Department of Gynecology and Obstetrics
Leverkusen Municipal Hospital, Germany
Director: Prof. Dr. med. A. K. Ertan

A RETROSPECTIVE ANALYSIS OF UNEXPECTED UTERUS MALIGNOMAS' APPEARANCE BY USING POWER MORCELLATION AND ELABORATION OF FOLLOW-UP DATA

BETWEEN 2008 AND 2016

LEVERKUSEN MUNICIPAL HOSPITAL

to obtain the degree of Doctor of medicine

at the University of Saarland

on the authority of Prof. Dr. med. E.-F. Solomayer

and in accordance with

the decision by the College of Deans.

by

Georgios Gitas

born on 22.11.1986

in Thessaloniki, Greece

Supervisor: **Prof. Dr. med. A. K. Ertan**
Co-Supervisor: **Dr. med. A. di Liberto**

Table of contents

1

V. **Discussion**

I. Abstract

Introduction: Due to the development of minimal invasive surgery (MIC), power electromechanical morcellation (EMM) has become a routine technique. Despite important advantages of morcellation, it may lead to dissemination of uterine tissue throughout the peritoneal cavity and thus spread of occult malignant cells which would result in upstaging of the cancer. The aim of this study was to estimate the frequency and clinical impact of unexpected malignoma after morcellation in a patient cohort at our department.

Materials and methods: This retrospective study included patients treated for symptomatic fibroids between 2008-2016 who underwent laparoscopic or robotic myomectomy or hysterectomy with use of EMM.

Results: A total of 471 patients were analysed, 51.7% had received laparoscopic supracervical hysterectomy (LASH), 17.9% total laparoscopic hysterectomy (TLH) and 30.6% laparoscopic myomectomy. An unexpected malignancy occurred in 3 of 471 patients representing 0.63%. All three cases histological report showed a diagnosis of sarcoma [2 x leiomyosarcoma (LS), 1 x endometrial stroma sarcomas (ESS)]. All patients underwent secondary surgery for complete surgical staging and no histological dissemination of sarcoma was found. However, two of three patients experienced tumor recurrence after 36 and 63 months. One of the patients with intraabdominal recurrence underwent a third surgery achieving complete resection once more. The second patient had a distant metastasis in the sternum. The third patient had no evidence of recurrence within follow-up of 31 months after surgical staging operation. At final follow-up all patients were in good general health.

Conclusion: There is an inherent risk of spreading occult malignoma in EMM. Potential risk factors indicating occult malignancies need to be considered preoperatively. In high-risk patients EMM should be avoided. The outcome of unexpected morcellated malignoma even with adequate secondary surgery and potential differences in prognosis remain unclear. The small number of cases within the cohort does not allow any definite statements.

Zusammenfassung

Einleitung: Durch die Entwicklung der minimal-invasiven Chirurgie wurde das elektromechanische Morcellement (EMM) als Routinetechnik etabliert. Trotz der wichtigen Vorteile des Morcellements, birgt das Verfahren jedoch prinzipiell das Risiko der Verbreitung von Uteruszellen im Bauchraum und daher bei okkultem Malignom zum Upstaging des Tumorstadiums. Das Ziel dieser Arbeit war die Erhebung der Prävalenz morcellierter maligner Befunde in unserer Abteilung und die Abschätzung der klinischen Konsequenzen für Patientinnen.

Patientinnen und Methodik: In dieser retrospektiven Studie wurden alle Patientinnen, die zwischen 2008-2016 aufgrund von symptomatischen Myomen in unserer Abteilung mittels laparoskopischer Myomektomie oder Hysterektomie behandelt wurden eingeschlossen.

Ergebnisse: Es wurden insgesamt 471 Patienten eingeschossen, hiervon hatten 51,7% eine LASH, 17,9 % eine TLH und 30,6% eine laparoskopische Myomektomie erhalten. Bei 3 von 471 Patientinnen wurde ein zufälliges Malignom entdeckt, dies entspricht 0,63%. In allen drei Fällen wurde histologisch ein Sarkom nachgewiesen [2 x Leiomyosarkom (LS), 1 x endometriales Stromasarkom (ESS)]. Die Patientinnen wurden mit einer Re-Operation zur Komplettierung des operativen Stagings behandelt, histologisch konnte keine Disseminierung des Sarkoms nachgewiesen werden. Jedoch kam es bei zwei von Patientinnen zu einem Rezidiv nach 36 und 63 Monaten. Eine der Patientinnen mit intrabdominalem Rezidiv konnte mit einer dritten Operation behandelt werden, wobei eine vollständige Resektion erreicht werden konnte. Bei der zweiten Patientin wurde eine Sternummmetastase festgestellt. Die dritte Patientin hatte nach Follow-up von 31 Monaten nach der Operation kein Hinweis für ein intraabdominales Rezidiv. Die Patientinnen waren alle beim letzten Follow-up in einem gutem Allgemeinzustand.

Schlußfolgerung: Es besteht ein inhärentes Risiko für die Disseminierung von okkulten Sarkomzellen bei Verwendung der EMM. Risikofaktoren für das Vorliegen von okkulten Uterusmalignomen sind präoperativ zu berücksichtigen. Bei

Patientinnen mit hohem Risiko für okkulte Malignome sollte ein EMM vermieden werden. Die prognostischen Auswirkungen nach akzidentellem Morcellement von Uterusmalignomen auch mit adäquater sekundärer Operation sind nicht eindeutig geklärt. Aufgrund der geringen Fallzahl innerhalb des Kollektivs können keine präzisen Aussagen getroffen werden.

II. Introduction

II. 1. Uterine malignancies

II. 1.1. Cervical Cancer

The organs in the female reproductive system include the uterus, ovaries, fallopian tubes, cervix, and vagina. The uterus is defined as a pear-shaped organ in the pelvis and, it is the place where a fetus may grow. The uterus has a muscular outer layer called the myometrium and an inner lining called the endometrium. The cervix is the narrow neck-like passage forming the lower end of the uterus and leads to the vagina[1].

Cervical cancer is the type of cancer that refers to the uterine cervix. According to the international data the incidence rate for this disease is 8.1 cases per 100,000 women per year in the United States and 13.6/100,000 women in Germany[2,3]. Approximately 6600 women are diagnosed in Germany with cervical cancer every year[4]. Moreover, there has been a continuous decrease in the incidence of carcinoma of the cervix since 1940, which continues to decline until today. The reason for this declination is the increasing effectiveness of screening procedures. Moreover, the FDA (US Food und Drug Administration) has approved two vaccines, Gardasil® and Cervarix®, which are highly effective in preventing persistent infections with HPV (Human Papilloma Virus) types including the 16 and 18, the two high-risk HPV types that cause the majority of cervical cancers. Gardasil® also protects against infections with HPV types 6 and 11, which cause about 90% of genital verrucae[5].

On top of that, symptoms of advancing cervical cancer may include bleeding, watery discharge, and signs associated with venous, lymphatic, neural, or ureteral compression. Besides, diagnosis of cervical cancer usually follows colposcopic examination and histologic evaluation of cervical biopsies. This cancer is staged

clinically, and stage is the most important indicator of long-term survival. Eventually, treatment varies and is typically dictated by this staging.

First and most importantly, there are two types of cervical carcinomas, which are called squamous cell carcinoma and adenocarcinoma. There are also two rare types of cervical carcinoma, named small cell carcinoma and cervical sarcoma and they both have a poor prognosis. Squamous cell carcinoma is referred to over 90% of cervical carcinomas, and adenocarcinoma to 5-9% of them. The first type starts in the surface cells lining the cervix, and the second type starts in glandular tissue. The treatment for both types as well as the survival rate is nearly the same, but the diagnosis of adenocarcinomas is more difficult. Correspondingly, adenocarcinoma is divided in four different types. The first type is called endocervical (60%), the second one endometrioid (10%), the third type clear cell carcinomas (10%) and the last one adenosquamous (20%). Moreover, the adenocarcinoma of the cervix has been often described as multifocal[6].

In reference to pre-invasive cervical cancer, it can progress to moderate dysplasia (CIN 2), after that to severe dysplasia and carcinoma in situ (CIN 3), and eventually to invasive carcinoma. Furthermore, it is also known as cervical intraepithelial neoplasia, as mild dysplasia and eventually Grade 1. Medical treatment consists of watchful waiting for spontaneous regression during the early stages of dysplasia (CIN 1) and, if no regression occurs, surgical treatment which may involve cryosurgery, cauterization, conization, laser treatment or hysterectomy. Moreover, conization is the most usual treatment for women who wish to have children, in contrast to total hysterectomy which is used for women who do not wish to have children or completed family planning. In addition, once the cervical cancer becomes invasive, it can spread locally to the upper vagina and into the tissues surrounding the upper vagina and the parametriam. Treatment for invasive cancer of the cervix depends on the extent of the disease. Patients whose cancer has invaded only the cervix and those whose disease has extended into the tissues next to the cervix or to the upper vagina can be treated effectively with either surgery or radiochemotherapy. Specifically, surgery may be a total or a radical hysterectomy (removal of the cervix,

uterus, parametrium, upper vagina and the pelvic lymph nodes) and according to radiation therapy it can either internal, external ionizing radiation therapy or both can be used. In this case, a chemotherapeutic drug cisdiamminedichloroplatinum (Cisplatin) is used as a radiosensitizer agent. Patients with cervical cancer that has spread to the pelvis, the lower part of the vagina or to the ureter are treated commonly only radiochemotherapy.

Patients with cancer that has spread to the pelvis, the lower part of the vagina or to the ureter are treated only with radiation therapy. Again, both internal and external radiation therapy can be used.

Moreover, it also grows toward the pelvic sidewall, hindering the tubes ureters. Eventually, it can spread to the bladder, rectum or distant parts of the body. Patients in this situation may be treated with chemotherapy in addition to surgery or radiation therapy. Chemotherapy is also used to treat patients whose disease recurs following treatment with surgery or radiation therapy.

Cervical tumor cells can invade the lymphatic system and spread to the lymph nodes in the pelvic wall and then to the aortic lymph nodes. Additionally, metastases can spread to the outer vagina, vulva, liver and through the bloodstream to lungs and brain[6,7].

II. 1.2. Endometrial cancer

Endometrial cancer (EC) is a cancer that arises from the endometrium, and it is the most commonly appearing cancer of the female reproductive system. Moreover, EC occurs more often to postmenopausal women and it is usually diagnosed after the age of fifty. After breast cancer, lung cancer and cancer of the colon and rectum, EC is the next most common cancer that affects women. It is also the seventh leading cause of death from malignancy in women. In most cases, EC presents early with abnormal vaginal bleeding (80% of cases, other signs and symptoms include uterine enlargement, pelvic pressure and pain in the lower abdomen) and lastly, in more advanced stages, it may cause general symptoms. It is important that any

postmenopausal bleeding should be assumed to be EC until proved otherwise. In the majority of EC cases (75-80%) a cancer called endometrioid adenocarcinoma is diagnosed, which is usually well differentiated, and it has a comparatively good prognosis. On the basis of differences in histology and clinical outcome, EC have long been divided into two types. Type I tumors comprise the large majority of EC, are mostly endometrioid adenocarcinomas, are associated with unopposed estrogen stimulation, and are often preceded by endometrial hyperplasia. Type II tumors are predominantly serous carcinomas and are commonly described as estrogen independent, arising in atrophic endometrium and deriving from intraepithelial carcinoma, a precancerous lesion. Type II tumors generally are less well differentiated and have poorer prognoses that type I tumors, and they account for a disproportionate number of endometrial cancer deaths (40% of the deaths, whereas they only acoount for 10-20% of cases). Uterine papillary carcinoma and uterine clear-cell carcinoma belong to the type II EM and they are aggressive tumors, which usually invade the myometrium, diagnosed in advanced tumor stage. Eventually, sarcomas, which are tumors that start in the uterine muscles, are rare and they constitute the 4% of cases. Furthermore, a malignant mixed Mullerian tumour, also termed uterine carcinosarcoma, is an extremely rare tumor, comprising only 1-2% of uterine neoplasms. These tumours are a dedifferentiated or metaplastic form of endometrial carcinoma. This tumor considered to be uterine epithelial carcinoma rather than sarcoma.

In regard to histologic differentiation of EC, which is really important, it is divided in three different categories[6, 10].

1. Highly differentiated (with better prognosis)

2. Differentiated with partly solid areas

3. Predominantly solid/undifferentiated.

Some of the main risk factors are obesity, diabetes, hormonal therapy, whether in postmenopausal or not, etc. Although in some cases, a more invasive examination with an endometrial biopsy should be done (dilatation and curettage) to prove or

exclude EM-Hyperplasia or EC. This biopsy can be accomplished with a small flexible tube (e.g. Pipelle®) with or without general anesthesia, on an outpatient basis. Moreover, blood tumor markers are not reliable for the diagnosis of EC, and if the CA-125 is elevated, a higher tumour stage could be suspected. In addition, if a woman is diagnosed with endometrial cancer, further tests, such as chest X-ray, computer tomography, magnetic resonance imaging, positron emission tomography, cystoscopy and proctoscopy, are recommended in order to define the stage of the cancer.

Referring to staging (FIGO classification, Fig. 1), it is defined as the process of classifying a tumor according to whether or not it has spread, in order to decide the best treatment options. EC has four different stages and each stage is divided into further categories:

Stage I[a]		Tumor contained to the corpus uteri
	IA	No or less than half myometrial invasion
	IB	Invasion equal to or more than half of the myometrium
Stage II		Tumor invades the cervical stroma but does not extend beyond the uterus[b]
Stage III[a]		Local and/or regional spread of tumor[c]
	IIIA	Tumor invades the serosa of the corpus uteri and/or adnexas
	IIIB	Vaginal and/or parametrial involvement
	IIIC	Metastases to pelvis and/or para-aortic lymph nodes
	IIIC1	Positive pelvic nodes
	IIIC2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV[a]		Tumor invades bladder and/or bowel mucosa and/or distant metastases
	IVA	Tumor invasion of bladder and/or bowel mucosa
	IVB	Disant metastases, including intra-abdominal metastases and or inguinal lymph nodes

Fig. 1: Endometrial cancer. Stage of endometrial cancer, by National Cancer Institute from the origin[11] on 22 April 2014.

In the 75% of cases, the tumor at the time of diagnosis is confined to the corpus uterus (first stage), and because of that, the survival rate is 75% or even higher (Table 1).

FIGO classification	TNM classification	5-year survival rates
Stage 1	T1, N0, M0	81%
Stage 2	T2, N0, M0	69%
Stage 3	T3, N0, M0	51%
Stage 4	any T, any N, M1	16%

Table 1: FIGO Classification of endometrial cancer [6,10], by National Cancer Institute from the origin[11] on 22 April 2014.

Initially, endometrial cancer treatment usually includes surgery. The basic treatment for cases that present to the first stage is total hysterectomy and bilateral salpingo-oophorectomy. At the same time as a hysterectomy, the surgeon may remove lymph nodes (pelvic and para-aortic lymph node) near the tumor to determine if the cancer has spread beyond the uterus. Guidelines for surgical treatment of EC vary between countries. German recommendation is to perform comprehensive pelvic and paraaortic lymphadenectomy up to the renal vessels in all patients except stage IA G1/2. In stages IB G1 and IB G2 lymph node dissection is optional, an all other cases obligatory [8]. Moreover, if the cervix shows any signs of invasion, a radical hysterectomy may be done, which involves removal of the uterus, the upper half of vagina, the parametrium and the pelvic and para-aortic lymph node. Finally, in case of advanced EC, a surgical treatment option is palliative debulking surgery to reduce symptoms. Further, after surgery, chemotherapy is used to destroy any remaining cancer cells and reduces the risk of cancer recurrence. Although, in case of advanced EC, it is used in order to relieve the symptoms. Moreover, it may be used after surgery if there is evidence of lymph node involvement. It may also be used as

therapy in women who are unsuitable for surgery. Definitely, combining chemotherapy and radiotherapy, after surgery, is an option for the gynecologist in certain cases. In addition, hormone therapy, such as high dosis of medroxyprogesterone acetate, can be used prior to surgery, or in advanced stages. Its main use is palliative treatment. Notably, this kind of therapy may be used in some cases of younger women who wish to maintain fertility preserving uterus and adnexa. Conservative treatment with progestins has been shown to be a feasible and safe fertility-sparing approach for women with low grade, early stage EC with no myometrial invasion[9].

II. 1.3 Uterine sarcoma

The uterine sarcomas, form a group of malignant tumors that arises from the smooth muscle or connective tissue of the uterus. This type of malignancy and the difficulty to diagnose them will interest us as an essential part of our study. To begin with, uterine sarcomas grow in connective tissue. Mainly, kinds of tumors can be found in the bones, muscles, tendons, nerves, cartilage, fat and blood vessels of the limbs, but they can normally appear anywhere. To continue, there are more than fifty types of sarcomas, however they can be divided them into two main kinds, the soft tissue sarcomas and the bone sarcomas or osteosarcomas (Fig. 2). (for more information see chapter II 1.3.2).
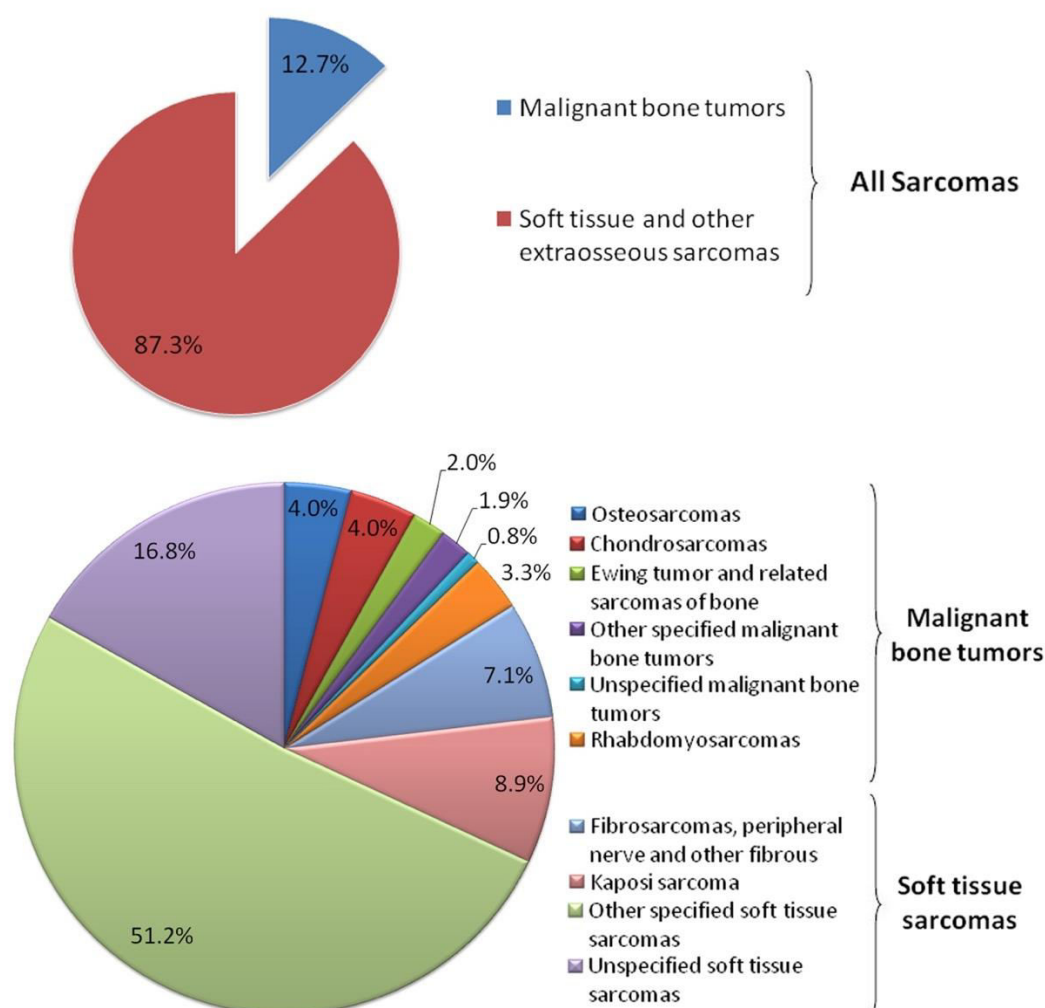
Fig. 2: Categorization of sarcomas[11].

Although infrequent, uterine sarcomas are among the most lethal of all uterine malignancies. The 5-year survival rate reportedly ranges from 30% to 68%. The confusion concerning nomenclature and diagnostic criteria is the reason why reports and results from sarcoma studies are difficult to interpret [12]. Uterine sarcomas are associated with poor prognosis [13]. The multiple tissues composing some of these malignancies (carcinosarcoma) have made their pathogenesis speculative. Several etiologic theories have been proposed. Leiomyosarcomas (LMS, Fig. 3) originate from smooth muscle, and endometrial stromal sarcomas (ESS) originate from

endometrial stroma tissue. The confusion concerns those sarcomas containing tissues foreign to the uterus . It is difficult to explain how cartilage, bone, fat, or skeletal muscle suddenly appears in a mature organ where the tissue does not normally reside [14,15]. The potential for intra-abdominal metastases and disruption of tissue planes within the pelvis increases the technical difficulty of surgery and perioperative risks. More important, the approach to staging is often subtly dissimilar to that of endometrial carcinomas. For example, because of the low rate of metastasis, it may be appropriate to sample only suspicious lymph nodes for leiomyosarcomas instead of performing a complete pelvic and para-aortic lymphadenectomy. In addition, it may be prudent to preserve the ovaries in a young woman with an ESS or LMS because the risk of adnexal metastasis is minimal. In general, a treatment plan is best organized preoperatively, if possible (for more information see chapter II. 1.3.5).

Many uterine sarcomas are not diagnosed until surgery or several days later when a pathology report is available. As a result, unstaged cases are common. If the diagnosis is made postoperatively, the decision to proceed with surveillance only, reoperation, or radiotherapy varies widely depending on the type of sarcoma and other circumstances. In general, these options are less straightforward than in typical endometrial carcinomas largely because of the rarity of these tumors and the comparatively limited data supporting one strategy compared with another.
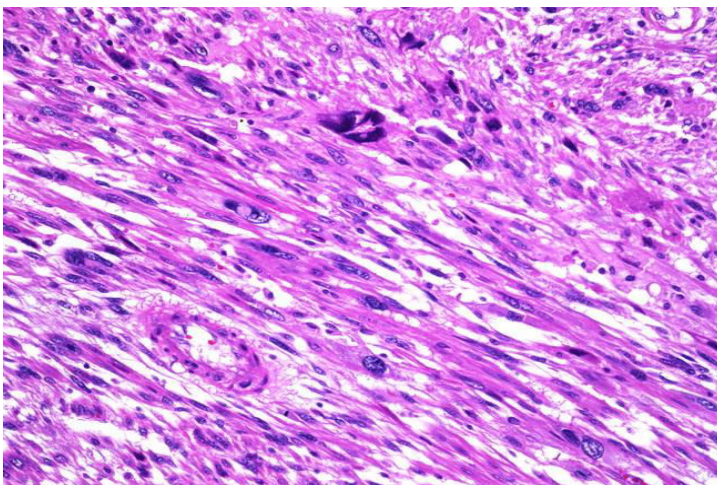
Fig. 3: The image shows a high-grade leiomyosarcoma arising in the uterus. One can appreciate the cytologic atypia of the smooth muscle cells consisting of hyper-chromatic pleomorphic nuclei with occasional prominent nucleoli. At least 2 mitotic figures can also be seen.
From: Webpathology.com: A Collection of Surgical Pathology images.

II. 1.3.1. Epidiomiology and risk factors.

Uterine sarcoma is a very rare kind of cancer that forms in the uterine muscles or in uterine connective tissue. Their reported incidence varies between 2.6% and 9.7% of all uterine corpus malignancies and accounts for 1% of all genital malignancies [16]. Black women have a twofold higher incidence of uterine sarcoma compared with non-Hispanic white [17]. Furthermore, being exposed to X-rays can increase the risk of uterine sarcoma. Risk factors for uterine sarcoma are past treatment with radiation therapy to the pelvis[18] and treatment with tamoxifen for breast cancer [19]. Symptoms are similar to those of endometrial carcinoma, but some women are first diagnosed as having a common benign uterine tumor called mimicking a myoma. After a rapidly growing, presumably benign myoma is surgically removed, the pathologist finds that it is a malignant tumor. Abnormal bleeding from the vagina (rare) and other symptoms may be caused by uterine sarcoma. Other reported symptoms include abdominal enlargement and pelvic discomfort, pain or a feeling of fullness in the abdomen or pollakisuria. There are no medical diseases common to patients with stromal sarcoma[20]. There are no classical risk factors as for example by the patients with EC. The clarification of risk factors of uterine sarcomaa is an important fact which concerns this study.

II. 1.3.2. Classification

Uterine sarcomas (US) are a heterogeneous group of malignancies (Table 2 and 3). Historically, US have been classified as carcinosarcomas (CS, about 40% of cases), leiomyosarcomas (40%) and endometrial stromal sarcomas (15%) [21,22,23]. The remaining 5% consist of a heterogeneous group of vascular, lymphatic and heterologic sarcomas.

Historical Classification of Uterine Sarcomas [21]		Recent Classification of Uterine Sarcomas [23]	
Carcinosarcoma	40%	Leiomyosarcoma	60%
Leiomyosarcoma	40%	Low-grade Endometrial Stromal Sarcoma	30%
Endometrial Stromal Sarcoma	15%	high-grade Undifferentiated Endometrial Sarcoma	5%
Uterine sarcomas-Other	5%	Adenosarcoma and other uterine sarcomas	5%

Table 2: Classifications of uterine sarcomas.

Pure Sarcomas	Pure homologous	Leiomyosarcoma, Stromal sarcoma, Endolymphatic stromal myosis, Angiosarcoma, Fibrosarcoma
	Pure heterologous	Rhabdomyosarcoma (including sarcoma botryoides), Chondrosarcoma, Osteosarcoma Liposarcoma
Mixed Sarcomas	Mixed homologous	
	Mixed heterologous (including mixed heterologous sarcomas with or without homologous elements)	
Mixed Malignant Müllerian Tumors (Mixed Mesodermal Tumors)	Mixed malignant müllerian tumor, homologous type (carcinoma plus leiomyosarcoma, stromal sarcoma, or fibrosarcoma, or mixtures of these sarcomas)	
	Mixed malignant müllerian tumor, heterologous type	
Sarcoma, Unclassified		
Malignant Lymphoma		

Table 3: A practical classification of uterine sarcomas by Kempson and Bari.

FIGO Classification

The 1988 International Federation of Gynecology and Obstetrics (FIGO) criteria for endometrial carcinoma have been used until now to assign stages for uterine sarcomas in spite of the different biologic behavior of both tumor categories. Recently, however, the valid FIGO classification (Table 4) and staging system has been specifically designed for uterine sarcomas in an attempt to reflect their different biologic behaviour[25].

This classification consists of as follows:

I	A Less than or equal to 5 cm
Tumor limited to uterus	B More than 5 cm
II	A. Adnexal involvement.
Tumor extends beyond the uterus, within the pelvis.	B. Involvement of other pelvic tissues.
III	A. One site
Tumor invades abdominal tissues (not just protruding into the abdomen)	B. More than one site
	C. Metastasis to pelvic and/or para-aortic lymph nodes
IV	A. Tumor invades bladder and/or rectum.
	B. Distant metastasis (lung, skin, soft tissues, liver etc.)

Table 4: Leiomyosarcomas and endometrial stromal sarcomas [25].

II. 1.3.3. Diagnostics of the uterine sarcomas

The definitive diagnosis is made by a pathologist evaluating either an office endometrial biopsy, tissue removed during a D&C (dilation and curettage) or the tissue specimen after hysterectomy. Although stromal and mixed mesodermal tumors are diagnosed from an endometrial biopsy or D&C, most leiomyosarcomas are diagnosed after a hysterectomy due to the assumption of benign uterine fibroids. Preoperative diagnosis of uterine sarcoma is very difficult, and currently, its diagnostic accuracy is not satisfactory. The following test and procedures can be used to detect and diagnose uterine sarcomas. The following tests and procedures may be used:

- Clinical pelvic examination.

- Clinical examination of the lymph nodes in the inquinal and supraclavicular region.

- Clinical examination of the abdomen to detect an enlarged liver, abdominal masses and excess fluid (ascites).

- Serum liver and kidney function tests.

- Cystoscopy and rectoscopy (occasionally).

- Specific gynaecologic examination.

- PAP-Test. Because uterine sarcoma begins inside the uterus, this cancer may not show up on the Pap test.

- Dilatation and curettage: Because uterine sarcoma begins inside the uterus, this cancer may not show up on this examination.

- Hysteroscopy

- Positron emission tomography scan (PET). Today, almost all PET scans are performed on instruments that are combined PET and CT scanners. The combined PET/CT scans provide images that pinpoint the anatomic location of abnormal metabolic activity within the body. This test can be helpful detection of disseminated malignancies in the whole body. It may also tell if a tumor is benign or malignant. PET scans are not routinely used to work-up a pelvic mass or abnormal bleeding in patients who are not known to have cancer.

- Chest X-ray to detect thorax metastasis.

- Pelvic and abdominal CT scans to detect pelvic extension of tumor, pelvic and aortic lymph nodes and liver metastases.

- Pelvic MRI (on occasion). One of the greatest advantages of MRI is the ability to change the contrast of the images. Small changes in radio waves and magnetic fields can completely change the contrast of the image. Moreover, MRI gives higher detail in soft tissues which is essential for the detection of uterine sarcomas.

- CA 125 assay: An increased CA 125 level in the blood is sometimes a sign of cancer or other condition.

II. 1.3.4. Prognosis

The National Cancer Institute SEER[26] (Surveillance, Epidemiology and End Results) program of USA has developed survival statistics based on women diagnosed with uterine sarcomas between 2004 and 2010. Moreover, SEER program gathers together the statistics by AJCC[27] (American joint Committee on Cancer) and FIGO[25] stage and uses three stages, called summary stages, the localized, the regional and the distant (Table 5). Firstly, localized is when the cancer is only in the uterus (stage I), secondly regional is when the cancer has spread to the nearby lymph nodes or tissues (stage II) and finally distant is when the cancer has spread further (stage IVA & IVB).

Type	Stage		
	Localized	Regional	Distant
Leiomyosarcoma	63%	36%	14%
Undifferentiated sarcoma	70%	43%	23%
Endometrial stromal sarcoma	99%	94%	69%

Table 5: Stage of metastasis in comparison with type of sarcoma.

National Cancer Institute SEER[26].

II. 1.3.5. Treatment

Many different types of treatment can be applied for patients with uterine sarcoma[28,29,30,31].

Firstly, for **leiomyosarcoma** the following treatment for each of the five stages are:

I.   Stage I (uterus):
- Total hysterectomy with bilateral salpingo-oophorectomy (BSO).
- Ovarian preservation could be used depending upon the circumstances (premenopausal women).
- Pelvic and para-aortic lymph node dissection or laparoscopic lymph node sampling may also be done by suspicion of metastasis.
- Post-operative adjuvant radiotherapy or adjuvant chemotherapy only in high risk patients. (clinical trial)

II.   Stage II (tumor spreads to the pelvis, no widely approved therapy has been established):
- Surgery to remove the whole tumor (includes removing the uterus and bilateral salpingo-oophorectomy), if debulking can be achieved; consider adjuvant chemotherapy (it is not clear that it is really helpful) +/- radiotherapy (may lower the chance of *local recurrence* but it doesn't seem ameliorate survival time, clinical trial)
- Pelvic and para-aortic lymph node dissection or lymph node sampling may also be done by suspicion of metastasis

III.   Stage III (tumor infiltrates abdominal tissues, no widely rapproved therapy has been established):
- Surgery to remove the whole tumor (total abdominal hysterectomy, bilateral salpingo-oophorectomy), if debulking can be achieved.
- Pelvic and para-aortic lymph node dissection

- If the tumor has spread to the vagina part
- After surgery, treatment radiation +/- chemotherapy may be offered to lower the risk of recurrence (clinical trial).

IV.

Stage IVA (tumor invades bladder or rectum, or both):

- Surgery to remove the whole tumor (exenteration), if debulking can be achieved.
- After surgery, treatment radiation +/- chemotherapy may be offered to lower the risk of recurrence (clinical trial).

Stage IVB (metastasis have appeared):

- Chemotherapy may be able to shrink the tumors for a time, but is not thought to be able to cure the cancer (clinical trial).
- Radiation therapy may also be an option (clinical trial).

There is no standard chemotherapy treatment. Doxorubicin, ifosamide, gemcitabine, docetaxel, trabectidin, dacarbazine, and cisplatin constitute the cytostatic agents that are usually used. Combination chemotherapy should be used only for patients in good general condition.

In the occasion of a recurrent disease physicians may act as follows:

- Operate the localized disease.
- Chemotherapy followed by CT scan to determine disease response.
- Palliative radiotherapy may be used for specific symptom control such as bleeding or pain. Where needed, patients should be considered for enrolment in a clinical trial.

Secondly, in the occasion of **adenosarcoma** options may include:

• Total hysterectomy with bilateral salpingo-oophorectomy (BSO).

• Surgery to remove the whole tumor in advanced cases, if debulking can be achieved.

• Adjuvant treatment is not typically required.

•Where possible, patients should be considered for enrolment in a clinical trial.

Thirdly**, endometrial stromal sarcoma** (formerly low-grade ESS) options may include:

• Total hysterectomy with bilateral salpingo-oophorectomy (BSO).

• Surgery to remove the whole tumor in advanced cases, if debulking can be achieved.

• Adjuvant treatment is not typically required (clinical trial).

• According to patients with advanced or metastatic disease, post-operative hormonal therapy with progestin (usually medroxyprogesterone acetate or megestrol), gonadotropin-releasing hormone agonist or aromatase inhibitors can be used.

Lastly**, undifferentiated endometrial sarcoma** (formerly high-grade ESS) options may include**:**

    I.   Stage I (when tumor restricted to the uterus):
- Total hysterectomy with bilateral salpingo-oophorectomy (BSO).
- Selective biopsy of pelvic +/- para-aortic lymph nodes

    II.   Stage II (tumor extends to the pelvis):
- Total hysterectomy with bilateral salpingo-oophorectomy (BSO).
- Surgery to remove the whole tumor, if debulking can be achieved.

    III.   Stage III (tumor invades abdominal tissues):
- Total hysterectomy with bilateral salpingo-oophorectomy (BSO).
- Surgery to remove the whole tumor, if debulking can be achieved.

IV.

        Stage IVA (tumor invades bladder or rectum or both):

- Surgery to remove the whole tumor, if debulking can be achieved.
- Neoadjuvant chemotherapy and later surgery to remove the whole tumor, if debulking can be achieved.
- Palliative radiotherapy, if surgery is not an option.
- Palliative chemotherapy, if surgery is not an option.

        Stage IVB (distant metastasis):

- Neoadjuvant chemotherapy and later debulking surgery.
- Palliative chemotherapy or radiotherapy, or both, if surgery is not an option.
- Palliative radiotherapy may be used for specific symptoms such as bleeding or pain.
- Palliative chemotherapy may be used in patients who have unresectable disease.

Palliative chemotherapy options include the following:

• There is no standard chemotherapy treatment.

• Doxorubicin, ifosamide, gemcitabine, docetaxel, dacarbazine, and cisplatin

constitute the agents that are usually used.

• Combination chemotherapy should be used only for patients in good general

condition.

 In the occasion of a recurrent disease we may act as follows:

• Operate the localized disease.

• Chemotherapy with periodic CT scan to determine tumor response.

• Palliative radiotherapy may be used for specific symptom control such as bleeding

or pain.

• Palliative chemotherapy may be used in patients who have unresectable disease.

Where needed, patients should be considered for enrolment in a clinical trial.

Hormonal therapy

A trial of hormonal therapy, such as palliative setting, should be taken into account for patients whose tumors express estrogen or progesterone receptors or both. GnRH analogs (i.e., leuprolide, goserelin), aromatase inhibitors (i.e., anastrozole, letrozole) and progestins (i.e., medroxyprogesterone acetate, megestrol acetate)[28,29,30,31].

II. 2. Hysterectomy

The word hysterectomy originates from the Greek υστέρα (hystera) and εκτομία (ektomia), the first means "womb" and the second one "a cutting out of". Hysterectomy is the surgical procedure to remove all of or a part of the uterus. Furthermore, it is more numerous done in non-cancerous conditions, to treat plenty of diseases that affect the uterus including uterine fibroids, abnormal bleeding, endometriosis and chronic pelvic pain, anatomic uterine defects, uterine prolapse and cancer[32,33]. Hysterectomy is still one of the most common and often performed operations for gynecologists[34]. The hysterectomy rate, between 2005 and 2006, for benign diseases of the genital tract among women over 20 years (3.6 out of 1000 women/year) in Germany was higher than in Sweden but lower than in the US or Australia[35]. The hysterectomy can be done using one of the following three main approaches, firstly laparoscopic hysterectomy (LH), secondly abdominal hysterectomy (AH) and thirdly vaginal hysterectomy (VH)[34]. In all the three approaches of hysterectomy the surgeon can remove the uterus and cervix both with and without removing the adnexa. Moreover, lymph nodes can be removed during laparoscopic and abdominal hysterectomy. There is evidence that vaginal hysterectomy was performed by Themison of Athens in 50 BC[36,37]. It is known that the procedure was performed by Soranus of Ephesus in 120 AD, by removing an

inverted uterus that had become gangrenous[36]. Beginning, the first authenticated vaginal hysterectomy was performed by the Italian anatomist Berengario da Carpi of Bologna in 1507. After many years, the professor of surgery at Heidelberg university Vincenz Czerny performed and described the first total hysterectomy by the vaginal route in 1879[36]. Moreover, the first recorded abdominal hysterectomy was performed by Charles Clay in Manchester, England, in 1843[36]. He was expecting a massive ovarian tumor, that is why he started performing an ovariectomy, and later he realized that it was a large fibroid uterus. Finally, Charles Clay performed a subtotal hysterectomy as a result of a huge uterine fibroid and the patient died of a massive hemorrhage in the immediate postoperative period[36]. The first planned subtotal hysterectomy for uterine fibroids was performed by John Bellinger of Charleston, in 1846 and the patient died on the 5th postoperative day, of sepsis[33]. At the beginning, the predecessor of the optical system of modern endoscopes was the cystoscope, developed by Maximilian Nitze in Germany in the 19th century. Moreover, in 1901, Georg Kelling in Dresden introduced a cystoscope into a dog's abdominal cavity and as a result he performed the first laparoscopy. Additionally, the first human laparoscopy was performed by Hans Christian Jacobaeus of Stockholm in 1911, by using pneumoperitoneum and the Nitze cystoscope[38]. Furthermore, it was Kurt Semm, a German gynecologist specialized in infertility who made gynecological laparoscopy popular in the 1960-70's and who is considered to be the father of modern gynecological laparoscopy. He invented the automatic insufflator, and hundreds of laparoscopic instruments, including a thermocoagulator, loop ligature, and devices for extracorporeal and intracorporeal endoscopic knot tying. He was one of the first proponents of video monitoring for laparoscopy, using a series of lenses and mirrors in an articulated arm to connect the laparoscope to a ceiling-mounted video camera. He developed laparoscopic techniques for ovarian cystectomy, myomectomy, treatment of ectopic pregnancy, appendectomy and hysterectomy. To add, in 1988 Harry Reich performed a total laparoscopic hysterectomy in Pennsylvania[39].

The most recent development in hysterectomy is the introduction of hysterectomy techniques which makes use of surgical robots. Nowadays, the robotic systems da

Vinci S, da Vinci SI and da Vinci XI are equipped with a double optic, which gives the operator three-dimensional view of the operative field, and with adjustable magnification, enabling much improved vision of the pelvis. Other benefits compared to conventional surgical procedures are decrease of postoperative length of stay, a reduction of post interventional need of analgetics, quickened period of recovery, reduced intraoperative blood loss respectively transfusion rate, reduced percentage of intraoperative and postoperative complications and shorter operation time[40]. In 2002, Diaz-Arrastia reported the first series of successful robotic laparoscopic hysterectomies[41].

The type of hysterectomy, which will be performed, depends on the reason of the surgery and of other factors such as age, the general health condition, the parity, the weight of the patient, the size of the uterus and the main disease. A review by Nieboer et al.[42] shows that, when technically feasible, vaginal hysterectomy (VH) should be performed in preference to abdominal hysterectomy (AH) because of more rapid recovery and fewer febrile episodes post-operatively. However, where VH is not possible, laparoscopic hysterectomy (LH) is used and has significant advantages over AH (including less operative blood loss, more rapid recovery, fewer febrile episodes, and wound or abdominal wall infections). On the other hand, these advantages are offset by longer operating time and more urinary tract (bladder or ureter) injuries. In these specific researches, there couldn't be found any advantages of LH over VH. Moreover, LH had longer operation time and more substantial bleeding, and specific total laparoscopic hysterectomy had more urinary tract injuries. To sum up, VH is probably the preferred route because it is quicker and cheaper than LH, with no other clear differences in outcome measures. On the other hand, LH has a number of advantages over AH such as shorter hospital stay and quicker return to normal activities. Whenever possible, hysterectomy should be minimally invasive [43]. The surgical approach to hysterectomy should be decided with the patient in light of the relative benefits and hazards. These benefits and hazards seem dependent of surgical expertise and may influence the decision.

In 1974, Piver-Rutledge-Smith[44] divided the radical hysterectomies into 5 classes, a classification respected by numerous surgeons and gynecologists. (table 6 below)

Type of surgery	Scope of procedure
Class 1	Extrafascial hysterectomy. As a matter of fact it is not a radical hysterectomy, it comprises only pushing the ureters away laterally without their preparation, which allows to clamp the vagina. The uterus is removed with a minimum of the parametrium and the vagina.
Class 2	Excision of the uterus along with the primary ligament which is intersected centrally in relation to the ureter. Excision of the sacro-uterine ligaments in the middle of their length and 1/3 of the upper vagina.
Class 3	It assumes the intersection of the primary ligaments laterally from the ureter by the pelvic wall and the intersection of the sacro- uterine ligaments as close to the sacrum as possible, i.e. hysterectomy with the removal of the entire broad and sacro-uterine ligaments as well as 1/2 of the vagina.
Class 4	Excision of the uterus and the periuretal tissue, resection of the upper vesical artery 3/4 of the vagina
Class 5	Resection of involved portions of the bladder or distal ureter with subsequent ureter reimplantation, if necessary anterior exenteration

Table 6: Types of operations according to *Piver, Rutledge and Smith (Piver 1974)*.
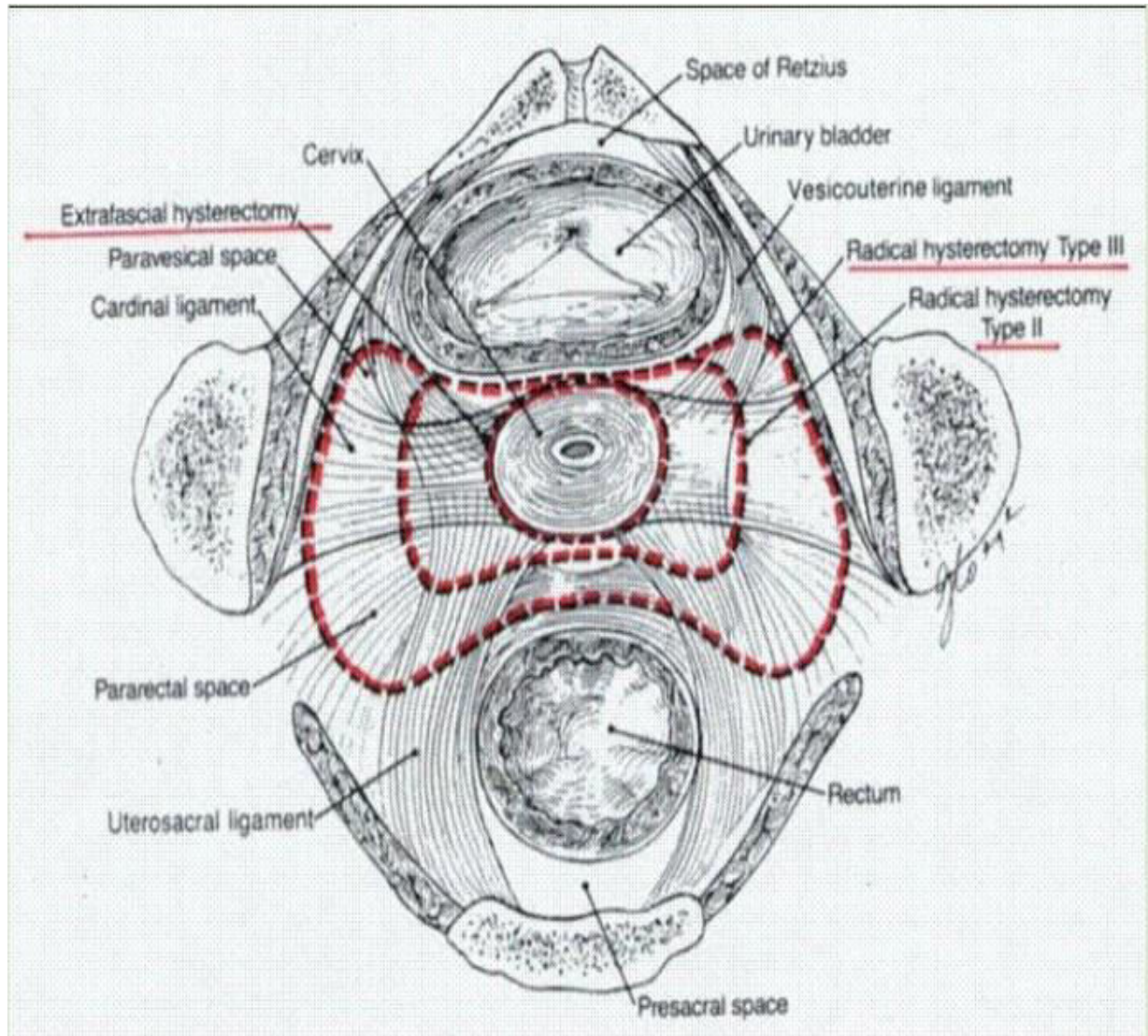
Fig. 4: Anatomical resection area for Type I, II and III of hysterectomy according to *Piver Classification*

Source: Clinalongology.com.ua.

Type of surgery	Scope of procedure
Type A	Extrafascial hysterectomy- Minimum resection of paracervix • Lateral parametrium removed to the ureter • Ureter not tunnelled • Anterior and posterior parametrium not removed • Vessels removed maximally close to the uterus • Vaginal resection is minimal without removal of the paracolpos
Type B	Transection of the paracervix at the urether • Ureter tunnelled • Partial resection of uterosacral and vesicouterine ligaments • Resection of paracervical ligament at the level of ureteral tunnel
Type C	C1. With autonomic nerve aparing preservation • Preservation of splanchnic nerves • Preservation of vesical brach of pelvis plexus • Preservation of hypogastric nerves C2. Without autonomic nerve sparing preservation • Intersection of the splanchnic nerve • Intersection of vesical branch of pelvic plexus • All branches of hypogastric nerve are dissected
Type D	Lateral parametrectomy • The line of resection runs between internal obturator internus muscle and lumbosacral plexus

Table 7: Querleu D, Morrow CP. Classification of radical Hysterectomy. Lancet Oncol 2008;9(3):297-303.

II. 3. Minimally invasive surgery

According to several studies, minimally invasive surgery which refers to hysterectomy for gynecologic conditions, displays improved surgical and disease-related results in comparison with laparotomy[42].

There are many important advantages follow, arising from minimally invasive surgery. Firstly, there is significantly less pain, secondly less blood loss and need for transfusion, thirdly less risk of infection, fourthly shorter hospital stay, quicker recovery and return to normal activities, and lastly small incisions for minimal scarring, better outcomes and more satisfied patients[45].

The laparoscopic method requires a direct magnified visualization of the surgery site and as a result, surgeries can be performed in areas that cannot be seen clearly with traditional surgical approaches[46]. Additionally, around half of the estimated 400,000 hysterectomies completed yearly in the United States for benign indications are performed via a minimally invasive surgical approach. Furthermore, more and more patients undergo minimally invasive myomectomy surgery, and they will increase as they have many benefits from having their uterine surgery performed this way[42].

Furthermore, surgical robot systems were invented due to the need of overcoming the disadvantages of the laparoscopic surgery, such as limitation in vision and flexibility. Robot surgical systems (Fig. 5) have various benefits over laparoscopic surgery as firstly it provides 3D visualization, secondly 7 degrees of freedom (in contrary with 4 degrees of freedom by the laparoscopic surgery) and thirdly stable camera function. Robotic surgery was introduced as one of the procedures of minimally invasive treatment for plenty fields, fed off the important advantages pointed before. On the other hand, important disadvantages are that robot surgical systems demand special training for the users and a really special and expensive equipment. Additionally, some minimally invasive procedures may take longer than open operations, because of the complicated equipment preparation. In addition, robot surgical systems have demerits in aspect of high cost and not yet defined long term postoperative results in most area. The lack of merits to overcome the high cost is also a problem that has to be solved. Moreover, most of the studies concerning

the robotic surgery are regarding technical feasibility and safety. What is more, the early postoperative outcomes of robotic surgery are equivalent to those of conventional open or minimally invasive procedures. Currently, robotic surgery system is used for general surgery, urology, gynecology, cardiothoracic surgery, and head and neck surgery.
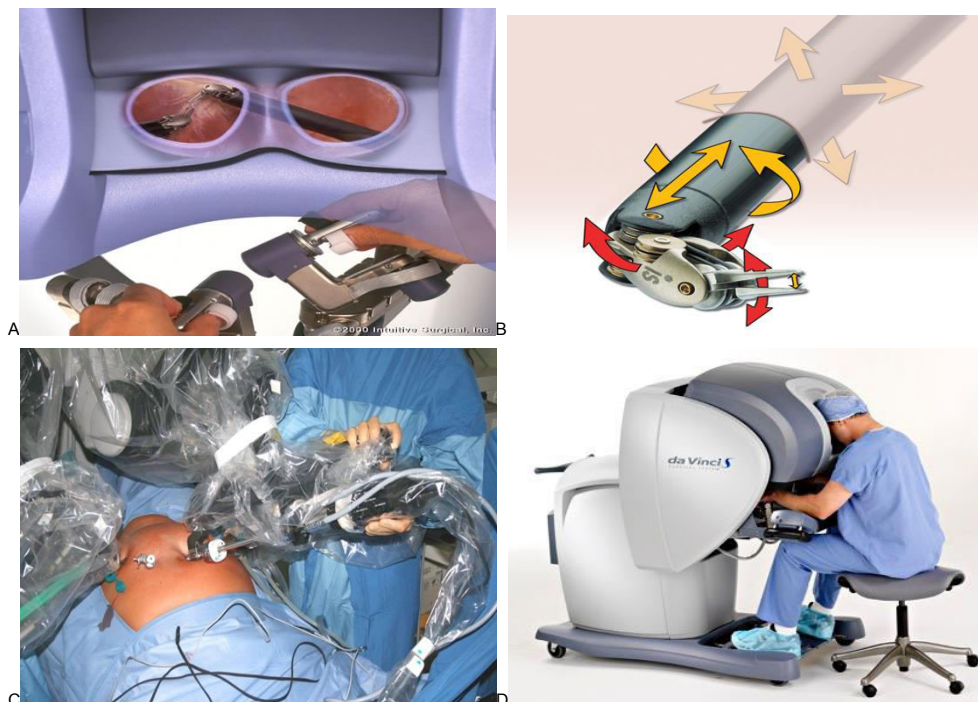
Fig. 5: The da Vinci surgical system, 2nd generation of the system da Vinci S

A. Heading section of the surgical console. Sterescopic viewer

B. Degrees of freedom of the Endowrist^{TM},

C. Intraoperative image with docking manoeuvre

D. Surgical console

source: Intuitive Surgical Inc., Sunnyvale, California

II. 4. Myomectomy

Myomectomy is the surgical procedure that preserves the uterus while treating myomas surgically. The treatment modalities for uterine myomas may include expectant management, medical therapy, conventional surgical options, and newer and less invasive approaches such as hysterectomy.

Various medications, both hormonal and non-hormonal, have been tried to control the symptoms produced by myomas (antifibrinolytics, nonsteroidal anti-inflammatory drugs, oral contraceptive pills, progestogens, danazol, levonorgestrel intrauterine devices, gonadotropin-releasing hormone analogs, aromatase inhibitors, mifepristone, ulipristal acetate). Most medical therapies cause a significant but temporary reduction in myoma size and improve symptoms in most cases.

A minimally invasive interventional radiological treatment for uterine myomas is the uterine artery embolization. This procedure, first described for management of myomas in 1995, attempts to reduce size and diminish growth by limiting the blood supply. Moreover, in October 2004, the FDA approved magnetic resonance imaging (MRI)-guided focused ultrasound treatment, another minimally invasive interventional treatment of uterine fibroids in humans, which is being sold as ExAblate™ in the United States. The rise in temperature of the tissue receiving the high intensity focused ultrasound and the resultant protein denaturation and irreversible cell damage form the basis of this treatment modality[47].

When a patient suffers from anemia, which could not be cured with medication, myomectomy may be the right treatment option. To add, it may also be a reasonable treatment option firstly for pressure or pain that is not cured by treatment with medication and secondly for a myoma that has modified the wall of the uterus. This last condition can sometime cause inability to conceive or recurrent miscarriages or complications during pregnancy and delivery. Underlining, a myomectomy is usually done before an in vitro fertilization, in order to improve the chances of pregnancy and successful full-term pregnancy[48] (mostly concerning submycosal myomas).

Moreover, myomectomy is suggested by available studies [49, 50, 51, 52] to have a higher risk of blood loss and more operative time, in comparison with hysterectomy.

On the other hand, myomectomy comparing with hysterectomy has a lower risk of ureteral injury. Garcia et al. report that 10% of women undergoing a myomectomy will require hysterectomy within 5 to 10 years. Also, after a myomectomy there is a 15% recurrence rate for myomas[49]. It is important that patients should be informed about the inherent risks of myomectomy, so that they are aware of the likelihood of hysterectomy at the time of a planned myomectomy. A preoperative anatomical (Fig. 6) evaluation using MRI of the abdomen can minimize this possibility. Until now, the vast majority of women with completion of family planning who require a surgical solution to cure symptomatic myomas are often treated with hysterectomy[50,51]. After laparoscopic surgery there is higher risk for recurrence of myomas, approximately a 33% risk at 27 months[53]. Furthermore, it has been reported that in 60% of cases come to adhesion formation postoperatively[54].
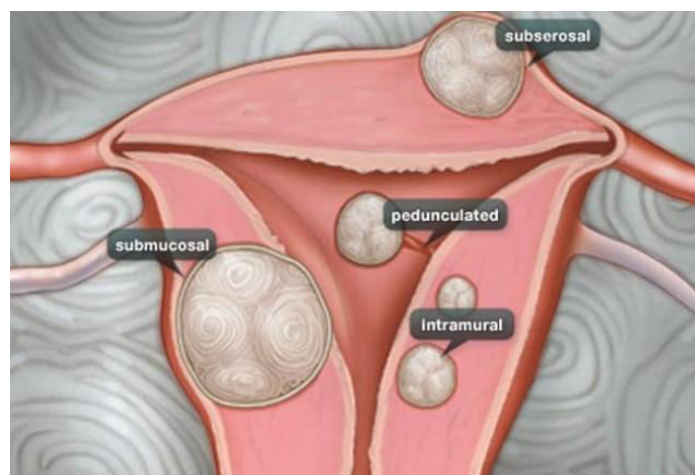

Fig. 6: Different localisation of uterine myomas.
Source: Professional Brooklyn Gynecology Services

During a laparoscopic hysterectomy or myomectomy, a surgical instrument calles a power morcellator is often used. Laparoscopic morcellators help the surgeon to divide and fragment tissue into smaller pieces to facilitate the removal of the tissue through small surgical incisions.

II. 5. The technique of power morcellation

Gynecologists use a medical device called laparoscopic power morcellator during different types of laparoscopic surgeries (LH, LASH, Myomectomy). Moreover, with this kind of tiny instrument (12-15mm diameter and more) operators cut large tissue masses into small fragments or pieces, and it is often used during laparoscopic surgeries to make the removal of tissue through small incision sites easier.
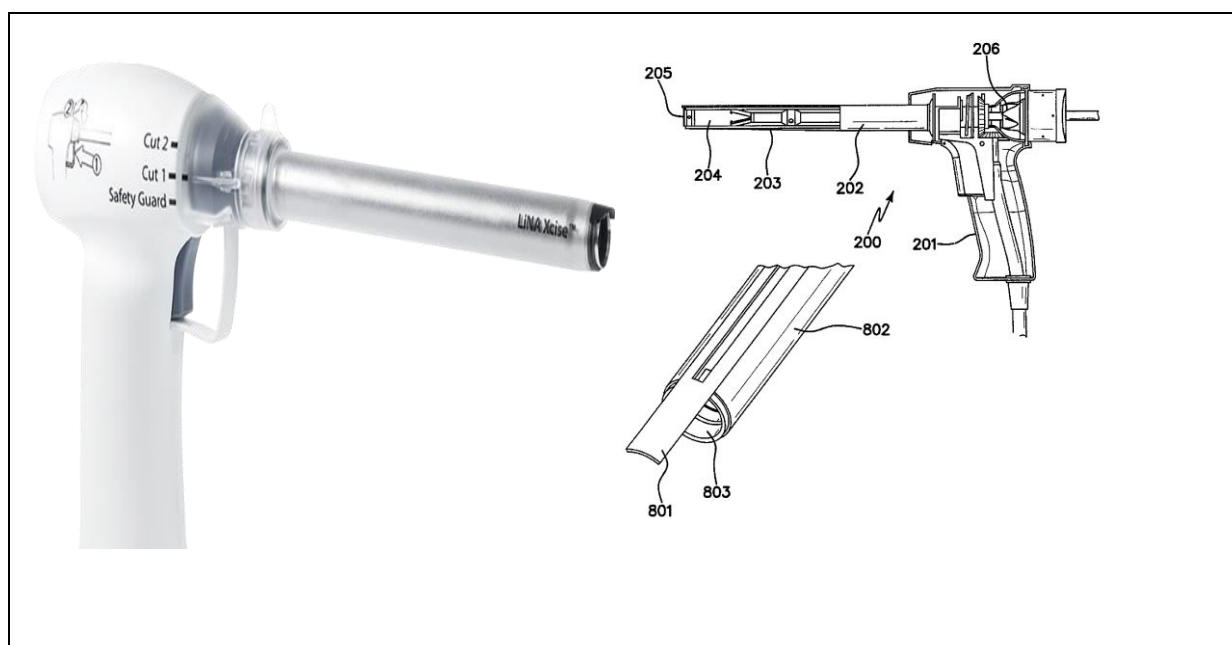
Fig. 7: Example for a power morcellation (LINA XCISE MORCELLATOR)

Source: APPLIED MEDICAL RESOURCES CORPORATION, CALIFORNIA

The first electric morcellator was introduced in 1993, prior to that morcellation of uterine specimens through the vaginal route or by minilaparotomy represented the common approach[55]. Currently, there are three general categories of uterine morcellation, the first one is called vaginal morcellation with a scalpel or morcellation knife through a culdotomy or colpotomy[42], the second one is done by a minilaparotomy (2-6 cm incision) /laparoendoscopic single site (LESS) morcellation with a scalpel[56], and the third one is called power morcellation (Fig. 7) or electromechanical morcellation (EMM)[57]. Power morcellation is performed to shred uterine tissue so that it can be removed during laparoscopic supracervical

hysterectomy, laparoscopic myomectomy, or laparoscopic total hysterectomy in case of very large uteri. Furthermore, regarding dissemination of an occult malignancy the former two approaches have been used for decades, but the risks are not systematic analyzed and studied in trials so we are not aware at the moment if they share equivalent risks as EMM. Vaginal retrieval of the uterine specimen has been long employed, with modifications of the technique for increased uterine size. With vaginal retrieval technique it is made much easier for gynecologists to observe the specimen and, if necessary, to incise it with a scalpel and eventually remove it from the uterus. The removal of the specimen may be accomplished through colpotomy or culdotomy for laparoscopic subtotal hysterectomy or myomectomy[58]. The mini-laparotomy is another common option to abdominal hysterectomy and myomectomy. Mini-laparotomy comparing to prolonged laparoscopic supracervical seems to be more cost-effective. It should be underlined that mini-laparotomy is not a suitable substitute for standard vaginal hysterectomy, which still is the most inexpensive procedure. To add, many variations of mini-laparotomy technique are currently available[59]. Furthermore, one choice for laparoscopic hysterectomy or myomectomy is to perform electromechanical or power morcellation to make specimen retrieval easier. Generally, the laparoscopic power morcellator device consists of a hollow cylinder that pierces the wall of the abdomen, which ends with a circular blade. Through this blade the surgeon inserts a grasper in order to pull out an extractable specimen. Besides, laparoscopic power morcellators typically use a blade, which rotates rapidly, to tissue into approximately 1-2.5cm diameter pieces that can be removed through a small incision. It is important to add that the FDA firstly approved the mechanical morcellation in 1995 and that it is not approved for transvaginal applications [60]. Moreover, in each of the methods summarized above, gynecologists may use a specimen retrieval bag to perform the surgery. According to LESS, it is currently being explored in gynecologic surgeries, but the literature is somewhat limited. As aforementioned, LESS is a technique that involves working with several endoscopic articulating instruments through one transumbilical incision [61].

Despite the well-established advantages of power morcellation during laparoscopy, the use of power morcellators is not completely used without concern. Like all

surgical procedures, the laparoscopic power morcellation also has complications, some of which are direct and some are indirect. The direct complications that literature reports are the injury of the small and large bowel, the vascular system und more often the iliac vessels. One of the most seldom complications that might appear is the injury of the ureter[62] analyzed the FDA's adverse event database "MAUDE" (Manufacturer and User Facility Device Experience) between 1992 and 2013, where injuries to the small and large bowel (31), large blood vessels (27), the kidney (3), ureter (3), bladder (1) and diaphragm (1) have been stated using power morcellation procedure. In the six cases pointed above, sometimes the result could be fatal. The common reasons for these complications are the non-experienced surgeons and the loss of visualization because of collapse of the capnopneumoperitoneum. If the operation lasts more than 3 to 4 hours, the percentages of the complications increase rapidly, which is not related with power morcellation[63]. When power morcellation is used, there is a risk that it will spread cells of the morcellated tissue inside the woman's abdominal and pelvic cavity. Furthermore, the most serious indirect complication may be the malignancy that comes as a result of the final histologically examination. In this case, the further treatment is not established. Although it is a benign pathology unlikely to cause complications, it is reported[62] that some of these women had a second surgery for symptoms such as pain. Surgery may also be indicated by a suspicion of malignancy when imaging is highly suspicious and preoperative pathology difficult to interpret. Unfortunately, power morcellation destroys the gross appearance of the specimen, thereby compromising pathological examination. For many women, minimally invasive surgeries are safe; however, when a "presumed myoma" is broken up inside the abdomen by a morcellator device, the end result can be a significant clinical problem if the mass turns out to be an unsuspected uterine cancer, such as a uterine leiomyosarcoma. The high speed of the morcellator blade spreads small macroscopic and microscopic fragments of tissue to other parts of the abdomen and pelvis. In a case report Paola Ordulu et al. report a case of disseminated peritoneal leiomyomatosis seven years after LASH for uterine leiomyoma. She proved this fact by using molecular cytogenetic analyses[64]. If there is an undetected uterine sarcoma

as reason of the uterine pathology, there is a high risk for tissue dissemination by power morcellation, and as a result this can worsen a woman's prognosis for long-term survival. The medical field and the media also underline the risk of using power morcellation in order to inform both gynecologists and patients about the danger of intraabdominal dissemination of uterine malignancy. Recent statements by the United States FDA [65] (April 2014) and Health Canada [66] (department of the government of Canada with responsibility for national public health) (May 2014) brought to public attention a case of Amy Reed, an anesthesiologist at Beth Israel Hospital in Boston. When Amy Reed, MD, was diagnosed with myomas in October 2013, her physician recommended what has become a routine procedure: hysterectomy with morcellation. Dr. Reed learned a few days after the surgery performed at Brigham and Women's Hospital that she had an uterine leiomyosarcoma, and the morcellation may have worsened her prognosis by spreading the cancer around her abdomen. Since then, Dr. Reed's husband, cardiothoracic surgeon Hooman Noorchashm, MD, PhD, has led a campaign calling for a ban on morcellation. After that FDA made detailed suggestions[65] to gynecologists about the treatment by using power morcellator. The recommendations, which support the careful use of power morcellators, as noticed by Health Canada[66] are presented as follows:

➢ Recognize the prevalence of unsuspected uterine sarcoma in patients under consideration for hysterectomy or myomectomy for the treatment of uterine fibroids.

➢ Consider the treatment alternatives for women with symptomatic uterine fibroids and review these options with each prospective surgical patient. Apart from a laparoscopic approach, alternative surgical procedures exist that do not require electric morcellation. Also, some surgeons and centers may recommend closed morcellation in a bag as a way to reduce the risk of inadvertent spread of uterine tissue.

> Be aware and inform patients that laparoscopic electric morcellation of unsuspected uterine sarcoma during hysterectomy or myomectomy may disseminate the disease and negatively impact prognosis.

II. 6. Preoperative differentiation between myomas and uterine sarcomas

The common characteristics between fibroids und sarcomas render the preoperative diagnosis almost impossible, and as a result they make the clinician's prediction very difficult. Besides there are some specific potential characteristics in uterine sarcomas such as growth, necrosis and increased vascularity, that help the treating physician to suspect their existence. However, these potential characteristics may also appear in beingn uterine myomas, and that encumbers the physician from recognizing the exact disease. Basically, there are no pathognomonic features predicting a LMS (Fig. 8) on any imaging technique [67,68].
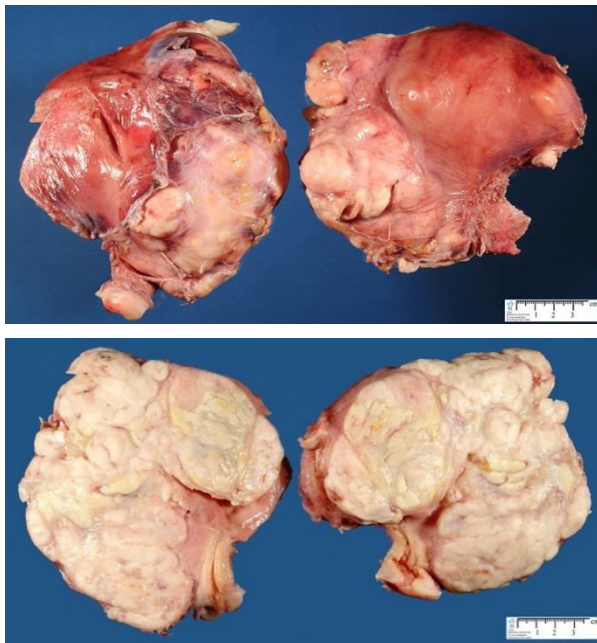
Fig. 8: Macroscopic pathological specimen of an uterine leiomyosarcoma

source: 1996-2016 Humpath.com - Human pathology

Rapid increase in size within 3 months has been reported in case reports of LMS [69,70] but it may also occur in myomas, and as a result it is still not distinctive[71]. It is a reassuring sign if the myomas don't grow in a 3 months' period, however this cannot

be judged if the patient receives GnRH analogues. Furthermore, sometimes myomas may escort the uterine sarcoma responding to GnRH and as well, due to its estrogen receptors it may be sensitive for estrogen deprivation itself. A retrospective study with 21 patients showed that from the 95% of the uterine specimens the leiomyosarcoma is solitary or it is the greatest mass. There is no specific localisation where leiomyosarcomas appear[72]. Additionally, in a study of Exacoustos, eight LMSs and three STUMPs (uterine smooth muscle tumors of uncertain malignant potential) have been compared with 225 myomas by using ultrasound, and the results have shown that LMSs are the greatest of all the uterine smooth muscle tumors[73]. LMSs were all solitary and seven of eight of them had a diameter bigger than 8 cm. Furthermore, in seven LMSs increased central und peripheral vascularity was illustrated, and in four LMSs degenerative cystic changes were noticed. In the diagnosis of LMS the sensitivity of increased central and peripheral vascularity was 100%, its specificity was 86%, but its positive predictive value was only 19%. Another way to recognize if the tumor is a myoma or a sarcoma may be 2D ultrasound Power Doppler (USPD), with a peak systolic velocity having a sensitivity of 80 % for detecting sarcoma with a specificity of 97 %[73]. It is important to know that LMS may have on ultrasound and MRI a similar appearance to myomas, despite all these diagnostic parameters. In spite of the rapid development of technology there are not yet any studies on sarcoma diagnosis measured by 3D USPD [69]. Until now, there are no systematic analyzed and studied trials which could define clear parameters for the preoperative differentiation between myomas and uterine sarcomas. Amant et al[23] and Hata et al[74] mentioned the characteristics that should increase the suspicion of existence of an LMS. Analytically, some of them are: Size larger than 8 cm, solitary, oval shape, highly peripheral and central vascularization, irregular heterogeneous myometrial tumor with central necrosis or degenerative cystic changes, lack of calcifications.

Diagnostic D&C was originally intended to detect intrauterine endometrial abnormalities and assist in the management of abnormal bleeding. However, D&C cannot guarantee the detection of malignances. For example, in one study it has

been demonstrated that 36% of sarcomas and 19% of endometrial cancer can be misdiagnosed[75]. Another study [143] demonstrated either positive or suspicious biopsy results in more than 51% of patients who were found to have leiomyosarcoma on final pathology. The detections rate was higher at post-menopausal patients with bleeding symptoms. Comprehensibly, there is low accuracy in the diagnosis of uterine sarcomas by using D&C, because they are cancers of the muscle or fibrous (connective) tissue of the uterus and in most of the cases they don't have connection with the endometrial cavity, thus D&C is not eligible to exclude sarcomas.

Further imaging may be needed for diagnosis in order to determine the true local extend of a lesion, to evaluate its relationship to adjacent structures, and to stage suspected malignancy. MRI can provide information for both diagnosis and staging and thus has emerged as the preferred modality for evaluating soft tissue tumors. MRI is ideally suited for this given its multiplanar capability and its ability to accurately assess both the bones and soft tissues. To outline the range and to assess the tissue of the leiomyoma it is preferable to use MR imaging and not CT scan[76]. Furthermore, the evaluation of tumor extension in the uterus and the segregation between leiomyoma and LMS may be assisted by MRI method and particularly by the T2-weighted sequences, which show both the normal anatomy and pathologic processes very well owing to the inherent differences in water content of different tissues, because pathology usually being depicted as an increase in water content[(77,78)]. In a prospective study with 227 patients it has been assumed that the use of dynamic MRI and serum measurement of LDH (isozymes type 3, LDH3) can help in the differential diagnosis of leiomyosarcoma from degenerated leiomyoma of the uterus. Moreover, the usefulness of gadolinium (Gd)-DTPA was examined. Specifically, contrast enhancement after administration of gadolinium (Gd)-DTPA was detected in all 10 LMSs, but it was not detected in 28 of 32 patients with degenerated uterine leiomyomas[79].

Moreover, positron emission tomography (PET) has a place in the diagnostic armamentarium of assumed myomas. In PET scanning the physician visualizes a radionuclide (tracer) on a biologically active molecule. Some molecules and especially fluorodeoxyglucose (FDG) are used in imaging of myomas (Fig. 9). In

general, the uptake of FDG in a myoma or a sarcoma is associated with the estrogen status, cellularity and the presence of malignancy. Adding, it has been reported that in few occasions deoxyfluorothymidine (FLT) or alphafluorobeta-estradiol (FES) was used in the diagnostic of assumed myomas with successful results[80]. Moreover, in a study with 76 patients with suspected uterine sarcoma it has been demonstrated that FES may be more reliable in distinguishing LMS from fibroids than FDG. The accuracy of the first one was 93% and from the second one 81%[81]. Three different imaging techniques (FDG PET, ultrasound PowerDoppler, dynamic MRI) in the case of suspected uterine sarcoma were compared by a retrospective study. There were five sarcomas, which were all detected by FDG PET (sensitivity 100%), two were detected by ultrasound PowerDoppler (sensitivity 40%) and four by dynamic MRI (sensitivity 80%)[82].
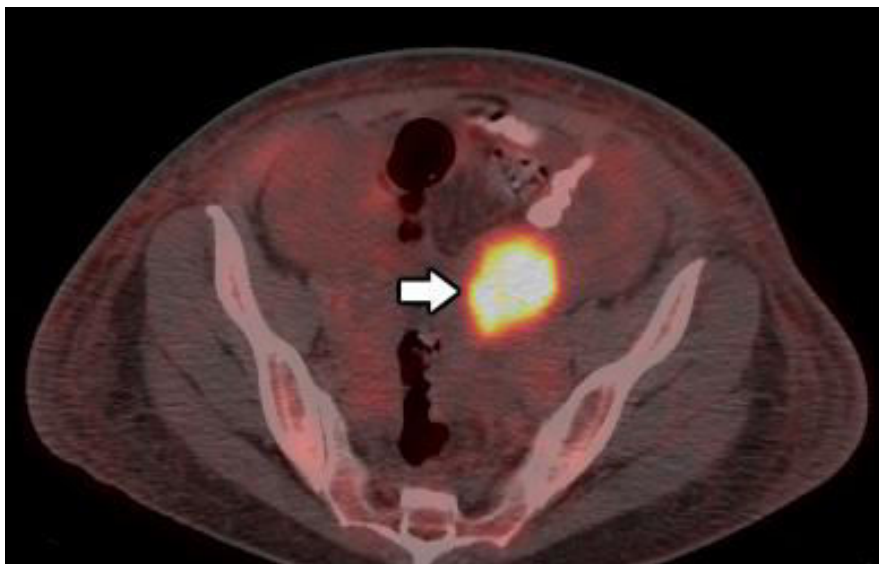
Fig. 9: The image above shows a uterine leiomyoma (arrow) with intense FDG activity. It has remained stable in size and activity on 4 years of follow-up PET/CT.

source: Roentgen Ray Reader, posted by Behrang Amini.

In the literature it is reported that serum CA 125 is increased in patients who suffer from LMS and mostly in advanced-staged LMS[70]. Clinical use of CA 125 is limited because there is increased level in serum mostly in advanced-staged LMS and rarely in early-stage uterine LMSs. That creates a significant overlapping of

preoperative serum CA 125 between the uterine leiomyoma group and LMS. However, in a study of 42 consecutive LMS, the values of preoperative serum CA 125 were significantly higher in the uterine LMS group than those in the uterine leiomyoma group [83].

Unfortunately, there are no high-quality data regarding the prevalence of sarcoma in women planning surgery for presumed benign leiomyomas. For other preoperative diagnostic methods such as operative hysteroscopy with deep endometrial and myometrial biopsy (e.g. Pipelle®) there are no sufficient data. On the other hand, in a large study from the Canadian Task Force III database with 68 women, who underwent endometrial sampling before surgery, it has been reported that there is no significant difference in the performance of the test between endometrial biopsy and dilation and curettage[84]. Moreover, preoperative imaging-guided biopsy of the mass (guided by pelvic imaging or laparoscopy) has been proposed but is generally not performed because of sampling errors and the risk that the procedure may spill malignant cells within the peritoneal cavity or elsewhere. Furthermore, intraoperative biopsy or frozen section is indicated if there are suspicious findings during surgery. On the other hand, frozen section analysis is not reliable for excluding uterine sarcoma while frozen section analysis typically depends upon a limited tissue sample. Thus, there is a high likelihood of a false-negative result even if a sarcoma is present[85]. These methods seem to be encouraging but without development they could not be established because of their limitations.

In conclusion, there are no reliable examinations to predict sarcomas and no effective testing that can distinguish between common benign myomas and ULMS before a surgical removal of the mass. Nowadays, experts suggest the preoperative assessment of presumed uterine fibroid tumors where power morcellation of tissue is outline to be used. Recommended preoperative studies include: imaging studies such as MRI or sonography, endometrial biopsy in cases with abnormal uterine bleeding and cervical cytology [86].

II. 7. Dilemma: Use or abandon electromechanical morcellation

The reported decreased risks of minimally invasive hysterectomy and myomectomy, their long term cost savings, and finally their efficiency encouraged gynecologists and also patients to support their use[42]. All this distinct advantages of MIS where fomented by the global health care system without taking the rarity of uterine sarcoma into consideration. As it had been mentioned before, the anesthesiologist from Beth Israel hospital in Boston (teaching hospital of Harvard medical school) Dr. Amy Reed, who had a personal experience, was the first who took the dangers of Laparoscopic Power Morcellation (LPM) public in December 2013 in the Wall Street Journal (a non-scientific magazine) article. Dr. Reed underwent a minimal invasive hysterectomy with expected LM, tissue extraction was done by power morcellation, after a week she was diagnosed with leiomysarcoma, and due to the performed surgical procedure it was upstaged to a FIGO Stage IV sarcoma because the sarcoma was spread iatrogenic intra-abdominally[87]. After the long-term analysis on the use of morcellators on unsuspected uterine sarcoma and the possibility to spread the malignant tissue within the abdomen and pelvis the literature is leaded to the question that follows: should morcellation technique be allowed to be continued, without the patient's approval, with the current known risks? Many investigations have taken place, especially by the US-FDA, about the important issue of the negative consequences of using a morcellator in hysterectomy patients. FDA warns against using laparoscopic power morcellators in the majority of women undergoing myomectomy or hysterectomy, and recommends physicians to inform their patients about these dangerous risks. After an analysis of the currently available data, FDA reports[65] that in 1 in 350 woman undergoing hysterectomy or myomectomy for the treatment of expected myomas, accidental uterine sarcoma has been detected. Some popular medical centers in the Boston area, such as Brigham and Women's Hospital, Boston Medical Center, Tufts Medical Center and Massachusetts General Hospital, have completely banned power morcellation devices after the FDA warning. Furthermore, it has been estimated that in the USA 2 to 5 women are diagnosed daily with ULMS, and for about 1000 women their cancer prognosis has

became worse due to minimally invasive hysterectomy technique. Additionally, for women younger than 35 years power morcellation has lower risk, as the incidence of leiomyosarcoma is rare in young patients. Pados et al.[171] in a study with 1216 patients in reproductive age (18-45 years old) who underwent laparoscopic morcellation of leiomyomas didn't report any unexpected sarcoma or atypical myomas. However, the risk of occult malignancy by using power morcellation is higher for women over 50 years age (perimenopausal and postmenopausal), as the incidence of uterine leiomyosarcoma increases within this age[88].

II. 8. Current data about electromechanical morcellation and occult malignancy

Jasmine Tan-Kim from Kaiser Permanente San Diego Medical Center, California, and colleagues published a retrospective review[89] on women who underwent laparoscopic hysterectomy with power morcellation. Analytically, their medical research included 3523 women, and thus they had a large series of laparoscopic hysterectomies and a long-term follow-up to examine. They pointed out that sarcoma was not associated with any preoperative conditions. Furthermore, 941 to 3523 women had hysterectomy with the use of a power morcellator and 0.6% of them were diagnosed with uterine sarcoma. Moreover, three of the 0.6% during the initial pathology review have been diagnosed with uterine sarcoma, and another three have been diagnosed with uterine sarcoma after 2 to 7 years. Moreover, no any cervical or endometrial cancer has been found accidentally in the examined cases. The study comes to the conclusion that already women over 40 years should be aware of the risks of power morcellation. In an another study, Seidman et al [90] had reviewed 1091 uterine morcellations and they pointed out that 1.2% of operated women had been diagnosed with uterine malignancy. Analytically, one was endometrial stromal sarcoma (ESS), one cellular leiomyoma (CL), six atypical leiomyomas (AL), three smooth muscle tumor of uncertain malignant potential (STUMP), and one leiomyosarcoma (LMS). For the majority of women diagnosed with uterine sarcoma, the treating gynecologists are only able to notify these

malignancies after the final pathology is confirmed and not during the presumed benign uterine myomas surgery. Moreover, after a follow-up laparoscopy examination it was found that in 64.3% of all the cases disseminated disease occurred. The authors concluded that dissemination of sarcomas increase the mortality, and they propose that literature should be reexamined, as the negative consequences of power morcellation are possibly underestimated. In another study[91] it is pointed that in sarcoma cases where EMM was performed, physicians are proposed to ensure that any residual peritoneal disease has to be resected by making a laparotomy. One study[92] that concentrated on LASH with unexpected malignances included 1584 patients, of these only 0.25% (4 patients) was diagnosed postoperatively with malignancy. Analytically, two of the four patients had leiomyosarcomas and the other two had endometrial cancers. Most of the patients (87.8%) received preoperative screening, which includes cytology (PAP-smear), ultrasound and curettage. Despite the preoperative screening the study shows that there is a small probability of unexpected malignances. Also, three of the patients were treated with staging laparotomy (multiple peritoneal biopsies, BSO, removal of the cervical stump, infragastric omentectomy) after a few days, and one of four with staging laparoscopy (multiple peritoneal biopsies) after 6 months. After 28-52 months of follow-up there was no evidence for recurrence. Another study[93] that compares the treatment of accidental endometrial cancer after only simple hysterectomy concluded that the group of patients, which received a complementary surgical staging, rather than an expectative follow-up, has significantly lower recurrence. The same where reported by Einstein et al.[94] in a retrospective study. Furthermore, the author reveals that there is a difference in 5-year survival between women with unexpected leiomyosarcoma who underwent a morcellation and with those who didn't undergo power morcellation. Namely, by using a power morcellator the percentage was 46% and without it was 73%. Moreover, after the power morcellation and histology shows leiomyosarcoma, there is need of reoperation to detect any spread of cancer. Chemotherapy would have been recommended only if tumor spread is detected[94]. In a recent study Serrano et al.[95] pointed out that after tumor morcellation of uterine LMS some issues were observed. Firstly, comparing to

the removal of ULMS by TAH (total abdominal hysterectomy) tumor morcellation had an important increased risk for tumor dissemination. Secondly, there was a really high risk of recurrence after the power morcellation and also the time to recurrence was shortened. The same results were presented by Park et al.[96] in a study with 56 patients with unexpected early low grade endometrial stromal sarcoma of the uterus who underwent power morcellation during surgery. These patients had a significant higher rate of recurrence and significant lower rate of 5-year disease-free survival than the patients who underwent abdominal hysterectomy without morcellation.

Moreover, iatrogenic endometriosis, complex atypical hyperplasia, peritoneal adenomyoma and peritoneal leiomyomatosis are some of the effects that prove the intense progress of morcellation-related pelvic implants[97]. As mentioned before, in some patients with morcellated myomas parasitic peritoneal leiomyomatosis appears. Namely, this kind of leiomyomatosis arises as a result of both the implantation and growth of sustainable leiomyoma particles disseminated[98]. The outcomes may include peritonitis, intra-abdominal abscesses or intestinal obstruction and they require another surgery or additional interference[62]. After a long research of various cases literature informs physicians that the frequency of the appearance of these complications is increasing. However, the actual frequency is not yet known, and probably underestimated [99]. In a relevant study, after EMM iatrogenic myomas were found on the appendix, implanted on the bladder, and in retroperitoneal spaces. In another similar study, after EMM scattered peritoneal leiomyomatosis throughout the pelvis has been found [100]. Additionally, after the EMM de novo endometriosis and adenomyosis have also been reported in patients without prior evidence of endometriosis [101].

After a few different researches professional societies, such as the American association of gynecologic laparoscopists (AAGL), took position on the issue[102]. Analytically, they pointed out that if the use of power morcellation was prohibited, many patients would be operated with open procedures and then the perioperative risk and recovery time would be increased, affecting mortality and morbidity of these patients[(102, 103)].

II. 9. Statement and recommendation of medical societies concerning laparoscopic morcellation and tissue extraction

The result of an AAGL analysis[102] reported that if all laparoscopic operations for uterine myomas were converted to open hysterectomies, there would be 17 women dying in the USA from complications of hysterectomy per year. The guidelines of AAGL on morcellation during uterine tissue extraction were published in May 2014, and they included the requirements that patients need to have in order to undergo EMM: firstly, they suggested informed consent to include a meticulous discussion of risks, benefits and alternatives. Secondly, they suggested that alternatives to EMM should be used among post-menopausal women because the majority of postoperative diagnoses for uterine cancer occur among this population. Furthermore, morcellation should only be considered in patients if the appropriate evaluation of the myometrium (with or without myomas) is reassuring. Laparotomy is an alternative to morcellation for patients in whom preoperative evaluation results in an increased suspicion for malignancy. When electromechanical morcellation (EMM) is likely to be done, the patient should be informed about the risks of encountering an undetected malignancy and the likelihood of worsening her prognosis. Patients have to be involved in the final decision to use EMM or not. Additionally, the surgeon who uses the morcellator has to be experienced and with sufficient skills. The use of specialised retrieval pouches should be investigated further for safety and outcomes in a controlled setting. Further important medical societies in laparoscopic surgery expressed the following:

SGO (Society of Gynecologic Oncology): A declaration [104] was reported in 10-11 July 2014 to the FDA's Obstetrics and Gynecology Medical Devices Advisory Committee concerning power morcellation. The SGO came to the decision not to support the ban on EMM.

ESGE (European Society for Gynaecological Endoscopy): a specific report [105] in May 2014 has been publisched concerning power morcellation. The report included that morcellation has the possibility to spread the sarcoma cells in the abdominal cavity.

Additionally, it highlights that patients should be informed about these negative effects in order to make a decision along with their gynecologist.

DGGG[106] (German Society of Gynecology and Obstetrics): the question of the patient safety will increase as a result of the abandon of EMM cannot currently be answered definitively. Benefits and risks of using EMM must be weighed up in discussions with each individual patient. The risk evaluation of occult malignancy and the deterioration of patients' prognosis after using EMM must be completely resolved. The information of the patients about the risk of EMM is obligatory, even those patients with minimal risk.

ISGE (International Society of Gynaecological Endocrinology): A review of the literature and recommendations[170] about the risk of laparoscopic morcellation during myomectomy and hysterectomy were published in June 2017 supporting the use of power morcellation in 'low risk' patients after preoperative examinations. It is underlined that prospective data is needed.

II. 10. Alternative Techniques to power morcellation

There are some alternative techniques that are used to avoid spread of the uterine tissue into the abdomen at the time of laparoscopic hysterectomy and myomectomy. The most well known techniques are laparoscopic-assisted minilaparotomy (a small incision 2-6 cm above the pubic symphysis), tissue removal through a vaginal incision and the use of an endoscopic retrieval bag.
In 1986 the suprapubic incision was first described by Kunster and recently modified by Pelosi[169]. The specimen could be morcellated with a scalpel. Extension of the umbilical or suprapubic trocar incision are the usually chosen locations to perform a mini-laparotomy. As it is obvious bigger incisions provide more rapid extraction of the tissue but on the other hand worse cosmesis. To maximize the small incision and

improve the visualization of the specimen, special self-retaining ring retractor (Alexis) could be used.

The first two methods should be considered (in case of myomectomy or supracervical hysterectomy) before intracorporal electric morcellation because they preserve the advantage of minimal invasive surgery and they minimize the risk of tumor dissemination. The implementation of these techniques is not always possible.

According to the third method, the endoscopic bag (Fig. 10) is situated in the abdomen, so the surgical area is isolated allowing the fragmentation of tissue only within the bag. Additionally, an endoscopic bag helps the surgeon to maintain control of the morcellator and keep the specimen away from the abdominal space.
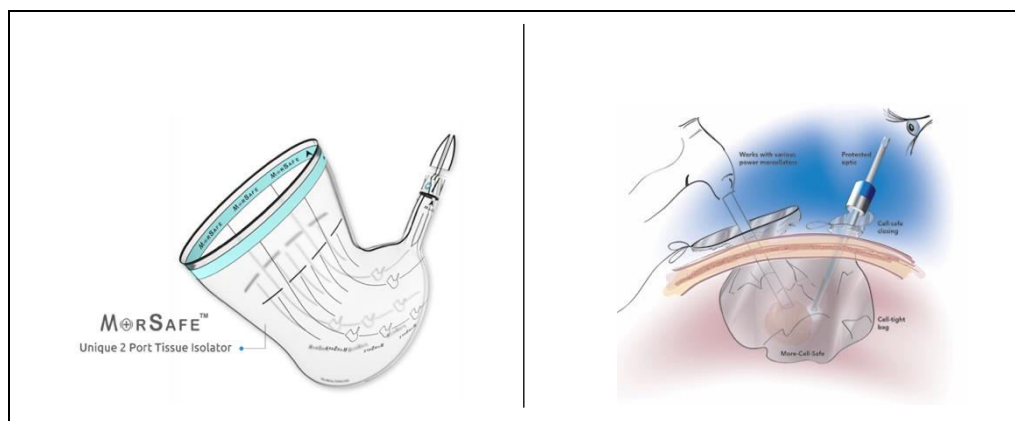
Fig. 10: Examples of specialised endoscopic morcellation bags.

Source: http://www.ami.at/en/produkt/more-cell-safe.

In a research of Menge et al.[108] it is pointed out that morcellation should be banned from the market, however it is supported that morcellation bag seems to be a really notable technique, by which tumor progression will be avoided. Moreover, Pasic et al[109] support and propose surgeons to always use the morcellation bag when suspicious tissues are morcellated. On the other hand, it is important to mention that morcellation bags were not produced for this purpose (less than 12 mm trocar) which could lead to high leakage rate[110]. At first the contained morcellation procedure was described as part of a single-port technique for LASH[157]. Afterwards, some studies showed the feasibility of contained power morcellation not only by single port but

also by multiport operations with many variations[158, 159, 160, 161]. Furthermore, the usage of morcellation bag has been described also in the urologic and general surgery studies [144,145]. A really important factor for a successful use of the retrieval bag is the skills of the surgeon and his extent of experience.

There is one more option, which is not listed above as typical alternative. In order to make the transabdominal removal of the tumor tissue by hand morcellation possible, the operator has to enlarge the surgical port incision after putting the tumor in a retrieval bag and through this incision to remove the tumor in small parts by using scissors or scalpel (Fig. 11).
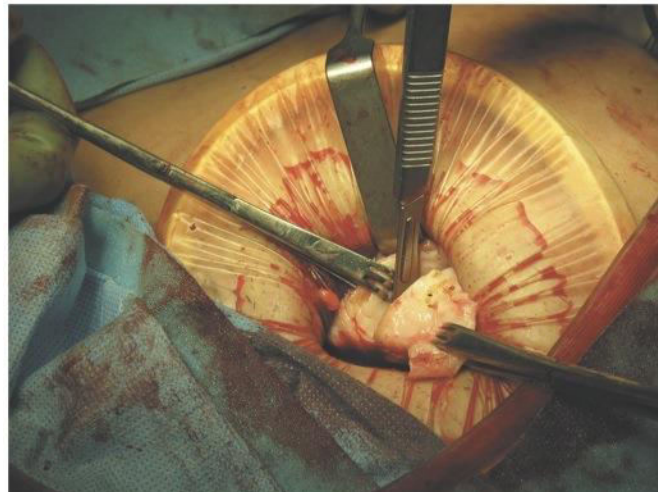
Fig. 11: Upward traction on the myoma is maintained with an additional Leaby clamp before the morcellated core is removed.
Source: MINIMALLY INVASIVE APPROACHES TO MYOMECTOMY Mojgan Mohammadi, Mark H. Glasser

If colpotomy is used to remove the uterus (the incision is made usually posterior in the fold between the uterosacral ligaments) after a supracervical hysterectomy, there are limitations (such as the size of the tumor) and usually the removal of a large tumor seems to be impossible[107].

In conclusion power morcellation has both advantages and disadvantages, which have to be carefully examined for each woman separately. Analytically, referring to the patient, the benefits are faster healing, faster recovery after the surgery with generally fast return to everyday life and reduced mortality. Additionally, referring to the surgeon, he is easily able to remove large tumors through small incisions. On the other hand, there is a high risk for spread of an occult malignomas, which can result in cancer upstaging. This dispersion may even cause worsening of the survival prognosis.

Naturally comes the dilemma: should morcellation be allowed to continue?

Is morcellator a useful or a dangerous surgical instrument?

III. Materials and methods

III. 1. Origin and type of the materials

This is a retrospective study carried out, in the Department of Gynecology and Obstetrics of Leverkusen Municipal Hospital in Germany during June 2008 and October 2016. Using the computerized database HL7-ADT_Nexus version 4 Software of the academic teaching hospital 'Klinikum Leverkusen' in Germany, we identified the women underwent an operation with the use of power morcellator. Their medical records were reviewed retrospectively, from their medical charts.

The patients were being treated long-term from local and regional gynecologists who are active in private offices and are allowed to make the regular gynecological examinations. The patients were sent to us with a medical of referral for the purpose of surgical treatment.

Patients who had a myomectomy or a hysterectomy performed by traditional laparoscopy, or robot-assisted laparoscopy, with power morcellation and without hand morcellation were included. The types of the laparoscopic and robotic assisted laparoscopic hysterectomies were LASH or TLH. Total laparoscopic hysterectomy is defined as removal of the uterus including the cervix. If the uterus was too large to extract specimen through the vagina, it was either dissected by laparoscopic power morcellation or by enucleating single myomas to retrieve each part separately by the vagina. Laparoscopic supracervical hysterectomy was defined as removal of the uterine corpus at the isthmocervical border followed by laparoscopic power morcellation to remove the specimen. The morcellation system, which was used for all operations, is produced from Karl Storz company and it is called Rotocut G1 morcellator. The standard placement of the ports was an umbilical 10mm port for the camera, a left 10mm and a right 5mm lower ancillary port for the instruments.

In this study, laparoscopic retrieval bags or specialized morcellation bags were not used.

Guided by the surgeons' list and operations' reports of the patients who underwent any type of morcellation conducted between June 2008 and October 2016, a data sheet of patients was generated. For this study, only data from morcellations using power morcellator (n=471 patients) were finally analysed.

All of the 471 eligible patients underwent an operation with the use of power morcellation. A total of three patients were diagnosed as malignant tumor postoperatively.

Two sub-groups were created concerning the age of the patient as a risk factor. The low risk group included the women under 45 years old and the high risk group the women from 45 and up. This age groups were chosen concerning the average female fertility upper limit. Regarding the average fertility age limits, we divided them in tumor groups. Group A patients > 45 years of age and Group B patients < 45 years of age.

We reviewed patient's data in four categories (anamnestic, diagnostic, clinic, histologic). The demographic data was not available for the total population of women studied. The recorded parameters are shown in the following table.

Statistical analysis was performed by utilizing the SPSS 19.0 software (IBM SPSS Statistics for Windows Armonk, NY: IBM Corporation, 2010)

The study is in compliance with the Helsinki declaration.

III. 2. Categorization

Basic data/ medical history	age
	parity
	menopausal status
	use of hormones
	use of the progestin intrauterine device
	history of previous abdominal surgery
Diagnostics	initial presenting symptoms
	ECOG-Status (anesthesiologist's protocol)
	preoperative diagnostics (Sonography, CT, MRI),
FIGO stage	tumor size, localization and extension
Procedure data	indication for operation
	surgical techniques
	procedures performed at initial surgery and reoperation
	duration of postoperative stay in hospital
	treatment of tumor dissemination
	examination of possible recurrence disease
	complications
	survival outcome
Histopathologic analysis	weight of the extracted specimen
	histological analysis with tumors stadium
	histological type
	tumor stage

Table 8: Protocol for the analysis of the patients' history.

III. 3. Histological evaluation

Postoperative two experienced pathologists, according to routine institutional guidelines, examined the specimens and generated the histopathological evaluation. This procedure lasted 2-3 days, and finally the pathologists transformed the reports in every patients' electronic medical record. Additional, these reports were examined cautiously in order to detect if there are any endometriosis, adenomyosis, fibroid tumors, cervical dysplasia, endometrial hyperplasia or malignancy.

At the macroscopically examination the pathologists weighed the specimen and inspected the surface for abnormalities. After that, the specimen were cut and they were examined thoroughly for abnormalities. Rarely we documented cases of myomectomy with use of power morcellation at the same time of TLH without morcellation. In these cases, the uterus was cut longitudinally starting from the cervix and ending to the fundus and representative samples were collected for further examination. According to morcellated specimens it was not always possible to identify whether they came from the uterus or cervix. Every specimen was submitted for formalin fixation except from the ones we send for frozen section. Additional, for every case standard surgical procedures were used both before and after the morcellation. To categorize the specimens for sarcomas 2009 FIGO system was used in every case. The pathologists also referred to FIGO staging in their reports.

Our study emphasizes on initial indication for the operation, examinations before the operation, the histological results and the appropriate therapy after dissemination of malignancy. Table 10 presents the indication spectrum for TLH, LASH or Myomectomy.

III. 4. Preoperative examination

- Premenopausal women with pathological ultrasound of the uterus

- Postmenopausal women with bleeding or pathological ultrasound of the

   uterus

- Women who had D&C before the operation

- Patients with very large myomas that have grown rapidly

Postoperative histological outcome

- Type of benign or malign results

- FIGO staging

Spectrum of treatment after accidental dissemination by power morcellation

- Control laparoscopy with biopsies

- Abdominal CT, chest X-ray, CT of the thorax

- Re-operation with laparotomy and complete staging with removal of cervical
   stump after LASH, infragastric omentectomy, Douglas cytology, multiple
   biopsies from peritoneum, appendectomy and bilateral salpingo-oophorectomy

- Adjuvant hormonal treatment

- Clinical follow-up

After appropriate information was gathered the three patients with dissemination of malignancy after power morcellation were interviewed one by one in order to pursue their health status. Additionally, there was cooperation with the external gynecologists in order to collect any further information about the patients. Moreover, Microsoft Excel 2013 was used to register all the collected informations follow up and subsequently to process and to update them.

III. 5. Limitations

In the meantime, during our research we came across to some limitations, which are pointed below.

- Firstly, there was difficulty in selecting the informations required for all the women and especially in the period of 2008 and 2009. Analytically, in this period the medical records were not properly saved and some items were missing.

- Secondly, we included young women with wish of children and uterine myomas in our study. In these cases, myomectomy was performed. The incidence of malignancy in these women is already decreased because of the young age.

III. 6. Research methods

Furthermore, we searched and analyzed all the published studies referring to power morcellation and dissemination of malignancy. Analytically, we examined all the published information (both in the Pubmed and medical books) and we combined them for the final outcomes and discussion. Moreover, foreign literature and articles were translated and used, as well as many different types of publications.

Finally, we used search engines as 'google' and 'bling' to help us to find these articles and publications. Below there are mentioned the most frequently used key words, sometimes combined altogether or in a different row:

✓ Power morcellation   ✓ Parasitic

✓ Myomectomy   ✓ Laparoscopy

✓ Malignancy   ✓ Dissemination

✓ Myomas   ✓ Sarcoma

"p values" <0.05 in two-sides tests were regarded as significant. Moreover, all statistical analyses were performed using SPSS for Windows (SPSS version 17.0; SPSS, Inc., Chicago, IL).

IV. Results

IV. 1. General results

We analysed 471 patients whose average age was 44.6, the youngest 23 years old and the oldest 68 years. We collected information referring to the parity from 121 patients (the informations for the rest of the patients were missing due to incomplete enquiry of the medical history), and the mean parity was 1.5 on average. The menopausal status was analyzed and showed that approximately 31% were postmenopausal, 7% perimenopausal and 62% premenopausal. Use of hormones (Tamoxifen) was observed only in 5 cases after breast cancer and in 12 cases use of progestin intrauterine device (Mirena®) was pointed. Moreover, the history of all the patients was observed and pointed that 33% of them have had an abdominal surgery for manifold reasons before.

Furthermore, in the preoperative examinations 61 patients (12.9%) underwent D&C, some of them because of suspicious endometrium, and the outcome was negative for malignancy, except in 2 cases endometrium hyperplasia without atypia was found. Anyway, patients who underwent D&C with diagnosis of malignancy were not eligible to our study.

The mean duration of hospital stay of the patients was 3.1 days. The average weight of morcellated tissue per operation, namely uterine myomas or uterus, was 232.9 grams. Analytically, the average weight of the myomas was 202.4 grams whereas of the uteri 263.3 grams. Additionally, in 59 cases (12.5%) of uterus morcellation the histological results have shown adenomyosis.

The most important issue of our study is that, in 3 of 471 patients unexpected malignancy has been detected, which represents 0.63 % incidence. In all three cases the malignancy was proved to be sarcoma (2 x LS, 1 x ESS). All these patients were examined according to the recommendation of DGGG (German society for gynecology and obstetrics) protocol.

IV. 2. Distribution of each operation's type

The operation techniques we used were conventional laparoscopic surgery in 74.5% of the patients and robot-assisted laparoscopic surgery in 25.5%. Adding, 69.6% of the operations were hysterectomies and 30.4% were myomectomies. The operative procedures we performed were LASH, TLH and single or multiple myomectomy. Their percentages are 51.7%, 17.9% and 30.6%, respectively.

Type of Operation	Conventional LSK procedures			Robot-assisted procedures			Total
	LASH	TLH	Myomectomy	LASH	TLH	Myomectomy	
n patients underwent power morcellation %	227 *47.9%*	47 *9.7%*	81 *16.9%*	20 *3.8%*	40 *8.2%*	66 *13.7%*	471 *100%*
Unexpected malignancy	3	0	0	0	0	0	3

Table 9: Analysis of the surgical procedures.
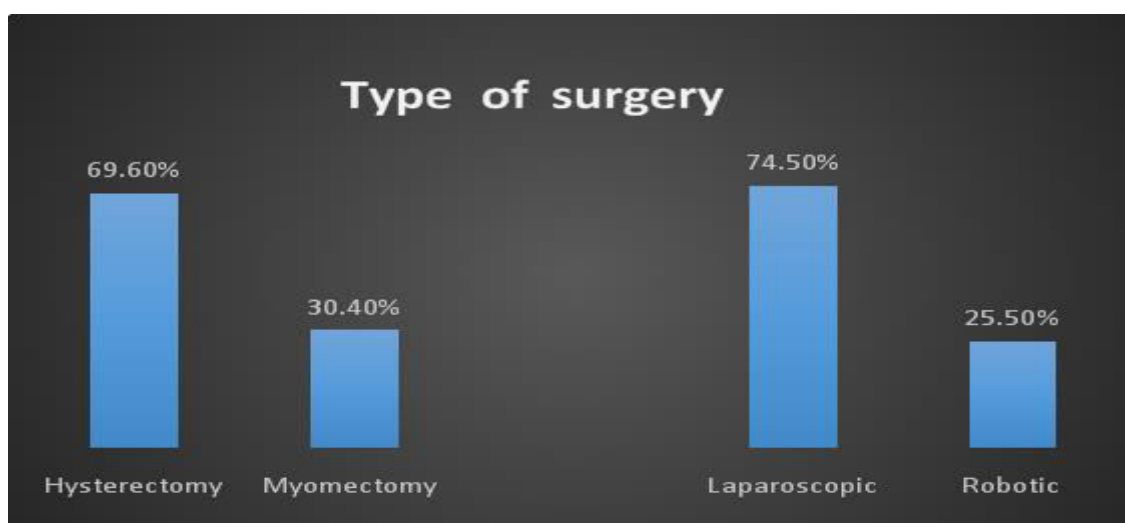
Fig. 12: Diagram of the types of surgery.

IV. 3. Surgical indications

In our research the most common indication for these operations were symptomatic myomas with 91.4%. Analytically, bleeding disorders by myomas were found in 40.8%, chronic pain, dysmenorrhea or suspicion of adenomyosis in 23.2%, documented growth in 21.7%, infertility in 4.6% and ischemia or necrosis of uterine myomas in 1.2%. Benign, simple hyperplasia of the endometrium confirmed by D&C could be found in 1.0% of the patients, and symptomatic pelvic organ prolapse combined with descensus surgery in 4.9% of them (such as laparoscopic sacrocolpopexy after LASH).

Indications for TLH, LASH, myomectomy	n patients underwent power morcellation	%
Bleeding disorders by uterine myomas	192	40.8
Chronic pain by myomas, dysmenorrhea or suspicion of adenomyosis	109	23.2
Suspected myomas with documented growth	102	21.7
Infertility and uterine myomas	22	4.6
Benign, simple hyperplasia of the endometrium confirmed by D&C	5	1.0
Symptomatic pelvic organ prolapse, combination with descensus surgery	23	4.9
Ischemia or necrosis of myomas	6	1.2
Other cases that cannot be categorized	12	2.6

Table 10: Presentation of the distribution surgical indication.

IV. 4. Subgroup analysis

The percentages of unexpected malignancy for the low risk sub-group for women (in reproductive age) under 45 years old was 0% and for the high risk group 1.37%. As it seems from the subgroup analysis, the risk is depending on age of the patients. There was no case of unexpected sarcoma for patients under 45 years old.

Risk sub-groups	n patients underwent power morcellation	Unexpected malignancy
Under 45 years old (low-risk)	253	0 (0%)
Over 45 years old (high-risk)	218	3 (1.37%)
All patients	471	3 (0.63%)

Table 11. Risk sub-groups analysis.

In the following we analyse these three cases by mentioning the medical history, the preoperative examinations, the intraoperative findings, the histological outcome, the treatment after dissemination and the clinical follow-up.

IV. 5. Case I (patient born on 20.12.1945)

The first patient was operated at the age of 66 years, in 2011. Her height was 165cm and her weight was 73 kilograms (BMI: 26.8 kg/m^2). We should also point out that she was a 5 gravida, 5 para, and she had 5 vaginal deliveries. She was

postmenopausal since the age of 46 years. The patient did not have any hormone replacement therapy. Furthermore, the gynecological medical check-up including cancer smear test took place in 2011, with an inconspicuous PAP test result. Mammography has not been done.

The patient had urge urinary incontinence (grade 3) and lower abdominal pain because of an assumed myoma which was located on the fundus of the uterus. This was the reason why the decision for surgical therapy was made. The enlargement of the assumed myoma, which was documented by her gynecologist, was pointed out as an important reason to operate.

Moreover, in the preoperative examination (Fig. 13 and 14) the uterus was 8.3 cm of length in sagittal orientation. The endometrium and the ovaries were completely normal. Additionally, no fluid accumulation in the pouch of Douglas was detected.
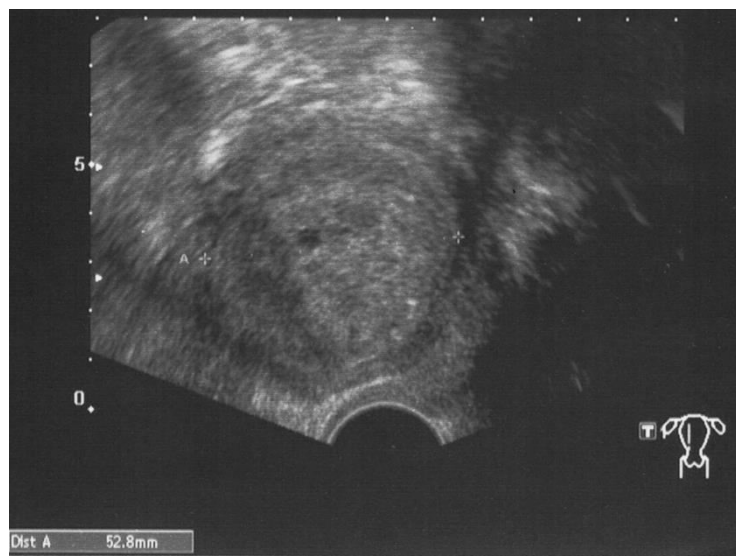
Fig. 13: Transvaginal ultrasound with size of the uterine mass in transversal orientation.

Toshiba Aplio ultrasound machine using 12-MHz probe. (Toshiba Medical System, Tokyo, Japan)

The assumed myoma was intramural, detected on the fundus of the uterus, and its size has grown to 5.3 cm. In the ultrasound examination neither signs of necrosis nor increased or intensified vascularization were presented.
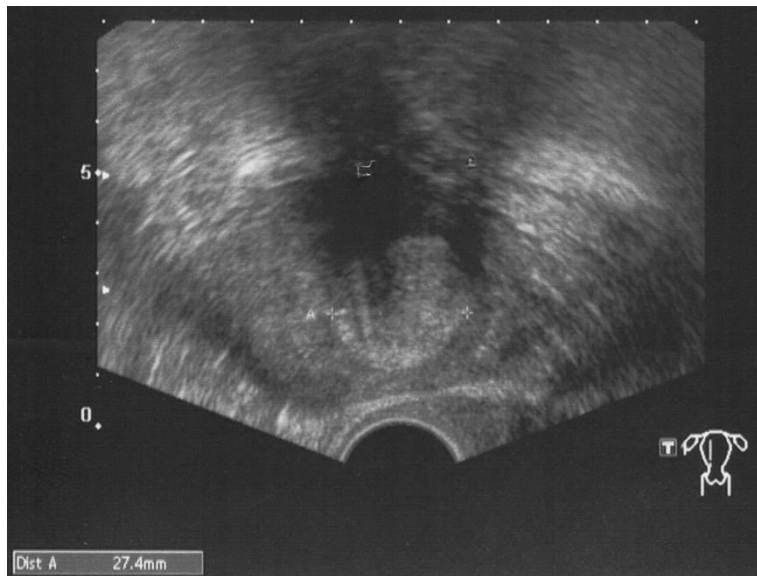
Fig. 14: Transvaginal Ultrasound with size of the uterine mass in transversal orientation.

The growth of the assumed myoma was the only suspicious sign for the possible appearance of malignant tumor. Prior to the operation D&C was not accomplished due to lack of postmenopausal bleeding and suspect endometrium. According to the patient's history, she didn't have any previous operation. To add, the patient had heart attacks in 1991 and 2001, and she suffers from pulmonary heart disease. Furthermore, she suffers from diabetes mellitus type II. According to the family history, there was no occurrence of gynecological malignomas. On 26th February 2011 the patient underwent a LASH. This type of surgery was indicated because of patient's wish after informed consent. During the surgery there was no suspicion of malignancy, and this is the reason why intraoperative frozen section has not been carried out (Fig. 15 and 16).
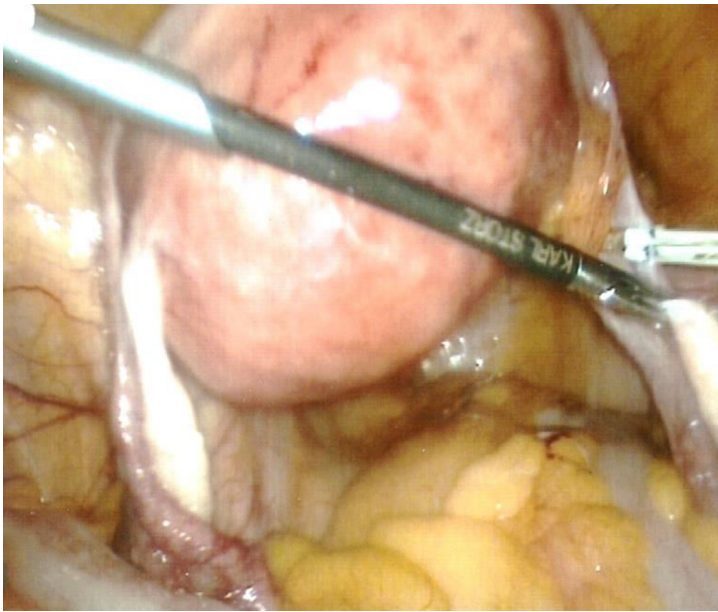
Fig. 15: Initial image of the uterus in the beginning of the operation; it shows inconspicuous uterus, peritoneum and adnexe.
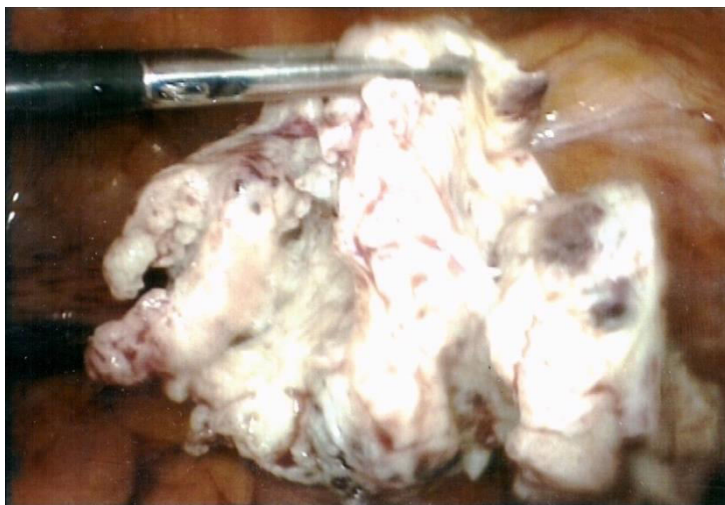
Fig. 16: Intraoperative image of morcellation of the uterine corpus with the Storz Rotocut® system.

The histological assessment showed a moderately differentiated leiomyosarcoma (G2, intermediate grade) of the uterus. The weight of the uterine corpus was 158 gr. After the operation she was transferred to the gynecological ward and stayed there for eight days, in order to start the staging classification of leiomyosarcoma.

The examinations that were performed after information about the histological assessment were CT of the abdomen and pelvis and chest X-ray. The results were unremarkable. There wasn't detected any other signs, i.e metastasis or distant manifestations of the sarcoma. The postoperative stay was completely normal without any complications.

In order to complete the surgical staging a reoperation with midline incision laparotomy followed on 29th March 2011. The open surgical procedure (laparotomy) contained removal of the cervical stump, infragastric omentectomy, retrieval of fluid in the pouch of Douglas for cytological examination, multiple peritoneal biopsies, colon sigmoid/ascending biopsies and bilateral salpingo-oophorectomy. The operation was performed without any complications. No dissemination of the sarcoma was observed during the operation. After the operation she was tranfered to the gynecological ward and stayed there for twelve days. The reason for such a long stay in the hospital was a urinary tract infection (UTI) she had, treated with antibiotics.

After discussing all the parameters of this case with the medical partners in our standard weekly oncology council, we concluded that adjuvant therapy would not be necessary respectively appropriate because there was no sign of dissemination or metastases. Only short-term follow-up examinations should be done according to the guidelines of the treatment after gynecological malignancies.

Furthermore, the patient was hospitalized for ileitis of indefinite origin in September 2011. During her stay in the hospital the following examinations took place: CT of the abdomen, chest X-ray, abdominal ultrasound, colonoscopy and gastroscopy with biopsies. Additionally, there wasn't anything unusual referring to the results either any sign of metastases. Moreover, ten days after receiving antibiotics the patient was discharged from the hospital.

A few months later, in November, she was again hospitalized, this time with pancreatitis. The following examinations have been done throughout the patient's stay in the hospital: chest X-ray, abdominal ultrasound, gastroscopy and CT of the abdomen. Again, the examinations didn't show anything unusual either any sign of metastases.

Furthermore, the patient was hospitalized a few months later due to abdominal pain and there was a clinical suspicion of coprostasis. Additionally, abdominal ultrasound, colonoscopy and gastroscopy with biopsies have been done, and the results were completely normal. Laxative therapy was required, and after that the patient was discharged from the hospital.

Moreover, in April 2014 the patient came urgently to the hospital with troponin positive coronary syndrome. Following, a heart catheterization was used to exclude the coronary heart disease. Additionally, chest X-ray, X-ray and ultrasound of the abdomen had followed without noticing anything abnormal. After appropriate cardiological treatment the patient was released from the hospital.

The patient was undergoing regular examinations by her gynecologist every 3 months, including MRI of the abdomen. 63 months after initial diagnosis of leiomyosarcoma a MRT examination (Fig. 17 and 18) showed an increase of a solid tumor mass of 9.2 x 8 cm at the right side of the lower abdomen with also pathological inguinal lymph node at the left side. Due to an important suspicion of recurrence the patient was referred to our department for further treatment.
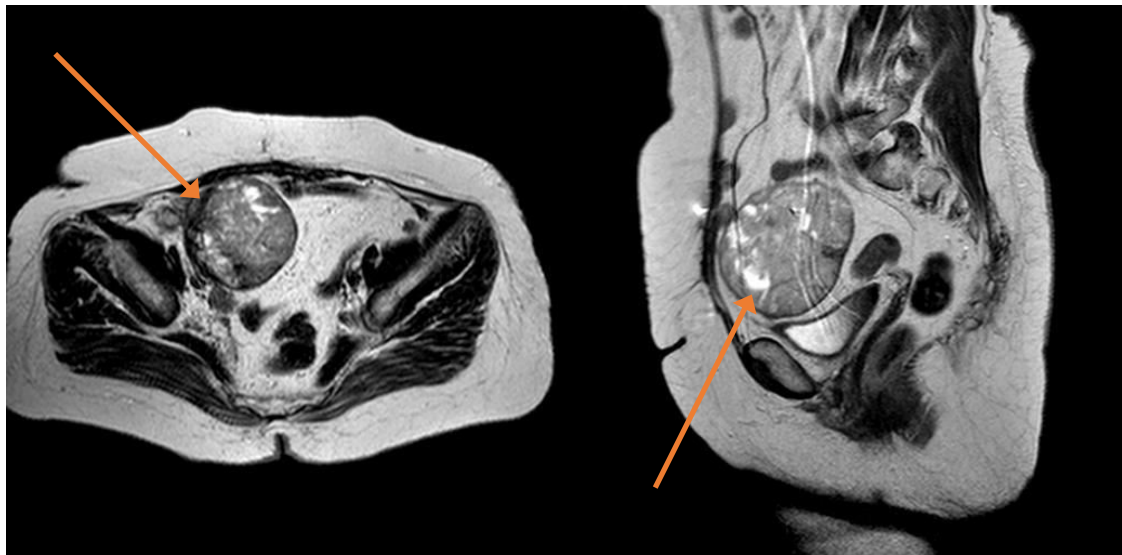
Fig. 17: MRI of the abdomen with a solid mass suspect of recurrence 9.2 x 8 cm at the right side of the lower abdomen (marked by orange arrows) 63 months after initial diagnosis of leiomyosarcoma (sagittal and axial abdomen slice view).
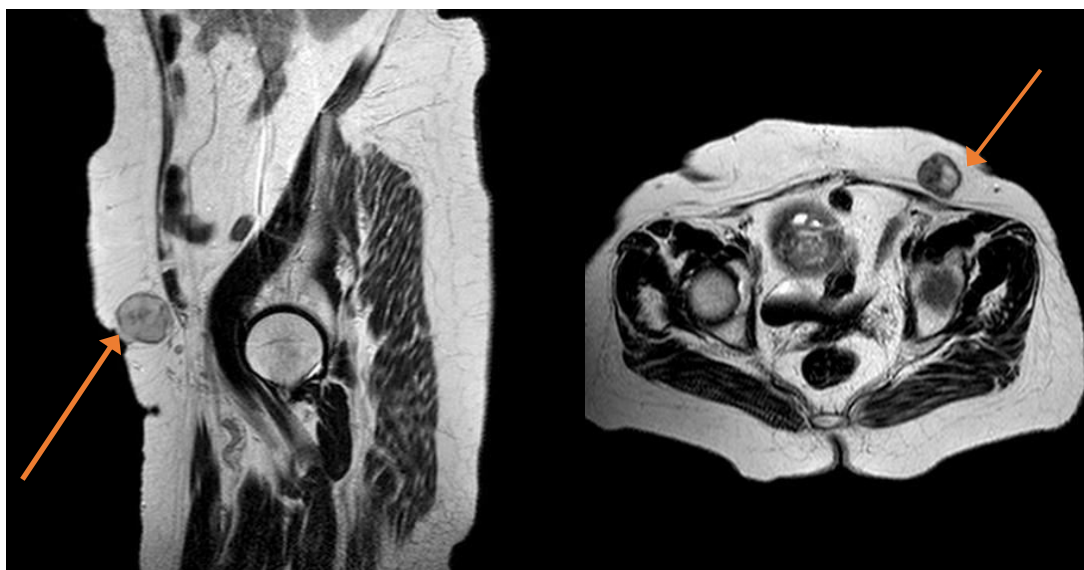
Fig. 18: MRI of the abdomen with tumor recurrence at the old trocar incisions (marked by orange arrows), mistakenly diagnosed intraperitoneal as inguinal lymph node metastasis.

In order to complete the tumor staging we proceeded to CT scan of the thorax but the results didn't reveal any further metastases. It revealed enlarged mediastinal lymph nodes which were unchanged compared to the previous examination from 03/2016 without suspicion of pulmonary metastases. The tumor marker CEA in blood was unsuspicious (0.6 µg/l). Due to the staging diagnosis the spreading of tumor was thought to be operable with good chance to succeed a complete resection, so it has been decided to perform a re-laparotomy.

The operation included resection of the tumor in the lower right abdomen, in the small pelvis and in the abdominal wall (at the area of the trocars incision on both sides, Fig. 19), appendectomy and biopsies from the omentum, mesentery (Fig. 20) and peritoneum. The resection of all tumors could be made without complications. Complete macroscopic tumor resection could be achieved.
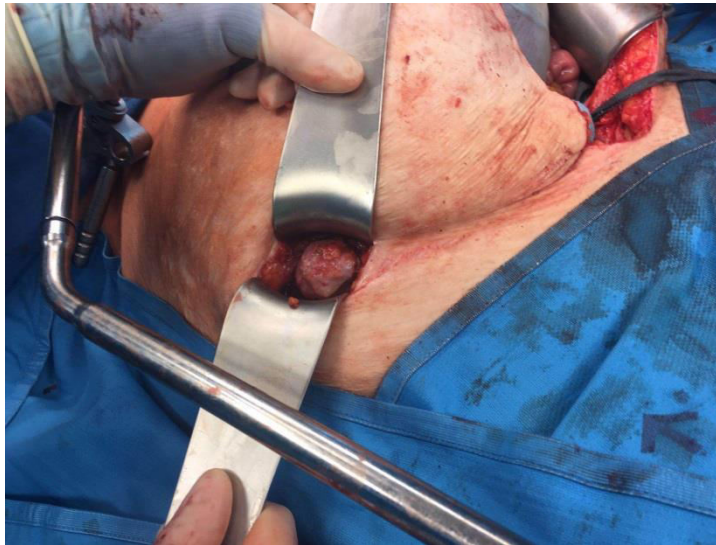
Fig. 19: Intraoperative image of dissemination of the leiomyosarcoma in the area of an old trocar incision. Here, a tumor knot of 3 cm size in the field of the right lower abdomen.
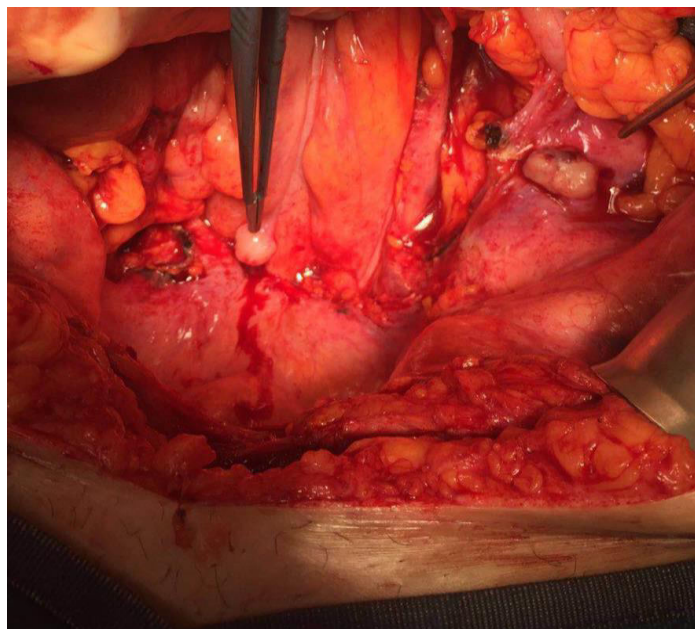
Fig. 20: Intraoperative image of dissemination of the known leiomyosarcoma in the mesenteric area.

The histological results showed a 9 x 9 cm metastasis at the right side of the lower abdomen with a well to moderately differentiated tumor grade (G1-2) metastasis from the previous diagnosed leiomyosarcoma in 2011.

Furthermore, the biopsies from the mesentery (1.5 cm), left and right abdominal wall (3.5 cm and 4.5 cm respectively), bedding tissue of the sigma (1.5 cm), and from the left pelvis wall (2.3 cm) were metastases from the pre-diagnosed leiomyosarcoma, as well. On the other hand, the biopsies from the skin, muscular fascia, sigma mesenterium, the infundibulopelvic ligament, the vermicular appendix, biopsies from the right peritoneum, the omentum majus, and Douglas fluid revealed no tumor cells. In summary, metastases were found from the pre-diagnosed leiomyosarcoma in both sides of the abdominal wall in the area where the trocars during the first operation were situated in 2011, in the right side of the small pelvis and a small metastasis at the mesenterium, left side of the pelvic wall and bedding tissue of the sigma.

 After discussing all the issues of this case with the medical partners at our standard weekly oncological conference, we concluded that adjuvant therapy would not be required because of well to moderately differentiated (G1-2) tumor grade and the macroscopic complete tumor resection. Additional reasons not to apply chemotherapy were at first that the recurrence is presented after a long time and at second the low response of leiomyosarcoma to chemotherapy. We could release the patient in good general health condition.

Furthermore, the patient was undergoing regular examinations by her gynecologist every 3 months, including CT of the abdomen once a year. After 7 months of follow-up there was no evidence of a further recurrence.

IV. 6. Case II (patient born on 09.07.1961)

The second patient was operated at the age of 51 years, in 2013. Her height was 180 cm and her weight 80 kilograms (BMI: 24.6 kg/m^2). We should also point out that she had never been pregnant, she was premenopausal, and her menstruation was abnormal (hypermenorrhea). The patient was not taking any hormone therapy. Furthermore, the last preventive gynecological checkup took place in March 2013,

with an inconspicuous PAP II test result. The last mammography was done 3 years ago. The patient did not have any unusual pain, and the reason why she was referred to surgical treatment was the abnormal bleeding (hypermenorrhea) and the enlargement of the pre-diagnosed assumed myoma. The enlargement of this mass, was documented by her gynecologist from 5.5 cm at July 2012 to 7.8 cm in 2013 (this was pointed as an additional reason to operate).

Moreover, in the preoperative examination the uterus was 9.9 cm in sagittal diameter. The endometrium was normal (0.9 cm), and the ovaries were completely unremarkable. Prior to the operation D&C was not accomplished because of unsuspicious endometrium. Additionally, fluid in the pouch of Douglas was not detected. The assumed myoma was intramural, detected on the fundus of the uterus, and its size has grown to 7.8 x 7.1 cm. In the ultrasound examination (Fig. 21) neither signs of necrosis nor increased vascularisation were observed.
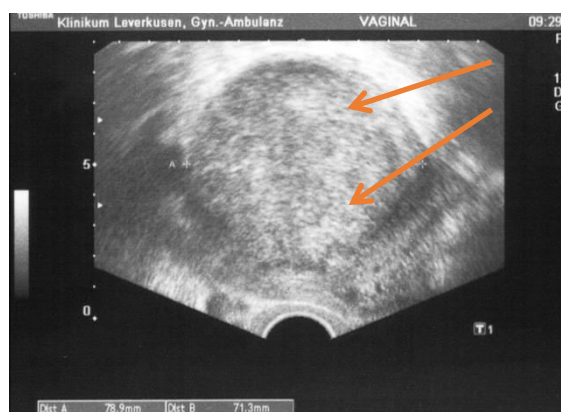
Fig. 21:
Transvaginal Ultrasound with presentation of the sarcoma from different orientations. Inhomogeneous appearance with mainly hyperechoic segments (orange arrows) which are atypical for myomas.
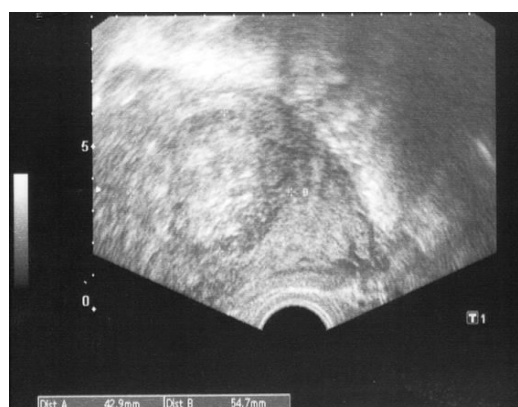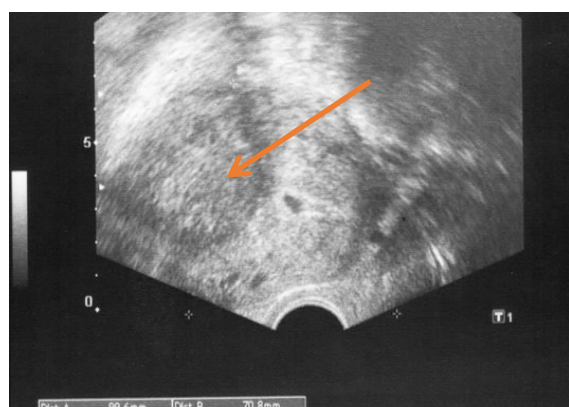
The growth dynamic of the assumed myoma and the sonographic atypical morphology for a myoma (inhomogeneous appearance with mainly hyperechoic sections) were, retrospectively, the only suspicious signs for the appearance a malignant tumor.

Regarding to the history of the patients, she didn't have any previous operation. To add, the patient was completely healthy, and she did not take any medication. According to the family history, her mother had bowel cancer, her father arteriosclerosis, and remarkably her older sister was diagnosed with sarcoma of the left breast one year before.

On 25th March 2013 the patient underwent a LASH procedure. During the surgery (Fig. 22) the appearance of malignancy was not recognized and this is the reason why intraoperative biopsy for frozen section did not take place. The marcoscopic appearance of myomas during power morcellation is very heterogeneous (due to different age of myomas, areas of recent and former necrosis, regions of calcifications) thus it is very difficult to attain a reliable clinical differential diagnosis of myomas versus sarcomas intraoperatively.
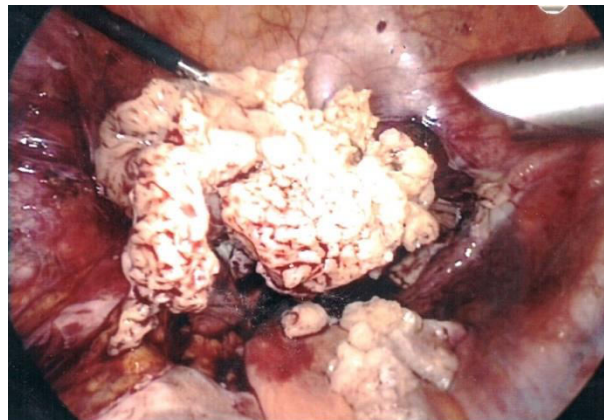
Fig. 22: Intraoperative morcellation aspect of the uterus (Rotocut ® system).

The histological evaluation showed well differentiated uterine leiomyosarcoma (G1, low grade). The weight of the uterine corpus was 375 gr.

Postoperatively she was transferred to the gynecological ward and stayed there for nine days in order to perform staging examinations after diagnosis of leiomyosarcoma. The postoperative stay was completely normal without any complications. After a few days she was hospitalized again for the purpose of completion the clinical staging. The examinations, which were performed, were MRI abdomen-pelvis and chest X-ray thorax. The results were inconspicious. There were no additional tumor manifestations detected.

With the intention to complete the surgical staging a re-operation with midline incision laparotomy was performed on 22nd April 2013. The open abdominal procedure included removal of the cervical stump, an infragastric omentectomy, retrieval of fluid in the pouch of Douglas for cytological evaluation, peritoneal biopsies, and bilateral salpingo-oophorectomy. The operation was performed without complications. §1§ Postoperatively she was transferred to the gynecological ward. The postoperative stay was completely normal without any complications.

After discussing all the findings of this case on the occasion of the interdisciplinary oncological conference, we concluded that adjuvant therapy would not be necessary because any of signs of metastasis or dissemination of the tumor. Only the close meshed follow-up care should be done according to the guidelines of the treatment after gynecological malignancies.

After 36 months a tumor recurrence appeared a bone metastasis of sternum but without any evidence for intraabdominal relapse. The patient was referred to an oncological department for further treatment, but until December 2016 she had refused any further treatment (selective radiotherapy). Further oncological treatment and care was done in external institution.

After 42 months of follow-up there has been observed no evidence of intraabdominal recurrence and the patient was in a good general condition (ECOG: 0), except a prominent sternal tumor.

IV. 7. Case III (patient born on 22.02.1962)

The third patient was operated at the age of 52 years, in 2014. Her height was 178 cm, and her weight was 67 kilograms (BMI: 21.5 kg/m^2). We should also point out that she had never been pregnant, she did not have bleeding disorders, and she was premenopausal. Thus, the patient did not take a hormone substitution. Furthermore, the preventive gynecological check up took place in March of 2013, the mammography on 12/2013 and the PAP test on 10/2013, with an inconspicuous result (PAP II). The patient did not have any unusual pain or abnormal bleeding, and the indication for surgical treatment was the enlargement of an assumed myoma which was already detected some years before.

Moreover, in the preoperative examination the uterus was 11.4 cm in sagittal diameter. The endometrium and the ovaries were completely normal. Additionally, minimal fluid in the pouch of Douglas was also detected but it was not remarkable. The assumed myoma was intramural, also it was detected on the posterior wall of the uterus, and its size has grown to 6 cm. Any sonomorphologic signs of necrosis were observed in the ultrasound examination (Fig. 23 and 24). The growth of the assumed myoma and the increased vascularization were suspicious indications of possible existence of a sarcoma retrospectively.
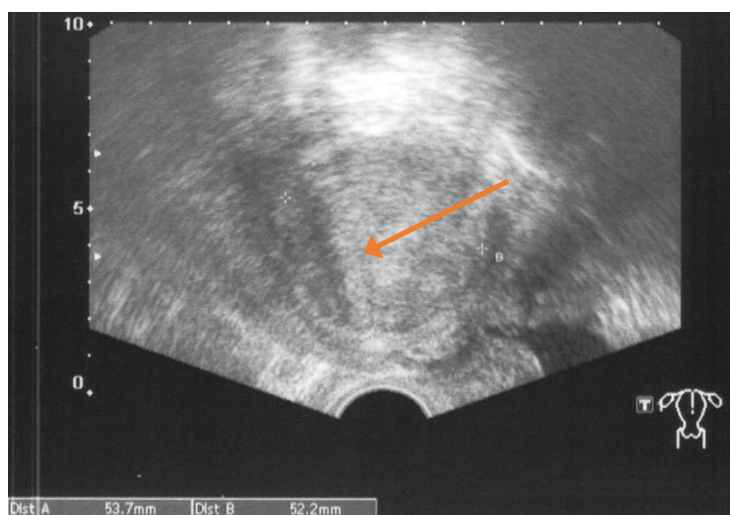
Fig. 23: Transvaginal transverse Ultrasound in sagittal diameter of the fundus of the uterus, measuring the size of the tumor. Inhomogeneous appearance with mainly hyperechoic areas (orange arrows) which are atypical for myomas.
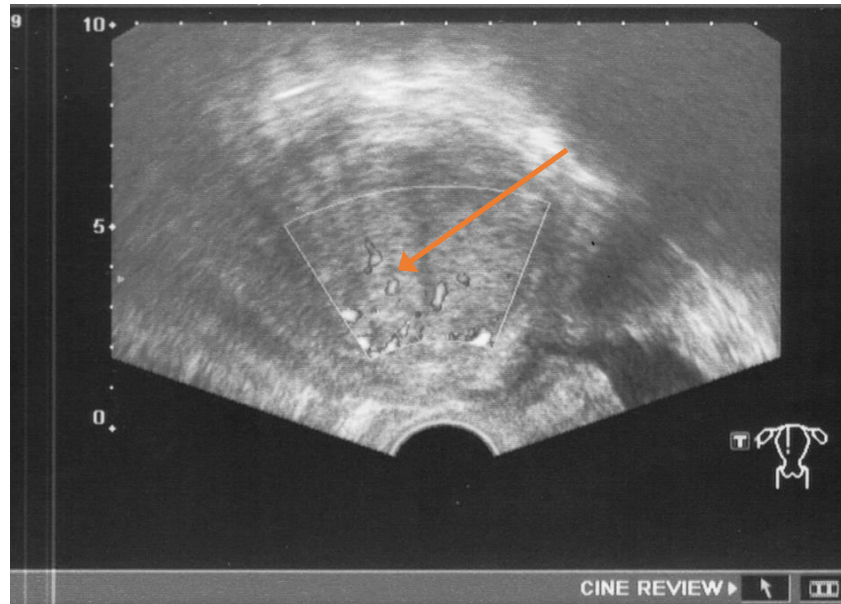
Fig. 24: Transvaginal Color Doppler Ultrasound image shows an increased central vascularization (orange arrow) in the heterogeneous tumor (transversal orientation of the ultrasound probe).

Preoperative D&C was not accomplished because of absence of bleeding disordes bleeding and suspect endometrium. Relating to the patient's history, she only had one laparoscopic ovarian cyst removal. To add, the patient was completely healthy, and she did not take any medication. In question of family history, her mother suffered from breast cancer at the age of 56 years. Prior to the operation we discussed about intraoperative biopsy, i.e. frozen section, if required.

On 22nd April 2014 the patient underwent a LASH procedure with bilateral prophylactic salpingectomy and adhesiolysis. During the surgery (Fig. 25 and 26) there was no macroscopic suspicion of malignancy, and this is the reason why intraoperative frozen section did not take place. The operation time was 86 min.
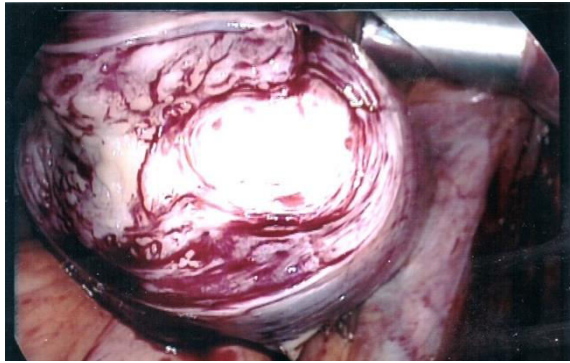
Fig. 25:
Intraoperative image during power morcellation with appearance of heterogeneous soft tissue of uterus retrospectively. Rotocut® system.
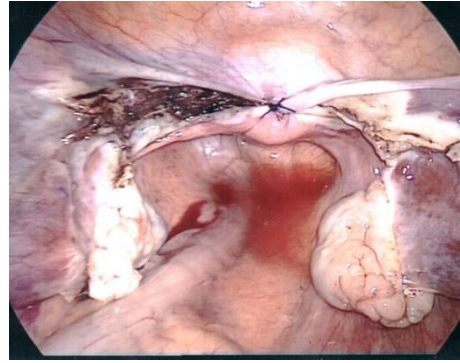
Fig. 26:
Final picture view into the pelvis with remaining ovaries, the cervical stump is covered by peritoneum, the fallopian tubes are removed. The ovaries are unremarkable; the pelvic peritoneum is normal, as well.

The histological evaluation revealed an endometrial stromal sarcoma (ESS). Postoperatively she was transferred to the gynecological ward and stayed there for four days. The postoperative stay was completely normal without any complications.

After diagnosis of ESS the staging examinations were performed: chest X-ray, CT abdomen and pelvis. The patient had these examinations on 30th April 2014. The results were inconspicious, i.e they did not show any signs of dissemination or distant metastatic formations.

With the objective to complete the surgical staging a reoperation with midline incision laparotomy was done on 2nd May 2014. The open abdominal procedure laparotomy operation contained removal of the cervical stump, infragastric omentectomy, retrieval of fluid in the pouch of Douglas for cytological examination, multiple peritoneal biopsies, paracolon fat tissue biopsies, bilateral oophorectomy, and excision of the trocar incisions. The operation was performed without complications. Any dissemination of the sarcoma was observed clinically during the operation. Remarkably, no rest of the morcellated uterus was found. Postoperatively she stayed one day on the intermediate care unit for surveillance. Afterwards she was transferred to the gynecological wand and stayed there for seven more days. The postoperative stay was completely normal without any complications.

After discussing all the results on the occasion of the interdisciplinary oncological conferences, we recommended a hormone therapy with gestagen, and the standardized follow up examinations according to the particular guidelines.

The patient stayed out of the hospital for five days, then she needed a readmission with upper abdominal pain and nausea. After the following examinations, including CT abdomen and pelvis, abdomen-ultrasound, and gastroscopy with biopsies, and in the overall view of examination results a gastritis was diagnosed.

Any evidence for recurrence has been observed after a follow up of 31 months, and the patient was in a good general condition. (ECOG: 0)

IV. 8. Overview of the procedure and facts after diagnosis of morcellated sarcomas

Treatment after dissemination	CT or MRI, chest X-ray	Re-operation with laparotomy	Therapy with hormone/ CTx	"Second look" laparoscopy	Clinical follow up (in months)	Recurrence
Patient I	+	+	-	-	63	+ *intra-peritoneal*
Patient II	+	+	-	-	36	+ *distant (sternal)*
Patient III	+	+	+ *gestagene*	-	31	-

Table 12. Diagnostic and therapeutic procedure after the diagnosis of morcellated sarcomas for all 3 patients and the further clinical follow up with documentation of the recurrence.

IV. 9. Overview of the risk factors of the patients for presence of malignancy

Risk factors	post-meno-pausal	tumor >8 cm	single fibroid	vascula-rization / necrosis	endo-metrium >5 mm	tumor markers / hormone therapy	abnormal bleeding	growth dynamic
Patient I	+	- 5.3cm	-	-	-	-	-	unclear
Patient II	-	- 7.8cm	+	-	+	-	+	unclear
Patient III	-	- 6.0cm	+	+	-	-	-	unclear

Table 13. Presentation of the risk factors of all 3 patients concerning their age, medical history, clinical symptoms, blood examinations and ultrasound findings.

V. Discussion

V. 1. Incidence of unexpected malignancy after EMM in comparison with the literature

The presented data showed that unexpected uterine malignancy existed in 3 to 471 women (0.63%) undergoing morcellation. Due to our subgroup analysis with women in high risk (older than 45 years), the incidence was higher and it was estimated in 3 to 218 women (1.37%). Analytically, one was an endometrial stromal sarcoma and two were leiomyosarcomas (G1 and G2), and all were detected after LASH operations in the age of 51, 52 and 66 years. Due to the small sample size we cannot generally define reliable results. After laparoscopic myomectomies and TLH no unexpected malignancy was observed. This forms a really important issue, as in only few relevant studies myomectomies are included. In this context, a study[111] with 4248 patients who underwent laparoscopic myomectomy displayed that the incidence of unexpected uterine sarcoma seems to be low (0.2%). Only 9 patients were identified with malignancy from which 8 were detected with endometrial stromal sarcoma and only one with leiomyosarcoma. Their histological results are in contrast with the generally approved fact that leiomyosarcoma is the most common type of sarcoma[112] .

In our cohort, 147 myomectomies took place, and no unexpected malignancy was observed. As it is reasonable a reliable conclusion can not be issued, irrespective of the number of cases. Supposing that the incident of leiomyosarcoma in myomectomy is 0.2 %[111] the number of cases would be 500 to detect one leiomysarcoma. However, we recognize the small evidence of our study, as it can show that there is a small risk of malignancy to appear by using EMM in myomectomies. Furthermore, as it seems from our subgroup analysis, the risk is depending on the age of the patients. Browl et al.[174] estimated the age-stratified risk of uterine sarcoma in an metanalysis with 10.120 patients who underwent myomectomy and concluded that it

ranges widely between age groups, from as high as ~1 in 100 for patients aged 75-79 years to <1 in 500 for those aged <30 years. Furthermore, Pados et al.[171] in a study with 1216 patients in reproductive age (18-45 years old) who underwent laparoscopic morcellation of leiomyomas didn't report any unexpected sarcoma or atypical myomas. For patients in reproductive age the risk seems to be low.

V. 2. Statement about laparoscopic myomectomy

Laparoscopic myomectomy seems to be a safe method, and we support the continuation of its use by low risk patients in reproductive age despite the newly general concern. Moreover, laparoscopic myomectomy seems to be very useful in young patients with wish for pregnancy, because the advantages it reveals, such as no large abdominal laparotomy incision, faster healing and recovery from surgery, less postoperative pain, lower risk of surgical site infection, and more rapid return to the usual activities[51], surpass the risk of unexpected malignancy. On the other hand, it is important to mention that Garcia et al.[49] reported that 10% of women undergoing a myomectomy will eventually require hysterectomy within 5 to 10 years. Also, after myomectomy there is a 15% recurrence rate for myomas. Moreover, Nezhat et al.[54] underline that after laparoscopic surgery there is higher risk for myomas to appear again, with a 33% recurrence risk within 27 months. Furthermore, it has been reported that postoperatively in 60% of cases there is adhesion formation[54]. Highlighting, when a myomectomy is done in order to improve the chances of pregnancy, the unexpected malignancy risk is low because of the patients' young age [48].

V. 3. TLH vs LASH and complications during EMM

It should be underlined that mostly in the first occasion (66 years old patient with small uterus, 158 gr) in which LASH technique has been used to reduce the urge urinary incontinence symptoms and down abdominal pain caused by the assumed myoma, we could insist more in the proposal of use of TLH, as there wouldn't be a necessity of EMM. In our hospital, we prefer TLH because both operation, techniques are comparable and almost equal referring to complication rates. The most important issues concerning the complication rates are the skillfulness and experience of the surgeon[113]. Furthermore, the arguments in favor to LASH in young women with frequent sexual activity hasn't been proved yet[114] thus preservation of the cervix referring to advantages of sexual fuction is currently only a hypothetical argument. In the reporting department it is favored to perform even in very large myomas or huge uterus a TLH in order to keep the laparoscopic possibility to enucleate the myomas or to dissect the uterus in few parts, and to retrieve the whole tissue via the vaginal opening, all with the aim to avoid EMM, which is associated with multiple and micro-fragmentation inclusively leaving uterine tissue intraabdominally. It is important to add that the surgeon has to be highly experienced, otherwise the iatrogenic injury risk is increasing. The most frequent and direct complications of power morcellation that literature reports are the injury of the small and large bowel, retroperitoneal vessels in particular the external iliac vessels[62]. Associated operative complications such as pneumonia, thrombosis, and embolism could be reduced with the use of TLH, as there wouldn't be need to undergo morcellation and, thus, the duration of the operation will be shorter. In our hospital we prefer TLH because both operational techniques are comparable and almost equal referring to complication rates. Furthermore, the arguments that women treated with LASH still maintain the sexual activity remain controversial[114].

The patients we operated with use of EMM had no complications during surgery. Afterwards, we observed two cases with postoperative bleeding and two cases of postoperative infection, which were easily handled. Additionally, after EMM was performed, it has been reported in the literature[99,100], endometriosis in patients without prior evidence of endometriosis, peritoneal leiomyomatosis and distance iatrogenic myomas. Donnez et al.[101] observed 1405 cases after LASH operation and found 8 cases (0.57%) of dyspareunia and pelvic pain caused by iatrogenic adenomyomas. Symptoms appeared between 2 and 9 years after surgery. Magnetic resonance imaging with injection of gadolinium contrast medium revealed vascularization of the adenomyomas, and for laparoscopic excision it has been required extensive dissection of the rectum and pararectal fossa. Although our histologic results of 59 patients who underwent hysterectomy with EMM showed adenomyosis, we didn't analyse the long term complications of benign results.

V. 5. Warning from FDA and further studies

After the warning of the FDA (specification of 1 in 350 with unexpected malignancy) against using laparoscopic power morcellators many studies with diverse results were published[65]. Seidman et al.[90] reviewed 1091 uterine morcellations, and they pointed out that 1.2% of operated women had been diagnosed with leiomyoma variants or atypical and malignant smooth muscle tumors. Analytically, there were one endometrial stromal sarcoma (ESS), one cellular leiomyoma (CL), six atypical leiomyomas (AL), three smooth muscle tumor of uncertain malignant potential (STUMPs) and one leiomyosarcoma (LMS). For the majority of women diagnosed with uterine sarcoma, the treating gynecologists are only able to notify these cases on the basis of final histopathologic results, and not during the presumed benign uterine myoma

surgery. Jasmine Tan-Kim[89] from Kaiser Permanente San Diego, California, and colleagues undertook a retrospective review of women who underwent laparoscopic hysterectomy with power morcellation. Analytically, their medical research included 3523 women, and so they had a large series of laparoscopic hysterectomies. They pointed out that 941 from 3523 women had hysterectomy with the use of a power morcellator and 0.6% of them were diagnosed with uterine sarcoma. Moreover, three of the 0.6% during the initial pathology review were diagnosed with uterine sarcoma, and another three were diagnosed with uterine sarcoma after 2 to 7 years indicating a considerable false negative note of histological results. Moreover, any cervical or endometrial cancer was found in the examined cases. A study[92] that concentrated on LASH with unexpected malignances included 1584 patients, from whom only 0.25% (4 patients) were diagnosed for malignancy after the operation. Analytically, two of the four patients had leiomyosarcoma and the other two had endometrial cancer. 87.8% of the patients received a preoperative screening with Pap test, ultrasound and D&C. By comparing our outcomes with the literature, it has to be stated in our data that the likelihood for unexpected malignancy after power morcellation is slightly higher (0.63%). As we mentioned before, the results for unexpected malignancies after power morcellation have a wide range, which proves the necessity for more studies in purpose of better understanding the dangers of morcellation, and to identify the specific risk factors for unexpected malignomas.

V. 5. Risk factors analysis for unexpected uterine sarcomas and comparison with the literature

Risk factors for uterine sarcoma have been analyzed in some studies[102, 75, 23]. Groups with a high risk to develop uterine sarcoma are blacks (Afro-Americans)[17], people being extensively exposed to X-rays, people who underwent radiation therapy to the pelvis in the past[18], and people who

received treatment with tamoxifen for breast cancer [19, 116]. The histories of the three patients in our analysis with unexpected malignancy we described above didn't include any of these risk factors. The level of evidence for the risk factors in our study do not allow us to give specific recommendations for the early detection of sarcoma; anywise this was not the aim of our study, due to the limitation of the case number (two LMS and one ESS), and the generally low incidence of uterine sarcomas. Most of our patients had received a preoperative screening with Pap test, ultrasound and D&C only where it was indicated. On the other hand, in the three cases with unexpected malignancy D&C was not performed, as we supposed we couldn't detect these types of malignancy with this method, because the sarcomas were intramural with any relation to the endometrium cavity. It has been mentioned that D&C is not supposed to be the appropriate examination to diagnose and to exclude or to prove the existence of malignancies except in case of concomitant operative hysteroscopy with the possibility of deep myometrial biopsy. In a study with 730 patients, who underwent preoperative endometrial sampling, Bansal et al.[75] concluded that endometrial sampling has a significantly lower predictive value in diagnosis of uterine sarcomas compared to epithelial uterine malignancies. Analytically, 36% of sarcomas and 19% of endometrium cancer could be misdiagnosed. Moreover, Theben et al.[92] showed that despite the good results of preoperative screening there is a small probability of unexpected malignancies. In her study, most of the patients (87.8%) received preoperative screening, which includes cytology (PAP-smear), ultrasound and D&C. Indications that include postmenopausal or abnormal bleeding, rapid growth of the assumed myoma with abdominal enlargement and pelvic discomfort, pain or abdominal bloating could be suspicious for sarcoma [20, 85].

From the three patients who where detected with unexpected malignancy in our data only one was postmenopausal. The risk factors of the first patient were her age (66 years old) and the growth of the assumed myomas. She had two myomas, both with size smaller than 8 cm, which has been reported

in the literature as cut-of for suspicion of sarcoma. Furthermore, tumor markers (CA 125, CEA, CA 15-3) and the endometrium were completely normal, and no uterine bleeding was observed. In all three cases there was no suspect of necrotic areas in the assumed myomas, and in one an increased vascularization was described, anyway, these two diagnostic parameters do not constitute a sufficient suspicion for uterine sarcoma[85]. The two other patients were premenopausal, and only one of them had uterine bleeding with increased endometrial thickening. In our study rapid increase of size within some months was not observed. On the other hand, rapid increase has been reported in other case reports of LMS. Rapid increase may also occur in histopathological proven myomas, and as a hint in some case reports it is still not representative[69, 70]. Moreover, it has been said that regular cycle anamnesis and homogeneity of the endometrium layer are important parameters for the detection of sarcomas in premenopausal women[117]. As we see, the patients' data were not very suspicious for malignancy, without having many risk factors. Due to the review[173] of the DGGG for the risk of occult sarcoma and problems of morcellation there are no clear criteria to evaluate suspicious findings detected during preoperative examination. Patient history, vaginal ultrasound examination and preoperative PAP-test or curettage of abnormalities could be useful, but these methods cannot exclude the possibility of sarcoma. More research and new methods of diagnostic are needed to develop reliable preoperative diagnosis of uterine sarcomas and to clarify the specific risk factors.

V. 6. Is a preoperative diagnosis of uterine sarcoma possible?

Nowadays, there are still no pathognomonic features predicting a LMS by imaging techniques with high specificity but only potential characteristics[67, 68]. To outline the range and to assess the tissue morphology of an assumed leiomyoma it is preferable to use MRI and not CT scan[76,118]. However, the

characteristics that arouse suspicion of LMS on MRI such as central necrosis, tissue signal heterogeneity, and ill-defined margins are characteristics that can be similarly related with benign degenerating uterine myomas. The same dilemma exists with ultrasound examination. Nevertheless, the evaluation of tumor extension in and around the uterus, and the segregation between leiomyoma and LMS may be assisted by MRI method and particularly by the T2-weighted sequences[77, 78].

Serum measurement of lactate dehydrogenase (LDH) isozymes (total LDH and LDH isozyme type 3) and dynamic MRI (contrast enhancement after administration of Gadolinium-DTPA) could help in the differential diagnosis of leiomyosarcoma. This was a prospective study[79] enrolling 298 patients with 100% diagnostic accuracy, but without any published confirmatory studies and with only comparing 10 LMS versus degenerating leiomyoma.

Positron emission tomography (PET) is also a way to diagnose assumed myomas along with molecules and especially fluodeoxyglucose (FDG) or alphafluorobeta-estradiol (FES). Zwang et al.[80] reported two cases of uterine leiomyosarcoma that presented with pulmonary metastases and unknown primary tumor. The primary malignancy was diagnosed by using FDG-PET-CT. Moreover, Yoshida et al.[81] reported in a study with 76 patients that FES-PET-CT may be more reliable in distinguishing LMS from myomas than FDG-PET-CT. The accuracy of the first one was 93%, and of the second one 81%. In another study[82], a comparison between FDG-PET, PowerDoppler and dynamic MRI for the preoperative diagnosis of uterine sarcoma in five patients with postoperative histopathologic confirmation of sarcoma, showed that FDG-PET had the best results. Analytically, FDG-PET examinations were 100% positive for the five sarcomas, PowerDoppler 80% positive (four of five cases) and dynamic MRI 40% positive (two of five cases). The review[173] of DGGG categorized CT, MRI or PET/CT as useful imaging technics in high risk patients for malignancy, but noticed that they also cannot rule out the presence of uterine sarcoma in every patient.

Furthermore, in the literature it is reported that serum CA-125 is increased in patients who suffer from LMS but mostly in advanced-staged LMS[70]. In our study CA-125 was not effective as tumor marker. Clinical use of CA-125 is limited because there is increased serum level mostly in advanced-staged LMSs, and rarely in early-stage uterine LMSs[83]. Until now, recommended preoperative studies include imaging examinations such as MRI or ultrasound, endometrial biopsy in cases with abnormal uterine bleeding, and cervical cytology[86].

V. 7. Update on treatment of uterine sarcoma after dissemination

Surgery remains the mainstay of treatment because effective adjuvant therapy to prolong survival has not yet been established. Adjuvant pelvic radiotherapy may improve local tumour control in high risk patients, but is not associated with an overall survival benefit. Similarly there is no good evidence for the routine use of adjuvant chemotherapy. Alternative approaches such as molecularly targeted therapies have not been explored[119]. Staging and treatment of the patients with morcellated leiomyosarcoma or endometrial stromal sarcoma in our study was staging with MRI or CT abdomen examination, chest X-ray, and re-operation with laparotomy contained removal of cervical stump, infragastric omentectomy, cytology from fluid in the pouch of Douglas, multiple peritoneal biopsies, bilateral salpingo-oophorectomy, lavage and maybe colon sigmoid-ascending biopsies. The recommendation[173] of the DGGG regarding the treatment of accidental uterine LMS is that a secondary open operation should be performed in a certified oncological institution and must include careful inspection of the entire abdomen due to the current oncological standards. A lymph node dissection was not performed because there was no suspicion of metastases. Anyway, in early stage of uterine leiomyosarcoma adnexal and

lymph node involvement is present in only 3% of the cases[120]. The staging examinations and laparotomy did not achieve any upgrade of tumor stages in our cases. However, two of the three patients showed recurrence after 63 months and after 36 months. The first patient revealed intraperitoneal recurrence which could be reached with a third operation where complete resection could be achieved. It is important to mention that signs of dissemination due to EMM were observed during the third operation with metastasis of the known leiomyosarcoma in both sides of the abdominal wall in the area where the trocars of the first operation in 2011 were situated, at the right side of the small pelvis and small metastases at the mesenteric, left side of the pelvic wall and bedding tissue of the sigma. It could be considered more favourable that the recurrence appeared after 63 months, which is a long duration and more than the estimated average disease free survival rate after leiomyosarcoma. The second patient presented a sternal metastasis. Until the completion of the analysis of this study all the patients were alive. The 5-years overall survival can be examined in only one case (case I) from 2011, who is alive 70 months after the diagnosis of LMS. The other two cases from March 2013 and April 2014 had a follow up 42 (case II) and 31 (case III) months after the operation. As a result, it is not ordinary to compare our results with these of other studies. Anyhow, the small number of patients does not allow any definite statements. Analysis of the literature data follows below. Concerning the sternal metastasis in one patient (case II) after 36 months it is supposed that it is not associated with the morcellation of the tumor rather than hematogenous dissemination, but for such a rare oncological case it is not completely clear, and a hematogenous metastasis as a result of morcellation cannot be excluded whereas, a least, a simultaneous peritoneal recurrence would be supposed. This is an interesting issue and demands further studies.

The oncological council of the reporting hospital concluded that adjuvant therapy would not be necessary for any of them because no signs of distant metastasis were revealed. Likewise, in the case of intraabdominal recurrence

adjuvant therapy was not necessary because of well to moderately differentiated (G1-2) tumor grade, and the macroscopic tumor free resection state. Only in the third case, where the tumor was an endometrial stromal sarcoma, we proposed the administration of hormone therapy with gestagen. In the literature it is pointed out that hormonal therapy appears to be helpful in cases of ESS[121]. Spano et al.[122] reported two cases of premenopausal women with ESS, who developed pulmonary metastases some years after initial treatment with hysterectomy. Under aromatase inhibitor therapy, both patients achieved a complete response, and they remain disease free with 14 and 7 years of follow-up. Although ESS is often sensitive to hormones, routine bilateral oophorectomy is not established as standard therapy. Moreover, referring to patients with ESS, lymph node dissection and ovarian preservation do not appear to have any effect on their overall survival[123]. In case of diagnosis of extrauterine disease of the uterine sarcoma, radiotherapy and chemotherapy are likely to be used after the operation. These patients are rather candidates for chemotherapy, and regarding to radiotherapy it is questionable if it is advantageous or not, despite reports that mention its usefulness[119]. A retrospective study of 182 patients, who were treated or not with adjuvant radiotherapy after surgery for uterine sarcoma, demonstrated an improved 2 and 5 years' local regional relapse-free survival for the patients treated with adjuvant radiotherapy (83.4% vs 70.3%; 78% vs 55.3%; p=0.013), especially those patients with leiomyosarcoma. The overall survival was longer for the patient group treated with adjuvant radiotherapy but without significant differences to the other one. Importantly, the subgroup of patients with leiomyosarcoma had a significant longer overall survival after adjuvant radiotherapy[124]. Moreover, combination of chemotherapy and radiotherapy is not examined thoroughly yet, however it is frequently applied in these cases[125]. Furthermore, other studies also reported that adjuvant pelvic radiotherapy for stage I of uterine sarcoma enhance the pelvic control of the disease but do not improve the overall

survival[126]. Further studies are needed to precise standardized recommendations for adjuvant first line or palliative treatment.

V. 8. Prognosis after using power morcellation in uterine malignancy

Seidman et al.[90] pointed out that after the surgery with power morcellation some patients with leiomyoma variants or atypical and malignant smooth muscle tumors were examined with follow-up laparoscopy, and the results have showed that in 64.3% of all cases disseminated disease occurred. Furthermore, 3 of 4 patients who were diagnosed with leiomyosarcoma have died with an average survival of 24.3 months. In another study from Oduyebo et al.[91], where also surgical re-exploration was used, it was found that two out of seven (28.5%) and one out of four patients (25%) with presumed stage I uterine LMS and STUMP respectively had to be upstaged. One of them with confirmed early uterine LMS and STUMP at the second surgery had intraperitoneal recurrence, while the other remain disease free. It was recommended to ensure that any potendial residual peritoneal disease has to be removed by realizing another surgery whose finding, could be used for accurate prognostication and contribution to the knowledge of progress of disseminated malignancy by EMM. Theben et al.[92] pointed out in their study that they treated three of four patients with unexpected malignancy (two uterine LMS, two EC) also with staging laparotomy after a few days and one with staging laparoscopy after 6 months. After 28-52 months of follow-up there was no evidence for recurrence. In a recent study, Serrano et al.[95] reported that after tumor morcellation of uterine LMS the following issues were observed: Firstly, comparing to the removal of uterine LMS by total abdominal hysterectomy (TAH) laparoscopic tumor morcellation had an important increased risk for dissemination of the tumor. Secondly, there is a really high risk of intraabdominal recurrence after the power morcellation and

also the time to recurrence. The same correlation was described by Einstein et al. [94] in a retrospective study. Furthermore, he reveals that there was a significant difference in 5-years survival between women with unexpected leiomyosarcoma who underwent a power morcellation compared with those who did not undergo morcellation. Namely, by using a power morcellator the 5-years survival rate was 46%, and without it was 73%. Furthermore, another very large study [140] with 125 occult uterine sarcomas compared power morcellation, nonpower morcellation, and intact removal of the uterus and revealed that morcellation is associated with decreased early (3-years) survival (54%, 51%, and 19%, respectively) between women with unexpected leiomyosarcoma who underwent morcellation compared with those who didn't undergo morcellation.

Moreover, after morcellation of assumed myoma, final histopathological result showing leiomyosarcoma, a re-operation would be mandatory to detect any tumor dissemination. Referred to Einstein et al.[94], approximately 15% of patients would be upstaged by re-exploration, particularly those with LMS who underwent EMM. Adjuvant chemotherapy would be recommended if tumor spreading is detected. The same results were represented by Park et al.[96] for patients with unexpected early low grade endometrial stromal sarcoma of the uterus who underwent power morcellation consistenly with the above mentioned. These patients had a significant higher rate of recurrence, and significant lower rate of 5-years disease-free survival than patients who underwent abdominal hysterectomy without EMM[96]. Moreover, George et al.[126] showed in a study of 58 patients that the median recurrence-free survival of patients with uterine leiomyosarcoma underwent power morcellation was significantly shorter (10.8 months) in comparison to patients treated with total abdominal hysterectomy (39.6 months). Similar to these findings, in a study including patients with FIGO stage I uterine LMS, 21 of them did not undergo tumor morcellation during surgery and 16 did, the outcome showed that there is significant difference in overall survival and also in disease free survival[128]. Without the use of power morcellation, the 5-

year survival rate for patients with stage I or II disease was pointed with 89.0%, in comparison to 50.3% for those with stage III or IV disease[129]. Consequently, it has to be stated from the literature that the use of power morcellation in unexpected uterine malignancies worsens the survival rate of the patients, while the exigence of complementary surgical staging is essential. The studies presented above are heterogeneous, thus a median prognosis rate for overall survival of patients after using power morcellation by uterine malignancy is difficult to be specified. The statement[173] of DGGG concluded that the intraabdominal morcellation of occult malignancy worsens the prognosis of the patient but precise figures about the extent of the deterioration of prognosis could not be made. Another interesting analysis concerning morcellation and endometrial hyperplasia and endometrial cancer found at time of hysterectomy for prolapse showed that these cases are more frequently (1-2%)[140] than unexpected sarcomas but on the other hand it seems that they don't have the same negative effects as in morcellated sarcoma cases [141,142].

V. 9. Use of alternative techniques to prevent dissemination

Frozen section analysis of suspicious leiomyoma during the operation may decrease the risk for unexpected malignancy and maintain the advantages of minimally invasive techniques. Tulandi et al.[85] presented two cases in which the feasibility of obtaining multiple biopsy specimens of uterine leiomyomas and frozen section could prevent laparoscopic morcellation. However, the reliability of frozen section analysis in detecting myometrial disease is controversial. Moreover, there is a risk for dissemination by the use of frozen section analysis as well, while trying to get tissue from the tumor during the operation. Due to the recommendation[173] of the DGGG, the histopathological evaluation should be done using a formalin-fixed surgical specimen. As far as

we know, there are no studies that can estimate this risk. Furthermore, other methods such as transcervical needle biopsy combined with MRI screening seem to be promising for the differential diagnosis between uterine sarcoma and leiomyoma. Kawamura et al.[130] performed transcervical needle biopsy in 435 patients with uterine myoma-like tumors. Of 435 patients, 7 had uterine sarcoma, 4 of them were diagnosed a sarcoma by needle biopsy alone and for the other 3 patients there was a suspicion. No sarcoma cases were included in the group of patients with totally unsuspicious examination results. However, fine needle aspiration is not recommended as a primary diagnostic modality, although it may be considered for confirming disease recurrence, or nodal metastases[175].

Alternative techniques to avoid peritoneal spreading of the uterine tissue by power morcellation are laparoscopic-assisted minilaparotomy, tissue removal through a vaginal incision and the use of a specialised endoscopic morcellation bag. These methods could minimize the risk of tumor dissemination and meanwhile they preserve the advantages of minimal invasive surgery, at least partially.

A retrospective analysis of 211 women who underwent laparoendoscopic single-site surgery (LESS) revealed that the risk for postoperative umbilical hernia is 2.4 % for all the patients and lower than 0.5 % for patients without significant comorbidities, which means that LESS seams not to increase the risk of hernia[163]. Moreover, some retrospective studies reported that there are no significant differences comparing complications rate and outcome between manual extraction and power morcellation [164, 165, 166]. On the other hand, it has been said that the performance of minilaparotomie is associated with longer operative time compared with power morcellation, both with and without use of containment bags [164, 166]. On the other hand, manual morcellation of the specimen can be done into a specimen bag which could make the extraction easier, especially for smaller specimens[168]. Nevertheless, minilaparotomy seems to be more cost effective compared with EMM.

If colpotomy is used to retrieve the uterus after a supracervical hysterectomy or after a myomectomy, there are limitations such as removal of a large tumor which usually seems to be impossible without fragmentation of the tissue, or runs the risk of higher grade vaginal injury. On the other hand, a report of colpotomy after laparoscopic myomectomy did not notice any increase of dyspareunia, infection or dehiscence[148].

Vaginal morcellation could be done after total laparoscopic hysterectomy with techniques such as coring, myomectomy, bivalving and wedge resection[146]. Wasson et al. reported that the estimated incidence of occult malignancy (including endometrial cancer) for women who undergo vaginal hysterectomy with morcellation at 0.82%, without negative results on prognosis and outcomes[147]. Furthermore, some studies demonstrating improved outcome after manual morcellation of malignant tissue through the vagina compared with power morcellation[154, 155]. Many reports have been published presenting the use of specimen bag after laparoscopic hysterectomy and before the vagina extraction[149, 150]. In most of the cases, the bag is introduced through colpotomy, the specimen is situated inside and then morcellated with one of the vaginal morcellation techniques. However, disruption of the bag was detected in approximately one third of cases by filling it with methylene blue after extraction[151]. We encourage the surgeons to use vaginal morcellation after TLH event by large uterus less than approximately 800 g, offering the opportunity to maintain the minimal invasive character of the operation. With larger uterus it seems that the abdominal approach could be more appropriate. Prospective studies are needed to evaluate the risk of dissemination by vaginal manual morcellation. However, up until now total abdominal hysterectomy is the surgery of choice for patients with suspicion of sarcomas[173]. The goal of surgery is to remove all of the cancer as one piece, with non-preservation of the uterus[106].

A research from Menge et al[131] in 2012 points out that power morcellation should be banned from the market, however supports that endoscopic bag seems to be a really notable technique, by which tumor dissemination and

consecutive tumor upstaging would be avoided. Other publications also underlined that the use of special retrieval bags minimizes the risk of dissemination[109, 107], without increasing the intraoperative complication rate. Furthermore, Trivedi et al[132] mentioned in a study of 21 cases of laparoscopic morcellation of myomas and uteri the safety of using so-called in-bag morcellation. The disadvantage referring to the use of the retrieval bag is the significant increase of surgery time and costs. Vargas et al.[133] pointed that the mean operative time was prolonged by 26 minutes with the use of in-bag morcellation and Srouji et al[134] reported a mean additional operative time approximately 30 minutes. On the other hand, it is mentioned that a usual retrieval bag is not designed for power morcellation, and there is high risk of tearing in the abdomen and of its contents to spill out into the peritoneal cavity, and in consequence to spread out the malignant tissue[135]. Cohen et al.[136] reported in a study to evaluate dissemination of tissue by using power morcellation with retrieval bags that in 7 of 76 cases (9.2%) leak of fluid or tissue was noted despite that all containment bags were intact. This study did not name the containment system used. On July 2015 a tissue isolator bag (MorSafe®, Fig. 27) produced in India from the company Veol Medical Technologies specifically for being used with a power morcellator received CE certification which means that the product complies with the essential requirements of the relevant European health safety system and may be legally placed on the market. This isolator bag was available in some markets since September 2014[137].
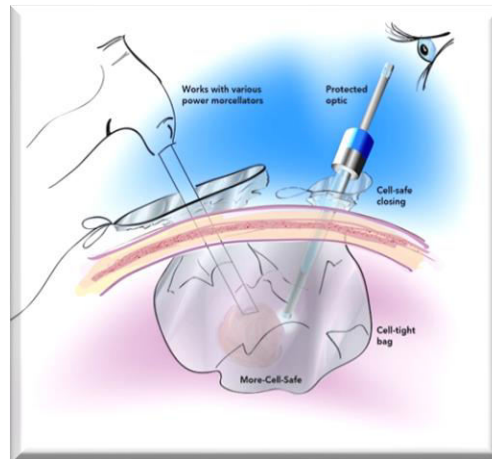
Fig. 27: MorSafe® isolator bag, Veol Medical Technologies, Mumbai, India

Source: http://www.cjmedical.com/products/specialties/gynaecology/more-cell-safe

Furthermore, on April 2016 the FDA allowed a company (Advanced Surgical Concepts Ltd) to merchandise its power morcellator tissue collection system (PneumoLiner, Fig. 28), but also remained the potential possibility of bag[138]. A really important factor for a successful and safe use of a retrieval bag is the skill of the surgeon and his level of experience. However, until now a definitive recommendation for the use of morcellation bags could not be made because of lack of evidence through the limited number of studies. The use of retrieval bags does not justify an uncritical use of morcellators[173].
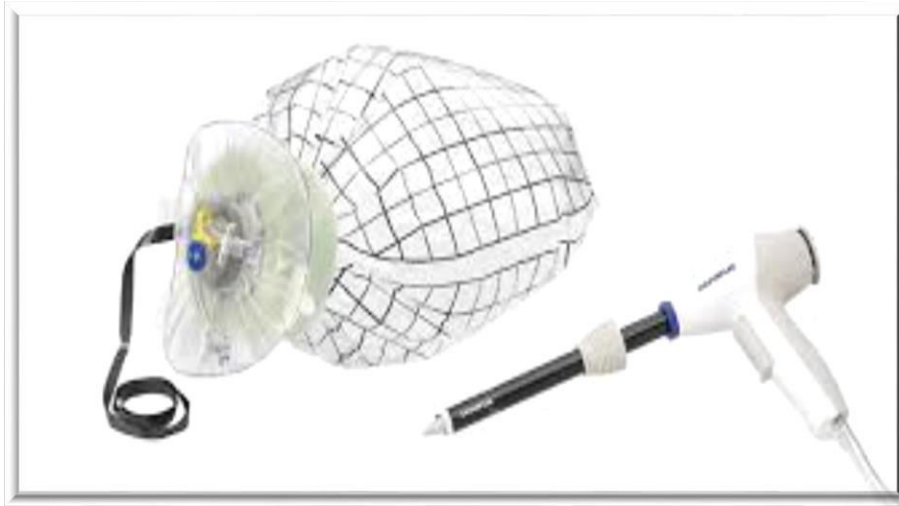
Fig. 28: PneumoLiner® isolator bag, Advanced Surgical Concepts Ltd, Ireland

Source: http://www.advancedsurgical.ie/Rest_of_World_Home_Page/Default.547.html/Rest_of_World_Home_Page/Default.547.html

V. 10. Conclusion

In conclusion, power morcellation has both advantages and disadvantages, which have to be carefully evaluated for each woman separately. Analytically, referring to the patient, the benefits of minimal invasive surgery are faster healing, faster recovery after the surgery and generally faster return to everyday life and on overall view reduced mortality. On the other hand, it is reported that there is a high risk for spreading of an occult uterine malignoma, which can result in tumor upstaging. This dispersion may even cause impairment of prognosis and premature death. In our study, there was no upstaging of the tumor during the secondary operation. However, two of three patients experienced tumor recurrence after 36 and 63 months. One of the patients with intraabdominal recurrence underwent a third surgery achieving complete resection once more. The second patient had a distant metastasis in the sternum. The small number of cases within the cohort does

not allow any definite statements about the outcome of the patients after unexpected morcellated malignoma with use of EMM. The statement[139] of the American Association of Gynecologic Laparoscopists (AAGL) to the FDA on power morcellation mentioned that the mortality from leiomyosarcoma and the potential dissemination through power morcellaton would be less than the mortality from open hysterectomy or in case of complete abandonment of minimal invasive surgery in these surgical entities. Analytically, the mortality from open hysterectomy was estimated 0.085% while from laparoscopic hysterectomy with power morcellation 0.077%. Concerning this statement, a reasonable conclusion is that the commitment of gynecologic surgeons is not only to look after patients with leiomyosarcoma, but also to take care of all patients which are candidates for MIS. More research with extended data is needed to enlighten the strategy of using power morcellation.

List of abbreviations

AAGL	American Association of Gynecologic Laparoscopists
BSO	Bilateral Salpingo-Oophorectomy
CIN	Cervical intraepithelial neoplasia
CS	Carcinosarcomas
D&C	Dilation and Curettage
DGGG	German Society for Gynecology and Obstrectics
EC	Endometrial cancer
EMM	Electromechanical Morcellation
ESS	Endometrial Stroma Sarcomas
FDA	Food und Drugs Administration
FDG	Fluodeoxyglucose
FES	Alphafluorobeta-estradiol
FIGO	International Federation of Gynecology and Obstetrics
FLT	Deoxyfluorothymidine
HPV	Human Papilloma Virus
LASH	Laparoscopic Supracervical Hysterectomy
LESS	Laparoendoscopic Single Site
LMS	Leiomyosarcomas
PET/CT	Positron emission tomography scan
STUMP	Uterine smooth muscle tumors of uncertain malignant potential
TAH	Total abdominal hysterectomy
TH	Total hysterectomy
LH	Laparoscopic hysterectomy
TLH	Total laparoscopic hysterectomy
US	Uterine Sarcomas
LPM	Laparoscopic Power Morcellation
LM	Leiomyoma
LS	Leiomyosarcoma

Literature

1.   MAHADEVAN, HAROLD ELLIS, VISHY. Clinical anatomy applied anatomy for students and junior doctors *(13th ed. ed.), 2013, Chichester, West Sussex, UK: Wiley-Blackwell. ISBN 9781118373767.*

2.   BERTZ B., HENTSCHEL S., HUNDSDÖRFER G., ET AL. Arbeitsgemeinschaft Bevölkerungsbezogener Krebsregister in Deutschland, editors. In collaboration with the Robert Koch-Institute. Krebs in Deutschland - Häufigkeiten und Trends. Cancer in Germany - Prevalences and Trends. *4th edited edition, Saarbrücken, 2004.*

3.   ROBERT KOCH-INSTITUTE. KREBS: Trends zu Inzidenz und Mortalität. Interaktive Datenbankabfrage. Cancer: Trends of incidence and mortality. Interactive database query. Accessed August 19, 2005.

4.   BOYLE P, MAISONNEUVE P, AUTIER P. Update on cancer control in women. *Int J Gynecol Obstet 2000; 70: 263–303.*

5.   FDA Approves New Indication for Gardasil to Prevent Genital Warts in Men and Boys. *FDA-Press release on 16. Oktober 2009.*

6.   AMERICAN CANCER SOCIETY. Cancer Facts and Figures 2015. *Atlanta, Ga: American Cancer Society; 2015.*

7.   YANG Y.-L., LIU L., WANG X.-X., WANG Y., WANG L. Prevalence and associated positive psychological variables of depression and anxiety among Chinese cervical cancer patients: A cross-sectional study. American Joint Committee on Cancer. Cervix Uteri. In: AJCC Cancer Staging Manual. *7th ed. New York, NY: Springer; 2010: 395-402.*

8.   AGO. Leitlinien zum Zervixkarzinom, zum Endometrium-Karzinom und zu den Trophoblasttumoren, Kommission Uterus der AGO e.V. (Hrsg.), *1. Auflage 2014, Zuckschwerdt Verlag München-Wien-New York.*

9.   STANFORD JL, BRINTON LA, BERMAN ML, MORTEL R, TWIGGS LB, BARRE TT RJWILBANKS GD& HOOVER RN. Oral contraceptives and endometrial cancer: do other risk factors modify the association? *International Journal of Cancer 1993.*

10.   D. CIBULA, A. GOMPEL, A.O. MUECK, C. LA VECCHIA , P.C. HANNAFORD L. DUSEK. Hormonal contraception and risk of cancer. *Hum. Reprod. Update (2010) 16 (6): 631-650.*

11.   NATIONAL CANCER INSTITUTE. "General Information About Endometrial Cancer". Wikipedia. *22 April 2014. Retrieved 3 September 2014.*

12.   NOVAK E, ANDERSON DF: Sarcoma of the uterus: Clinical and Pathologic study of fifty-nine cases. *Am J Obstet Gynecol 1937; 34: 740.*

13.   D'ANGELO E, SPAGNOLI LG, PRAT J. Comparative clinicopathologic and immunohistochemical analysis of uterine sarcomas diagnosed using the World Health Organization classification system. *Hum Pathol 2009; 40:1571–85.*

14.   PAPANICOLAOU GN, MADDI FV: Observations on the behavior of human endometrial cells in tissue culture. *Am J Obstet Gynecol 1958; 76: 601.*

15.   OBER WH: Uterine sarcomas: Histogenesis and taxonomy. *Ann NY Acad Sci 1959; 74: 568.*

16.   NIEMINEN U, SODERLIN E: Sarcoma of the corpus uteri: Results of the treatment of 117 cases. *Strahlentherapie 1974; 148: 57.*

17.   SHERMAN ME, DEVESA SS. Analysis of racial differences in incidence, survival, and mortality for malignant tumors of the uterine corpus. *Cancer. 2003; 98(1): 176.*

18.   HAGIWARA T, MORI T, KAKU T EUR J. Development of endometrial cancer following radiation therapy for cervical carcinoma. *Gynaecol Oncol. 2005; 26(2): 191.*

19. WICKERHAM DL, FISHER B, WOLMARK N, BRYANT J, COSTANTINO J, BERNSTEIN L, RUNOWICZ CD J. Clinical association of tamoxifen and uterine sarcoma. *Oncol. 2002; 20(11): 2758.*

20. BLYTHE JG, BARI W, BUCHSBAUM HJ. Uterine Sarcoma Clinico-Pathologic Study, St John's Mercy Medical Center, St Louis, MO, University of Iowa, 1974 *unpublished data.*

21. MCMEEKIN DS. Sarcoma of the uterus. In: DiSaia, Greasman: Clinical Gynecologic Oncology. Seventh edition ed. Philadelphia: *Mosby Elsevier; 2007.*

22. MC CLUGGAGE W.G. Malignant biphasic uterine tumours: carcinosarcomas or metaplastic carcinomas? Department of Pathology, Royal Group of Hospitals Trust, Northern Ireland; J Clin Pathol. 2002 May; 55(5): 321–325.

23. AMANT F, COOSEMANS A, DEBIEC-RYCHTER M, TIMMERMAN D, VERGOTE I. Clinical management of uterine sarcomas. *Lancet Oncol 2009; 10: 1188-1198.*

24. KEMPSON RL, BARI W: Uterine sarcomas: Classification, diagnosis and prognosis. *Hum Pathol 1970; 1: 331.*

25. staging for uterine sarcomas. *Int J Gynaecol Obstet 2009; 104: 179.*

26. AMERICAN NATIONAL CANCER INSTITUTE SEER (Surveillance, Epidemiology and End Results), Uterine Sarcomas. https://seer.cancer.gov/statfacts/html/corp.html.

27. AJCC official website (American join Committee on Cancer). https://cancerstaging.org/Pages/default.aspx.

28. NATIONAL COMPREHENSIVE CANCER NETWORK. Clinical Practice Guidelines in Oncology: Uterine Neoplasms. *December 13, 2010. BC Cancer Agency. Cancer Management Guidelines.*

29.   NCCN. *Guidelines* Gynecological Sarcomas: Management. *Retrieved on June 15, 2010. https://www.nccn.org/professionals/physician_gls/default.aspx.*

30.   AMERICAN NATIONAL CANCER INSTITUTE. Uterine Sarcoma Treatment. *Retrieved: June   15,   2010. https://www.cancer.org/content/dam/CRC/PDF/Public/8861.00.pdf.*

31.   DGGG. German Society for Gynaecology and Obstetrics. (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe). *Langfassung der Leitlinie "Uterine Sarkome".http://www.awmf.org/uploads/tx_szleitlinien/015-074l_S2k_Uterine_Sakro-   me; 2015-08.pdf.*

32.   REICH H., ROBERTS L. Laparoscopic hysterectomy in current gynaecological practice. *Rev Gynaecol Pract. Vol. 3,* 2003; *pp. 32–40.*

33.   BASKETT TF. Hysterectomy: evolution and trends. Best Pract Res. *Clin Obstet Gynaecol 2005; 19: 295-305.*

34.   CLAYTON R.D. Hysterectomy. *Best Practice & Research Clinical Obstetrics and Gynaecology.* 2006; *Vol. 20, No. 1, pp. 73–87.*

35.   STANG A., MERRILL R.A., KUSS O. Nationwide rates of conversion from laparoscopic or vaginal hysterectomy to open abdominal hysterectomy in Germany. *Eur J Epidemiol.* 2011; 26, 125–133.

36.   SUTTON C. Past, Present and Future of Hysterectomy. *J Minim Invasive Gynecol 2010; 17(4): 421-35.*

37.   LAU WY, LEOW CK, LI AK. History of Endoscopic and Laparoscopic surgery. *World J Surg 1997; 21: 444-53.*

38.   HIMAL HS. Minimally invasive (laparoscopic) surgery. *Surg Endosc 2002; 16: 164752.*

39.   REICH H, DECAPRIO J, MCGLYNN F. Laparoscopic hysterectomy. *J Gynecol Surg 1989; 5: 213-6.*

40.   ERTAN AK., ULBRICHT M, HUEBNER K, DI LIBERTO A. The technique of robotic assisted laparoscopic surgery in gynaecology, its introduction into the clinical routine of a gynaecological department and the analysis of the perioperative courses - a German experience. *J Turk Ger Gynecol Assoc. 2011 Jun 1;12(2): 97-103.*

41.   VISCO AG, ADVINCULA AP. Robotic Gynecologic Surgery. *Obstet Gynecol 2008; 112: 1369-84.*

42.   NIEBOER TE, JOHNSON N, LETHABY A, TAVENDER E, CURR E, GARRY R, VAN VOORST S, MOL BW, KLUIVERS KB. Surgical approach to hysterectomy for benign gynecological disease. *Cochrane Database Syst Rev. 2009 Jul 8;(3).*

43.   BRUMMER TH, JALKANEN J, FRASER J, HEIKKINEN AM, KAUKO M, MÄKINEN J, SEPPÄLÄ T, SJÖBERG J, TOMÁS E, HÄRKKI P. FINHYST, a prospective study of 5279 hysterectomies: complications and their risk factors. *Hum Reprod. 2011 Jul;26(7): 1741-51.*

44.   PIVER MS, RUTLEDGE F, SMITH JP. Five classes of extended hysterectomy for women with cervical cancer. Obstet Gynecol 1974; 265–272.

45.   AAGL Advancing Minimally Invasive Gynecology Worldwide. AAGL position statement: route of hysterectomy to treat benign uterine disease. *J Minim Invasive Gynecol 2011; 18(1): 1-3.*

46.   ROSERO EB, KHO KA, JOSHI GP, GIESECKE M, SCHAFFER JI. Comparison of robotic and laparoscopic hysterectomy for benign gynecologic disease. *Obstet Gynecol 2013 Oct;122(4): 778-786.*

47.   TERZIC M. Focused ultrasound for treatment of uterine myoma: from experimental model to clinical practice. *Srp Arh Celok Lek. 2008; 136: 193–195.*

48.   AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS. Alternatives to hysterectomy in the management of leiomyomas. *(2008, reaffirmed 2012). ACOG Practice Bulletin No. 96. Obstetrics and Gynecology, 112 (2, part 1): 387–399.*

49.   GARCIA CR. Management of the symptomatic fibroid in women older than 40 years of age: hysterectomy or myomectomy? Obstet Gynecol Clin North Am 1993; 20(2): 337–47.

50.   LEFEBVRE G, ALLAIRE A, JEFFREY J, VILOS G. Hysterectomy. SOGC Clinical Practice Guidelines *No. 109, January 2002. J Obstet Gynaecol Can 2002; 24(1): 37–48.*

51.   SEINERA P, ARISIO R, DECKO A, FARINA C, CRANA F. Laparoscopic myomectomy: indications, surgical technique and complications. *Hum Reprod 1997; 12: 1927–30.*

52.   DUBUISSON JB, CHAPRON C, LEVY L. Difficulties and complications of laparoscopic myomectomy. *J Gynecol Surg 1996; 12: 159–65.*

53.   NEZHAT FR, ROEMISCH M, NEZHAT CH, SEIDMAN DS, NEZHAT CR. Recurrence rate after laparoscopic myomectomy. *J Am Assoc Gynecol Laparosc 1998; 5: 237–40.*

54.   AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS. Surgical alternatives to hysterectomy in the management of leiomyomas. *ACOG Prac. Bull (May) 2000; 16: 1–8.*

55.   STEINER RA, WIGHT E, TADIR Y. Electrical cutting device for laparoscopic removal of tissue from the abdominal cavity. *Obstet Gynecol 1993; 81: 471–4.*

56.   LE HUU NHO R, MEGE D, OUAISSI M, SIELEZNEFF I, SASTRE B. Incidence and prevention of ventral incisional hernia. *J Visc Surg 2012 Oct;149(5 Suppl): 3-14.*

57.   WRIGHT KN, JONSDOTTIR GM, JORGENSEN S, SHAH N, EINARSSON JI. Costs and outcomes of abdominal, vaginal, laparoscopic and robotic hysterectomies. *JSLS 2012 Oct-Dec;16(4): 519-524.*

58.   WANG CJ, YUEN LT, LEE CL, KAY N, SOONG YK. A prospective comparison of morcellator and culdotomy for extracting of uterine myomas laparoscopically in nullipara. *J Minim Invasive Gynecol 2006; 13: 463–6.*

59.   GLASSER M. MINILAPAROTOMY: A minimally invasive alternative for major gynecologic abdominal surgery. *Perm J 2005; 9: 41–5.*

60.   SAVAGE GM, CHRISTIAN JJ, DILLOW DC. Disposable laparoscopic morcellator. *US Patent 6,039,748A. 2000.*

61.   UPPAL S, FRUMOVITZ M, ESCOBAR P, RAMIREZ PT. Laparoendoscopic single site surgery in gynecology: review of literature and available technology. *J Minim Invasive Gynecol 2011; 18: 12–23.*

62.   MILAD MP, MILAD EA. Laparoscopic morcellator-related complications. *J Minim Invasive Gynecol 2014; 21(3):486–491.*

63.   CATANZARITE T, SAHA S, PILECKI M, KIM J, MILAD M. The effect of operative time on preoperative morbility after laparoscopic hysterectomy. *Obstet Gynecol. 2014; 2015.0012.*

64.   ORDULU PDC, WILSON WS. CHONG, KWONG WC, CHARLES L, MICHAEL GM, BRADLEY JQ, CYNTHIA CM. Disseminated Peritoneal leiomyomatosis after laparoscopic supracervical hysterectomy with characteristic molecular cytogenetic findings of uterine leiomyoma. Genes Chromosomes and Cancer. 2010 Dec; 49(12): 1152–1160.

65.   FOOD AND DRUG ADMINISTRATION. Quantitative Assessment of the Prevalence of Unsuspected Uterine Sarcoma in Women Undergoing Treatment of Uterine Fibroids. Summary and Key Findings. *Published April 17, 2014. Accessed April 17, 2014.*

66.   HEALTH CANADA. Laparoscopic electric morcellators risk of spread of unsuspected uterine sarcoma—notice to hospitals. Ottawa: *Government of Canada; 2014. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/42885a-eng. php.*

67.   AVIRAM R, OCHSHORN Y, MARKOVITCH O, FISHMAN A, COHEN I, ALTARAS MM ET AL. Uterine sarcomas versus leiomyomas: gray-scale and Doppler sonographic findings. *J Clin Ultrasound 2005, 33(1):10–13.*

68.   FUKUNISHI H, FUNAKI K, IKUMA K, KAJI Y, SUGIMURA K, KITAZAWA R ET AL. Unsuspected uterine leiomyosarcoma: magnetic resonance imaging findings before and after focused ultrasound surgery. *Int J Gynecol Cancer 2007, 17(3):724–728.*

69.   MILMAN D, ZALEL Y, BIRAN H, OPEN M, CASPI B, HAGAY Z ET AL. Unsuspected uterine leiomyosarcoma discovered during treatment with a gonadotropin-releasing hormone analogue: a case report and literature review. *Eur J Obstet Gynecol Reprod Biol 1998; 76(2):237–240.*

70.   VELLANKI VS, RAO M, SUNKAVALLI CB, CHINAMOTU RN, KAJA S. A rare case of uterine leiomyosarcoma: a case report. *J Med Case Rep 2010; 4:222.*

71.   PARKER WH, FU YS, BEREK JS. Uterine sarcoma in patients operated on for presumed leiomyoma and rapidly growing leiomyoma. *Obstet Gynecol 1994; 83:414–418.*

72.   SCHWARTZ LB, DIAMOND MP, SCHWARTZ PE. Leiomyosarcomas: clinical presentation. *Am J Obstet Gynecol 1993; 168(1 Pt 1):180–183.*

73.   EXACOUSTOS C, ROMANINI ME, AMADIO A, AMOROSO C, SZABOLCS B, ZUPI E ET AL. Can gray-scale and color Doppler sonography differentiate between uterine leiomyosarcoma and leiomyoma? *J Clin Ultrasound 2007; 35(8):449–457.*

74.   HATA K, HATA T, MAKIHARA K, AOKI S, TAKAMIYA O, KITAO M ET AL. Sonographic findings of uterine leiomyosarcoma. *Gynecol Obstet Investig 1990; 30(4):242.245.*

75.   BANSAL N, HERZOG TJ, BURKE W, COHEN CJ, WRIGHR JD. The utility of preoperative endometrial sampling for the detection of uterine sarcomas. *Gynecol Oncol. 2008 Jul; 110(1):43-8.*

76.   Janus C, White M, Dottino P, Brodman M, Goodman H. Uterine leiomyosarcoma–magnetic resonance imaging. *Gynecol Oncol 1989; 32(1):79–81.*

77.   Melia P, Maestro C, Bruneton JN, Gasperoni A, Peyrottes I, Teissier E et al. MRI of uterine leiomyosarcoma. Apropos of 2 cases. *J Radiol 1995; 76(1):69–72.*

78.   Pattani SJ, Kier R, Deal R, Luchansky E. MRI of uterine leiomyosarcoma. *Magn Reson Imaging1995; 13(2):331–333.*

79.   Goto A, Takeuchi S, Sugimura K, Maruo T. Usefulness of Gd-DTPA contrast-enhanced dynamic MRI and serum determination of LDH and its isozymes in the differential diagnosis of leiomyosarcoma from degenerated leiomyoma of the uterus. *Int J Gynecol Cancer 2002; 12(4):354–361.*

80.   Zhang HJ, Zhan FH, Li YJ, Sun HR, Bai RJ, Gao S. Fluorodeoxyglucose positron emission tomography/computed tomography and magnetic resonance imaging of uterine leiomyosarcomas: 2 cases report. *Chin Med J (Engl) 2011; 124(14): 2237–2240.*

81.   Yoshida Y, Kiyono Y, Tsujikawa T, Kurokawa T, Okazawa H, Kotsuji F. Additional value of 16 alpha-[18F] fluoro-17 beta-oestradiol PET for differential diagnosis between uterine sarcoma and leiomyoma in patients with positive or equivocal findings on [18F] fluorodeoxyglucose PET. *Eur J Nucl Med 2011; Mol Imaging 38 (10):1824–1831.*

82.   Umesaki N, Tanaka T, Miyama M, Kawamura N, Ogita S, Kawabe J et al. Positron emission tomography with (18) fluorodeoxyglucose of uterine sarcoma: a comparison with magnetic resonance imaging and power Doppler imaging. *Gynecol Oncol 2001; 80(3):372–377.*

83.   Juang CM, Yen MS, Horng HC, Twu NF, Yu HC, Hsu WL. Potential role of preoperative serum CA125 for the differential diagnosis between uterine leiomyoma and uterine leiomyosarcoma. *Eur J Gynaecol Oncol 2006; 27(4):370–374.*

84.   Hinchcliff EM, Esselen KM, Watkins JC. The role of endometrial biopsy in the preoperative detection of uterine leiomyosarcoma. *J Minim Invasive Gynecol 2016; 23:567.*

85.   Tulandi T, Ferenczy. A. Biopsy of uterine leiomyomata and frozen sections before laparoscopic morcellation. *J Minim Invasive Gynecol 2014; 21:963-6.*

86.   Hagemann IS1, Hagemann AR, LiVolsi VA, Montone KT, Chu CS. Risk of occult malignancy in morcellated hysterectomy: a case series. Int J Gynecol Pathol. *2011 Sep;30(5):476-83.*

87.   Levitz J. Fibroid Surgery Puts Doctor Fighting Cancer Diagnosis in the Spotlight, *The Wall Street Journal, December 19, 2013.*

88.   Rauh-Hain JA, Oduyebo T, Diver EJ, et al. Uterine leiomyosarcoma: *An updated series. Int J Gynecol Cancer. 2013;23.*

89.   **Tan-Kim J, Hartzell KA, Reinsch CS, et al. Uterine sarcomas and parasitic myomas after laparoscopic hysterectomy with power morcellation. *Am J Obstet Gynecol 2015;212.***

90.   Seidman MA, Oduyebo T, Muto M, Crum C, Nucci M, and Quade B. Peritoneal dissemination complicating morcellation of uterine mesenchymal neoplasms, *PLoS One. 2012; 7(11).*

91.   Oduyebo T, Rauh-Hain AJ, Meserve EE, Seidman MA, Hinchcliff E, George S, et al. The value of re-exploration in patients with inadvertently morcellated uterine sarcoma. *Gynecol Oncol 2014 Feb;132(2):360-365.*

92.   Theben JU, Schellong RM, Altgassen C, Kelling K, Schneider S, Grosse-Drieling D. Unexpected malignancies after laparoscopic-assisted supracervical hysterectomies (LASH): an analysis of 1,584 LASH cases. *Arch Gynecol Obstet. 2013*

Mar;287(3):455-62.

93.   AYHAN A, KART C, CUVEN S, BOYNUKALIN K, KUCUKALI T. The role of reoperation in the management of endometrial carcinoma found in simple hysterectomy. *J Surg Ongol. 2006 Apr 1;93(5):373-8.*

94.   EINSTEIN MH, BARAKAT RR, CHI DS, ET AL. Management of uterine malignancy found incidentally after supracervical hysterectomy or uterine morcellation for presumed benign disease. *Int J Gynecol Cancer. 2008;18(5):1065–1070.*

95.   SERRANO C, ODUYEBO T, MANOLA J, FENG Y, MUTO MG, GEORGE S. Impact of tumor morcellation on the natural history of uterine leiomyosarcoma (ULMS), Paper 011, Session 4: Uterine Leiomyosarcomas, *Final Program, Connective Tissue Oncology Society 18th Annual Meeting, New York, NY.*

96.   PARK JY1, PARK SK, KIM DY, KIM JH, KIM YM, KIM YT, NAM JH . The impact of tumor morcellation during surgery on the prognosis of patients with apparently early uterine leiomyosarcoma. *Gynecol Oncol. 2011 Epub 2011 May 12.*

97.   KILL LM, KAPETANAKIS V, MCCULLOUGH AE, MAGRINA JF. Progression of pelvic implants to complex atypical endometrial hyperplasia after uterine   morcellation. *Obstet Gynecol 2011; 117:447–9.*

98.   CUCINELLA G, GRANESE R, CALAGNA G, SOMIGLIANA E, PERINO A. Parasitic myomas after laparoscopic surgery: an emerging complication in the use of morcellator? *Description of four cases. Fertil Steril 2011 96: 90-96.*

99.   HILGER WS, MAGRINA JF. Removal of pelvic leiomyomata and endometriosis five years after supracervical hysterectomy. *Obstet Gynecol 2006 Sep;108): 772-774.*

100.   TAKEDA A, MORI M, SAKAI K, MITSUI T, NAKAMURA H. Parasitic peritoneal leiomyomatosis diagnosed 6 years after laparoscopic myomectomy with electric tissue morcellation: report of a case and review of the literature. *J Minim Invasive Gynecol*

2007;14(6): 770-775.

101.   DONNEZ O, SQUIFFLET J, LECONTE I, JADOUL P, DONNEZ J. Posthysterectomy pelvic adenomyotic masses observed in 8 cases out of a series of 1405 laparoscopic subtotal hysterectomies. *J Minim Invasive Gynecol 2007 Mar-Apr;14(2): 156.160.*

102.   AAGL (Advancing Minimally Invasive Gynecology Worldwide). Morcellation During Uterine Tissue Extraction. *Report 6 May 2014.*

103.   TUCKER, MIRIAM E. FDA Advisory Panel Voices Concern About Morcellation Risk, *July 14, 2014, Accessed July 28, 2014*

104.   SGO. Statement of the Society of Gynecologic Oncology to the FDA's Obstetrics and Gynecology Medical Devices Advisory Committee Concerning *Safety of Laparoscopic Power Morcellation, July 10-11, 2014.*

105.   ESGE (European Society for Gynaecological Endoscopy), *Statement on Morcellation, May, 2014. http://www.esge.org/wp-content/uploads/2017/02/ESGE-Statement-on-Morcellation-02-May-2014.pdf.*

106.   DGGG (German Society of Gynecology and Obstetrics). Sarcoma of the Uterus. *Guideline of the DGGG S2k-Level, AWMF Registry No. 015/074, August 2015.*

107.   COHEN SL Einarsson JI, Wang KC, Brown D, Boruta D, Scheib SA, Fader AN, Shibley T. Contained Power Morcellation Within an Insufflated Isolation Bag *Obstet Gynecol 2014; 124:491–7.*

108.   MENGE F, HARTMANN E, MATHEW M, KASPER B, HOHENBERGER P. The impact of operative techniques to the onset of peritoneal tumor dissemination in patients with uterine leiomyosarcomas, Paper 010, Session 4: Uterine Leiomyosarcomas, *Final Program Connective Tissue Oncology Society 18th Annual Meeting, New York, NY.*

109.   PASIC P, BRILL A, LEVINE R. A Practical Manual of Laparoscopy and Minimally Invasive Gynecology: *A Clinical Cookbook" CRC Press, May 2007.*

110.   UCCELLA S, CROMI A, BOGANI G, CASARIN J, SERATI M, GHEZZI F. Transvaginal specimen extraction at laparoscopy without concomitant hysterectomy. *J Minim Invasive Gynecol. 2013;20(5): 583-590.*

111.   JI. ZHANG, JU. ZHANG, Y. DAI, L. ZHU, J. LANG, J. LENG. Clinical characteristics and management experience of unexpected uterine sarcoma after myomectomy, *International Journal of Gynecology and Obstetrics 2015; 130 195–199.*

112.   D'ANGELO E, PRAT J. Uterine sarcomas: a review. *Gynecol Oncol 2010; 116(1):131–9.*

113.   BOOSZ A, LERMANN J, MEHLHORN G, LOEHBERG C, RENNER SP, THIEL FC, SCHRAUDER M, BECKMANN MW, MUELLER A. Comparison of re-operation rates and complication rates after total laparoscopic hysterectomy (TLH) and laparoscopy-assisted supracervical hysterectomy (LASH). *Eur J Obstet Gynecol Reprod Biol. 2011 Oct;158(2): 269-73.*

114.   STRAUSS B, JÄKEL I, KOCH-DÖRFLER M, LEHMANN-WILLENBROCK E, GIESE KP, SEMM K. [Psychiatric and sexual sequelae of hysterectomy--a comparison of different surgical methods]. *Geburtshilfe Frauenheilkd. 1996 Sep;56(9): 473-81.*

115.   LUM DA, SOKOL ER, BEREK JS, SCHULKIN J, CHEN L, MCELWAIN CA, WRIGHT JD. Food and Drug Administration, Quantitative Assessment of the Prevalence of Unsuspected Uterine Sarcoma inWomen Undergoing Treatment of Uterine Fibroids. *Summary and Key Findings. J Minim Invasive Gynecol. 2016 May-Jun;23(4): 548-56.*

116.   YILDIRIM Y, INAL MM, SANCI M, YILDIRIM YK, MIT T, POLAT M, TINAR S. Development of uterine sarcoma after tamoxifen treatment for breast cancer: report of four cases. *Int J Gynecol Cancer. 2005 Nov-Dec;15(6): 1239-42.*

117.   DUEHOLM M, JENSEN ML, LAURSEN H, KRACHT P. Can the endometrial thickness as measured by trans-vaginal sonography be used to exclude polyps or hyperplasia in pre-menopausal patients with abnormal uterine bleeding? *Acta Obstet Gynecol Scand 2001 Jul;80(7): 645-5.*

118.   RUSSELL DJ. Med Clin. North Am. The female pelvic mass. Diagnosis and management. *1995 Nov;79(6); 1481=93.Rewiew.*

119.   NAM J.H., PARK J.Y. Update on treatment of uterine sarcoma. *Curr Opin Obstet Gynecol 2010;22: 36-42.*

120.   LEITAO MM, SONODA Y, BRENNAN MF, BARAKAT RR, CHI DS. Incidence of lymph node and ovarian metastases in leiomyosarcoma of the uterus. *Gynecol Oncol 2003;91: 209 12.*

121.   SEDDON BM, DAVDA R. Uterine sarcoma recent progress and future challenges. *Eur J Radiol 2011;78(1):30–40.*

122.   SPANO JP, SORIA JC, KAMBOUCHNER M, PIPERNO-NEUMAN S, MORIN F, MORERE JF. Long-term survival of patients given hormonal therapy for metastatic endometrial stromal sarcoma. *Med Oncol 2003; 20(1):87–93.*

123.   SHAH JP, BRYANT CS, KUMAR S, ALI-FEHMI R, MALONE J MORRIS RT. Lymphadenectomy and ovarian preservation in low-grade endometrial stromal sarcoma. *Obstet Gynecol 2008; 112(5):1102–8.*

124.   HOU HL, MENG MB, CHEN XL, ZHAO LJ, ZHU L, ZHANG BL, WANG P. The prognosis factor of adjuvant radiation therapy after surgery in uterine sarcomas. *Onco Targets Ther. 2015 Aug 28; 8:2339-44.*

125.   CANTRELL LA, BLANK SV, DUSKA LR. The prognosis factor of adjuvant radiation therapy after surgery in uterine sarcomas.. *Gynecol Oncol. 2015 Jun;137(3):581-8.*

126.   Magnuson WJ, Petereit DG, Anderson BM, Geye HM, Bradley KA. Impact of adjuvant pelvic radiotherapy in stage I uterine sarcoma. *Anticancer Res. 2015 Jan;35(1):365-70.*

127.   George S, Barysauskas C, Serrano C, Oduyebo T, Rauh-Hain JA, Del Carmen MG, Demetri GD, Muto MG. Retrospective cohort study evaluating the impact of intraperitoneal morcellation on outcomes of localized uterine leiomyosarcoma. *Cancer. 2014 Oct 15;120(20):3154-8.*

128.   Perri T, Korach J, Sadetzki S, Oberman B, Fridman E, Ben-Baruch G. Uterine leiomyosarcoma: does the primary surgical procedure matter? *Int J Gynecol Cancer 2009;19:257–60.*

129.   Chan JK, Kawar NM, Shin JY, Osann K, Chen LM, Powell CB, et al. Endometrial stromal sarcoma: a population-based analysis. *Br J Cancer 2008;99(8):1210–5.*

130.   Kawamura N, Ichimura T, Ito F, Shibata S, Takahashi K, Tsujimura A, et al. Transcervical needle biopsy for the differential diagnosis between uterine sarcoma and leiomyoma. *Cancer 2002;94(6):1713–20.*

131.   Menge F, Hartmann E, Mathew M, Kasper B, Hohenberger P. The impact of operative techniques to the onset of peritoneal tumor dissemination in patients with uterine leiomyosarcomas, Paper 010, Session 4: Uterine Leiomyosarcomas, *Final Program Connective Tissue Oncology Society 18th Annual Meeting, New York, NY.*

132.   Trivedi PH, Patil SS, Parekh NA, Gandhi AC, Trivedi SP, Abreo MO. Laparoscopic Morcellation of Fibroid and Uterus In-Bag. *J Obstet Gynaecol India. 2015 Dec;65(6): 396-400.*

133.   Vargas MV, Cohen SL, Fuchs-Weizman N, Wang KC, Manoucheri E, Vitonis AF, Einarsson JI. Open power morcellation versus contained power morcellation within aninsufflated isolation bag: comparison of perioperative outcomes.*J Minim Invasive Gynecol. 2015 Mar-Apr;22(3): 433-8.*

134. Srouji SS, Kaser DJ, Gargiulo AR. Techniques for contained morcellation in gynecologic surgery *Fertil Steril. 2015; 103: 34.*

135. Uccella S, Cromi A, Bogani G, Casarin J, Serati M, Ghezzi F. Transvaginal specimenextraction at laparoscopy without concomitant hysterectomy. *J Minim Invasive Gynecol. 2013;20(5): 583-590.*

136. Cohen SL, Morris SN, Brown DN, Greenberg JA, Walsh BW, Gargiulo AR, Isaacson KB, Wright KN, Srouji SS, Anchan RM, Vogell AB, Einarsson JI. Contained tissue extraction using power morcellation: prospective evaluation of leakage parameters. *Am J Obstet Gynecol. 2016 Feb;214(2):257.e1-6.*

137. Veol Medical Technologies. MorSafe Power Morcellation Bag Receives CE Pvt. *Ltd Medical Posted 13th July 2015. http://www.safemorcellation.com/MorSafe-CE-Press-Release.pdf.*

138. FDA Approves Morcellator Bag to Prevent Cancerous Tissue Spread Posted *April 12th, 2016 by Michelle Llamas & filed under FDA News & Recalls. https://www.drugwatch.com/2016/04/12/fda-approves-morcellator-bag-preventing-cancer-spread/*

139. Brown J., AAGL advancing minimally invasive gynecology worldwide: statement to the FDA on power morcellation. *J Minim Invasive Gynecol. 2014 Nov-Dec;21(6): 970-1.*

140. Raine-Bennett T, Tucker LY, Zaritsky E, Littell RD, Palen T, Neugebauer R, et al. Occult uterine sarcoma and leiomyosarcoma: incidence of and survival associated with morcellation *[published erratum appears in Obstet Gynecol 2016; 127: 405]. Obstet Gynecol 2016;127: 29–39.*

141. Frick AC, Walters MD, Larkin KS, Barber MD. Risk of unan- ticipated abnormal gynecologic pathology at the time of hysterectomy for uterovaginal prolapse. *Am J Obstet Gynecol 2010; 202:507.e1–4.*

142.   HILL AJ, CARROLL AW, MATTHEWS CA. Unanticipated uterine pathologic finding after morcellation during robotic-assisted supracervical hysterectomy and cervicosacropexy for uterine prolapse. *Female Pelvic Med Reconstr Surg 2014;20: 113–5.*

143.   HINCHCLIFF EM, ESSELEN KM, WATKINS JC, ODUYEBO T, RAUH- HAIN JA, DEL CARMEN MG, ET AL. The role of endometrial biopsy in the preoperative detection of uterine leiomyosarcoma. *J Minim Invasive Gynecol 2016;23: 567–72.*

144.   TULANDI T, LEUNG A, JAN N. Nonmalignant sequelae of unconfined morcellation at laparoscopic hysterectomy or myomectomy. *J Minim Invasive Gynecol 2016;23: 331–7.*

145.   URBAN DA, KERBL K, MCDOUGALL EM, STONE AM, FADDEN PT, CLAYMAN RV. Organ entrapment and renal morcellation: permeability studies. *J Urol 1993;150: 1792–4.*

146.   PELOSI MA III, PELOSI MA. The Pryor technique of uterine morcellation. *Int J Gynaecol Obstet 1997;58: 299–303.*

147.   WASSON M, MAGTIBAY P II, MAGTIBAY P III, MAGRINA J. Incidence of occult uterine malignancy following vaginal hysterectomy with morcellation. *J Minim Invasive Gynecol 2017;24: 665–9.*

148.   GHEZZI F, CASARIN J, DE FRANCESCO G, PUGGINA P, UCCELLA S, SERATI M. Transvaginal contained tissue extraction after laparoscopic myomectomy: *a cohort study. BJOG 2017 [Epub ahead of print].*

149.   SERUR E, ZAMBRANO N, BROWN K, CLEMETSON E, LAKHI N. Extra-corporeal manual morcellation of very large uteri within an enclosed endoscopic bag: our 5-year experience. *J Minim Inva- sive Gynecol 2016;23: 903–8.*

150.   KLIETHERMES C, WALSH T, GUAN Z, GUAN X. Vaginal tissue extraction made easy. J *Minim Invasive Gynecol 2017;24: 726.*

151.   SOLIMA E, SCAGNELLI G, AUSTONI V, NATALE A, BERTULESSI C, BU-SACCA M, ET AL. Vaginal uterine morcellation within a specimen containment system: a study of bag integrity. *J Minim Invasive Gynecol 2015;22:1244–6.*

152.   GREENE AK, HODIN RA. Laparoscopic splenectomy for massive splenomegaly using a Lahey bag. *Am J Surg 2001;181: 543–6.*

153.   LANDMAN J, VENKATESH R, KIBEL A, VANLANGENDONCK R. Modified renal morcellation for renal cell carcinoma: laboratory experience and early clinical application. *Urology 2003;62: 632–4.*

154.   BOGANI G, CLIBY WA, ALETTI GD. Impact of morcellation on survival outcomes of patients with unexpected uterine leiomyosarcoma: a systematic review and meta-analysis. *Gynecol On- col 2015;137: 167–72.*

155.   PRITTS EA, PARKER WH, BROWN J, OLIVE DL. Outcome of occult uterine leiomyosarcoma after surgery for presumed uterine fibroids: a systematic review. *J Minim Invasive Gynecol 2015;22: 26–33.*

156.   VAN DEN HAAK L, ARKENBOUT EA, SANDBERG EM, JANSEN FW. Power morcellator features affecting tissue spill in gynecologic laparoscopy: an in-vitro study. *J Minim Invasive Gynecol 2016; 23: 107–12.*

157.   SHIBLEY KA. Enclosed morcellation using a large bowel isolation bag. Available: *http://www.mdedge.com/obgmanagement/article/80278/surgery/enclosed-morcellation using-large-bowel- isolation-bag. Retrieved September 24, 2017.*

158.   COHEN SL, EINARSSON JI, WANG KC, BROWN DN, BORUTA D, SCHEIB SA, ET AL. Contained power morcellation within an insufflated isolation bag. *Obstet Gynecol 2014;124: 491–7.*

159.   McKenna JB, Kanade T, Choi S, Tsai BP, Rosen DM, Cario GM, et al. The Sydney contained in bag morcellation technique. *J Minim Invasive Gynecol 2014;21: 984–5.*

160.   Cholkeri-Singh A, Sasaki K, Steller C, Johnston M, Miller CE. Contained morcellation techniques during laparoscopy. *J Minim Invasive Gynecol 2015;22: 126.*

161.   Einarsson JI, Cohen SL, Fuchs N, Wang KC. In-bag morcellation. *J Minim Invasive Gynecol 2014;21: 951–3.*

162.   Boruta DM, Shibley T. Power morcellation of unsuspected high-grade leiomyosarcoma within an inflated containment bag: 2-year follow-up. *J Minim Invasive Gynecol 2016;23: 1009–11.*

163.   Gunderson CC, Knight J, Ybanez-Morano J, Ritter C, Escobar PF, Ibeanu O, et al. The risk of umbilical hernia and other complications with laparoendoscopic single-site surgery. *J Minim Invasive Gynecol 2012;19: 40–5.*

164.   Gujral H, Vilkins A, Clark NV, Vogell AB, Wright KN. Deter- mining a learning curve for contained hand tissue extraction: perioperative outcomes and operative time. *J Minim Invasive Gynecol 2017;24: 103–7.*

165.   Dubin AK, Wei J, Sullivan S, Udaltsova N, Zaritsky E, Yama- moto MP. Minilaparotomy versus laparoscopic myomectomy after cessation of power morcellation: rate of wound complications. *J Minim Invasive Gynecol 2017;24: 946–53.*

166.   Meurs EAIM, Brito LG, Ajao M, Goggins ER, Vitonis AF, Einarsson JI, et al. Comparison of morcellation techniques at time of laparoscopic hysterectomy and myomectomy. *J Minim Invasive Gynecol 2017;24: 843–9.*

167.   VENTURELLA R, ROCCA ML, LICO D, LA FERRERA N, CIRILLO R, GIZZO S, MORELLI M, ZUPI E, ZULLO F. In-bag manual versus uncontained power morcellation for laparoscopic myomectomy: randomized controlled trial. *Fertil Steril 2015; 105:1369–1376.*

168.   EINARSSON JI, COHEN SL, FUCHS N, WANG KC. In-bag morcellation. *J Minim Invasive Gynecol 2014;21: 951–3.*

169.   PELOSI MA, 3RD, PELOSI MA. The suprapubic cruciate incision for laparoscopic-assisted microceliotomy. *JSLS. 1997 Jul–Sep;1(3):269–72.*

170.   ALESSANDRO LODDO, ROBERT ZURAWIN, BRUNO VAN HERENDAEL, DUSAN DJOKOVIC. Assessing the risk of laparoscopic morcellation of occult uterine sarcomas during hysterectomy and myomectomy: *Literature review and the ISGE recommendations. European Journal of Obstetrics & Gynecology and Reproductive Biology 220 (2018) 30–38.*

171.   PADOS G., TSOLAKIDIS D, THEODOULIDIS V., MAKEDOS A, ZARAMBOUKAS T, TARLATZIS B. Prevalence of occult leiomyosarcomas and atypical leiomyomas after laparoscopic morcellation of leiomyomas in reproductive-age women Human Reproduction, *Vol.32, No.10 pp. 2036–2041, 2017.*

172.   QUERLEU D, MORROW CP. Classification of radical hysterectomy. Lancet Oncol. 2008 Mar;9(3): 297-303.

173.   BECKMANN MW, JUHASZ-BÖSS I, DENSCHLAG D, GASS P, DIMPFL T, HARTER P, MALLMANN P, RENNER SP, RIMBACH S, RUNNEBAUM I, UNTCH M, BRUCKER SY, WALLWIENER D. Surgical Methods for the Treatment of Uterine Fibroids - Risk of Uterine Sarcoma and Problems of Morcellation: *Position Paper of the DGGG. Geburtshilfe Frauenheilkd 2015; 75(2): 148-164.*

174.   Brohl AS, Li L, Andikyan V, Običan SG, Cioffi A, Hao K, Dudley JT, Ascher-Walsh C, Kasarskis A, Maki RG. Age-stratified risk of unexpected uterine sarcoma following   surgery for presumed benign leiomyoma. *Oncologist. 2015 Apr;20(4):433-9.*

175.   Adam Dangoor, Beatrice Seddon, Craig Gerrand, Robert Grimer, Jeremy Whelan, Ian Judson. UK guidelines for the management of soft tissue sarcomas. *Clin Sarcoma Res. 2016; 6: 20.*

Acknowledgement

First of all, I would thank my former director Prof. A. K. Ertan und our associated director Dr. A. di Liberto for guiding and assisting me with all their will to accomplish this work.

I would like also thank my family and analytically my father, my mother, my brother and especially my wife and my sons for giving me the power and the mental tranquillity to continue.

Of course, I would like to thank the University of Saarland and especially Prof. Solomayer for giving me this opportunity.