučaju mioma maternice. Trodimenzionalna UZ metoda 3D MultiPlane najpouzdanija je metoda za određivanje volumena mioma maternice.

Ključne riječi: *Fibroid maternice; Ultrazvuk; 3-D slikovne tehnike; Volumen tumora; Histopatologija*