Peritoneal Surface Oncology Group International

PSOGI World News

February 2025
Issue #2

A quarterly newsletter with the latest news, views and announcements

IN THIS ISSUE

Section 1: Progress in Clinical or Laboratory Research

Laparoscopic and Robotic CRS. Current state-of-the-art.

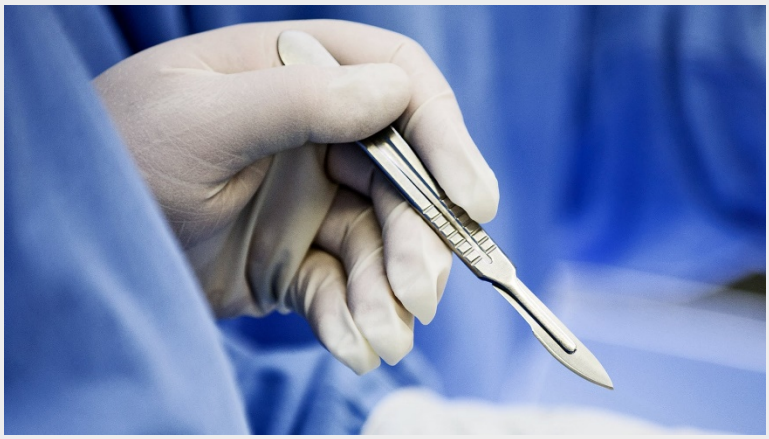
By Pompiliu Piso

Introduction

Minimally invasive surgery has been established as an efficient tool to treat gastrointestinal cancer by surgery with less adverse events and improved quality of life compared to open surgery. Therefore, it is not surprising that in the field of peritoneal surface malignancies, minimally invasive techniques have also been performed. However, to this point in time the published experience is small and it has not been investigated in a systematic approach (including prospective studies). It is not surprising that the use of minimally invasive techniques in peritoneal surface malignancies is currently a controversial subject within the medical community. Minimally invasive surgery has generated heated discussions at surgical meetings. Therefore, I would like to highlight this discussion and provide some guidelines for the selection of appropriate patients for this treatment modality.

Assessment of the extent of peritoneal surface malignancies

Peritoneal metastases or primary tumors progressing within the peritoneal spaces are potentially disseminated widely into the entire peritoneal cavity. Preoperative radiologic diagnostics have limited accuracy for small lesions, with a low detection rate. A laparoscopic evaluation of the abdominal and pelvic cavity increases this detection rate. Nevertheless, during an open surgical exploration in most patients more lesions are detected than during laparoscopy. Consequently, there is an underestimation of the extent of the disease in patients with peritoneal metastases located in several abdominopelvic regions. This underestimation of the extent of disease is often combined with mucinous ascites.



For decades the management of a small extent of peritoneal metastases has been open surgery plus HIPEC. The results long-term have been excellent.

Minimal invasive peritonectomy procedures

In theory all parietal and visceral peritonectomy procedures can be performed by minimally invasive procedures. This is the case in particular for single procedures, e.g. right upper quadrant peritonectomy or omentectomy-splenectomy. It becomes very difficult and time consuming for a combination of several or all peritonectomy procedures. For example, a right upper quadrant peritonectomy takes up to an hour by open surgery. By minimally invasive surgery, it

takes 2 to 3 hours. Currently, minimally invasive procedures are only performed in patients with a limited disease and low tumor load. Until now the average published PCI (peritoneal cancer index) is lower than 5. Most published papers refer to laparoscopic techniques with just a few reports on robotic procedures. The largest reported series is from the laparoscopic PSOGI (Peritoneal Surface Oncology Group International) registry which includes 323 patients (*Eur J Surg Oncol* 2023:49).

More recently, the laparoscope plus laparoscopic HIPEC has been recommended for selected patients with peritoneal metastases.

Combination with hyperthermic intraperitoneal chemotherapy (HIPEC)

The minimally invasive surgery can be combined with other treatment modalities. This may include a laparoscopic or robotic resection plus a laparoscopic or robotic HIPEC. The placement of the in- and outflow catheters is similar to the open procedure and the principles of perfusion the same. The port-sites can be used for the drains. Contrary to earlier data, the risk of port-site recurrence is very low after minimally invasive procedures and it may be near zero after using HIPEC. However, there are no data published as yet regarding this issue. Although speculative and based on my personal experience, the target temperature and the outflow parameters may be more frequently impaired as compared to open surgery.

Preoperative patient selection for minimally invasive surgery

Preoperative selection focuses on assessing resectability. Estimates of the amount of tumor are based on radiologic imaging. A low PCI score and a high probability of complete macroscopic cytoreduction would favor a minimally invasive approach. The assessment may include DW-MRI (diffusion weight magnetic resonance imaging) and/or laparoscopy if small bowel disease has to be excluded. Moreover, well-differentiated tumors may be more appropriate because the infiltration pattern usually allows a more accurate dissection within anatomic planes.

Indications for laparoscopic/robotic CRS (and HIPEC)

Generally, all indications for a CRS with a curative intent may be considered for minimally invasive procedures. Favored diagnoses include appendiceal malignancies with LAMNs (low-grade appendiceal mucinous neoplasms) and HAMNs (high-grade appendiceal mucinous neoplasms) with limited PMP (pseudomyxoma peritonei). A right colon cancer with peritoneal metastases limited to the right paracolic sulcus and omentum, or a gastric cancer with localized peritoneal seeding in the left upper quadrant may be ideal cases. In these patients, the primary can be resected and the peritoneal metastases removed concomitantly. Of course, the PCI must be low (most lower than 5 points) and the disease occupies only one or two abdominopelvic regions. In these cases, a complete macroscopic cytoreduction can occur with an open surgery or minimally invasive surgery. In contrast, minimally invasive procedures should not be performed in patients with extensive disease with multiple peritoneal nodules and mucinous ascites, such as PMP patient with PCI of 30.

PROs and CONs

The PROs for a minimally invasive approach include the low morbidity and rapid recovery. The absence of a large incision diminishes the risk of hernias. This may be of advantage in particular for limited diseases that may be treated effectively with a low number of peritonectomy procedures and a minimally aggressive tumor biology.

If the peritoneal cavity is not affected by adhesions, a laparoscopic exploration of the occult PSM (peritoneal surface malignancy) sites can be performed. These may include the inferior duodenal-jejunal fossa and/or the inferior recess of the left paracolic sulcus. However, there are some differences to the routine laparoscopy. First, the surgeon has to be aware of these occult sites of disease. Second, he/she will need to approach the abdominal cavity with at least three trocars in order to scroll the small bowel and visualize optimally the entire abdomen and pelvis. Third, it is recommendable to perform the exploration by an experienced surgeon. We do not have data on how often occult sites of disease are missed in a laparoscopic procedure. However, for properly selected cases, there is probably no difference to the open approach. Findings that need palpation, adhesions, large tumor masses, tumor penetration in several quadrants are not suitable for minimal invasive approaches.

The CONs for a minimally invasive approach include limitation to patients with low PCI and a less aggressive tumor biology, longer operating time, higher costs, and limited availability. Minimally invasive procedures, in particular robotic procedures, are more time consuming than open procedures. However, after a learning curve this will be less evident. Docking times have to be taken into consideration for robotic operations as they prolong the intervention.

As in open surgery, extensive parietal peritonectomy procedures require new highly specialized expertise. Surgical teams, familiar for example with laparoscopic right or left colon resections, do need additional skills to manage PSM. These can be achieved by collaboration in specialized peritoneal surface malignancy centers, ideally within a fellowship as offered by the ESPSO (European School of Peritoneal Surface Oncology).

Future developments

By an evaluation of the rapid developments and the extension of indications of laparoscopic and robotic surgery, we may predict an increasing proportion of patients treated by minimally invasive cytoreductive surgery. The increased awareness towards peritoneal surface malignancies will increase the number of patients with early-stage disease that are suitable for these techniques. Nevertheless, it will remain a “niche” indication with a limited number of patients. We need to prospectively collect more long-term results regarding the quality of life, regional recurrence rate and survival in these patients as compared to open procedures. A clinical trial to demonstrate safety and efficacy of minimally invasive surgery as compared to open surgery, as has occurred with several other gastrointestinal cancers, is indicated.

Although limited by monetary constraints, the robotic cytoreductive surgery has been used for a small extent of peritoneal surface malignancy. HIPEC is required after a complete resection.

Section 2: Exposition of progress and productivity of a PSOGI/PSM established Center of Excellence

China's First PSOGI/PSM Established Center of Excellence. We Have Come a Long Way and We Have a Long Way to Go.

By Xin-Li Liang, Zhong-He Ji, Yan Li

Peritoneal metastases from gastrointestinal and gynecologic cancer remains the most difficult pattern of disease spread to treat in oncology. This problem is especially acute in China. Based on our most recent nationwide epidemiology study[1], in the year 2020 alone, there were 766,664 patients with newly diagnosed peritoneal metastases from gastric cancer, colorectal cancer, ovarian cancer, pseudomyxoma peritonei and peritoneal mesothelioma. Among this huge number of patients, there were at least 435,414 patients who should have been treated with standardized cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC). Currently, 1,194 expert centers specialized in this comprehensive treatment strategy are needed. Less than 200 high-volume expert centers have been active in this technique in China. Therefore, we remain vigilant and clear-headed that the road towards controlling peritoneal metastasis is long and hard.

Yet, we have come a long way (Figure 1). This story shows how a series of bench-to-bedside studies have changed the landscape of peritoneal surface oncology in China.

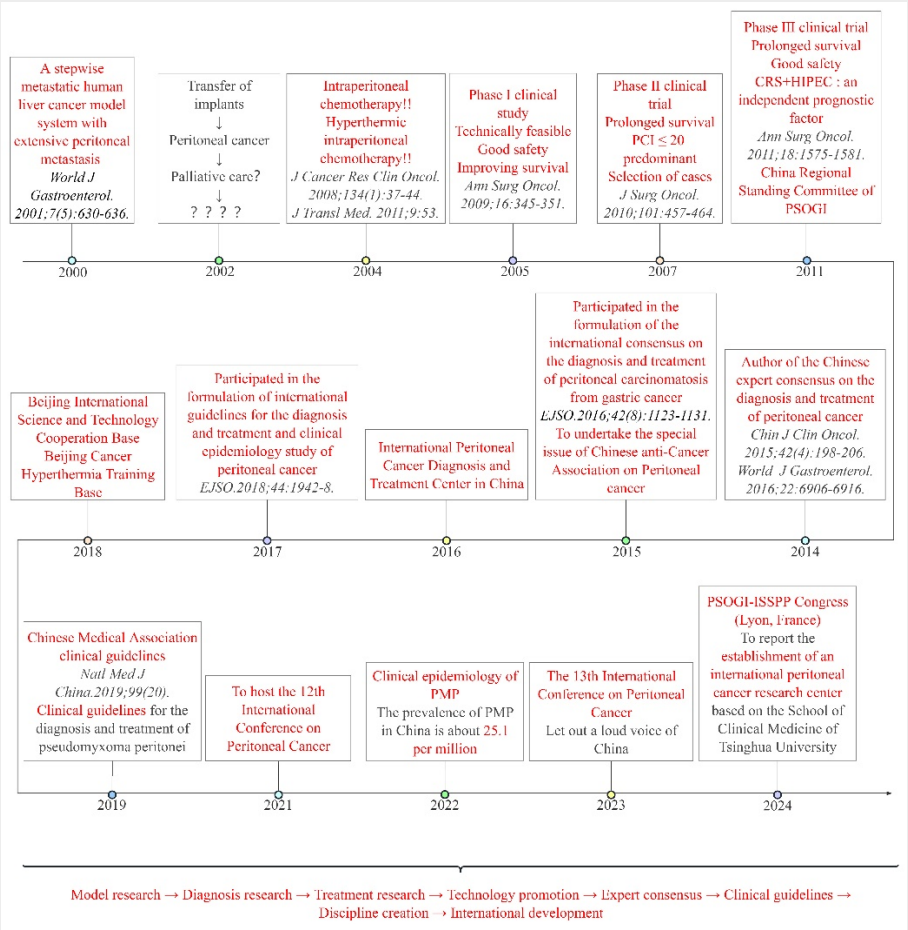


Figure 1. Our timeline shows the innovative exploration of diagnosis, prevention and treatment of peritoneal metastases. A strategic victory in the control of peritoneal cancer in China has been achieved.

As early as 2000, we found from animal model studies that cancer metastasis could be a stepwise, selective and progressive process. Various subpopulations of cancer cells have a preferred potential for liver metastases, pulmonary metastases or peritoneal metastases. The distinctive tumor biology underlying cancer peritoneal metastases called for an individualized and peritoneum-focused approach to this problem[2]. Based on this understanding, we showed that intraperitoneal chemotherapy and intraperitoneal hyperthermic chemotherapy would have a much better effect in reducing peritoneal metastases and improving survival. This was demonstrated in a series of experimental studies involving small and large animal models[3, 4]. Later on, consecutive phase 1, 2 and 3 clinical studies have demonstrated that CRS+HIPEC results in a survival advantage with acceptable safety profiles for peritoneal metastases from gastric and colorectal cancer[5-9]. After these landmark successes, we expanded our treatments to other primary sites for cancer peritoneal metastases, including ovarian cancer, primary peritoneal carcinoma, pseudomyxoma, peritoneal mesothelioma, retroperitoneal sarcoma and miscellaneous other tumors. Since our first clinical research with CRS+HIPEC in 2004, we have treated over 3,000 patients with this innovative approach. History making survival records have been made:

The longest disease-free survivor with gastric cancer with limited peritoneal metastases is over 9 years.

The longest disease-free survivor with colorectal cancer with limited peritoneal metastases is over 18 years.

The longest disease-free survivor with hepatocellular carcinoma, bloody ascites and extensive peritoneal metastases is over 8 years.
The longest disease-free survivor with pseudomyxoma peritonei is more than 20 years. CRS+HIPEC was used twice.
The longest disease-free survivor with extensive, diffuse peritoneal mesothelioma is over 9 years.
The list can go on and on.

Currently, 8 to 12 CRS+HIPEC procedures are performed at our center each week. In our second decade, building on the foundation established in the previous period, we have focused on continuing education and promoting the application of advances in peritoneal surface malignancy to oncology. In 2015, Professor Li Yan left Wuhan University, which had become a highly experienced peritoneal metastases treatment center, and moved to Beijing. There, he successfully established the Peritoneal Cancer Center at both the School of Oncology at Capital Medical University and the School of Clinical Medicine at Tsinghua University. Following this, peritoneal tumor diagnosis and treatment training centers were created under the auspices of the Beijing Municipal Health Commission, the China Anti-Cancer Association, and the China Medical Doctors Association. To date, we have helped ten leading hospitals in China establish peritoneal metastases treatment centers and create a national cooperative network focused on peritoneal cancers. We have trained over 200 healthcare professionals specialized in peritoneal cancer, published five expert consensus documents, and released a monograph on peritoneal oncology. Additionally, we have actively promoted the application and dissemination of theories and practical techniques related to peritoneal cancers throughout China.

In 2015, we published the first expert consensus on CRS+HIPEC for peritoneal cancer in China, which initiated the nationwide promotion of this technology.

In 2016, we organized the first Continuing Education Workshop on Peritoneal Surface Oncology.

In 2017, we hosted a session on the peritoneal metastasis of gastric cancer during the 12th World Gastric Cancer Congress (Beijing).

In 2021, we hosted the 12th International Congress on Peritoneal Surface Malignancies, which attracted over 5,000 online participants, setting a new record for attendance at Peritoneal Surface Oncology Group International (PSOGI) conferences.

In 2024, the Peritoneal Tumor Disciplinary Alliance was founded in China, with Beijing Tsinghua Changgung Hospital serving as the core institution.

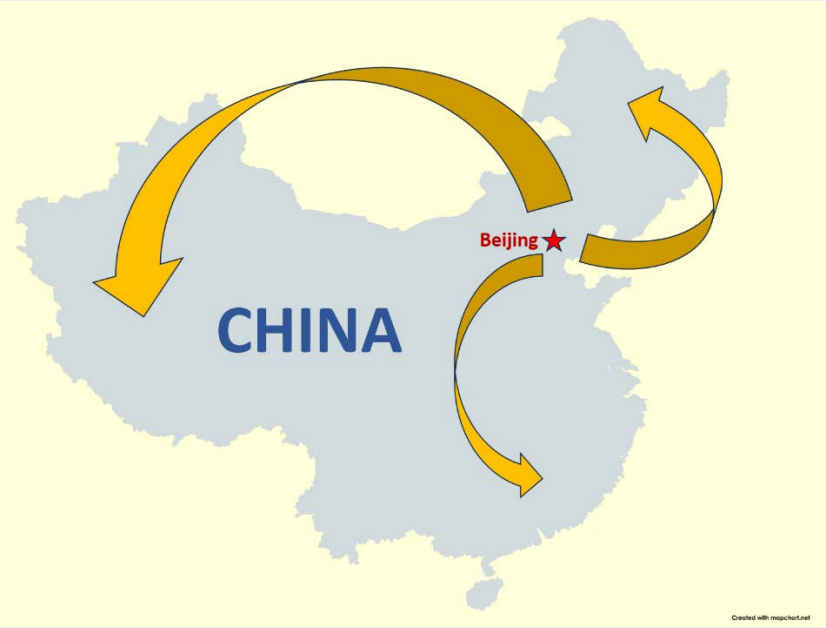
The treatment of peritoneal metastases challenges traditional oncology theories, making progress in this area quite difficult. After facing skepticism, ridicule and criticism, the field of peritoneal oncology is now thriving and flourishing in China, emerging as a prominent focus in cancer research.

Our efforts show that we have come a long way. We have a long way to go.

With close collaboration with PSOGI, we will set up an International Research Center on Peritoneal Surface Oncology (IRCPSO). This institution covers three fields: basic research, translational research, and clinical research. IRCPSO will become a new research hub for PSOGI Executive Committee in China. We foresee a far-reaching production of high-quality clinical evidence to support the global cause of conquering peritoneal surface malignancy.

References

1. Yang R, Su YD, Ma R, Li Y. Clinical epidemiology of peritoneal metastases in China: The construction of professional peritoneal metastases treatment centers based on the prevalence rate. Eur J Surg Oncol, 2023, 49(1): 173-178.
2. Li Y, Tang ZY, Ye SL, Liu YK, Chen J, Xue Q, Chen J, Gao DM, Bao WH. Establishment of cell clones with different metastatic potential from the metastatic hepatocellular carcinoma cell line MHCC97. World J Gastroenterol, 2001, 7(5): 630-636.
3. Li PC, Chen LD, Zheng F, Li Y. Intraperitoneal chemotherapy with hydroxycamptothecin reduces peritoneal carcinomatosis: results of an experimental study. J Cancer Res Clin Oncol, 2008, 134(1): 37-44.
4. Tang L, Mei LJ, Yang XJ, Huang CQ, Zhou YF, Yonemura Y, Li Y. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy improves survival of gastric cancer with peritoneal carcinomatosis: evidence from an experimental study. J Transl Med, 2011, 9: 53.
5. Yang XJ, Li Y, Hassan A, Yang GL, Liu SY, Lu YL, Zhang JW, Yonemura Y. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy improves survival in selected patients with peritoneal carcinomatosis from abdominal and pelvic malignancies: results of 21 cases. Ann Surg Oncol, 2009, 16(2): 345-351.
6. Yang XJ, Li Y, Yonemura Y. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy to treat gastric cancer with ascites and/or peritoneal carcinomatosis: Results from a Chinese center. J Surg Oncol, 2010, 101(6): 457-464.
7. Yang XJ, Huang CQ, Suo T, Mei LJ, Yang GL, Cheng FL, Zhou YF, Xiong B, Yonemura Y, Li Y. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from gastric cancer: final results of a phase III randomized clinical trial. Ann Surg Oncol, 2011, 18(6): 1575-1581.
8. Huang CQ, Feng JP, Yang XJ, Li Y. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from colorectal cancer: a case-control study from a Chinese center. J Surg Oncol, 2014, 109(7): 730-739.
9. Huang CQ, Yang XJ, Yu Y, Wu HT, Liu Y, Yonemura Y, Li Y. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy improves survival for patients with peritoneal carcinomatosis from colorectal cancer: a phase II study from a Chinese center. PLoS One, 2014, 9(9): e108509.
10. Li Y, Zhou YF, Liang H, Wang HQ, Hao JH, Zhu ZG, Wan DS, Qin LX, Cui SZ, Ji JF, Xu HM, Wei SZ, Xu HB, Suo T, Yang SJ, Xie CH, Yang XJ, Yang GL. Chinese expert consensus on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal malignancies. Chin J Clin Oncol. 2015, 42(4): 198-206.



Beijing's Tsinghua Changgung Hospital is a center for advanced studies in Peritoneal Surface Malignancy with an outreach throughout China.

Section 3: Listing of upcoming events

Meeting	Date	Venue	Registrations
CONFERENCES			
2nd Middle East PSOGI Conference	8-10th February, 2025	Jeddah, Saudi Arabia	Open https://psogi-me.ksau-hs.edu.sa/home/index
8th INDEPSO-ISPSM Annual Update in Peritoneal Malignancies	5-7th June, 2025 Preceded by a one-day video workshop on the 4th June, 2025	Calicut, India	Open https://www.onlinesbi.sbi/sbicollect/icollecthome.htm?corpID=639211
15th International Congress on Peritoneal Surface Malignancies	29-31st October, 2025	Barcelona, Spain	To open in March 2025 https://psogicongress2025.com/
WORKSHOPS			
Preconference Video Workshop on Cytoreductive Surgery 20th Congress of the Asia-Pacific Federation of Coloproctology	13th February, 2025	Kota Kinabalu, Malaysia	Open https://www.apfcp2025.org/registration
ESSO Advanced Course on the Management of HIPEC after CRS	6-8th March, 2025 Preceded by a one-day video workshop and live surgery on the 5th March, 2025	Berlin, Germany	Open https://www.essoweb.org/courses/esso-advanced-course-on-the-management-of-hipec-after-crs-2025/
Turkish Society of Colorectal Surgery PSM Video Workshop	11-12th July, 2025	Izmir, Turkey	To be announced
FIRST ANNOUNCEMENT			
5th LATAM Latin American Congress on Peritoneal Surface Malignancies	2026 (dates will be announced in due course)	Colombia, South America	---

INDEPSO and ISPSM Meeting in Namakkal, India, 10-12 January 2025

By Aditi Bhatt

This quarter, there is one meeting that needs a special mention. It was a regional meeting of the two Indian societies on peritoneal malignancy, INDEPSO and ISPSM, held in a small southern India town, Namakkal from the 10-12 January, 2025. Namakkal, is home to the Thangam Cancer Centre, that hosted the meeting. It is a high-volume center for the treatment of peritoneal malignancies. The main purpose of this meeting was to create awareness about the treatment options for peritoneal malignancies in the region among oncologists, general physician, surgeons, gynecologists and surgical oncology trainees. The challenge was to provide the latest updates to those who were already involved in the treatment of peritoneal malignancies and touch upon the basics for others. The meeting focused on colorectal cancer, gastric cancer, ovarian cancer and the basics of management of peritoneal malignancy for two whole days and was supplemented by a video workshop on day three. The faculty included the most experienced surgeons from the country and two French experts which greatly enhanced the scientific value and level of the meeting.

Nearly two hundred clinicians attended the meeting (30 online participants). There was extensive discussion on various aspects of management of PM including perioperative management and socioeconomic considerations. New data on systemic treatment for gastric PM was shared by the French surgeons that may in the future be practice changing. Some new data and research projects were presented by the Indian groups too.

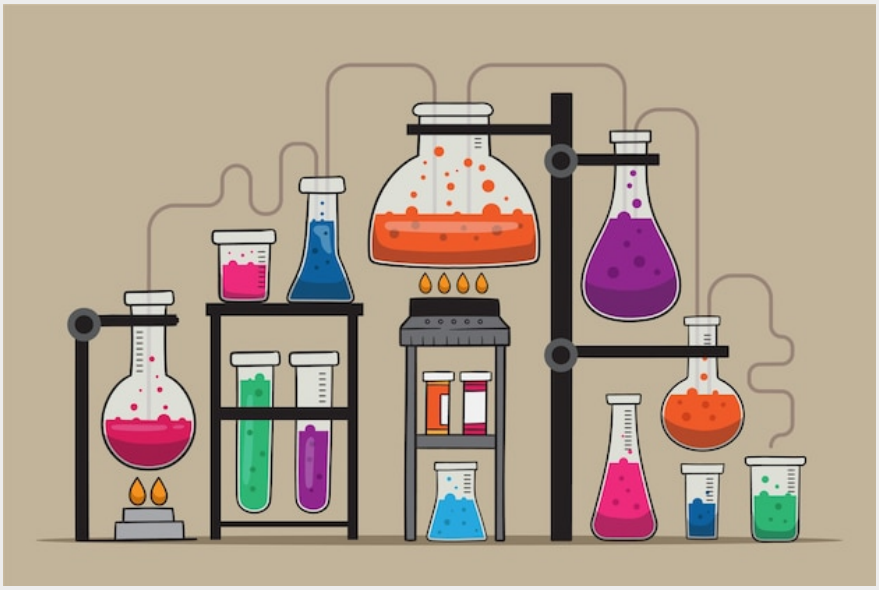
Namakkal is a relatively difficult place to access compared to other Indian cities. Most surgeons had to spend one day each travelling back and forth, while for the overseas faculty it was over 24 hours of travel. This did not dim the enthusiasm and it was heartening to see such a large number of participants travelling from different corners of the country to attend this meeting. This meeting underlined the interest in the management of PM in the region and the country. More of such meetings are needed to disseminate correct knowledge regarding the treatment of PM which will in turn enable more and more patients to get the right treatment at the right time.

Namakkal, home of the Thangam Cancer Centre, hosted a regional Peritoneal Surface Malignancy Meeting with discussions led by experts from India and Europe.

Section 4: Alternatives to traditional HIPEC

Innovations in Intraperitoneal Drug Delivery: UPy-PEG Hydrogel and its Promise in Treating Peritoneal Metastases

By: Anne G. W. E. Wintjens, Patricia Y. W. Dankers, Nicole D. Bouvy, and Ignace H. J. T. de Hingh



Peritoneal metastases (PM) remain a challenge in the treatment of colorectal cancer, affecting about 10% of patients with advanced disease. Despite advances in systemic chemotherapy and cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC), therapeutic hurdles persist. Early detection of PM is often difficult due to its asymptomatic nature and nonspecific presentation and the limitations of imaging modalities to detect microscopic lesions. Consequently, many patients are diagnosed at advanced stages where curative options are no longer viable. These challenges underscore the urgent need for innovative solutions in both detection and treatment.

While CRS and HIPEC remain the gold standard treatment for selected PM patients, its therapeutic efficacy is limited by the short residence time of the chemotherapeutic agents in the peritoneal cavity, with subsequent short exposure of the cancer cells and unwanted systemic effects through rapid uptake. Drug delivery systems (DDSs), such as injectable hydrogels, offer an innovative opportunity to address this challenge. DDSs aim to achieve sustained, local drug exposure while minimizing systemic side effects.

The ureido-pyrimidinone poly(ethylene glycol) (UPy-PEG) hydrogel, a pH-responsive supramolecular hydrogel, has gained interest due to its potential for sustained drug release suitable for application in the peritoneal cavity. The hydrogel is designed with supramolecular interactions, such as hydrogen bonds, providing dynamic but also mechanical robustness. Unlike temperature-responsive hydrogels, which are prone to fragmentation in the dynamic peritoneal environment, the more robust UPy-PEG adheres uniformly to peritoneal surfaces, enhancing its therapeutic potential. The hydrogel's biocompatibility and controlled release properties have positioned it as a promising candidate for intraperitoneal drug delivery.

This article summarizes our key findings in the development, safety, pharmacokinetics, and therapeutic efficacy of UPy-PEG hydrogel in preclinical models, emphasizing its potential for intraperitoneal therapies.

Preclinical development and safety assessment

In preclinical experiments using healthy WAG-Rij rats, a novel UPy-PEG formulation optimized for intraperitoneal administration with a pH of 9 and a weight percentage of 6 was developed. This formulation formed a sticky, cohesive layer adhering uniformly to all intraperitoneal surfaces, including the abdominal wall. Given that PM are often widely disseminated throughout the peritoneal cavity, achieving a uniform distribution of the hydrogel is crucial to maximize its therapeutic potential as drug depot. Safety evaluation revealed no significant weight loss, discomfort, or macroscopic organ damage over a 28-days follow-up period. Histological analysis identified vacuolated macrophages in several intraperitoneal organs, e.g. the liver and spleen, which is a known response to PEG degradation. While this macrophage activation did not result in immediate adverse effects, the potential long-term response remains to be investigated.

UPy-PEG safety and anastomotic healing

As CRS most often involves resecting the affected colon segment and forming a subsequent anastomosis, the impact of UPy-PEG on anastomotic healing was evaluated. Mitomycin C (MMC), a widely used agent in HIPEC, was incorporated in the UPy-PEG hydrogel and administered to healthy rats that just received a colonic anastomosis. Control groups received either the unloaded hydrogel or saline. Although a higher occurrence of anastomotic leakage was found in the unloaded hydrogel group, this difference did not remain statistically significant after correction. Other outcome parameters did not show significant differences, including bursting pressure and histological features of the anastomotic site.

However, 48% of animals in hydrogel-treated groups experienced serious adverse events and were taken out of the experiment, primarily due to intraluminal bleeding or animal discomfort. Notably, this occurred regardless of MMC loading, raising concerns that the hydrogel itself may have negatively affected the outcomes. Histopathological analysis revealed lymphatic congestion, likely caused by the recruitment of vacuolated macrophages during hydrogel degradation. This may have led to blood vessel damage near the anastomosis. It is hypothesized that this is caused by the large hydrogel volume administered (20 mL/kg), needed to cover the peritoneal surface in small mammals with high surface-to-volume ratio. However, in ongoing preclinical studies in larger animals (i.e. minipigs) there are no indications of negative effects on wound healing, suggesting that the administered volume per animal model requires optimization.

Pharmacokinetics of MMC released from UPy-PEG

To demonstrate the increased residence time of MMC in the peritoneal cavity, the pharmacokinetics of MMC delivered via the UPy-PEG hydrogel were compared to MMC dissolved in phosphate-buffered saline (PBS). MMC delivered via UPy-PEG exhibited a plateau-shaped plasma concentration, indicative of sustained drug release, contrasting with the peak-shaped profile observed in the PBS-MMC group. This sustained release profile shows a pharmacological advantage by maintaining prolonged local exposure while reducing systemic toxicity. These results provide strong evidence that the UPy-PEG hydrogel enhances the pharmacokinetic profile of MMC, making it a promising vehicle for intraperitoneal drug delivery.

Therapeutic efficacy in rodent PM model

Finally, the therapeutic efficacy of the MMC-loaded hydrogel was evaluated in a validated PM model with WAG-Rij rats bearing CC531 tumor cells. Animals treated with MMC-loaded UPy-PEG demonstrated a trend toward improved survival, with 78% surviving the 120 days follow-up period compared to 38% in the PBS-MMC group ($p = 0.087$). Although not statistically significant, these findings highlight the hydrogel's potential to enhance intraperitoneal drug delivery and therapeutic outcomes. Furthermore, this experiment demonstrated the ability to monitor longitudinal intraperitoneal tumor progression minimally invasively using bioluminescence imaging.

Conclusions

The UPy-PEG hydrogel holds promise to improve intraperitoneal drug delivery as preclinical studies highlight its potential to improve therapeutic outcomes. To enable translation to the clinic, remaining challenges related to dosing, administration, and safety are currently being addressed in large animal models that more closely resemble human anatomy and clinical setting. By addressing these issues, UPy-PEG hydrogels could play an important role in enhancing therapeutic efficacy of intraperitoneal therapies and improving outcomes for patients with PM. The startup company UPyTher is continuing the development of innovative DDSs to bridge the gap between preclinical promise and clinical application, offering new hope for managing this challenging disease.

Section 5: Pioneers of progress in peritoneal surface malignancy

Who was Shigemasa Koga, MD?

By Yutaka Yonemura, Toshiyuki Kitai, Paul H. Sugarbaker

After John S. Spratt published his methodology for the first HIPEC in 1980, no interest in this technology for prevention or treatment of peritoneal metastases was evident in either the United States or in Europe. Had it not been for Professor Shigemasa Koga, the invention of HIPEC by John Spratt may have gone unnoticed. Dr. Koga recognized the potential application of HIPEC to prevention of peritoneal metastases. Also, he introduced mitomycin as the drug of choice for hyperthermic intraperitoneal chemotherapy after gastrectomy for serosal-positive disease. The first application of heated intraperitoneal chemotherapy used in the operating room to control peritoneal metastases from gastric cancer is a contribution of Shigemasa Koga.

Dr. Koga was born in Fukuoka, Japan on December 11, 1925. His medical school education was at Kyushu University in Fukuoka, Japan. In April of 1975, he was appointed Second Professor of Surgery at Tottori University. He became the Director of Tottori University Hospital in 1988.

Dr. Koga was an intellectual leader in the description of the mechanisms of peritoneal dissemination of gastric cancer. In 1984 in the *Journal of Cancer Research Clinical Oncology*, he showed that there was a profound prognostic significance of free intraperitoneal cancer cells in patients having a complete resection of gastric cancer. In 84 of 171 patients who underwent curative surgery, cancer invasion into the gastric serosa was histologically confirmed. Twenty patients (24%) had free cancer cells in the peritoneal cavity. In Patients with both serosal cancer invasion and free cancer cells the 5-year survival rate was 13% as compared with 85% for patients who had neither. For the patients who had serosal invasion but no free peritoneal cancer cells, the survival was 40%. These definitive data regarding invasion of the wall of the stomach resulting in peritoneal metastases led Professor Koga to utilize Spratt's HIPEC methodology for resectable gastric cancer with serosal invasion. These data on the natural history of peritoneal metastases in gastric cancer were Professor Koga's first step in his efforts to improve surgery for gastric cancer.

A second step in using HIPEC was to test the efficacy of HIPEC in an animal model. He administered cancer cells by the intraperitoneal route. In the rat model, untreated animals had the shortest survival, heat alone or chemotherapy alone treatment caused a modest prolongation of survival. By far, the best results were in rats treated with both 42°C heat plus chemotherapy within four days of the administration of cancer cells. These data were published in the journal *Cancer* in May of 1984.

A new and promising chemotherapy agent for intraperitoneal administration was available to Dr. Koga. This was mitomycin C. This new drug was developed and manufactured in Japan. As a single agent, the objective response rate in gastric cancer patients was reported to be 24%. Dr. Koga's pharmacologic studies showed an increased local-regional drug concentration after intraperitoneal administration. This increased concentration of mitomycin C within the peritoneal space would maximize the destruction of gastric cancer cells. Also, the cytotoxicity of mitomycin C was shown to be increased by heat with this new HIPEC methodology. Dr. Koga proceeded to perform a phase II study in patients confirmed histologically to have serosal invasion of gastric cancer. The survival of 45 HIPEC mitomycin C-treated patients was compared to 78 gastric cancer patients with the same histology. At three years after potentially curative gastrectomy, 73.7% of patients treated with HIPEC survived. This was significantly greater than 52.7% in the control group. The survival difference was significant with a $p<0.04$.

With these promising phase II data, Dr. Koga went on to perform a randomized controlled study of patients with serosal-positive gastric cancer who had a complete gastric cancer resection. One group of patients had gastrectomy plus HIPEC mitomycin C and the control group gastrectomy only. There were 60 patients in the randomized trial. Thirty-two patients in the HIPEC-treated group had a thirty-month survival of 83.0%. Twenty-eight patients in the control group had a survival of 67.3%. Although the trend toward improved survival was impressive, the limited number of patients in the trial and the abbreviated follow-up caused the differences in survival to be non-significant.

The report of this groundbreaking clinical research was reported in the journal *Cancer* in January of 1988. The limited duration of the study was for an unfortunate reason. Dr. Koga himself died of gastric cancer on September 7, 1989. This was just one year after his clinical trials were published.

Although the research with peritoneal metastases from gastric cancer of Shigemasa Koga continued for less than a decade, he must be credited with a recognition of the value of HIPEC and its first implementation in gastrointestinal cancer. Because of his disciplined laboratory and clinical studies, interest in HIPEC caused a flood of activity in peritoneal surface malignancy not only throughout Japan but also throughout the United States and Europe. Yonemura and coworkers in Kanazawa, Japan credits Dr. Koga as the spark that led to great progress with peritoneal surface malignancy in Japan. Fujimoto in Funabashi, Japan was greatly influenced by Dr. Koga. Loggie from Winston-Salem, North Carolina, Sugarbaker from Washington, DC and Gilly from Lyon, France traveled to Japan in the early 1990s to learn from the extensive experience of the Japanese gastric cancer surgeons with HIPEC. Professor Yutaka Yonemura remembers Professor Koga as a teacher of HIPEC. Yonemura began HIPEC for gastric cancer after he heard Professor Koga's special lecture at Japanese Surgical Congress, where he presented the mechanisms of peritoneal metastases by experimental and clinical studies.

Young gastric cancer surgeons who trained under Professor Koga have great admiration for his mentorship. Surgical training with him was severe but always accompanied by full credit for productivity. He instructed his medical staff to write a number of scientific papers and promoted studying abroad. Professor Koga's personal achievements in gastrointestinal surgery gave him a leadership position in surgery in Japan. He exhibited deep understanding in the diagnosis and pathology of gastrointestinal cancer. He made heroic efforts to transfer his depth of understanding to his surgical and research trainees. Professor Koga was an established authority, nevertheless he was humble and a good student himself. Before attending a research seminar, he always checked previous literatures and present status of the research in detail. Younger attending surgeons sometimes felt ashamed for their lack of diligence. His research meetings sometimes continued until after midnight.

Professor Koga playing baseball with his surgical colleagues at Tottori University.

After the meeting, Professor Koga would advise his trainees regarding the management of personal affairs while in a taxi towards the airport or to home. He was impatient about the stagnation of the research work at the University and always encouraged his trainees to investigate unsolved problems in gastrointestinal surgery. He was filled with passion for progress but always humble and gentle.

Section 6: Focus of an important PSM protocol

Adjuvant Intraperitoneal Versus Intravenous Chemotherapy for Epithelial Peritoneal Mesothelioma After Complete Cytoreductive Surgery

By Paul H. Sugarbaker

The epithelial type of malignant mesothelioma has an unusual natural history that is ideal for testing the efficacy of local-regional cancer chemotherapy. It has an aggressive tumor biology that rapidly advances over one to two years to cause a loss of gastrointestinal function. Yet with this abdominal and pelvic progression, systemic manifestations of the disease rarely occur. If successful treatments can control the intraperitoneal disease, a major improvement in progression-free survival, quality of life and overall survival is expected.

The clinical trial, "A study of additional chemotherapy after surgery for people with malignant peritoneal mesothelioma", seeks to determine if intraperitoneal chemotherapy is more effective that systemic chemotherapy to delay the progression of disease (NCT06057935). The study contact is Garrett Nash, MD at Memorial Sloan Kettering Cancer Center. There are 13 locations that can enter patients and the trial is actively recruiting patients. All patients who meet the eligibility requirements and are enrolled in the trial will undergo cytoreductive surgery. The surgery must achieve a complete or near-complete cytoreduction. After the surgery, all patients are given HIPEC. By parallel assignment, two different methods for administering cancer chemotherapy following surgery plus HIPEC are followed. In the intravenous chemotherapy arm (IVC), patients receive intravenous pemetrexed and intravenous cisplatin chemotherapy. Patients will receive 4 cycles of intravenous treatments, but if the drugs are tolerated well, a total of 6 cycles may be administered. If cisplatin causes too much toxicity, intravenous carboplatin may be substituted.

In the other arm of the trial, the cancer chemotherapy is given by the intraperitoneal route. This method for chemotherapy administration is called normothermic intraperitoneal chemotherapy (NIPEC). In the operating room after the cytoreductive surgery plus HIPEC, an intraperitoneal access device will be inserted through the abdominal wall. This intraperitoneal port will allow the pemetrexed and cisplatin to be administered directly into the peritoneal cavity. If cisplatin is too toxic, carboplatin may be substituted. At least 4 but up to 6 cycles of NIPEC are to be administered.

The progression-free survivals of the IVC arm and NIPEC arm will be compared.

A strong rationale to simultaneously compare the efficacy of IVC and NIPEC comes from clinical data concerning treatment of patients with epithelial malignant peritoneal mesothelioma by Sugarbaker and Chang at the Washington Cancer Institute (*Ann Surg Oncol, 2021*). In this study, the addition of intraperitoneal pemetrexed and intravenous cisplatin to cytoreductive surgery plus HIPEC was determined using propensity matched survival in 74 patients. In the patients receiving NIPEC, there was a significant improvement in survival (p=0.0263). Five-year survival increased from 76.9% to 92.7%. This study suggested that HIPEC was necessary for treatment of epithelial peritoneal mesothelioma but

was not sufficient. Long-term intraperitoneal chemotherapy was needed for optimal results. The current trial hosted by Memorial Sloan Kettering Cancer Center seeks to confirm these data.

Objective evidence that intraperitoneal pemetrexed combined with intravenous cisplatin resulted in a reduction in the peritoneal tumor burden was provided by Le Roy and colleagues from the Gustave Roussy (*Ann Surg Oncol, 2017*). Laparoscopic evaluation was used as a selection criteria perioperatively. Twenty patients had high laparoscopic PCI and were not suitable for upfront CRS plus HIPEC. These patients were treated with the bidirectional chemotherapy. The objective response recorded at the second laparoscopy was 60%. Ten patients had a conversion CRS plus HIPEC with a two-year survival of 83.3%. The bidirectional chemotherapy was well tolerated and facilitated a conversion surgery in half of these advanced peritoneal mesothelioma patients.

Xin-Li Liang and colleagues from Shijitan Hospital, Beijing performed a case-controlled study comparing adjuvant intraperitoneal chemotherapy to adjuvant intravenous chemotherapy (*Eur J Surg Oncol, 2024*). All 152 patients had CRS and HIPEC from malignant peritoneal mesothelioma. The CRS was optimal in 89 (58.6%) of patients and incomplete in 63 (41.4%). When adjuvant intraperitoneal chemotherapy was compared to adjuvant intravenous chemotherapy in the complete CRS group, no differences were seen. However, in the incomplete CRS group, the use of 5 cycles of adjuvant intraperitoneal chemotherapy more than doubled overall survival (p=0.005). Median overall survival increased from 10.3 months to 24.5 months. In this manuscript, NIPEC with cisplatin was effective in patients with malignant peritoneal mesothelioma who had gross residual disease after CRS. This study did not utilize intraperitoneal pemetrexed.

These data taken together suggest that a regional approach to the management of malignant peritoneal mesothelioma is in need of a definitive randomized controlled study. The protocol now active at Memorial Sloan Kettering Cancer Center seeks to provide this information. The trial is a challenging one in that this is a rare disease with 300-500 new cases per year in the United States. Recruitment of a sufficient number of patients within a reasonable time period will be a challenge. Almost all patients will be required to travel considerable distances for treatment and follow-up. Also, maintenance of an intraperitoneal access device for 4-6 months can be problematic. Nevertheless, cytoreductive surgery plus HIPEC took malignant peritoneal mesothelioma from a median survival of 1 year to 4 years. Now, the contribution of NIPEC with pemetrexed to improve survival in patients with this disease is definitely needed.

Section 7: Editorial

The Unstoppable Evolution of Minimally Invasive Surgery in the Management of Peritoneal Metastases

By Jesus Esquivel

Surgery is the first form of treatment described for the management of solid tumors. It has been more than 200 years since the first colectomy for cancer and 130 years ago, Doctor William Halsted, reported the use of a radical mastectomy for the treatment of breast cancer. This procedure continued to be the standard of care until the early 1970s. Today, surgery continues to be the cornerstone of solid cancer treatments.

Better understanding of cancer biology, earlier detections, improvements in technology, and the addition of neoadjuvant and adjuvant therapies have been able to decrease the need for some more radical procedures like permanent colostomies in rectal cancer and amputations in extremity tumors.

Since its original description 45 years ago, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) continue to play an ever-increasing role in the management of patients with peritoneal surface malignancies (PSM) of gastrointestinal, gynecological, or peritoneal origin.

Traditionally, this therapy required a large midline incision and many hours in the operating room. Consequently, the patients required a prolonged hospitalization and even though there was a low mortality rate, the procedure carried a significant morbidity. Reports of the first feasibility, morbidity and outcome study using minimally invasive surgery done via the laparoscopic route in patients with low peritoneal cancer index (PCI $\leq$ 10) were published in 2011 (*Annals of Surgery, Volume 253, Number 4, 764-768*). Since then, there are approximately 200 publications on this subject. These studies show lower morbidity, decrease in length of hospital stay and no difference in oncological outcome compared to the open procedures.

The use of robotic assisted, minimally invasive surgery has been gaining popularity in the last two decades. Advantages include better ergonomics, 3D visualization with a X 10 magnification, the simplicity of Indocyanine Green (ICG) to evaluate perfusion of bowel prior to an anastomosis, and the increased ability to perform intracorporeal anastomosis. Consequently, the robotic approach is rapidly replacing laparoscopy for complex oncological procedures. Hundreds of publications have been reported, including a few in patients with peritoneal metastases.

In my opinion, this unstoppable evolution has allowed us to optimize our approach to the management of patients with peritoneal metastases: Step 1, patients whose CT scan shows evidence of peritoneal carcinomatosis are taken to the operating room for a diagnostic laparoscopy, determination of the peritoneal cancer index (PCI), multiple biopsies including frozen sections and if the diagnosis of cancer is established, a Mediport catheter is placed during the same anesthesia. Step 2, determine the currently relevant histopathological, genetic, and molecular evaluations that exist

including microsatellite instability status (MSI), tumor mutational burden (TMB), genomic profile analysis (GPA), consensus molecular subtypes (CMS), BRCA and HRD status to name a few. Step 3, present the case at a multidisciplinary tumor board conference and discuss the best neoadjuvant therapy available. If one is available, start the therapy and after 3 or 4 cycles restage the patient and repeat the laparoscopy. Step 4, if the patient has demonstrated an appropriate response, determine at the time of laparoscopy if the remaining disease will be able to be removed using minimally invasive surgery. If not, discuss the role of additional therapies or proceeding with an open cytoreductive surgery and HIPEC if all the disease can be removed.

I believe that as time goes by, better neoadjuvant treatments will come along, and patients will need smaller surgical resections that will be performed robotically-assisted. Also, better adjuvant treatments will help us maintain the complete surgical response within the abdomen and pelvis and thereby improve the quality and quantity of life of our patients.

Peritoneal metastases when optimally treated can be cured; in selected patients peritoneal metastases can be prevented. The ultimate goal is to eliminate local-regional recurrence and peritoneal metastases from the natural history of gastrointestinal and gynecologic malignancy.


PSOGI
Barcelona 2025
October 29th • 31st, 2025
Peritoneal Surface Oncology Group International
PSOGI
SEOQ
The 15th PSOGI International Congress on Peritoneal Surface Malignancies
Fira Barcelona
CONGRESS CHAIRS
Dr. Fernando Pereira
Madrid, Spain
Dr. Pedro Bretcha-Boix
Alicante, Spain
Preliminary agenda
With the collaboration of:
ISSPP
European Society of COLOPROCTOLOGY
ESCP
https://psogicongress2025.com

Scientific and Organizing Committee

Luis Gonzalez-Bayón, *Surgical Oncology (Madrid, Spain)*
Lana Bijelic, *Surgical Oncology (Barcelona, Spain)*
Santiago González-Moreno, *Surgical Oncology (Madrid, Spain)*
Álvaro Arjona, *Surgical Oncology (Córdoba, Spain)*
Pedro Cascales, *Surgical Oncology (Murcia, Spain)*
Jorge Barriuso, *Medical Oncology (Madrid, Spain)*
Frederic BibeaU, *Pathology (Besançon, France)*
Max Lahaye, *Radiology (Amsterdam, The Netherlands)*

PSOGI Board

Paul H. Sugarbaker - *Washington (USA)*
Aditi Bhatt - *Bangalore (India)*
S.P. Somashekhar - *Bangalore (India)*
David L. Bartlett - *Pittsburgh, Pa (USA)*
Marcello Deraco – *Milano (Italy)*
Olivier Glehen - *Lyon (France)*
Diane Goéré - *Paris (France)*
Santiago González-Moreno - *Madrid (Spain)*
Ignace de Hingh - *Eindhoven (The Netherlands)*
Yan Li - *Beijing (China)*
Brendan John Moran - *Basingstoke (United Kingdom)*
David Morris - *Sydney (Australia)*
Aviram Nissan - *Tel Aviv (Israel)*
Pompiliu Piso - *Regensburg (Germany)*
Beate Rau - *Berlin (Germany)*
Vic Verwaal - *Lund (Sweden)*
Yutaka Yonemura - *Kyoto (Japan)*
Claudio Quadros - *Salvador Bahía (Brasil)*

Key topics

- Controversies in appendiceal neoplasms
- Advanced Surgical Techniques in PSM
- Neoadjuvant therapy in PSM
- Minimally invasive surgery in PSM
- Patient Advocacy session
- Most expected Clinical Trials in PSM
- Young Surgeons in PSM
- Prehabilitation
- Peritoneum-plasma barrier and Pharmacokinetics of HIPEC
- Historical PSOGI consensus
- Radiomics in PSM
- Tumor Board sessions
- Pro/Con Debate sessions
- ISSPP sessions
- Joint sessions with other societies:
  1. European Society of Coloproctology (ESCP)
  2. European Society of Gynaecological Oncology (ESGO)