ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΣΠΟΥΔΩΝ:
‘‘ΕΛΑΧΙΣΤΑ ΕΠΕΜΒΑΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ,
ΡΟΜΠΟΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ ΚΑΙ ΤΗΛΕΧΕΙΡΟΥΡΓΙΚΗ’’

ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ
ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

ΘΕΜΑ:

ROBOTIC SURGERY IN MANAGEMENT OF OVARIAN CANCER. REVIEW OF THE LITERATURE.

ΜΕΤΑΠΤΥΧΙΑΚΟΣ ΦΟΙΤΗΤΗΣ:

ΓΕΩΡΓΙΟΣ ΔΙΑΚΑΚΗΣ

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Του Μεταπτυχιακού Φοιτητή Γεώργιου Διακάκη

Εξεταστική Επιτροπή

- Νικόλαος Νικητέας, Αναπλ. Καθηγητής Χειρουργικής, **Επιβλέπων**
- Χρήστος Π. Τσιγκρής, Καθηγητής Χειρουργικής & Επιστημονικός Υπεύθυνος του Π.Μ.Σ
- Θεόδωρος Διαμαντής, Καθηγητής Χειρουργικής

Η Τριμελής Εξεταστική Επιτροπή η οποία ορίσθηκε από την ΓΣΕΣ της Ιατρικής Σχολής του Παν. Αθηνών Συνεδρίαση της.....ης .... 20.... για την αξιολόγηση και εξέταση του υποψηφίου κύριου Γεώργιου Διακάκη, συνεδρίασε σήμερα .../.../....

Η Επιτροπή διαπίστωσε ότι η Διπλωματική Εργασία του Κύριου Γεώργιου Διακάκη με τίτλο: *ROBOTIC SURGERY IN MANAGEMENT OF OVARIAN CANCER. REVIEW OF THE LITERATURE*, είναι πρωτότυπη, επιστημονικά και τεχνικά άρτια και η βιβλιογραφική πληροφορία ολοκληρωμένη και εμπεριστατωμένη.

Η εξεταστική επιτροπή αφού έλαβε υπ' όψιν το περιεχόμενο της εργασίας και τη συμβολή της στην επιστήμη, με ψήφους .... προτείνει την απονομή του Μεταπτυχιακού Διπλώματος Ειδίκευσης (Master's Degree), στον παραπάνω Μεταπτυχιακό Φοιτητή.

Στην ψηφοφορία για την βαθμολογία ο υποψήφιος έλαβε για τον βαθμό «ΑΡΙΣΤΑ» ψήφους ...., για τον βαθμό «ΛΙΑΝ ΚΑΛΩΣ» ψήφους ...., και για τον βαθμό «ΚΑΛΩΣ» ψήφους .... Κατά συνέπεια, απονέμεται ο βαθμός «.....................».

Τα Μέλη της Εξεταστικής Επιτροπής

Νικόλαος Νικητέας, **Επιβλέπων**	(Υπογραφή)	________________
Χρήστος Π. Τσιγκρής,	(Υπογραφή)	________________
Θεόδωρος Διαμαντής,	(Υπογραφή)	________________

Αφιέρωση

Στη μνήμη του πατέρα μου Διακάκη Ιωάννη,
Χειρουργού, Μαιευτήρα- Γυναικολόγου.

Ευχαριστίες

Ευχαριστώ θερμά την οικογένεια μου.

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INTRODUCTION

The risk of a woman to develop ovarian cancer (OC) is 1: 70 and is the second most common pathology of the female reproductive tract, representing 3% of all cancer cases [1]. OC is difficult to diagnose at an early stage due to insidious symptoms and lack of markers and tests for early detection. Early stages of the disease represent only 15% to 20% with 5-year survival rate >90%. Patients with stage III have a 5-year survival rate of 46% [2]. Even though the ovary seems to be the origin of the cancer, recent study suggested that the fallopian tube and the peritoneal cavity can be the sources of the disease [3]. The objective of this article is to review the published scientific literature regarding robotic surgery (RS) as a surgical tool of minimally invasive surgery (MIS) and its applications in management of OC. We report the history of RS and the role of gynecologists in its evolution, and analyze its role in borderline ovarian tumors (BOTs) and early stage OC, but also in the more advanced and recurrent OC. We give emphasis about the feasibility, efficacy and safety of RS in OC management and its future perspectives.

PART 1

1.1 EVOLUTION OF ROBOTS IN MEDICINE

1.1.1 HISTORY OF ROBOTIC SURGERY

In 1985 an industrial robot called PUMA adapted in stereotactic neurosurgery [4]. The robotic system PROBOT was manufactured for transurethral resection of prostate gland with guidance from a preoperatively constructed 3-D image [5]. Furthermore ROBODOC was used for total hip replacement in 1992 [6]. The concept of these early designs was their autonomous function with a preoperative plan. In 1994 the US Food and Drug Administration (FDA) first time approved AESOP (Automated Endoscopic System for Optimal Positioning; Computer Motion, Inc, Galeta, California), which was a single robotic arm that controlled the camera by voice command [7]. This active robotic device had motorized joints that were activated via the HERMES speech recognition program [8]. Gynecologists had evaluated this technology and one study by Mettler et al [9] compared the system to a surgical assistant holding the laparoscope during gynecologic surgery and concluded that less time is needed due to the fact that the surgeons are able to use both their hands. The first surgical system that made the concept of telesurgery reality, meaning that the surgeon operates at a distance from the patient at a console, was ZEUS with the addition of 2 robotic arms in 1999 [10]. In 2001the first transcontinental telesurgery so called " Lindbergh " was done by a surgeon in New York performing laparoscopic cholecystectomy in a patient in Strasbourg, France [11,12]. Gynecologists reported successful application of ZEUS in tubal anastomosis in a prospective study [13]. Today the only surgical robotic system which is actively produced and FDA approved is the da Vinci Robotic System (DRS). Intuitive Surgical, Inc, acquired Computer Motion, Inc, in 2003 and phased out the ZEUS [14]. At April 2005 got clearance for use in gynecologic procedures.

1.1.2 DA VINCI ROBOTIC SYSTEM

The DRS is composed of 3 components. The first component is the surgeon console which consists of a stereoscopic viewer, hand and foot controls. At the console, the surgeon controls the robotic arms and the EndoWrist instruments with natural hand and wrist motions that mimic movements performed in open surgery. The EndoWrist instruments are designed with seven degrees of freedom, one more than the human hand. Furthermore, the robotic system is able to remove human tremor and is ergonomic for the surgeon. Foot pedals located at the base of the console facilitate positioning of the camera, focus adjustment, activation of monopolar or bipolar energy sources, repositioning of the handgrips via a clutch mechanism, and toggling between instruments. The second component of the DRS is the InSite vision system, which provides 3D stereoscopic imaging via a 12-mm endoscope with 10 to 15 times higher magnification and high definition analysis. The third component of DRS is the patient-side cart with EndoWrist instruments and either 3 or 4 robotic arms. According to the above the DRS has several advantages over conventional laparoscopy such as 3-D stereoscopic imaging, seven degrees of movement, improved dexterity over laparoscopy, elimination of the fulcrum effect of laparoscopy, independency and less fatigue for the operating surgeon. Furthermore, RS allows less experienced laparoscopic surgeons to perform more complex procedures due to its faster learning curve comparing to conventional laparoscopy. However it has several disadvantages including lack of haptic feedback, increased cost, bulky machine habitus and need for additional staff and training [15].

1.1.3 ROBOTIC SURGERY IN GENERAL GYNECOLOGY AND GYNECOLOGIC ONCOLOGY

The DRS is well adapted in nearly every subspecialty of gynecology. It is increasingly used in hysterectomies, myomectomies, adnexal surgery, tubal anastomosis, sacrocolpopexies, ovarian transposition but the most profound application of robotic surgery is in the field of gynecologic oncology[16-21].
Marchal et al were first to describe 30 case series of simple and radical hysterectomies in 2005 using the DRS [22]. Later on, Sert and Abeler published the first case-control study of robotic and laparoscopic radical hysterectomy which showed no significant difference in perioperative parameters. However, blood loss was less and hospital stay was shorter in the robotic group [23]. Since then numerous studies followed that established the feasibility of robotic radical hysterectomy with reasonable operative time, low blood loss, less hospital stay, comparable lymph node yields and less morbidity compared with open surgery and can be considered as an alternate option for surgical management of cervical cancer without compromising the oncologic outcome [24-33]. For endometrial cancer RS has become the first choice for many institutions with reasonable operative time, less blood loss, short hospital stay, less morbidity and good oncologic outcome [34-41]. Lim et al [42] showed that RS has an easier and faster learning curve compared to laparoscopy, and Bell et al concluded that open surgery is the most expensive surgical approach followed by RS and laparoscopy when operating for endometrial cancer [43]. The evolving role of RS in ovarian cancer management has started to grow in the last few years, and below we review its major applications.

1.2 ROBOTIC SURGERY IN OVARIAN CANCER

1.2.1 TECHNIQUES FOR STAGING OVARIAN CANCER

The staging of OC is in compliance with the International Federation of Gynecology and Obstetrics (FIGO) staging system. The comprehensive surgical staging of the presumed early-stage OC is very important because it will lead to upstaging in 16% to 35% of the cases [44]. This includes upfront surgery with peritoneal washings, hysterectomy, bilateral salpingo-oophorectomy (BSO), omentectomy, appendectomy, multiple peritoneal biopsies, pelvic lymphadenectomy (PLD), and para-aortic lymphadenectomy (PALD). When preservation of fertility is desired and the disease seems to be confined to one ovary, the uterus and controlateral ovary is preserved.
For advanced OC maximal cytoreduction is needed with excision of all visible disease with the purpose of complete or optimal cytoreduction (residual disease <1cm). This in most of cases is a difficult radical operation involving the whole abdominal cavity from the diaphragmatic surfaces to lower pelvis [45-48]. In recurrent disease again maximal debulking of a localized recurrent platinum-sensitive OC prolongs survival [83]. In most of the above cases platinum and taxanes-based, intravenous or intraperitoneal chemotherapy follows. However cytoreduction to microscopic disease is not possible in all cases at the initial surgery, so neoadjuvant chemotherapy with interval cytoreduction has emerged as an alternative to primary surgery [49]. It has been shown that cytoreduction has a more significant influence on survival than the extent of a metastatic disease observed before surgery. This target has value in the primary cytoreduction, in interval debulking surgery after neoadjuvant chemotherapy, and in secondary cytoreduction in platinum-sensitive recurrent ovarian cancer patients. Extensive upper abdominal debulking surgery increases the rate of optimal cytoreduction and it is related to improved survival rates in advanced ovarian cancer undergoing primary cytoreduction and interval debulking surgery. Hepatic resection [84], splenectomy [85-86], video-assisted thoracic surgery [87], and diaphragmatic resection [88] have been considered as components of primary cytoreduction when necessary.
The inherent problem of RS is to safely and adequately operate in all four quadrants of abdominal cavity. For apparent early-stage OC, docking the robot for pelvic surgery between patients legs is usually enough but to accomplish a comprehensive surgical staging and optimal cytoreduction in more advanced cases different techniques have been proposed. Magrina et al [67] in their article about robotic radical hysterectomy, after finishing the operation in pelvis, undocked the robot, rotated the operating table 180°, inserted new ports more caudally and redocked the robotic column. So instead of the DRS to be between patients legs for the pelvic part of the operation, it is now behind patients head. With this technique they adequately completed PALD as described below and operated in the upper abdominal cavity.
Nezhat et al [68] developed a hybrid technique in which both conventional laparoscopy and RS are used in the surgical management of OC. They used

conventional laparoscopy for omentectomy and upper abdominal debulking in the first part and then they docked the robotic column on the left side of the patient, in order to complete the operation in the pelvis.

1.2.2 PARA-AORTIC LYMPHADENECTOMY

The infrarenal lymph nodes have been reported as one of the most common site of nodal metastases in OC [50]. Especially the left infrarenal nodes are the most difficult to remove both in laparoscopy and RS and are located in an area with potential vessel anomalies and therefore at higher risk of vascular injuries. Magrina et al [51] described the sovrapubic approach for infrarenal nodal dissection. In order to perform this dissection, and upper abdominal procedures, the robot is undocked after completion of pelvic surgery, the table is rotated 180°, additional trocars are inserted more caudally and the robot is redocked with the camera in a suprapubic position. A similar infrarenal nodal excision was performed by Zanagnolo et al [52] in their study with 51 patients with the vast majority having OC. The above studies showed that infrarenal aortic lymphadenectomy with the sovrapubic approach is feasible, safe and oncologically adequate. The operating time was acceptable and aortic nodes was similar between RS and laparoscopic studies [53-56]. Vizza et al described robotic transperitoneal aortic lymphadenectomy without relocating the robotic column or the patient [57]. In their study with 20 patients, 12 had OC. They placed the laparoscope supraumbilically and used 3 robotic arms and 1 assistant trocar. With the above mentioned setup, they managed to perform both pelvic and aortic lymphadenectomy- including left infrarenal nodes- with safety, and comparable nodal yields in a fast and simple approach. Lambaudie et al [58] in their study about robotic PALD up to the left renal vein, they executed 3 types of PALD in 53 patients with cancer : isolated extraperitoneal PALD, isolated transperitoneal PALD and combined transperitoneal PALD with other procedures. There were 4 patients with ovarian and tubal cancers. In 3 of them they performed combined transperitoneal PALD together with omentectomy and appendectomy. In the above 3 cases they set the robotic platform between the patients legs and the 12mm optical port in a high supraumbilical position. In the remaining 1 case, isolated extraperitoneal PALD was performed, setting the robot on patient’s right shoulder and all the ports in the lower abdomen. They found that more lymph nodes were excised in the isolated technique and in case of combined procedures the surgical approach should be modified regarding the patient body mass index (BMI) and the associated procedure to increase lymph node count.

1.2.3 EARLY EXPERIENCE. MIXED AND VARIOUS OVARIAN CANER CASES

The first data on the application of RS in management of OC were from mixed series of gynecological cancers (table 1), where perioperative parameters were not specifically reported for the subset of patients with OC. These early experiences clearly demonstrate the feasibility of applying RS to gynecologic cancer staging without an increase in complication rate or compromise to surgical technique [52, 57, 59-66]. S.J. Lee et al [66] evaluated the feasibility and safety of same-day discharge after robotic assisted hysterectomy. In their study with 200 patients with various indications, there were 5 with OC. They used DRS Si dual console platform with 4 arms and a assistant port. Intraoperative ketorolac and trocar site bupivacaine was used in several patient and prior to fascial closure, positive pressure ventilations were administered to decrease residual pneumoperitoneum and reduce postoperative pain. All patients received a similar oral pain and bowel medication regimen and were discharged if they had normal vital signs, adequate oxygenation, no nausea, pain control with oral medications and voided postoperatively. They concluded that same-day discharge after robotic assisted hysterectomy for benign and malignant conditions is feasible and safe.

Van Dam et al [119] reported the first case of robotic-assisted laparoscopic cytoreductive surgery for a metastatic lobular carcinoma of breast to both ovaries, where hysterectomy, bilateral adnexectomy and pelvic lymph node sampling was performed. They used the 4-arm DRS "S" model and 2 assistant ports. The operation lasted 200 min and blood loss was 300 mL.

1.2.4 FEASIBILITY OF ROBOTIC SURGERY IN BORDERLINE OVARIAN TUMORS (BOTs) AND EARLY-STAGE OVARIAN CANCER

BOTS account for approximately 10-15% of cases of early-stage OC. Most of the cases of BOTs present at an early stage, with 5-year survival rate after surgical excision of more than 95% [69]. Several studies so far showed the feasibility and safety of laparoscopic surgery in management of BOTs without compromising the oncologic outcome if adherence to surgical oncologic principles is applied [70-74]. Some of them addressed the importance of complete staging due to possibility the disease to be upstaged [75-76].

Early-stage OC is defined as cancer limited to one or both ovaries according to FIGO stage I. Laparoscopic studies demonstrated the feasibility, safety of MIS in management early-stage OC again without compromising the oncologic outcome when performed by gynecologic oncologists having perioperative benefits such as decreased blood loss, faster return of bowel function and lower hospital stay [77-81]. Nezhat et al [82] in part of their study examined perioperative outcomes, including complications rates of conventional laparoscopy (CL) versus robotic-assisted laparoscopy (RALS) in evaluation and management of early-stage OC. For early-stage OC they did a retrospective analysis of a prospectively maintained database of

22 operations : 9 RALS, 10 CL and 3 laparoscopic converted to laparotomy (LT) (Table 2). As mentioned before [68] they used the DRS via a hybrid technique in patients with upper and abdominal disease. BMI was greater in CL compared to RALS and there were no differences in past medical and surgical history between the 3 groups. The 3 conversions were due to 1 large uterine fibroid, 1 large pelvic mass and 1 due to dense adhesions. No difference between CL and RALS in estimated blood loss (EBL) or length of hospital stay (LOS), however the minimal invasive techniques had significantly less EBL and LOS than LT($p<0.05$). No significant difference in operating room time among the 3 groups. No intraoperative complications for CL and RALS. In LT there was an enterotomy repaired with bowel resection and primary end-to-end anastomosis. There was no significant difference in postoperative complications among the 3 groups. No significant difference between CL and RALS in PLD and PALD lymph node yields.
Magrina et al [89] compared perioperative and survival results of RS with CL and LT for primary surgical treatment of OC and showed decreased EBL and shorter LOS for patients with early disease undergoing type I debulking operated with RS and CL ($p<0.05$). Patients characteristics, operating time, complications, overall survival(OS) and progression free survival (PFS) were not statistically significant between the 3 surgical modalities for type I debulking.

1.2.5 FEASIBILITY OF ROBOTIC SURGERY IN ADVANCED OVARIAN CANER

Very few studies of MIS exist for advanced stage OC. Laparoscopic debulking of advanced OC have been published concluding that is feasible with minimal morbidity and acceptable survival [90-91].
Magrina et al [89], in their retrospective case-control analysis, compared 25 cases of RS to 27 cases of CL and 119 cases of LT for staging OC matched by age, BMI, number and type of procedures done. Patients were divided in 3 groups according to type of debulking. FIGO staging III-IV was 60%, 75% and 87% for RS, CL and LT respectively. Neoadjuvant chemotherapy was similar between the groups around 25%. Complete debulking was achieved in 84% for RS, 93% for CL and 56% for LT ($p<0.05$). Intraoperative complications were similar for type I debulking, lower for RS and CL for type II debulking and similar for RS and LT in type III debulking (no CL type III debulking). For type I interventions, there was a significant reduction in EBL and LOS in both RS and CL compared to LT. The operating times were comparable in all 3 groups : 282 min for RS, 249 min for CL and 230 min for LT. For type II debulking EBL was smaller and LOS was shorter for RS and CL versus LT ($p<0.05$), but operating time of RS was 78 min longer than CL and 86 min longer than LT ($p<0.05$). For type III debulking EBL and intraoperative complications were reduced for RS compared to LT (there was no CL group in type III debulking), but the mean operating time was 138 min longer for RS. Postoperative complications and LOS were similar in 2 groups. 3-year OS was similar between the 3 surgical modalities but 3-year PFS was higher for RS and CL, most likely due to selecting an open approach

for patients with more disseminated disease. However, the fact that no difference in OS and PFS was noted between RS and LT with complete and incomplete debulking shows that complete disease removal is more important that the type of surgical approach. There was only 1 conversion in CL group. None of the patients developed port-site metastases. The above results are summarized in table 3. The authors concluded that RS and CL are preferable for patients with OC requiring primary tumor excision alone or with one additional major procedure. LT is preferable for patients requiring two or more additional major procedures and survival is not affected by the type of surgical approach. There is potential for several biases due to heterogeneity of patients within and between the cohorts analyzed in the above study. For example no CL and only 2 cases undergoing RS in type III debulking. Furthermore the different percentages of advanced OC between the surgical groups could bias the study in favor of RS and CL. Despite the biases, we could say that RS is feasible and safe for early stage OC and selected patients with advanced stage disease not requiring multiple major procedures without compromising the oncologic outcome.

Feuer et al [92] in their retrospective study evaluating the perioperative outcomes and survival rates, compared 63 RS cases to 26 LT cases for initial staging or debulking after neoadjuvant chemotherapy of OC. Patients characteristics were matched for age, BMI and uterine weight but prior abdominal surgery was more common in LT group ($p<0.05$). Neoadjuvant chemotherapy was 52% in RS group and 15% in LT group ($p<0.05$). Patients with tumors <15 cm who did not require multiple advanced procedures were operated with RS, while patients with extensive disease or requiring multiple procedures were operated with LT. FIGO staging III-IV was 59% for RS and 73% for LT. The type and numbers of procedures performed were similar, except the lack of diaphragm stripping in LT group and the lack of bowel resection in RS group. Spleen and liver resection was not performed in 2 groups. Operating time was 139 min for RS group and 95 min for LT group ($p<0.05$), but EBL was smaller and LOS was shorter for RS group ($p<0.05$). Overall and major complication rates were similar between the 2 groups. Complete debulking was achieved in 73% of RS and 50% of LT group. At 1 year, survival and no evidence of disease rates were equivalent. There were no conversions and only 1 port-site metastasis. The results are summarized in table 3. The authors concluded that RS is feasible and effective for management of OC including patients treated with neoadjuvant chemotherapy. There are several biases such as higher percentage of patients with neoadjuvant chemotherapy and lower percentage with advanced disease in RS group and that large tumor masses were excluded from RS group. Interesting is that RS mean operating time is shorter than that of Magrina's study. This happened due to higher robotic ports placement, which allowed to reach 80% of the peritoneal cavity without redocking. Furthermore, the proper selection of patients with extensive pre-surgical laparoscopic assessment allowed RS to be completed in the majority of cases with a single dock. Finally we can say that the judicious use of neoadjuvant chemotherapy and proper patient selection not requiring multiple major procedures allowed the authors to successfully include more advanced cases amenable to RS with good outcomes.

Nezhat et al [82] also compared RALS, CL and LT in advanced/recurrent OC regarding perioperative outcomes and complications rates. Of the 47 cytoreductive operations performed for advanced/recurrent disease, 29 were CL, 10 were RALS and 8 were LT. The 8 LT cases are conversions from CL. The 3 groups were matched by age, BMI, medical and surgical history. The authors use liberally neoadjuvant chemotherapy in cases in which maximum cytoreduction does not appear feasible based on preoperative imaging and/or initial exploratory laparoscopic evaluation [93]. For recurrent disease, cytoreductive surgery was utilized for localized recurrences. EBL was smaller and LOS shorter in RALS and CL group when compared to LT group ($p<0.05$). Operating time was 245 min for CL, 320 min for RS and 374 min for LT ($p>0.05$).Complete cytoreduction was achieved in 72% in CL group, 100% in RALS and 63% in LT group ($p>0.05$). intraoperative and postoperative complications were similar between the 3 groups. 2 patients had port-site metastases in CL group and at the same time both presented with recurrent intraperitoneal disease. It seems that in carefully selected patients of advanced/recurrent OC, CL and RALS are acceptable approaches.

Lambrou et al [94] in their retrospective analysis, compared 24 RALS cases with 34 LT cases of primary or recurrent ovarian and fallopian tube cancer. Patients were matched by age, BMI and histology. Advanced/recurrent stage was 85% for LT group and 66% for RALS group ($p<0.05$). Multiple tumor masses were more frequent in the LT group ($p<0.05$). There was no significant difference in operative times between RALS and LT (mean 163 min vs 157 min). EBL was less and LOS shorter in RALS compared to LT ($p<0.05$). There were no differences in the intra-operative or post-operative complication rate, percentage of optimal cytoreduction, and overall survival between groups. Authors concluded that in appropriately selected patients with primary or recurrent OC this surgical approach is feasible and should be considered.

Chen et al [95] retrospectively analyzed 15 cases of ovarian/fallopian tube cancer that underwent robotic surgical management. 12 women received surgical staging procedures and 3 women received secondary debulking surgery due to ovarian cancer recurrence. For the 12 patients who underwent surgical staging, operating time was 120 min, EBL was 108 mL, lymph node dissection yield was 25 and LOS was 3 days. For the 3 patients that underwent secondary cytoreduction for recurrent disease, operating time was 150 min, EBL was 50 mL, lymph node dissection yield was 23 and LOS was 4 days. There were no conversions or postoperative complications in 2 groups. All patients are still alive and follow-up continues. Interesting was the case of a 13 week pregnant woman who underwent robotic surgical staging where the uterus and right ovary were preserved.

For advanced OC it has been described a novel anterior pelvic exenteration technique by Farghaly [96] utilizing the DRS. Six ports are inserted through the abdominal wall. A 12 mm trocar is inserted 25 cm above the pubic symphysis (4 cm above the umblicus) for the camera. Two 8 mm trocars placed at the lateral borders of the rectus sheath (8 cm from the supraumblical port in horizontal plane). An Additional 8 mm robotic trocar is inserted 8 cm lateral and just superior to the left robotic port. Two additional ports a 12 mm trocar is placed superior and lateral to the camera port, and a

5 mm tocar is inserted lateral to the right robotic port. In addition a V-care uterine manipulator is placed. DRS is used to perform the urinary cystectomy, total hysterectomy, bilateral salpingo-oophrectomy, PLD and PALD. The anterior pelvic exenteration procedure involves wide perivesical dissection. Then the robot is undocked and ileal conduit is performed via a 6 cm lower midline incision. Estimated operative time 4.6 hours, average blood loss 210 ml and hospital stay for 5 days.

1.2.6 FEASIBILITY OF ROBOTIC SURGERY IN RECURRENT OVARIAN CANCER

Secondary cytoreductive surgery is an acceptable treatment for patients with recurrent ovarian cancer platinum sensitive with progression free survival (PFS) of at least 6 months, having a good performance status, relatively isolated single region tumor recurrences and who can subsequently undergo platinum-based salvage chemotherapy [97-100]. Optimally resected patients have an 18 to 25 months survival advantage over those left with bulky disease and completely resected patients have overall median survival in excess of 44 months [101-103].
Hepatic resection of recurrent ovarian and fallopian tube cancers has been reported with high percentage of complete metastases resection and a median survival of 62 months. Fifty percent of patients also required diaphragm resection in this series [104]. Robotic-assisted major and minor hepatic resections have been described for management of benign and malignant liver lesions [105-106]. Resected hepatic parenchymal metastases in patients with primary epithelial ovarian carcinoma have favorable outlook with an actuarial 3 year cancer survival of 78% after resection. Diaphragm resection and repair has been described using traditional and robotic-assisted laparoscopy in the urologic literature [107-108].
Holloway et al [109] reported the first hepatic and diaphragm resection of recurrent OC using the DRS. The lesion was 3.4 cm and located high on the dome of right liver. The 12-mm camera port was placed superior and lateral to the umbilicus approximately 12 cm from the right costal margin in its midpoint. Two robotic operative 8.5 mm ports were placed 1 cm off the right costal margin, approximately 10 cm from the camera port. The fourth robotic port was placed in the right flank and a 12 mm assist port was placed in the right upper quadrant. The DRS was docked at patient’s right shoulder. Successful resection of the hepatic lesion and full thickness diaphragm revealed a high grade recurrent papillary serous OC with negative hepatic and diaphragmatic margins. EBL was 100 mL and total operative time 137 min with the patient discharged on day 5 after drainage of cytology negative pleural effusion. The above mentioned case report showed that isolated upper abdominal recurrent OC can be managed safely and effectively with RS.
Magrina et al [110] retrospectively analyzed 52 patients with recurrent OC that underwent secondary cytoreduction. 9 were operated with CL, 33 with LT and 10 with RS. Patients with a single or multiple recurrence sites and no ascites were considered candidates for minimally invasive surgery. These patients had undergone primary debulking followed by platinum based chemotherapy with 12 or more months

of disease-free interval and were in adequate functional status. None of them received chemotherapy prior to secondary cytoreduction. Patients in the 3 surgical groups were matched by age, BMI, number of previous surgeries, tumor type and grade, and by the number and type of major procedures performed. There were no differences for operating times, intra and postoperative complications between the 3 groups($p>0.05$). Statistically significant differences were noted for decreased EBL and LOS for the RS and CL groups($p<0.05$). Complete debulking was achieved in 70%, 72.7% and 88.9% for the RS, LT and CL group respectively($p>0.05$). OS at 3 years was 85.7%, 48.4% and 66.7% for RS, LT and CL group respectively($p>0.05$). Results of the above study are summarized in table 4. The authors concluded that LT is more appropriate for disease involving several abdominal quadrants and in case of widespread adhesions due to improved exposure –in particular for mesenteric peritoneal implants-, possibly decreased risk of bowel injury, avoidance of additional trocar placement, and -in the case of RS- the inability of the robotic arms to reach the four abdominal quadrants without redocking. The use of RS is preferable for isolated recurrences particularly in the diaphragms, liver, retrorectal area and in the pelvis. CL is preferable with limited disease and when redocking would be necessary. The above study shows that for a small number of carefully selected patients with limited OC recurrences, RS and CL is feasible and safe with smaller blood loss and shorter hospital stay than LT, without compromising the oncologic outcome.

Escobar et al [111] in their retrospective multi-institutional study assessed the feasibility and surgical outcomes of RS in the management of recurrent OC, which is the largest series in the literature so far. 48 patients were identified by preoperative screening, having a disease-free interval (DFI) after primary surgery and platinum/taxane based first line chemotherapy of at least 6 months. Patients with carcinomatosis were excluded for robotic management of recurrent OC. There were 4 conversions to LT. Most patients (~70%) had high grade serous histology, and 20% had mixed histology. 75% of patients who underwent robotic secondary cytoreduction recurred in a single region, of which 40% were in the pelvis and 35% were in the abdomen, with some having more than one mass within that region. 23% of patients recurred in both the abdomen and pelvis, and 1 patient recurred in both the pelvis and diaphragm. Fourteen patients had disease recurrences isolated to the lymph nodes (pelvic and/or para-aortic). For the 44 patients that underwent robotic cytoreduction, median operative time was 180 min, median EBL was 50 mL and median LOS was 1 day. 82% of these patients had a complete cytoreduction. Median follow-up for 36/44 patients managed robotically was 28.1 months with median PFS of 24.5 months and median OS of 50.1 months. Perioperative outcomes and surgical procedures of the above study are summarized in table 4. Despite the retrospective nature, the heterogeneity of recurrent disease and limited follow-up, this study clearly shows that RS is feasible, safe and effective for secondary cytoreduction of recurrent OC in limited sites without carcinomatosis.

Estape et al [112] in their retrospective review assessed the feasibility, perioperative and survival outcomes of RS for secondary cytoreduction of recurrent OC. 22 patients underwent 38 robotic secondary debulking procedures. The majority (19 of 22) were initially stage III or IV. 19 were platinum sensitive (DFI>6 months). 84% had a successful robotic secondary debulking, which included debulking parts of the following: organ or peritoneal surface (63%), retroperitoneum (31%), diaphragm (22%), colon resection with anastamosis or colostomy (18%), liver wedge resection (16%) or splenectomy (4%). Mean operative time was 71 min and mean blood loss was 85ml. Mean hospital stay was 1.6 days. They concluded that robotic secondary debulking is feasible in a subset of patients that have moderate volume disease (<8 cm) and do not have a small bowel obstruction at time of surgery.

Fagotti et al [113] retrospectively analyzed the feasibility of laparoscopic/robotic secondary cytoreductive surgery and hyperthermic intraperitoneal intraoperative chemotherapy(HIPEC) in a series of isolated platinum sensitive recurrent OC. Of the 10 patients meeting the criteria, 7 were managed with CL and 3 with RS. Complete debulking achieved in all cases. The procedures performed for the 3 cases treated with RS were: ahesiolysis/radical omentectomy for 1 patient and only radical omentectomy for the other 2. For the CL group splenectomy performed in 2 cases, adhesiolysis/selective peritonectomy in 4 cases and radical omentectomy in 1 case. The median operative time excluding HIPEC phase was 122 min, median EBL was 50 mL, median LOS was 4 days for the whole group with no big differences between CL and RS. There were no intraoperative complications with only one patient developing atrial fibrillation in early postoperative period. After a median follow-up of 10 months, there were no deaths or secondary recurrences. Despite the small number of cases, MIS and HIPEC is feasible in isolated recurrent OC in terms of postoperative complications, blood loss and hospital stay. There are studies that support the role of secondary cytoreductive surgery and HIPEC in platinum sensitive recurrent OC [114-115] and evidence from pharmacokinetics studies that strongly support the benefit of HIPEC administration in the context of MIS [116-118].

1.3 ROBOTIC SURGERY CONCERNS FOR OVARIAN CANCER MANAGEMENT

The feasibility, safety and efficacy of RS in OC management was addressed previously but there are some general issues regarding minimally invasive techniques staging OC

1.3.1 TUMOR RUPTURE

Tumor rupture during CL and RS to treat early-stage OC is of great concern. It will lead to immediate upstaging of the disease and may cause spread of tumor cells, compromising the prognosis. However there are no prospective studies to prove it. Nevertheless appropriate patient selection, liberal use of endobag and controlled aspiration are essential to reduce tumor rupture [120-122].

1.3.2 PORT-SITE METASTASES

Like CL there is also concern that circulating cancer cells in peritoneal cavity may implant at a robotic trocar entry and cause a tumor metastasis. CL studies showed that the overall incidence of port-site metastases is low ranging from 1% to 2% and is more common in patients with advanced disease and carcinomatosis [123-125]. From the other hand the development of port-site metastases has not been shown to affect overall survival [126]. This review article and robotic studies [127,128] confirm that port-site metastases are uncommon during robotic surgical procedures. Proper patient selection, oncologic principles maintenance and fast as possible start of adjuvant chemotherapy will result in low incidence of port-site metastases.

1.3.3 EFFECTS OF CO_2 ON TUMOR GROWTH

The effect of pneumoperitoneum is also another subject and the few studies conducted so far in vitro and in vivo show conflicting or limited results on tumor growth [129-132].

1.4 FUTURE OF ROBOTIC SURGERY

The currently available surgical robotic system is large and bulky. It requires a lot of space in the operating room and someone to drive and lock the system in place. This reduces ease of repositioning the patient or the flexibility of access to various quadrants in a surgical cavity. The heaviness of the system also prevents its use as a mobile device, so lowering the weight of a robotic system would open the opportunities for providing remote surgical care, perhaps in underserved environments. Therefore miniaturization will greatly expand the use of robots. Currently, one of the most promising technologies is the Micro Electro-Mechanical Systems (MEMS). These are made up of components of 1-100 µm in size and are extremely reliable and energy efficient. The use of such MEMS components will permit a dramatic reduction in size, increase in accuracy and speed. Revolutionary micro-and nanotechnology will change totally the concept of surgery. Intraluminal microrobots that are remotely controlled by the console or perhaps multiple tiny robots that are inserted intra-abdominally and controlled as a ‘‘squad’’ of robots each with a specific function and the surgeon acting like a commander, regulating the motion of the multiple robots are some future examples [133,134]. Although such robots exist today [135] the full development is still years away.
The lack of haptic feedback is a drawback in robotic surgery. Hence, it is key to develop instruments that will sense the forces against various structures such as blood vessels, and prevent damage to those structures by closed loop feedback, or record hand motions and forces as a medical record of the performance of the procedure. The hope is that information about the forces that a surgical robot experiences during the course of a surgery can be converted to electrical signals that can then distort the shape of telemanipulators being handled by the surgeon so that the surgeon receives some form of touch sensation feedback about the interactions with the tissues [136,137].
Emerging nonhaptic technologies that will augment robotic surgery capabilities will include embedding nonhaptic sensors into the tips of the instruments that will be able to provide real-time tissue physiology information, such as using the same microscopic size LED (light-emitting diodes) that are used in a pulse oximeter to provide information about tissue oxygenation and blood flow data to the surgeon [138-141] . The clinical relevance is that instead of haptic feedback telling the surgeon how much force is being applied to the tissues, a more valuable metric might be whether the forces applied are causing tissue ischemia. Tissue-specific fluorescent tags (fluorophobes) that can be attached to a given cell type (also referred to as ‘‘tumor paint’’) promise to be another adjunct in feedback. Through these special fluorescent-tagged antibodies targeting specific tumor cells, cancers can be visualized with hyperspectral imaging sensors so that a surgeon can avoid inadvertent tumor violation during extirpative procedures[142]. Coupling the visual data from the tumor paint and unique software control algorithms, the surgical robot can be engineered to physically prevent a surgeon from moving instruments into the tumor. These ‘‘virtual

fixtures'' can be assigned to any structure in the operative field and not only may be marked for tumors, but also used for creating ''no-fly'' or ''no-go'' zones to avoid dangerous structures such as delicate vasculature and tissues [143].
Ultimately, autonomous surgical procedures will be performed, where part or the complete surgical procedure is done by a robot once the procedure has been rehearsed by the surgeon, edited to be sure there are no errors, and then sent to the robot to be performed in half the time with no errors.

PART 2

OBJECTIVES

The objective of this article is to review all the published scientific literature regarding RS and its applications in OC management. We tried to address the feasibility, safety and efficacy of RS in early, advanced and recurrent OC. Part of this review is the history, evolution and future of RS.

MATERIAL AND METHODS

Relevant sources were identified searching PubMed, Medline, ScienceDirect and Scopus till date using the key words “robotic surgery” and “ovarian cancer management”.

TABLES

Table 1. RS in OC (mixed series)

Author	N	OR Min	EBL mL	hospital stay days	Type of operation	Lymph node count	Indications	Complications Intraoperative	Complications Postoperative
Lambaudie et al [59]	32	175.25	110	3.9	H +/- BSO+PLD or PALD	25	**Ovarian cancer (1)**, endometrial cancer (7), cervical cancer-dysplasia (24)	No	No
Field et al [60]	41	302	253	2.5	Type 1 H, RH, LD	_	**Ovarian cancer (3)**, endometrial cancer (3), cervical cancer (14)	Robot failure, bleeding, colotomy, bradycardia	Shoulder palsy
Velojovich et al [61]	118	213	71.3	1.35	Type 1 H +/- LD, staging LD, oophorectomy, RH type 3 + LD	15.4	**Ovarian cancer or LMP (9)**, *fallopian tube cancer (2)*, uterine cancer (35), cervical cancer or CIS (14), other cancers (6)	Vascular injury (2)	Vaginal cuff dehiscence (2), venous thromboembolism (2), bowel obstruction (1), ICU admission (1)
Diaz-Arrastia et al [62]	11	270-600	300	2	Type 1 H, staging	_	**Ovarian cancer (1)** CIN3 or pelvic mass (6), endometrial cancer (4)	Bleeding, blood transfusion	No
Kho et al [63]	91	128	79	1.4	Type 1 H +/- adnexectomy +/- LD	_	**Ovarian cancer (18)**	Enterotomy	Heart failure, pneumonia, ileus, vaginal cuff abscess, C difficile infection
Reynolds et al [64]	7	257	50	2	Type 1 H, staging	15	**Ovarian cancer or LMP (2)**, *fallopian tube cancer (1)*, endometrial cancer (4)	No	Sinusitis

Table 1 continued

Author	N	OR Min	EBL mL	hospital stay days	Type of operation	Lymph node count	Indications	Complications Intraoperative	Postoperative
Enrico Vizza et al [57]	20	224	1.3 g/dL hg fall	2	PALD, RH, PLD, adnexectomy, omentectomy	12.5	**Ovarian cancer (12)**, cervical cancer (2), endometrial cancer (6)	Bleeding from right common iliac vein	No
Thumuluru Kavitha Madhuri et al [65]	104	197	155.24	3	Type 1 H, PALD, RH, PLD, adnexectomy, omentectomy, RT	16.22	**Ovarian cancer (5)**, endometrial cancer (51), cervical cancer or dysplasia (34)	Vascular injury (3), bladder injury (3), robot failure (1)	1 death on day 7 from sepsis due to bowel obstruction, 1 mild cerebral oedema, 2 late bowel perforations, 3 temp. branchial plexus neuropraxia
Stephen J. Lee et al [66]	200	136	50	5.23 hours	H +/- BSO, PALD, PLD, omentectomy, appendectomy,	_	**Ovarian cancer (5)**, endometrial cancer (82), cervical cancer (8), others	Intraoperative vaginal laceration (4)	pelvic or abdominal wall hematoma (3), fever, trocar infection, incarcerated hernia, retained foreign body
V. Zanagnolo et al [52]	51	285	50	3	PLD and PALD +/- H	29.2	**Epithelial ovarian cancer (31)**, **nonepithelial ovarian cancer(9)**, *tubal cancer (4)*, cervical cancer (1) endometrial cancer (6)	Bleeding (2)	Chylous ascites (7), ureteral fistula (1), port-site hernia (2), lymphocele (4), lymphatic ascites (1)

BSO=bilateral salpingo-oophorectomy; C difficile=Clostridium difficile; CIN3=cervical intraepithelial neoplasia, grade 3; EBL=estimated blood loss; H=hysterectomy; ICU=intensive care unit; LD=lymphadenectomy; LMP=low malignant potential tumor; N=number of operations; OR=operating room; PALD=para-aortic lymphadenectomy; PLD=pelvic lymphadenectomy; RH=radical hysterectomy; RT=radical trachelectomy

Table 2. Early-stage OC. Comparison of surgical modalities

		N	OR Min	EBL mL	hospital stay days	Type of operation	Lymph node count	Histology	Complications Intraoperative	Postoperative	Conversions
FR Nezhat et al [82]	RALS	9	304.5	125	2	Staging	Pelvic: 10.5 Aortic: 12	Invasive epithelial (6), BOTs (2), germ cell (1)	NO	Wound infection (1), FUO (1)	0
	CL	10	190	100	1	Staging	Pelvic: 9 Aortic: 11	Invasive epithelial (2), BOTs (3), germ cell (4), stromal (1)	NO	Fever and possible and possible vaginal cuff cellulitis (1)	3
	LT	3	242	500	5	Staging	_	BOTs (3)	Enterotomy (1)	Ileus (1)	

BOTs=borderline ovarian tumors; CL=conventional laparoscopy; EBL=estimated blood loss; FUO=fever of unknown origin; LT=laparotomy; N=number of operations; OR=operating room; RALS=robotic-assisted laparoscopy

Table 3. RS in OC (pure cases). Primary Surgical Treatment. Comparison of surgical modalities

		N	OR Min	EBL mL	hospital stay days	Type of operation	Lymph node count	Complications: Intraoperative	Complications: Postoperative	Complete debulking %	OS %	PFS %
Javier F. Magrina et al [89]	robotic	25	315	164	4.2	Type I debulking, type II debulking, type III debulking	25.3	bladder injury (2), aortic injury (1)	vaginal cuff dehiscence (2), pleural effusion (1), bleeding (1), ileus (1), trocar site infection (1), pulmonary edema (1)	84	67.1 (at 3 years)	74.2
	laparoscopy	27	254	267	3.2	Type I debulking, type II debulking	22.8	enterotomy (1), bleeding (2)	pelvic abscess (1)	93	75.6 (at 3 years)	62.6
	Laparotomy	119	261	1307	9.4	Type I debulking, type II debulking, type III debulking	23.1	bleeding (6), intestinal injuries (5), bladder injury (2), ureteral injury (2), partial gastrectomy due to gastric ischemia (1)	wound (10), intestinal (11), cardiovascular (7), pulmonary (7), UTI (2), pelvic abscess (2), bleeding (1), pelvic hematoma (1), hand compartment sy. (1), death (1) due to sepsis	56	66 (at 3 years)	40.2
Gerald A. Feuer et al [92]	robotic	63	138.6	94.9	2.3	Debulking for localized disease, debulking for clinical Stage II-IIIC	13.3	hypogastric artery bleed (1), vena cava laceration (1), cystotomy (1), vaginal tear (1)	cuff dehiscence and fistula (1), pelvic abscess (1), aspiration/p. edema/ileus (1), PE/ATN/p. edema/transfusion (1), ICU/transfusion/ileus/p. edema (1) cholecystitis/pelvic abscess (1), cuff dehiscence (1), ileus (3), fever (1), umbilical infection (1), lymphedema (1), lower extremities edema (1), transfusion (1), wound infection (1), seroma (1)	73	97.2 (36/63 at 1 year)	80.6
	Laparotomy	26	95.2	385.4	6.2	Debulking for localized disease, debulking for clinical Stage II-IIIC	10.7	bleeding (2), cystotomy/postopc ileus (1), vena cava tear/postopc ileus/ pelvic hematoma (1)	hernia (1), abdominal pain (1), UTI/pain (1), fever/UTI/DVT (1), hypertension/pneumonia (1)	50	90 (20/26 at 1 year)	85

ATN=acute tubular necrosis; DVT =deep vein thrombosis; EBL=estimated blood loss; ICU=intensive care unit; N=number of operations; OR=operating room; OS=overall survival; p.=pulmonary; PE=pulmonary embolism; PFS=progression free survival; sy.=syndrome; type I debulking= hysterectomy, adnexectomy, omentectomy, pelvic and aortic lymphadenectomy, appendectomy and removal of metastatic peritoneal disease if present; type II debulking= type I debulking and one additional major procedure; type III debulking = type I debulking and 2 or more major procedures(modified posterior pelvic exenteration with low colorectal anastomosis, sigmoid resection with high anastomosis, transverse colon resection, ileocecal resection, and/or small bowel resection, full thickness diaphragm resection, resection of liver disease, and splenectomy); UTI=urinary tract infection;

Table 4. RS in OC recurrent disease. Comparison of surgical modalities

Study	Modality	N	OR Min	EBL mL	hospital stay days	Type of operation	Complications: Intraoperative	Complications: Postoperative	Conversions	Complete debulking %	OS %	PFS %
Javier F. Magrina et al [110]	robotic	10	220.6	206.3	3.4	Resection of superficial pelvic implants (6), resection of superficial abdominal implants(9), small bowel resection (1), colon resection (2), PLD(6),PALD (4), liver metastases resection (5), diaphragm resection(5), segmental bladder/ureteral resection(1), resection of invasive pelvic recurrences (1), omentectomy(1), adhesiolysis(1), additional operations(4)	Vena cava injury(1)	Pleural effusion (1), rectosigmoid anastomotic leak (1)	No	70	85.7 (6/10 at 3 years)	43.8
	laparoscopy	9	177	127.8	4.1	Resection of superficial pelvic implants (5), resection of superficial abdominal implants(6), splenectomy (1), small bowel resection (1), PLD(2),PALD (1), liver metastases resection (1), diaphragm resection(3), resection of invasive pelvic recurrences(5), omentectomy(4), adhesiolysis(3), additional operations(3)	Enterotomies (2)	Trocar site hernia (1), pneumothorax(1), pleural effusion(1) pericardial effusion (1)	No	88.9	66.7 (8/9 at 3 years)	22.9
	Laparotomy	33	222.3	936.7	9.9	Resection of superficial pelvic implants (19), resection of superficial abdominal implants(31), splenectomy (4), small bowel resection (10), colon resection (11), PLD(11),PALD (13), liver metastases resection (5), diaphragm resection (6), segmental bladder/ureteral resection(2), resection of invasive pelvic recurrences (10), omentectomy(12), vaginectomy (2), adhesiolysis(7), additional operations(12)	Enterotomies (2), cystotomies(3), major vein injuries (2)	Pleural effusion (4), pneumonia (2), wound complications (2), jejunal leak (1) with re-operation, sigmoid perforation with re-operation, bleeding (1) with transfusion, sepsis (1) with reoperation, bowel obstruction (1) with re-operation, ureteral fistula (1) with reoperation		72.7	48.4 (24/33 at 3 years)	33.1

Table 4 continued

		N	OR Min	EBL mL	hospital days	Recurrence sites	Type of operation	Complications Intraoperative	Complications Postoperative	Conversions	Complete debulking %	OS m.	PFS m.
PF Escobar et al [111]	robotic	44	180	50	1	Single region (33), multiple region (11)	Organ sparing (35), appendectomy (1), large bowel resection (3), large bowel and small bowel resection (1), liver and large bowel resection (1), diaphragm resection (2), splenectomy (1)	No	PTX(1), ileus (2), C. diffile infection (1), cellulitis (1), sepsis (1), wound infection (1)	4	82	50.1 (36/44 at 28.1 m.)	24.5
	Laparotomy	4	247	250	6	Single region (3), multiple region (1)	Organ sparing (2),	No	No		100	-	-

EBL=estimated blood loss; N=number of operations; OR=operating room; OS=overall survival; PALD=para-aortic lymphadenectomy, PFS=progression free survival; PLD=pelvic lymphadenectomy; PTX=pneumothorax

DISCUSSION

The main concern about RS in management of OC is the feasibility to operate in all 4 quadrants of the peritoneal cavity due to bulkiness and inflexibility of the current DRS. For early-stage OC docking the DRS for pelvic surgery is usually enough. For more advanced cases, rotation of the table, hybrid robotic-conventional laparoscopic technique, insertion of trocars higher than usual have been reported.

RS is superior to CL with respect to visualization, dexterity, ergonomics and surgeon's learning curve. However these advantages are not seen yet in OC management where RS and CL show similar perioperative results but robotic operating time is usually longer.

RS is feasible and safe without compromising the oncologic outcome in early-stage OC and selected patients with advanced and recurrent disease. It shows smaller EBL, shorter hospital stay and fewer complications than LT.

The literature regarding RS in OC management consists of studies with mixed gynecologic malignancies, case reports, reviews, case-control analyses and nonrandomized comparative observational studies all with retrospective nature. Furthermore, the reviewed studies have several biases especially in advanced OC regarding patient selection and type of procedure performed with only short term outcomes.

As experience grows, well designed prospective studies as well as cost effective analyses comparing RS with CL and LT will help characterize the true advantages and disadvantages of this technology and determine the appropriate applications in OC management. Limitations such as absence of tactile feedback, bulky design, high cost and lack of standardized training method will need to be addressed.

CONCLUSION

Although still in its infancy, RS is a cutting-edge-technology that has already demonstrated far-reaching implications in gynecologic oncology especially as far as uterine and cervical cancer is concerned. Regarding OC RS just started to develop. With the current technology the application of RS is limited to selected OC patients but the studies conducted so far give promising results for the future of RS. As technology evolves into smaller machines and specialty-specific instruments, RS will almost inevitably become part of all surgical specialties.

ΠΕΡΙΛΗΨΗ

Μετά την έγκριση της από τον αμερικανικό οργανισμό τροφίμων και φαρμάκων για γυναικολογική χειρουργική, η χρήση της ρομποτικής χειρουργικής στην γυναικολογική ογκολογία έχει αυξηθεί ραγδαία. Παρά τους αρχικούς ενδοιασμούς για την εφαρμογή της πιο προηγμένης τεχνολογικά, ελάχιστα επεμβατικής χειρουργικής στην γυναικολογική ογκολογία, η χειρουργική αυτή προσέγγιση έχει φανεί ότι είναι τόσο ασφαλής όσο και εφικτή και τουλάχιστον ισοδύναμη με την συμβατική λαπαροσκοπική χειρουργική στην αντιμετώπιση του καρκίνου του τραχήλου και του σώματος της μήτρας. Ωστόσο επικρατεί σκεπτικισμός σχετικά με την ασφάλεια της ρομποτικής χειρουργικής στην αντιμετώπιση του ωοθηκικού καρκίνου όσον αφορά στην εκτίμηση, διάγνωση και σταδιοποίηση του προφανούς ωοθηκικού καρκίνου αρχικού σταδίου, της πρωτογενούς ή μετά από προεγχειριτική χημειοθεραπεία κυτταρομείωσης του ωοθηκικού καρκίνου προχωρημένου σταδίου και την εφαρμογή της στην κυτταρομείωση των υποτροπών της νόσου. Η βιβλιογραφική αυτή ανασκόπηση προσπαθεί να αναδείξει τις κύριες εφαρμογές και τον δυνητικό ρολό της ρομποτικής χειρουργικής στην αντιμετώπιση του ωοθηκικού καρκίνου. Στο μέλλον απαιτούνται τυχαιοποιημένες προοπτικές μελέτες για να στηρίξουν τον ρόλο της ρομποτικής χειρουργικής στην αντιμετώπιση του ωοθηκικού καρκίνου.

ABSTRACT

Since its approval by the FDA in 2005 for gynecological surgery, the use of robotic surgery (RS) in gynecologic oncology has increased dramatically. Despite initial considerations about the application of the most technologically advanced modality of minimally invasive surgery (MIS) in oncogynecology, this surgical approach has been shown to be both safe and feasible and at least equal to conventional laparoscopic surgery in management of cervical and uterine cancer. However there are feasibility and safety concerns regarding the role of RS in management of ovarian cancer (OC) as far as evaluation, diagnosis and staging of apparent early stage OC, primary or postneoadjuvant chemotherapy debulking of advanced OC and its use in cytoreduction of recurrent disease. This review of the literature tries to address the main applications and the potential role of RS in OC management. Future prospective randomized control studies are needed to support the role of RS in management of OC.

REFERENCES

[1] American Cancer Society. Cancer Facts and Figures, 2011. Atlanta, GA: American Cancer Society; 2011.

[2] Jemal A, Siegel R, Xu J,Ward E. Cancer Statistics, 2010 [published correction appears in CA Cancer J Clin. 2011;61:133-134]. CA Cancer J Clin. 2010;60:277–300.

[3] Crum CP, McKeon FD, XianW. BRCA, the oviduct, and the space and time continuum of pelvic serous carcinogenesis. Int J Gynecol Cancer. 2012;22:S29–S34.

[4] Kwoh YS, Hou J, Jonckheere EA, Hayati S. A robot with improved absolute positioning accuracy for CT-guided stereotactic brain surgery. IEEE Trans Biomed Eng. 1988;35:153–160.

[5] Davies BL, Hibberd RD, Coptcoat MJ, Wickham JEA. A surgeon robot prostatectomy: a laboratory evaluation. J Med Eng Technol. 1989;13:273–277.

[6] Bauer A, Borner M, Lahmer A. Clinical experience with a medical robotic system for total hip replacement. In: Nolte LP, Ganz R, editors. Computer-assisted Orthopedic Surgery. Bern, Switzerland: Hogrefe & Huber; 1999. p. 128–133.

[7] Hockstein NG, Gourin CG, Faust RA, Terris DJ. A history of robots: from science fiction to surgical robotics. J Robotic Surg. 2007;1:113–118.

[8] Talamini MA. Robotic surgery: is it for you? Adv Surg. 2002;36:1–13.

[9] Mettler L, Ibrahim M, Jonat W. One year of experience working with the aid of a robotic assistant (the voice-controlled optic holder AESOP) in gynecologic endoscopic surgery. Hum Reprod. 1998;13:2748–2750.

[10] Marescaux J, Rubino F. The ZEUS robotic system: experimental and clinical applications. Surg Clin North Am. 2003;83:1305–1315.

[11] Marecaux J, Leroy J, Gagner M. Transatlantic robotic-assisted telesurgery. Nature. 2001;413:379–380.

[12] Marescaux J, Leroy J, Rubino F, et al. Transcontinental robot-assisted remote telesurgery: feasibility and potential applications. Ann Surg. 2002;235:487–492.

[13] Falcone T, Goldberg JM, Margossian H, Stevens L. Robotically assisted laparoscopic microsurgical anastomosis: a human pilot study. Fertil Steril. 2000;73:1040–1042.

[14] R. Peplinski, "Past, present and future of the Da Vinci robot," in *2nd UK Robotic Urology Course*, Guy's Hospital, London, UK, 2006.

[15] Jennifer E. Cho, Farr R. Nezhat. Robotics and Gynecologic Oncology: Review of the Literature. Journal of Minimally Invasive Gynecology (2009) 16, 669–681

[16] J. E. Cho, A. H. A. Shamshirsaz, C. Nezhat, C. Nezhat, and F. Nezhat, "New technologies for reproductive medicine: laparoscopy, endoscopy, robotic surgery and gynecology. A review of the literature," *Minerva Ginecologica*, vol. 62, no. 2, pp. 137–167, 2010.

[17] R. W. Holloway, S. D. Patel, and S. Ahmad, "Robotic surgery in gynecology," *Scandinavian Journal of Surgery*, vol. 98, no.2, pp. 96–109, 2009.
[18] C. A. Matthews, "Applications of robotic surgery in gynecology," *Journal of Women's Health*, vol. 19, no. 5, pp. 863–867, 2010
[19] A. Tinelli, A. Malvasi, and S. Gustapane, "Robotic assisted surgery in gynecology: current insights and future perspectives," *Recent Patents on Biotechnology*, 2011.
[20] A. C. Frick and T. Falcone, "Robotics in gynecologic surgery," *Minerva Ginecologica*, vol. 61, no. 3, pp. 187–199, 2009
[21] C. C. G. Chen and T. Falcone, "Robotic gynecologic surgery: past, present, and future," *Clinical Obstetrics and Gynecology*, vol. 52, no. 3, pp. 335–343, 2009.
[22] Marchal F, Rauch P, Vandromme J, et al. Telerobotic-assisted laparoscopic hysterectomy for benign and oncologic pathologies: initial clinical experience with 30 patients. Surg Endosc 2005; 19:826–831.
[23] Sert B, Abeler V. Robotic radical hysterectomy in early-stage cervical carcinoma patients, comparing results with total laparoscopic radical hysterectomy cases. The future is now? Int J Med Robot 2007; 3:224–228.
[24] Magrina JF, Kho RM, Weaver AL, et al. Robotic radical hysterectomy: comparison with laparoscopy and laparotomy. Gynecol Oncol 2008; 109:86–91.
[25] Estape R, Lambrou N, Diaz R, et al. A case matched analysis of robotic radical hysterectomy with lymphadenectomy compared with laparoscopy and laparotomy. Gynecol Oncol 2009; 113:357–361.
[26] Sert MB, Abeler V. Robot-assisted laparoscopic radical hysterectomy: comparison with total laparoscopic hysterectomy and abdominal radical hysterectomy; one surgeon's experience at the Norwegian Radium Hospital. Gynecol Oncol 2011; 121:600–604.
[27] Lowe MP, Chamberlain DH, Kamelle SA, et al. A multiinstitutional experience with robotic-assisted radical hysterectomy for early stage cervical cancer. Gynecol Oncol 2009; 113:191–194.
[28] Ko EM, Muto MG, Berkowitz RS, Feltmate CM. Robotic versus open radical hysterectomy: a comparative study at a single institution. Gynecol Oncol 2008; 111:425–430.
[29] Maggioni A, Minig L, Zanagnolo V, et al. Robotic approach for cervical cancer: comparison with laparotomy: a case control study. Gynecol Oncol 2009; 115:60–64.
[30] Persson J, Reynisson P, Borgfeldt C, et al. Robot assisted laparoscopic radical hysterectomy and pelvic lymphadenectomy with short and long term morbidity data. Gynecol Oncol 2009; 113:185–190.
[31] Boggess JF, Gehrig PA, Cantrell L, et al. A case–control study of robot-assisted type III radical hysterectomy with pelvic lymph node dissection compared with open radical hysterectomy. Am J Obstet Gynecol 2008; 199:e351–e357.
[32] Cantrell LA, Mendivil A, Gehrig PA, Boggess JF. Survival outcomes for women undergoing type III robotic radical hysterectomy for cervical cancer: a 3-year experience. Gynecol Oncol 2010; 117:260–265.

[33] Obermair A, Gebski V, Frumovitz M, et al. A phase III randomized clinical trial comparing laparoscopic or robotic radical hysterectomy with abdominal radical hysterectomy in patients with early stage cervical cancer. J Minim Invasive Gynecol 2008; 15:584–588.
[34] Cardenas-Goicoechea J, Adams S, Bhat SB, Randall TC. Surgical outcomes of robotic-assisted surgical staging for endometrial cancer are equivalent to traditional laparoscopic staging at a minimally invasive surgical center. Gynecol Oncol 2010; 117:224–228.
[35] Boggess JF, Gehrig PA, Cantrell L, et al. A comparative study of 3 surgical methods for hysterectomy with staging for endometrial cancer: robotic assistance, laparoscopy, laparotomy. Am J Obstet Gynecol 2008; 199:e361–e369.
[36] DeNardis SA, Holloway RW, Bigsby GE 4th, et al. Robotically assisted laparoscopic hysterectomy versus total abdominal hysterectomy and lymphadenectomy for endometrial cancer. Gynecol Oncol 2008; 111:412–417.
[37] Gehrig PA, Cantrell LA, Shafer A, et al. What is the optimal minimally invasive surgical procedure for endometrial cancer staging in the obese and morbidly obese woman? Gynecol Oncol 2008; 111:41–45.
[38] Gocmen A, Sanlikan F, Ucar MG. Comparison of robotic-assisted surgery outcomes with laparotomy for endometrial cancer staging in Turkey. Arch Gynecol Obstet 2010; 282:539–545.
[39] Seamon LG, Fowler JM, Richardson DL, et al. A detailed analysis of the learning curve: robotic hysterectomy and pelvic-aortic lymphadenectomy for endometrial cancer. Gynecol Oncol 2009; 114:162–167.
[40] Holloway RW, Ahmad S, DeNardis SA, et al. Robotic-assisted laparoscopic hysterectomy and lymphadenectomy for endometrial cancer: analysis of surgical performance. Gynecol Oncol 2009; 115:447–452.
[41] Gaia G, Holloway RW, Santoro L, et al. Robotic-assisted hysterectomy for endometrial cancer compared with traditional laparoscopic and laparotomy approaches: a systematic review. Obstet Gynecol 2010; 116:1422–1431.
[42] Lim PC, Kang E, Park do H. A comparative detail analysis of the learning curve and surgical outcome for robotic hysterectomy with lymphadenectomy versus laparoscopic hysterectomy with lymphadenectomy in treatment of endometrial cancer: a case-matched controlled study of the first one hundred twenty two patients. Gynecol Oncol 2011; 120:413–418.
[43] Bell MC, Torgerson J, Seshadri-Kreaden U, et al. Comparison of outcomes and cost for endometrial cancer staging via traditional laparotomy, standard laparoscopy and robotic techniques. Gynecol Oncol 2008; 111:407–411.
[44] Stier EA, Barakat RR, Curtin JP, et al. Laparotomy to complete staging of presumed early ovarian cancer. Obstet Gynecol. 1996;87:737–40.
[45] Bristow RE, Tomacruz SR, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta analysis. J Clin Oncol. 2002; 20:1248–1259.

[46] Winter WE III, Maxwell GL, Tian C, et al. Gynecologic Oncology Group Study. Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2007;25:3621–3627.
[47] Winter WE III, Maxwell GL, Tian C, et al. Gynecologic Oncology Group. Tumor residual after surgical cytoreduction in prediction of clinical outcome in stage IV epithelial ovarian cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2008;26:83–89.
[48] Du Bois A, Reuss A, Pujade-Lauraine E, Harter P, Ray-Coguard I, Pfisterer J. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials; by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d' Investigateurs Nationaux pour les Etudes des Cancers l'Ovaire (GINECO). Cancer. 2009;115:1234–1244.
[49] Vergote I, Trop_e CG, Amant F, et al. European Organization for Research and Treatment of Cancer-Gynaecological Cancer Group; NCIC Clinical Trials Group. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med. 2010;363:943–953.
[50] Pereira A, Magrina JF, Rey V, et al. Pelvic and aortic lymph node metastasis in epithelial ovarian cancer. Gynecol Oncol. 2007; 105:604-608.
[51] Magrina JF, Long JB, Kho RM, et al. Robotic transperitoneal infrarenal aortic lymphadenectomy: technique and results. Int J Gynecol Cancer. 2010;20:184–187.
[52] V. Zanagnolo, D. Rollo, T. Tomaselli, P. G. Rosenberg, L. Bocciolone, F. Landoni, G. Aletti, M. Peiretti, F. Sanguineti, and A.Maggioni. Robotic-Assisted Transperitoneal Aortic Lymphadenectomy as Part of Staging Procedure for Gynaecological Malignancies: Single Institution Experience. Obstet Gynecol Int. 2013;2013:931318.
[53] Kohler C, Tozzi R, Klemm P, et al. Laparoscopic paraaortic left-sided transperitoneal infrarenal lymphadenectomy in patients with gynecologic malignancies: technique and results. Gynecol Oncol. 2003;91:139-148.
[54] Abu-Rustum NR, Chi DS, Sonoda Y, et al. Transperitoneal laparoscopic pelvic and para-aortic lymph node dissection using the argon-beam coagulator and monopolar instruments: an 8-year study and description of technique. Gynecol Oncol. 2003;89:504-513.
[55] Ghezzi F, Cromi A, Uccella S, et al. Laparoscopy versus laparotomy for the surgical management of apparent early stage ovarian cancer. Gynecol Oncol. 2007;105:409-413.
[56] Schlaerth JB, Spirtos NM, Carson LF, et al. Laparoscopic retroperitoneal lymphadenectomy followed by immediate laparotomy in women with cervical cancer: a gynecologic oncology group study. Gynecol Oncol. 2002;85:81-88.
[57] Enrico Vizza, Emanuela Mancini, Ermelinda Baiocco, Cristina Vicenzoni, Lodovico Patrizi, Maria Saltari, Monica Cimino, Stefano Sindico, Giacomo Corrado, Robotic Transperitoneal Aortic Lymphadenectomy in Gynecologic Cancer: A New Robotic Surgical Technique and Review of the Literature. Ann Surg Oncol (2012) 19:3832–3838.
[58] Eric Lambaudie, Fabrice Narducci, Eric Leblanc, Marie Bannier, Camille Jauffret, Francesco Cannone, Gilles Houvenaeghel. Robotically assisted laparoscopy for paraaortic lymphadenectomy: technical description and results of an initial experience. Surg Endosc (2012) 26:2430–2435.

[59] Lambaudie E, Houvenaeghel G, Walz J, et al. Robot- assisted laparoscopy in gynecologic oncology. Surg Endosc. 2008;22:2743–2747.
[60] Field JB, Benoit MF, Dinh TA, Diaz-Arrastia C. Computer-enhanced robotic surgery in gynecologic oncology [published online ahead of print December 19, 2007]. Surg Endosc. 2007;21:244–246.
[61] Veljovich DS, Paley PJ, Drescher CW, Everett EN, Shah C, Peters WA III. Robotic surgery in gynecologic oncology: program initiation and outcomes after the first year with comparison with laparotomy for endometrial cancer staging. Am J Obstet Gynecol. 2008;198:679. e1–679.e10.
[62] Diaz-Arrastia C, Jurnalov C, Gomez G, Townsend C Jr. Laparoscopic hysterectomy using a computer-enhanced surgical robot [published online ahead of print June 27, 2002]. Surg Endosc. 2002;16:1271–1273.
[63] Kho R, Hilger W, Hentz J, Magtibay P, Magrina J. Robotic radical hysterectomy: technique and initial outcomes. Am J Obstet Gynecol. 2007;197:113. e1–113.e4.
[64] Reynolds RK, Burke WM, Advincula AP. Preliminary experience with robot-assisted laparoscopic staging of gynecologic malignancies. JSLS. 2005;9:149–158.
[65] Thumuluru Kavitha Madhuri, Imran Hamzawala, Anil Tailor, Simon Butler-Manuel. Robot assisted surgery in gynaecologic oncology – starting a program and initial learning curve from a UK tertiary referral centre: the Guildford perspective. Int J Med Robotics Comput Assist Surg 2012; 8: 496–503.
[66] Stephen J. Lee, Bianca Calderon, Ginger J. Gardner, Allison Mays, Stephanie Nolan, Yukio Sonoda, Richard R. Barakat, Mario M. Leitao Jr. The feasibility and safety of same-day discharge after robotic-assisted hysterectomy alone or with other procedures for benign and malignant indications. Gynecol Oncol (2014), http://dx.doi.org/10.1016/j.ygyno.2014.04.006.
[67] Javier F. Magrina , Rosanne Kho, Paul M. Magtibay. Robotic radical hysterectomy: Technical aspects. Gynecologic Oncology 113 (2009) 28–31.
[68] Farr R. Nezhat, Tanja Pejovic, Tamara N. Finger, Susan S. Khalil. Role of Minimally Invasive Surgery in Ovarian Cancer. Journal of Minimally Invasive Gynecology (2013) 20, 754–765.
[69] Lenhard MS, Mitterer S, Kumper C, et al. Long-term follow-up after ovarian borderline tumor: relapse and survival in a large patient cohort. Eur J Obstet Gynecol Reprod Biol. 2009;145:189–94.
[70] Romagnolo C, Gadducci A, Sartori E, Zola P, Maggino T. Management of borderline ovarian tumors: results of an Italian multicenter study. Gynecol Oncol. 2006;101:255–60.
[71] Donnez J, Munschke A, Berliere M, et al. Safety of conservative management and fertility outcome in women with borderline tumors of the ovary. Fertil Steril. 2003;79:1216–21.
[72] Tinelli R, Malzoni M, Cosentino F, et al. Feasibility, safety, and efficacy of conservative laparoscopic treatment of borderline ovarian tumors. Fertil Steril. 2009;92:736–41.

[73] Camatte S, Morice P, Atallah D, et al. Clinical outcome after laparoscopic pure management of borderline ovarian tumors: results of a series of 34 patients. Ann Oncol. 2004;15:605–9.
[74] Fauvet R, Boccara J, Dufournet C, Poncelet C, Darai E. Laparoscopic management of borderline ovarian tumors: results of a French multicenter study. Ann Oncol. 2005;16:403–10.
[75] Darai E, Tulpin L, Prugnolle H, Cortez A, Dubernard G. Laparoscopic restaging of borderline ovarian tumors. Surg Endosc. 2007;21:2039–43.
[76] Querleu D, Papageorgiou T, Lambaudie E, et al. Laparoscopic restaging of borderline ovarian tumours: results of 30 cases initially presumed as stage IA borderline ovarian tumours. BJOG. 2003;110:201–4.
[77] Tozzi R, Schneider A. Laparoscopic treatment of early ovarian cancer. Curr Opin Obstet Gynecol. 2005;17:354–358.
[78] Weber S, McCann CK, Boruta DM, Schorge JO, Growdon WB. Laparoscopic surgical staging of early ovarian cancer. Rev Obstet Gynecol. 2011;4:117–122.
[79] Nezhat FR, Ezzati M, Chuang L, et al. Laparoscopic management of early ovarian and fallopian tube cancers: surgical and survival outcome. Am J Obstet Gynecol. 2009;200:83–85.
[80] Angioli R, Muzii L, Battista C, et al. The role of laparoscopy in ovarian carcinoma. Minerva Gynecol. 2009;61:35–43.
[81] Childers JM, Lang J, Surwit EA, Hatch KD. Laparoscopic surgical staging of ovarian cancer. Gynecol Oncol. 1995;59:25–33.
[82] FR Nezhat, TN Finger, P Vetere, AR Radjabi, M Vega, L Averbuch, S Khalil, SK Altinbas, D Lax. Comparison of Perioperative Outcomes and Complication Rates Between Conventional Versus Robotic-Assisted Laparoscopy in the Evaluation and Management of Early, Advanced, and Recurrent Stage Ovarian, Fallopian Tube, and Primary Peritoneal Cancer. Int J Gynecol Cancer 2014;24: 600-607.
[83] R. Salani, A. Santillan, M.L. Zahurak, R.L. Giuntoli II, G.J. Gardner and D.K. Armstrong et al. Secondary cytoreductive surgery for localized, recurrent epithelial ovarian cancer: analysis of prognostic factors and survival outcome. Cancer 109 (2007), pp. 685–691.
[84] M.A. Merideth, W.A. Cliby, G.L. Keeney, T.G. Lesnick, D.M. Nagorney, K.C. Podratz. Hepatic resection for metachronous metastases from ovarian carcinoma. Gynecol. Oncol. 89 (2003), pp. 16–21.
[85] S.M. Eisenkop, N.M. Spirtos, W.C. Lin. Splenectomy in the context of primary cytoreductive operations for advanced epithelial ovarian cancer. Gynecol. Oncol. 100 (2006), pp. 344–348.
[86] P.M. Magtibay, P.B. Adams, M.B. Silverman, S.S. Cha, K.C. Podratz. Splenectomy as part of cytoreductive surgery in ovarian cancer. Gynecol. Oncol. 102 (2006), pp. 369–374.
[87] M.M. Juretzka, N.R. Abu-Rustum, Y. Sonoda, R.J. Downey, R.M. Flores, B.J. Park. The impact of video-assisted thoracic surgery (VATS) in patients with suspected advanced ovarian malignancies and pleural effusion. Gynecol. Oncol. 104 (2007), pp. 670–674.
[88] W. Cliby, S. Dowdy, S.S. Feitoza, B.S. Gostout, K.C. Podratz. Diaphragm resection for ovarian cancer: technique and short-term complications. Gynecol. Oncol. 94 (2004), pp. 655–660.

[89] Magrina JF, Zanagnolo V, Noble BN, Kho RM, Magtibay P. Robotic approach for ovarian cancer: Perioperative and survival results and comparison with laparoscopy and laparotomy. Gynecol Oncol 2011;121:100–105.
[90] Nezhat FR, DeNoble SM, Liu CS, et al. The safety and efficacy of laparoscopic surgical staging and debulking of apparent advanced stage ovarian, fallopian tube, and primary peritoneal cancers. JSLS. 2010; 14:155–168.
[91] Fanning J, Yacoub E, Hojat R. Laparoscopic-assisted cytoreduction for primary ovarian cancer: success, morbidity and survival. Gynecol Oncol. 2011;123:47–49.
[92] GA Feuer, N Lakhi, J Barker, S Salmieri, M Burrell. Perioperative and clinical outcomes in the management of epithelial ovarian cancer using a robotic or abdominal approach. Gynecologic Oncology 131 (2013) 520–524.
[93] Fagotti A, Ferrandina G, Fanfani F, et al. A laparoscopy-based score to predict surgical outcome in patients with advanced ovarian carcinoma: a pilot study. Ann Surg Oncol. 2006;13:1156–1161.
[94] N. Lambrou, R. Diaz, T. Gatcliffe, L. Gil, A. Eisermann. Robotic-assisted laparoscopy for primary or recurrent ovarian cancer: A comparison with laparotomy. Gynecologic Oncology 125 (2012) S122
[95] Chen C-H, Chiu L-H, Liu W-M. Robotic Approach for Ovarian-Fallopian Tube Cancer Surgical Staging and Secondary Debulking Surgery for Focal Recurrent Ovarian Cancer. Journal of Minimally Invasive Gynecology, Volume 20, Issue 6, Supplement, November–December 2013, Pages S169-S170.
[96] Farghaly SA. Robotic-assisted laparoscopic anterior pelvic exenteration in patients with advanced ovarian cancer: Farghaly's Technique. Eur J Gynecol Oncol 2010; 31(4): 361-363.
[97] Chi DS, McCaughty K, Diaz JP, Huh J, Schwabenbauer S, Hummer AJ, et al. Guidelines and selection criteria for secondary cytoreductive surgery in patients with recurrent, platinum−sensitive epithelial ovarian carcinoma. Cancer 2006 May 1;106(9):1933–1939.
[98] Onda T, Yoshikawa H, Yasugi T, Yamada M, Matsumoto K, Taketani Y. Secondary cytoreductive surgery for recurrent epithelial ovarian carcinoma: proposal for patients selection. Br J Cancer 2005 Mar 28;92(6):1026–1032.
[99] Salani R, Santillan A, Zuhurak ML, et al. Secondary cytoreductive surgery for localize recurrent epithelial ovarian cancer. Analysis of prognostic factors and survival outcomes. Cancer 2007;109:685–691.
[100] Harter P, duBois A, Hahmann M, et al. Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR trial. Ann Surg Oncol 2006;13:1702–1710.
[101] Janicke F, Holscher M, Kuhn W, von Hugo R, Pache L, Siewert JR, Graeff H. Radical surgical procedure improves survival time in patients with recurrent ovarian cancer. Cancer 1992;70:2129–2136.
[102] Gadducci A, Iacconi P, Cosio S, Fanucci A, Cristofani R, Genazzani AR. Complete salvage surgical cytoreduction improves further survival of patients with late recurrent ovarian cancer. Gynecol Oncol 2000;79:344–349.
[103] Eisenkop SM, Friedman RL, Spirtos NM. The role of secondary cytoreductive surgery in the treatment of patients with recurrent epithelial ovarian carcinoma. Cancer 2000;88:144–153.

[104] Yoon SS, Jarnagin WR, Fong Y, DeMatteo RP, Barakat RR, Blumgart LH, Chi DS. Resection of recurrent ovarian or fallopian tube carcinoma involving the liver. Gynecol Oncol 2003;91:383–388.
[105] Giulianotti PC, Coratti A, Sbrana F, Addeo P, Bianco FM, Busch NC, Annechiarico M, Benedetti E. Robotic liver surgery: Results for 70 resections. Surgery 2011;149: 29–39.
[106] Idrees K, Bartlett DL. Robotic liver Surgery. Surg Clin N Am 2010;90:761–774.
[107] Aron M, Colombo Jr JR, Turna B, Stein RJ, Haber G-P, Gill IS. Diaphragmatic repair and/or reconstruction during upper abdominal urologic laparoscopy. J Urol 2007;178:2444–2450.
[108] Moskowitz RM, Young JL, Box GN, Pare LS, Clayman RV. Retroperitoneal transdiaphragmatic robotic-assisted laparoscopic resection of a left thoracolumbar neurofibroma. J Soc Laparosc Surg 2009;13:64–68.
[109] Holloway RW, Brudie LA, Rakowski JA, Ahmad S. Robotic-assisted resection of liver and diaphragm recurrent ovarian carcinoma: Description of technique. Gynecol Oncol 2011;120:419–422.
[110] Magrina JF, Cetta RL, Chang YH, Guevara G, Magtibay PM. Analysis of secondary cytoreduction for recurrent ovarian cancer by robotics, laparoscopy and laparotomy. Gynecol Oncol 129 (2013) 336–340.
[111] PF Escobar, KL Levinson, J Magrina, MA Martino, RR Barakat, AN. Fader, MM. Leitao Jr. Feasibility and perioperative outcomes of robotic-assisted surgery in the management of recurrent ovarian cancer: A multi-institutional study. Gynecol Oncol (2014), http://dx.doi.org/10.1016/j.ygyno.2014.05.007
[112] R. Estape, E. Quinoa, R. Estape, T. Noel, O. Vega. Robotic secondary debulking in the management of recurrent ovarian cancer. Gynecologic Oncology 125 (2012) S121–S122.
[113] A. Fagotti, M. Petrillo, B. Costantini, F. Fanfani, V. Gallotta, V. Chiantera, L.C. Turco, C. Bottoni, G. Scambia. Minimally invasive secondary cytoreduction plus HIPEC for recurrent ovarian cancer: A case series. Gynecologic Oncology 132 (2014) 303–306.
[114] Fagotti A, Costantini B, Petrillo M, Vizzielli G, Fanfani F, Margariti PA, et al. Cytoreductive surgery plus HIPEC in platinum-sensitive recurrent ovarian cancer patients: a case–control study on survival in patients with two year follow-up. Gynecol Oncol 2012;127:502–505.
[115] Bakrin N, Cotte E, Golfier F, Gilly FN, Freyer G, Helm W, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for persistent and recurrent advanced ovarian carcinoma: a multicenter, prospective study of 246 patients. Ann Surg Oncol 2012;19:4052–4058.
[116] Thomas F, Ferron G, Gesson-Paute A, HristovaM, Lochon I, Chatelut E. Increased tissue diffusion of oxaliplatin during laparoscopically assisted versus open heated intraoperative intraperitoneal chemotherapy (HIPEC). Ann Surg Oncol 2008;15:3623–3624.
[117] Esquis P, Consolo D, Magnin G, Pointaire P, Moretto P, Ynsa MD, et al. High intraabdominal pressure enhances the penetration and antitumor effect of intraperitoneal cisplatin on experimental peritoneal carcinomatosis. Ann Surg 2006;244:106–112.
[118] Jacquet P, Stuart OA, Chang D, Sugarbaker PH. Effects of intra-abdominal pressure on pharmacokinetics and tissue distribution of doxorubicin after intraperitoneal administration. Anticancer Drugs 1996;7:596–603.

[119] Peter A. van Dam, Pieter-Jan H.H. van Dam Luc Verkinderen, Peter Vermeulen, Filip Deckers, Luc Y. Dirix. Robotic-assisted laparoscopic cytoreductive surgery for lobular carcinoma of the breast metastatic to the ovaries. Journal of Minimally Invasive Gynecology (2007) 14, 746–749.
[120] Vergote I, De Brabanter J, Fyles A, et al. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. Lancet. 2001;357:176–182.
[121] Sjovall K, Nilsson B, Einhorn N. Different types of rupture of the tumor capsule and the impact on survival in early ovarian carcinoma. Int J Gynecol Cancer. 1994;4:333–336.
[122] Smorgick N, Barel O, Halperin R, Schneider D, Pansky M. Laparoscopic removal of adnexal cysts: is it possible to decrease inadvertent intraoperative rupture rate? Am J Obstet Gynecol. 2009;200:237 e1–3.
[123] Ramirez PT, Wolf JK, Levenback C. Laparoscopic port-site metastases: etiology and prevention. Gynecol Oncol. 2003;91:179–189.
[124] Ramirez PT, Frumovitz M, Wolf JK, Levenback C. Laparoscopic port-site metastases in patients with gynecological malignancies. Int J Gynecol Cancer. 2004;14:1070–1077.
[125] Zivanovic O, Sonoda Y, Diaz JP, et al. The rate of port-site metastases after 2251 laparoscopic procedures in women with underlying malignant disease. Gynecol Oncol. 2008;111:431–437.
[126] Vergote I, Marquette S, Amant F, Berteloot P, Neven P. Port-site metastases after open laparoscopy: a study in 173 patients with advanced ovarian carcinoma. Int J Gynecol Cancer. 2005;15:776–779.
[127] N Rindos, CL Curry, R Tabbarah, V Wright. Port-Site Metastases After Robotic Surgery for Gynecologic Malignancy. JSLS (2014)18:66–70
[128] BT Ndofor, PT Soliman, KM Schmeler, AM Nick, M Frumovitz, PT. Ramirez. Rate of Port-Site Metastasis Is Uncommon in Patients Undergoing Robotic Surgery for Gynecological Malignancies. Int J Gynecol Cancer 2011;21: 936-940.
[129] Smidt VJ, Singh DM, Hurteau JA, Hurd WW. Effect of carbon dioxide on human ovarian carcinoma cell growth. Am J Obstet Gynecol. 2001;185:1314–1317.
[130] Zhang X, Guo X, Zhang A, Wang Y, Zhao J. Influence of carbon dioxide pneumoperitoneum environment on adhesion and metastasis of a human ovarian cancer cell line. Surg Endosc. 2009;23:108–112.
[131] Leng J, Lang J, Jiang Y, Liu D, Li H. Impact of different pressures and exposure times of a simulated carbon dioxide pneumoperitoneum environment on proliferation and apoptosis of human ovarian cancer cell lines. Surg Endosc. 2006;20:1556–1559.
[132] Azuar AS, Matsuzaki S, Darcha C, et al. Impact of surgical peritoneal environment on postoperative tumor growth and dissemination in a preimplanted tumor model. Surg Endosc. 2009;23:1733–1739.
[133] Rentschler ME, Dumpert J, Platt SR, et al. Natural orifice surgery with an endoluminal mobile robot. Surg Endosc. 2007;21:1212-1215.

[134] Edd J, Payen S, Rubinsky B, et al. Biomimetic propulsion for a swimming surgical micro-robot. In Intelligent Robots and Systems, 2003. IROS 2003.
In: Proceedings of the 2003 IEEE/RSJ International Conference. Las Vegas, NV, October 28-29, 2003;3:2583-2588.
[135] Wortman TD, Meyer A, Dolghi O, et al. Miniature surgical robot for laparoendoscopic single-incision colectomy. Surg Endosc. 2012;26:727.
[136] Choi B, Choi HR, Kang S. Development of tactile sensor for detecting contact force and slip. In: Intelligent Robots and Systems (IROS 2005) IEEE/RSJ International Conference. Edmonton, Alberta, Canada, August 26, 2005. 2005:2638-2643.
[137] Jung K, Kim KJ, Choi HR. A self-sensing dielectric elastomer actuator. Sensors Actuators A: Physical. 2008;143:343-351.
[138] Roan PR, Wright AS, Lendvay TS, et al. An instrumented minimally invasive surgical tool: design and calibration. Appl Bionics Biomech. 2011;8:173-190.
[139] Borisov SM, Klimant I. Optical nanosensors-smart tools in bioanalytics. Analyst. 2008;133:1302-1307.
[140] Basiri A, Edelstein DL, Graham J, et al. Detection of familial adenomatous polyposis with orthogonal polarized spectroscopy of the oral mucosa vasculature. J Biophotonics. 2011;4:707-714.
[141] Palmer GM, Viola RJ, Schroeder T, et al. Quantitative diffuse reflectance and fluorescence spectroscopy: tool to monitor tumor physiology in vivo. J Biomed Optics. 2009;14:024010.
[142] Veiseh M, Gabikian P, Bahrami S-B, et al. Tumor paint: a chlorotoxin: Cy5.5 bioconjugate for intraoperative visualization of cancer foci. Cancer Res. 2007;67:6882-6888.
[143] Park S, Howe R, Torchiana D. Virtual fixtures for robotic cardiac surgery. In: Medical Image Computing and Computer-Assisted Intervention-MICCAI 2001. Berlin, Germany: Springer; 2001: 1419-1420.