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Conclusions: There is a high prevalence of burnout, depression & anxiety in oncology residents which may be due to a low doctor-patient ratio & a lack of resident work hour limits. With an expected increased in cancer burden in the next decade, psychological issues in oncology caregivers can be expected to increase. Further studies would be needed to determine interventions that would reduce psychological distress.

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COMBINATIVE TREATMENT OF NONRESECTABLE CHOLANGIOCELLULAR CANCER COMPLICATED BY OBSTRUCTIVE JAUNDICE.

Artem Shiryaev¹, Igor Reshetov¹, Viktor Loschenov², Maxim Loschenov², Vladimir Makarov², Aleksandr Borodkin². ¹The First University clinical hospital I.M. Sechenov Moscow State Medical University, Surgical Oncology and Combinative Methods of Treatment, Moscow, Russian Federation; ²Prokhorov General Physics Institute of the Russian Academy of Sciences, Prokhorov General Physics Institute of the Russian Academy of Sciences, Moscow, Russian Federation

Background: The five-year survival rate for successful surgical treatment of cholangiocellular cancer is only 20–40%, in the case of an unresectable tumor, the life expectancy does not exceed 6 months. These terms decrease with the presence of jaundice due to the spread of the tumor process along the bile ducts, leading to their obstruction.

The objectives of our study were to improve the diagnostic and treatment approaches using combined surgery and noninvasive methods for the patients with unresectable liver cholangiocarcinoma complicated by obstructive jaundice [1].

Materials and Methods: The group included 34 patients. The treatment included (i) percutaneous transhepatic biliary excision under ultrasound and fluoroscopic control; (ii) transfusion endoscopic video fluorescent diagnosis with targeted biopsy; (iii) intraperitoneal PDT; (iv) stenting of bile ducts. Photosensitizers (PS) based on aluminum phthalocyanine (Fotosens, Russia) and chlorin e6 (Radachlorine, Russia and Photolon, Belorussia) were used for fluorescence diagnostics and PDT. For the first time in Russia, a video-fluorescent module for endoscopy and minimally invasive surgery was used. Video fluorescence images of the bile duct tumor were obtained and the photosensitizer concentration in it was determined. Photodynamic therapy was carried out using a fiber-optic system with, if required, a controllable balloon catheter at the distal end which allows straightening the stricture and carrying out the illumination along it uniformly. The average power density of laser radiation (LFT-670-01-BIO-SPEC, 670 nm, longer wavelength laser was chosen to increase the depth of the therapeutic effect) was 200 mW/cm², the total light dose of radiation was 110–130 J/cm². No complications occurred during surgery.

Results: All patients noted PS accumulation in tumor tissue in a concentration sufficient for PDT. Video fluorescence images of the bile duct tumor were obtained, the photosensitizer concentration in it was determined. Morphologically cholangiocellular cancer was confirmed in 25 patients. The effectiveness of treatment was assessed by the patient's life expectancy. The longest life expectancy was 32 months (mean 16±2 months). 11 patients are under dynamic observation, for a period of 4 to 17 months. Seven patients died within 3±1 months after the treatment and initially had multiple distant metastases and entered the clinic in a serious condition (Karnovsky index 30).

Conclusions: The developed technique allows to diagnose tumor tissue, which is the only possible objective method for diagnosing malignant lesions of the bile ducts. Stenting of bile ducts in combination with anti-neoplastic photodynamic therapy of stricture allows to achieve a treatment positive result, without reducing the patient life quality.

1. Shiryaev A.A., et. al., Combined treatment of nonresectable cholangiocarcinoma complicated by obstructive jaundice. Photodiagnosis and Photodynamic Therapy. 2019. Vol.26:218–223.

P-451

WOMEN IN SURGERY ITALIA: PERCEIVED GENDER BIAS AMONG ITALIAN SURGEONS

Gaya Spolverato¹, Marianna Purgato², Federico Tedeschi², Daniela Molena², Roberto Salvia⁴, Elda Baggio⁴, Corrado Barbui², Isabella Frigerio⁵. ¹Università degli Studi di Padova, DiSCOG - Department of

Surgery, Padova, Italy; ²Università di Verona, Psychiatry, Verona, Italy; ³Memorial Sloan Kettering Cancer Center, Surgery, New York, USA; ⁴Università di Verona, Surgery, Verona, Italy; ⁵Ospedale Pederzoli, Surgery, Peschiera del Garda VR, Italy

Background: Over the last decade Italian women surgeons are increasing in number, consistently with the growing rate of female surgeons worldwide. The number of first-year residents in 2016 was 47% compared to 23% in 2000, confirming a trend toward a further rise in the number of trained surgeons in the next 10 years. Nevertheless, surgery in Italy is still a male dominated field and female surgeons perceive gender-related discriminations during their professional career. We sought to investigate the perceived gender bias among Italian residents and surgeons.

Materials and Methods: A modified version of the Career Barriers Inventory—Revised was administered to male and female surgical residents and surgical faculty members of the major Italian surgical societies using an online survey tool. Likert-type scales were used to measure respondents' agreement with each survey item. Chi-square test (or Fisher's exact test, where appropriate) was used to identify significant differences on the basis of gender.

Results: A total of 134 (65.7% female) surgeons completed the online survey. Sixty-six percent of women experienced sex-related discrimination during training versus 21% of men (P<0.001). Women were also more discriminated than men during job interview (19.8%, P 0.035) and during early-career development (27.9%, P 0.028). Despite 95.2% of responders reported to have had a mentor, in only 9.0% of cases the model was a woman. Men were two-folds more likely to have kids compared to women (M = 79.5% versus F = 36.8%; P<0.001). Although 36.8% of women had kids, 73.5% wished to have more and those (n = 26) who decided not to have more children due to professional reasons are twice those who did so for personal reasons (n = 12). In-hospital child-care was considered very helpful by the 93.6% of responders but only 28.9% of surgeons could rely on it. Finally, 70.2% of all participating women surgeons considered female gender to be an obstacle to a surgical career.

Conclusions: Although the number of women in surgical training has significantly increased over the last decade, strong gender-related discrimination is still frequent among Italian surgeons. Mentorship and networking with other women at a national and international level might empower women surgeons, create opportunities for career advancement and hopefully change the overall surgical male-dominant mentality into an equal opportunity environment for all the surgeons.

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METABOLIC ACIDOSIS IN CANCER: A NEW STRATEGY USING A PH ACTIVATED IMAGING AGENT FOR FLUORESCENCE-GUIDED SURGERY IN HUMANS

Pieter Steinkamp¹, Floris Voskuil², Bert van der Vegt³, Jan Johannes Doff⁴, Tian Zhao⁵, Jeff Hartung⁶, Yalia Jayalakshmi⁷, Baran Sumer⁸, Jiming Gao⁹, Max Witjes¹⁰, Gooitzen van Dam¹¹. ¹University Medical Center Groningen, Surgical Oncology, Groningen, Netherlands; ²University of Groningen, Department of Maxillofacial Surgery, Groningen, Netherlands; ³University Medical Center Groningen, Pathology & Medical Biology, Groningen, Netherlands; ⁴University Medical Center Groningen, Pathology and Medical Biology, Groningen, Netherlands; ⁵OncoNano Medicine Inc, OncoNano Medicine Inc, Texas, USA; ⁶JPH Clinical Development Inc, JPH Clinical Development Inc, San Diego, California, USA; ⁷Onconano Medicine Inc, Onconano Medicine Inc, San Diego, California, USA; ⁸University of Texas Southwestern Medical Center, Department of Otolaryngology Head and Neck Surgery, Dallas, Texas, USA; ⁹University of Texas Southwestern Medical Center, Department of Pharmacology, Dallas, Texas, USA; ¹⁰University Medical Center Groningen, Department of Maxillofacial Surgery, Groningen, Netherlands; ¹¹University Medical Center Groningen, Department of Surgery & Medical Imaging Center, Groningen, Netherlands

Background: Extracellular acidosis of the tumor environment is a general phenomenon observed in solid tumors due to the Warburg Effect where tumor cells preferably convert glucose into lactic acid despite the presence of oxygen. Up to now, this hallmark of cancer has not been successfully used in diagnostic or therapeutic settings. ONM-100 is a micelle-based

polymer imaging agent conjugated with ICG with an exquisitely pH-sensitive, binary off/on mechanism that can be used for intraoperative tumor detection and margin assessment. Micelles dissociate in acidic environments resulting in fluorescent activation of ICG. By targeting metabolic vulnerabilities of cancer with this unique pH-activated approach, ONM-100 could overcome the limitations of other fluorescent imaging agents which lack a broad tumor applicability due to tumor type-specific targeting. This first-in-human study investigates the safety and feasibility of ONM-100 as diagnostic agent for fluorescent imaging of various solid tumors.

Materials and Methods: In this Phase 1 study, ONM-100 was IV administered 24±8h prior to surgery in accordance with a dose escalation scheme (0.1-1.2mg/kg), and a selected dose was further evaluated in a subsequent cohort with multiple solid tumors. Patients with breast cancer (BC), head and neck squamous cell carcinoma (HNSCC), colorectal cancer (CRC) and esophageal cancer (EC) were included. Blood was drawn for safety and pharmacokinetic data. Intraoperative images were collected before and after tumor excision, from the surgical cavity and of the specimen directly after excision using a standardized method. Fluorescence images were obtained from serially sliced specimens and correlated with standard histopathological assessment.

Results: Thirty patients (11 BC, 13 HNSCC, 3 EC, 3 CRC) were enrolled. No treatment-related (serious) adverse events higher than CTCAE grade 1 were observed. A sharply demarcated fluorescent signal was observed in all 29 patients with viable tumor tissue with *in vivo* and/or *ex vivo* imaging, (median Tumor-to-Background Ratio of 4.3; IQR of 3.1) which correlated with tumor on final histopathology, irrespective of the tumor type or ONM-100 dose. One patient showed complete pathological response after neoadjuvant treatment. All tumor positive surgical margins in BC and HNSCC (N=9) and occult peritoneal metastasis could be detected by intraoperative fluorescence imaging. Pharmacokinetic data showed a strong correlation between dose and exposure.

Conclusions: This study demonstrates that ONM-100 appears safe and may allow generic fluorescent-based tumor visualization both *in vivo* and *ex vivo* in various solid tumors with high tumor-to-background fluorescence ratios and excellent correlation with histopathology. These data support the potential clinical utility of ONM-100 towards improving the detection of positive margins and occult disease.

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HYPERTHERMIC INTRATHORACIC CHEMOTHERAPY (HITHOC) IN OVARIAN CARCINOMA – CASE REPORT

Dejan Stojiljkovic¹, Srdjan Nikolic², Ana Cvetkovic³, Vladimir Jokic⁴, Igor Spurnic⁴, Stevan Jokic⁴, Merima Goran⁴, Milan Kocic⁴, Tanja Stojiljkovic⁵. ¹Thoracic Surgery, Surgery, Belgrade, Serbia; ²Institute for Oncology and Radiology of Serbia, Surgery, Belgrade, Serbia; ³Institute for Oncology and Radiology of Serbia, Anesthesiology, Belgrade, Serbia; ⁴Institute for Oncology and Radiology of Serbia, Surgery, Belgrade, Serbia; ⁵Medical Center Smederevo, Radiology, Smederevo, Serbia

Background: Hyperthermic Intrathoracic Chemotherapy (Hithoc) is based on the known principle that by increasing concentration of cytotoxic agents the level of tumor cell destruction is also increased. This method is based on the synergistic effect of increased temperature and high cytotoxic concentration on tumor cells. Hithoc as a relatively new method has gained application in treating pleural mesothelioma, thymoma and also in advanced malignancies of the abdominal and pelvic cavity origin.

Materials and Methods: A female patient aged 42, begun oncological treatment for advanced ovarian carcinoma in June 2016. Considering intraoperative findings, cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) were performed. After that, the treatment continued with adjuvant chemotherapy. In March 2018, the computed tomography (CT) examination showed the progression of the disease on the pleura in the form of carcinomatosis with increased in the level of tumor markers. In April 2018, in our institute, total parietal pleurectomy, partial visceral pleurectomy, and then Hithoc with cisplatin were performed. The procedure went properly, as did the postoperative course. Patient was discharged from our institute on the 13th postoperative day with no major complications regarding the operation.

Results: Three months after the surgery, CT showed no signs of any

disease relapse.

Conclusions: This is a relatively new method of treating pleural carcinomatosis. Real results are to be expected with a larger series of patients and longer postoperative period.

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A SEARCH FOR NEW BIOMARKERS IN PERITONEAL SURFACE MALIGNANCIES OF DIFFERENT ORIGIN TREATED WITH CYTOREDUCTIVE SURGERY AND HIPEC

Marco Tonello¹, Barbara Montini², Nayana Lazzari², Maria Assunta Piano², Rocco Cappellesso³, Carlo Riccardo Rossi⁴, Pierluigi Pilati¹, Antonio Sommariva¹, Maria Luisa Calabrò². ¹Veneto Institute of Oncology IOV-IRCCS, Surgical Oncology of the Esophagus and Digestive Tract, Padova, Italy; ²Veneto Institute of Oncology IOV-IRCCS, Immunology and Molecular Oncology, Padova, Italy; ³University of Padova, Surgical Pathology Unit- Department of Medicine DIMED, Padova, Italy; ⁴Veneto Institute of Oncology IOV-IRCCS, Surgical Oncology, Padova, Italy

Background: There are many evidences suggesting a major role of epithelial-mesenchymal transition (EMT) in promoting cancer development and aggressiveness. This biological process converts static epithelial cells in migratory and microenvironment-interacting mesenchymal cells. EMT is also implicated in the modulation of proteins linked to stemness and aggressiveness of tumor cells. So far the relevance of factors linked to EMT and regulated by this process in peritoneal surface malignancies (PSM) has not been fully elucidated. In this pilot study, the expression of EMT-related and -regulated genes was measured in surgical specimen derived from patients affected by PSM of different origin treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), to look for mesenchymal marker(s) preferentially expressed in specific tumor histotypes and potentially linked to biological behavior.

Materials and Methods: The expression of 8 EMT-related genes was analyzed by qRT-PCR (structural mesenchymal proteins: vimentin and ASMA, transcriptional repressors: ZEB1 and SIP1, proteins modulated by EMT factors and associated to tumor aggressiveness: periostin (POSTN) and mesothelin (MSTN), stemness markers: OCT4 and NANOG). Transcripts levels were normalized on a housekeeping and expressed as normalized relative quantification (nRQ), using two samples of activated mesothelium. Patient characteristics and survival variables were extracted from a prospectively collected clinical database. Demographic and clinical variables were analyzed using appropriate tests with SPSS software v. 20.0.

Results: After Ethical Committee approval in 2016, 38 patients affected by PSM of different origins have been enrolled: 19 pseudomyxoma peritonei (PMP), 12 colorectal carcinoma (CRC), 7 peritoneal malignant mesothelioma (MM). Preliminary analyses disclosed that POSTN (P=0.044) and MSTN (P=0.026) genes were significantly differentially expressed. Specifically, POSTN was found to be more expressed in CRC and PMP, whereas MSTN was highly expressed in MM and mucinous CRC. Interestingly, high POSTN expression was significantly associated with high grade rather than low-grade PMP (P=0.02). MSTN expression was significantly higher in mucinous compared to not-mucinous CRC (P=0.03). The association with biological behavior did not reach statistical significance; nevertheless higher rate of local recurrence was observed in MM with high MSTN expression and in low-grade PMP and CRC with elevated POSTN expression.

Conclusions: These preliminary data suggest that two markers of aggressiveness modulated during EMT might show a preferential expression in specific PSM histotypes; these markers could therefore represent novel therapeutic targets and could be exploited as recurrence indicators in their circulating forms. Further studies in a larger sample size are needed.

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RISK FACTORS AND MANAGEMENT FOR COMPLICATION IN CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

Ali Ekrem Unal¹, Ogün Erşen¹, Cemil Yüksel¹, Serdar Çulcu², Salim İlksen Başçeken¹, Ümit Mercan¹, Ferit Aydın², Ömer Yalkın³. ¹Ankara University, Surgical Oncology, Ankara, Turkey; ²Ankara Oncology Hospital, Surgical