ORAL PRESENTATIONS

S1 – HOW TO IMPROVE TREATMENT OUTCOMES OF ONCOLOGY PATIENTS WITH COLORECTAL CARCINOMA

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Colorectal cancer (CRC) surgery has experienced major improvements regarding decision making through multidisciplinary teams, perioperative treatment and minimally invasive surgical techniques. The overall survival of colorectal patiens has been considerably improved with earlier diagnosis and novel medical treatment options. The cornerstone in the treatment of colorectal cancer is surgery but multimodal perioperative treatment modalities significantly affect outcomes. Implementation of enhanced recovery after surgery programs (ERAS) has shown significantly improved various key outcome measures including reduced overall complication rates, length of hospital stay (LoS), improved postoperative recovery and patient satisfaction. Minimally invasive surgery (MIS) has demonstrated many benefits in colorectal procedures. Laparoscopic surgery for colorectal cancer is associated with all advantages of minimally invasive surgery along with better short-term outcomes, survival and recurrence rates comparable to these of open surgery. On the other hand, it has some technical limitations and difficulties especially when performing total mesorectal excision (TME). Robotic colorectal cancer resections are becoming the standard approach worldwide. However, uncertainties still exist regarding benefits of robotics when compared to other MIS options. Surgical robot systems have been offering different improvements that may overcome some of the limitations of laparoscopic surgery. Robotic surgery allow immersive 3D visualization with enhanced depth perception, allows changes in ergonomics, more precise and complex movements with elimination of surgeon´s tremor, articulating instruments and infrared technology. All of these facilitates access to deep pelvis and enhances identification and manipulation of structures during TME with decreased learning curve compared to laparoscopy. Robotic surgery for CRC offers improved outcomes defined as LoS less of 5 days, absence of 30-day complications, readmissions, and mortality for right and left colectomy. These advantages have not been demonstrated in low anterior resection (LAR). When comparing postoperative outcomes, robotic and laparoscopic resections have comparable rates of anastomotic leak. However, longer surgery time, absence of tactile sensation and docking still remain problematic.

Keywords: colorectal cancer; laparoscopy; minimally invasive surgery; robotics; enhanced recovery after surgery

S2 – COLORECTAL CANCER DIAGNOSTICS (CRC): PROPER STAGING IS CRUCIAL FOR TREATMENT INITIATION

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Introduction: Proper selection of diagnostic methods for colorectal cancer can initially determine the stage of the disease as accurately as possible. The use of magnetic resonance imaging (MRI) for local staging of colorectal cancer can determine the relationship between the primary tumor and pathological lymph nodes concerning the mesorectal fascia. If the mesorectal fascia is intact, surgical resection of the primary tumor is possible, which is marked as a negative circumferential margin.

Using MSCT, a more accurate disease stage can be obtained – confirming or ruling out metastases in the lung or liver parenchyma. For poorly differentiated lesions in the liver parenchyma after CT, an MRI of the liver is recommended for better characterization of the lesions as malignant or benign.

Rarely, if insufficient information is obtained with MRI, the patient may be referred for PET CT.

Aim: Our goal is to present the diagnostic methods used to determine the disease stage as accurately as possible in colorectal cancer. Accurate disease staging with imaging methods directs patients to either surgical treatment, neoadjuvant therapy, or, in the case of metastatic disease evidence, systemic treatment.

Methods: In our institution, each patient with colorectal cancer undergoes MRI of the pelvis following colonoscopy and PHD-confirmed colorectal cancer. The rectal cancer protocol does not require contrast medium for MRI but only agents to reduce bowel motility. All patients also undergo MSCT of the thorax and abdomen, and if necessary, for differentiating focal lesions in the liver parenchyma, MRI of the abdomen.

We used a 1.5 Tesla MRI device and MSCT. MRI is performed natively with T2 sequences in all three planes (transverse, coronal, and sagittal) and transverse diffusion sequences through the pelvis, i.e.,

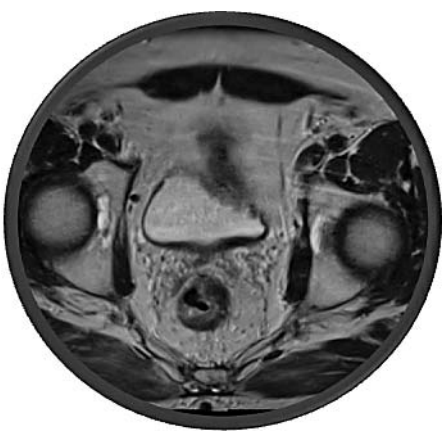

Figure 1. T3a – Extension through the muscularis propria into mesorectal fat <1 mm

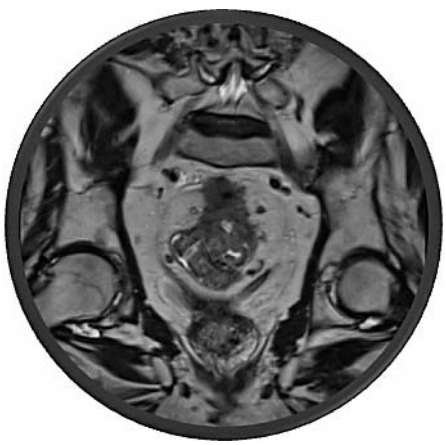

Figure 2. T3d – Extension through the muscularis propria into mesorectal fat >15 mm

through the affected colorectal area. CT is initially performed using a multiphase protocol with iodine contrast.

Results: Proper patient preparation and MRI for colorectal cancer provide adequate imaging of the rectal segment previously described/diagnosed by colonoscopy. T2-weighted sequences through the affected rectal area in millimeter sections enable optimal spatial and contrast resolution, while diffusion-weighted sequences show the volume of active malignant disease and functional regression after neoadjuvant therapy.

Conclusions: Proper selection of diagnostic methods with high accuracy can determine the disease stage, enabling optimal treatment for each colorectal cancer patient.

Keywords: colorectal cancer; diagnostic methods; staging; MRI; MSCT

S3 – BREAST DIAGNOSTICS – WHAT'S NEW?

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Introduction: The role of the radiologist in presenting a patient to the multidisciplinary breast cancer team is to determine the size of the tumor and the involvement of lymph nodes as accurately as possible, including the number of lymph nodes and their axillary levels. If there is insufficient information, the patient is referred for additional tests, whether imaging or invasive procedures such as core biopsy.

Aim: Our goal is to present the diagnostic imaging and interventional methods needed to accurately determine the extent of the disease in patients with breast cancer in terms of primary tumor size, lymph node involvement, and the presence of distant metastases.

Methods: In the multidisciplinary team, each patient should have a PHD verified breast cancer by core biopsy. In the case of suspected metastases, axillary lymph nodes can be confirmed either cytologically or by core biopsy. If the tumor is HER2-positive and the lymph nodes are cytologically positive, it is recommended to perform a biopsy of the pathological lymph node to ensure the best therapeutic approach, similarly is done for Luminal A tumors with positive axilla.

If fewer than three pathological lymph nodes are involved, a tissue marker is placed in the axilla after a core biopsy of the pathological lymph node, and such patients are later considered for eventual targeted axillary dissection (TAD) after the neoadjuvant chemotherapy.

Each patient undergoes a core biopsy, ultrasound (US) of both breasts and axilla, and if lymph nodes are positive or the tumor is aggressive, an MSCT of the thorax, abdomen, and pelvis is performed. If axillary lymph nodes are negative, an abdominal ultrasound and chest X-ray are done. Every patient with breast cancer should have a mammogram and, if necessary, an MRI of the breasts. The size of the primary tumor is usually determined by breast MRI, but if MRI is not possible, ultrasound with mammography or optionally contrast mammography is sufficient.

If a neoadjuvant approach is chosen, the primary tumor must be marked with a tissue marker. In our institution, a tissue marker is always placed after biopsy as proof of the intervention. If lesions are smaller than 5 mm, the primary tumor may be removed by core biopsy, leaving only the tissue marker in the final pathological report.

If fewer than three pathological lymph nodes are involved, a tissue marker should be placed in one of the initially pathological lymph nodes for a TAD surgical approach after neoadjuvant therapy.

Results: With well-prepared patients in terms of disease volume, we can optimize the surgical approach as accurately as possible. The introduction of preoperative wire marking allows for the marking of small non-palpable tumors or tissue markers placed after neoadjuvant therapy.

In targeted axillary approaches after neoadjuvant therapy (TAD), a wire guide is also placed in the initially pathological lymph node within the axilla, which was marked with a tissue marker before neoadjuvant therapy.

The assessment of neoadjuvant therapy is always done with MRI, ideally on the same machine with the same contrast medium, and the targeted surgical approach is chosen based on the comparison of old and new findings.

Figure 1. Mammographic image of specimen after neoadjuvant therapy, wire placed in tissue marker

Conclusions: With well-prepared patients in terms of disease volume, we can optimize the surgical approach as accurately as possible. The introduction of preoperative wire marking allows the marking of small non-palpable tumors or tissue markers placed after neoadjuvant therapy. In targeted axillary approaches after neoadjuvant therapy, a wire guide is also placed in the initially pathological lymph node within the axilla, which was marked with a tissue marker before neoadjuvant therapy. The assessment of neoadjuvant therapy is always done with MRI, ideally on the same machine with the same contrast medium, and the targeted surgical approach is chosen based on the comparison of old and new findings.

Keywords: breast cancer; diagnostic imaging; interventional methods

S4 – SIGNIFICANCE OF PREOPERATIVE PET/CT FOR TREATMENT PLANNING IN PATIENTS WITH HIGH RISK MELANOMA

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Introduction/Aim: To evaluate the importance od 18F FDG PET/CT in staging of patients with high risk melanoma regarding further therapy decision-making.

Methods: In this ongoing study, 85 patients with high risk melanoma, confirmed by histopathological and immunohistochemical analysis, performed PET/CT 5-6 weeks after the primary excision of the tumour, 48 men and 37 women of the mean age 66 years. Melanomas were located in the head and neck in 17 patients, on the trunk in 32 patients and in 36 patients on the extremities. The average tumour thickness was 5.3 mm, the average mitotic rate 11.3 per mm square, with 68 melanomas histologically ulcerated.

Results: Positive PET/CT scans were indentified in 22 patients (26%) with high risk melanoma, in 2 sites near the primary tumour, in 19 in the regional lymph nodes and 5 distant metastases. Positive lymph nodes were confirmed with ultrasound/cytological puncture and underwent lymph node dissection. Later on, 1 patient was treated surgically, 1 patient underwent radiotherapy, 13 patients received adjuvant targeted BRAF/MEK inhibitor therapy and 5 patients with metastatic disease received immunotherapy (2 patients refused further treatment). PET/CT revealed incidental benign tumours in 9 patients and additional malignant tumours in 4 patients. PET/CT scans were true negative in 45 (71%) of all negative scans confirmed with SLNB, while in 18 (29%) scans SLNB was positive in at least one regional lymph node (subcapsular micrometastases). These patients were subsequently treated surgically (1), with radiotherapy (2), targeted therapy (4), immunotherapy (2), on regular follow-ups with no active treatment required (8), 1 patient refused further treatment. Due to the PET/CT findings of disseminated disease, 22 patients (26%) did not undergo SLNB. The positive predictive value of PET/CT in this group of patients is 95% and negative predictive value 71%.

Conclusions: Since preoperative PET/CT changed the treatment plan for 26 patients (31%), we support the importance of PET/CT in the primary evaluation of patients with high risk melanoma, thus influencing on the best future treatment modalities and quality of patient's life, stresssing the need for recommendation of routine PET/CT diagnosis and follow-up in these patients. The increasing availability of different types of therapy for people with high risk of disease spread at presentation urge the necessity of the accurate primary staging.

Keywords: melanoma; PET/CT; staging

S5 – HOW BRCA STATUS AFFECTS THE THERAPEUTIC PLAN AND DECISION MAKING OF MULTIDISCIPLINARY TEAM IN PATIENTS WITH BREAST CANCER

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The lifetime risk of developing breast cancer in general population is about 11%, while in carriers of pathological variants (PV) of the BRCA1 gene it is 57-72%, and of the BRCA 2 gene 45-69%. It is estimated that 10% of all breast cancers are related to hereditary forms of breast cancer, while about 3% are related to PV BRCA1/2 genes. When PV BRCA 1/2 genes are identified, genetic counseling should be performed, which should clarify the medical and potential psychological implications for both individuals and their families.

Carriers of the PV BRCA 1/2 gene require lifelong screening, not only for breast cancer, but also for other tumors, such as ovarian and pancreatic cancer. To reduce the risk of disease, we have available risk-reducing drugs and surgical procedures (prophylactic mastectomy).

Consideration of disease risk should be individualized and, when available, validated tools should be used to aid decision-making. Diagnostics and follow-up of patients with PV BRCA 1/2 gene should be carried out in multidisciplinary, specialized, tertiary institutions.

Detection of breast cancer in PV BRCA 1/2 carriers at an early stage is based on the shorter screening intervals that should begin at age 30 or 5 years earlier than the youngest family member with breast cancer. For BRCA1 carriers, a 6-month examination interval is recommended, the optimally with MRI. For BRCA1 carriers, regardless of age, there is little benefit from mammography screening, however, there may be additional benefit of mammography for BRCA2 carriers. If a 6-month MRI examination is unavailable, an annual MRI is recommended, which should be supplemented (between annual MRIs) with ultrasound or mammography.

Risk-reducing medications are an option for women who delay or do not undergo risk-reducing surgery. In randomized studies, the selective estrogen receptor modulators, tamoxifen and raloxifene, and the aromatase inhibitors, anastrozole and exemestane, have been shown to reduce the incidence of breast cancer by 30%-60%. The absolute risk of serious side effects was low, especially for premenopausal women.

Prophylactic mastectomy with or without reconstruction is the most effective method for reducing the risk of breast cancer among PV BRCA1/2 carriers. In all affected high-risk carriers of PV BRCA1/2, contralateral prophylactic mastectomy reduces the incidence of contralateral breast cancer without a significant effect on overall survival. Prophylactic mastectomy reduces the risk of recurrence from breast cancer by about 90%, depending on the study and the type of surgery performed. It must be noted that no randomized controlled studies have been conducted. The greatest benefit of prophylactic mastectomy is if it is performed after the age of 30, because by the age of 30, the cumulative risk of breast cancer for BRCA1/2 carriers is 4%. Prophylactic mastectomy is an extensive procedure that should be carefully discussed with patients, taking into account benefits, complications, and psychosocial impact. After bilateral prophylactic mastectomy, an MRI should be performed in the first year after surgery to assess the amount of residual breast tissue, and further imaging decisions should be made accordingly on a case-to-case basis.

A multidisciplinary approach to treatment is required in patients with breast cancer who are carriers of PV BRCA1/2. In planning surgical treatment, bilateral mastectomy with or without reconstruction is recommended. If the patients are not prone to bilateral mastectomy, intensive postoperative monitoring is required, as is for PV BRCA1/2 carriers who have not suffered from breast cancer and have not undergone prophylactic mastectomy. In certain breats cancer patients with PV BRCA1/2, it is possible to prescribe adjuvant PARP inhibitors such as olaparib or talazoparib.

In conclusion, it must be emphasized that the approach to the treatment of PV BRCA1/2 carriers, as well as breast cancer patients who are PV BRCA1/2 carriers, must be multidisciplinary. This is best done in specialized, tertiary centers that have all the necessary services that are needed in the care of such patients, and at the same time, it is necessary to provide psychological help. Monitoring of PV BRCA 1/2 carriers is more intensive, along with monitoring it is recommended to carry out treatment that reduces the risk of breast cancer, preferably bilateral prophylactic mastectomy with reconstruction. In patients diagnosed with breast cancer and carriers of PV BRCA 1/2, it is also best to perform a bilateral mastectomy with reconstruction, with the inclusion, in certain patients, of PARP inhibitors in adjuvant treatment. A special approach is needed in patients who are not prone to bilateral mastectomies, who require intensive and frequent monitoring. In the future, we expect progress in the pharmacological reduction of breast cancer risk in PV BRCA 1/2 carriers.

Keywords: breast cancer; BRCA 1/2 mutattion; PARP inhibitors**;** prophylactic mastectomy

S6 – SURGERY AFTER NEOADJUVANT TREATMENT – WHEN IS THE RIGHT MOMENT

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Introduction: Neoadjuvant chemotherapy in breast cancer used to be reserved for patients with locally advanced breast cancer with the aim of shrinking the tumor to allow surgery. The first studies that began to investigate the impact of neoadjuvant treatment on overall survival rate and local recurrence-free survival rate have shown that they were associated with a complete pathological response to neoadjuvant chemotherapy.

Aim: To investigate whether the timing of surgery after the end of neoadjuvant chemotherapy affects overall survival rate and local recurrence-free survival rate.

Methods: By browsing the Pubmed literature, the most significant studies on the influence of time passed from the end of neoadjuvant chemotherapy to surgery on overall survival rate and recurrence-free survival rate were extracted.

Results: Previous studies have shown that a time interval of 4 to 8 weeks from the end of neoadjuvant chemotherapy was optimal for surgery. A time interval longer than 8 weeks increases the index of residual tumor and is therefore associated with worse overall survival rate and a higher risk of disease recurrence, and an interval shorter than 4 weeks is associated with a higher rate of surgical complications. The meta-

analysis showed statistically significantly better overall survival rate and recurrence-free survival rate when the interval to surgery was shorter than 8 weeks. At the same time, the studies showed no difference in the overall survival rate and the local recurrence rate, depending on whether a radical or sparing surgery was performed. The factor that most influences the postponement of surgery is an additional outpatient examination, and the size of the tumor on the post-therapy MRI was significantly correlated with the size of the tumor on the final pathohistological findings.

Conclusions: The optimal time for surgery after neoadjuvant chemotherapy is 4 to 8 weeks after completion. Waiting up to 8 weeks is unlikely to result in a clinically significant increase in residual tumor size. The type of surgery has to be planned as early as possible in the treatment phase in order to reduce the number of outpatient examinations.

Keywords: breast cancer; neoadjuvant therapy; surgery

S7 – TREATMENT OF T1AN0 AND T1BN0 BREAST TUMORS

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Introduction: Small breast tumors represent a diagnostic and therapeutic challenge, but also the best chances for long-term survival. The lecture will cover diagnostic and therapeutic difficulties in the framework of breast anatomy, lymphatic drainage and technical possibilities. Also, the results of the treatment of 76 patients with initial (T1a and T1b) breast cancer treated at the University Hospital for Tumors during 2022 will be presented. Potential new technologies in the treatment of small tumors will also be presented.

Aim: To present the results of the treatment of small breast tumors from the available literature and compare them with our own results (Department of Oncoplastic and Reconstructive Surgery, 2022).

Methods: Retrospective analysis of a group of patients with T1a and T1b breast tumors treated during 2022 at the Department of Oncoplastic and Reconstructive Surgery.

Results: Small breast tumors in this group of patients were most often of favorable biology (DCIS and luminal HER2 negative tumors). HER2 positive tumors had a share of 10.5%, and TNBC 2.6%. The axilla was affected in 8% of cases.

Conclusions: Small breast tumors have an excellent prognosis but represent a diagnostic and therapeutic challenge. Pathohistological staging of the axilla for small tumors of low and medium grade is not necessary, but for now there are no long-term results according to the biology of the tumor, considering that the biological classification was established in 2012 (St. Gallen). Alternative methods to surgical treatment, such as BLES and cryoablation, are currently not recommended, given the unsatisfactory results of complete tumor removal.

Keywords: breast cancer; stage T1a and T1b; staging of axilla

S8 – COLORECTAL CANCER-NEWS IN TREATMENT

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Treatment options in colorectal cancer, the most common GI malignancy have improved in the recent years, still the three main treatment options in locally advanced rectal cancer remain radiotheraphy, surgery and chemotheraphy. Recently results from the multicentre phase II/III noninferioty study PROSPECT suggest that in patient with cT2 node-positive, T3 node-negative or T3 node-positive neoadjuvant FOLFOX with selective use of chemoradiotheraphy was noninferior to chemoradiotheraphy with respect to disaese free survival over a median follow up of 58 months thus potencially deescalating treatment. In the very advanved (ugly) rectal cancer cT4, or cT3 with involement of the mesorectal fascia, cirfumerenctial resection margin, positive lateral nodes the prefered approcah remains total neoadjuvant theraphy. For a small subset of patients with mismatch repair deficient (dMMR) status or microsatellite instability-high(MSI-H) phenotype, a phase 2, single arm study showed that in 18 patients with locally advanced rectal cancer neoadjuvant treatment with the programmed death (PD)-1 inhibitor dostarlimb after 6 months of treatment achived clinical complete response (cCR) with organ-sparing non-operative management.

In the metastatic colorectal cancer it is crucial to determine the predicitive biomarkers mismatch repair (MMR) status, KRAS, NRAS and BRAF mutations for selecting first-line therapy.

On the basis of randomized phase 3 study Keynote 177 patients with MSI-H or dMMR shoud be offered monoimunotheraphy pembrolizumab, but results from the randomized phase 3 study CheckMate 8HW study with nivolumab and ipilimumab that showed 79% reductiom in the risk of disease progression or death compared with standard therapy support this combination as a new potential standard of care in this subset of patients.

For patients with microsatelite stable (MSS) or proficient mismatch repair (pMMR) left RAS wild type the standard remains doublet chemotheraphy with anti-epidermal growth factor (EGFR) antibody,while for RAS mutated and right RAS wt tumors the recommended treatment according to guidelines is doublet or triplet chemotherapy with anti-VEGF theraphy. In the second line treatment encorafenib plus cetuximab should be offered to patients with previously treated BRAF V 600E-mutant mCRC according to phase 3 BEACON trial that resulted in significantly longer overall survival and a higher response rate than standard therapy in patients with metastatic colorectal cancer with the BRAF V600 mutations, this combinatin is currently being investigated in BREAKWATER trial in the first line setting and we are waiting for the results. The greatest unmet need currently are the microsatelite stable,immune *cold tumor* in which imunotheraphy alone but also combinations of immunotheraphy with chemotheraphy has so far shown in multiple trials limited clinical efficacy.

The new standard of care in third line setting is the combination of trifluridine- tipiracil and bevacizumab that in the SUNLIGHT study resulted in longer overall survival than trifluridine-tipiracil alone. There is also, the evolving landscape of targeted therapeutic options and it is ever more important to identify patients with next generation sequencing (NGS) that could benefit from these targeted treatments.

In conclusion the treatment paradigm of colorectal cancer is changing and evolving and the centers of excellence and multidisciplinary teams should be mandatory in management of patients with this disease.

Keywords: colorectal cancer; treatment options; predictive biomarkers

S9 – PANCREATIC DUCTAL ADENOCARCINOMA – NEOADJUVANT AND ADJUVANT TREATMENT; ADVANCES IN TREATMENT

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Pancreatic ductal adenocarcinoma (PDAC) is 14th most common type of cancer in the world and 7th most common cause of cancer-related death according to latest Global Cancer Observatory data. The prediction is that it will be the 3rd most common cause of death by the year 2025. Most PDAC develop as a result of spontaneous mutations, although about 5% develop because of germline mutations in BRCA1, BRCA2 and PALB2 genes. There is no established screening method for earlier diagnosis od PDAC, even in patients with proven germline mutations in cancer susceptibility genes. Some diagnostic methods, such es endoscopic ultrasound (EUS) and magnetic resonance (MR), were investigated but their role in screening is yet to be established. At initial diagnosis only 10-20% of PDACs are suitable for upfront resection, while more then 50% are metastatic. High-quality imaging is very important when establishing a diagnosis, preferably done in high-volume centres with expertise in treatment of PDAC. PDAC can, based on imaging, be clasified regarding its resectability in resectable, borderline resectable, locally advanced and metastatic. In globally accepted guidelines (NCCN) resectability status is defined according to its arterial and venous infiltration. Resectability assessment influences therapeutic decisions and approach, which should be made in consensus at multidisciplinary meeting. Resectable PDAC should underwent upfront resection or neoadjuvant chemotherapy and then resection upon achieving tumor response. Borderline resectable and locally advanced unresectable PDAC should always go neoadjuvant treatment, neoadjuvant chemotherapy and, in some cases, radiotherapy. Then again the assessment of resectabilty should be done and rasponsive tumors be subjected to resection. Metastatic disease is treated with palliative intent, with systemic chemotherapy. In metastatic disease testing for germline BRCA1/2 mutations or next generation sequencing should be carried out in order to distinguish tumors that may have benefit from treatment with PARP inhibitors or other targeted therapies.

Resectable PDAC, which comprises for about 10-20% of all PDAC, is usually subjected to upfront surgery. Regardless od pathological findings all patients should undergo adjuvant chemotherapy because of tumor aggressiveness. An indicator of aggressive behaviour is the data that 25% of tumors recurr within 6 months and that median overall survival is 20 to 50 months. When resectable PDAC is accompanied with some other high-risk features, such as high Ca 19-9, large tumor burden, bulky regional lymph nodes, severe anorexia or pain, neoadjuvant treatment should be preffered. American Society of Clinical Oncology (ASCO) guidelines simplified and concisely select patients for whom neoadjuvant approach should be considered: they have no clear extrapancreatic disease, Ca 19-9 is not that high that indicates metastatic disease and there is no clear involvement of blood vessels according to resectability criteria. They also pont out patients who are not fit for upfront surgery but colud be resected upon recovery of nutritive status or frailty. There is not a lot of evidence for preferred neoadjuvant regimens and most recommendations are extrapolated from metastatic setting. Recommended protocols are FOLFIRINOX (fluorouracil + leucovorin + irinotecan + oxaliplatin) and gemcitabin + albumin-bound paclitaxel. For known BRCA1/2 or PALB2 mutations platinum derivates should be used.

Borderline resectable PDAC is an increasingly common term due tu advances in diagnostics and surgical techniques. All cases sholud be discussed in mutlidisciplinary boards and prefferably treated in high-

volume centres. Treatment options include upfront surgery followed by adjuvant chemotherapy, neoadjuvant chemotherapy +/- radiotherapy followed by resection or inclusion in clinical trials. The goal of neoadjuvant treatment is tumor shrinkage so the most effective regimens are used as mentioned above.

Patients with locally advanced PDAC have subclinical metastases in 50% of cases, often accompanied with high tumor burden and symptoms such as pain, gastric outlet obstruction and anorexia. In patients with good performans status (PS) intensive approach should be considered, e.g. neoadjuvant therapy then resection, and in those with poor PS, palliative approach.

Metastatic PDAC (more then 50%) has poor outcomes and prognosis. Medan overall survival is less then one year and 5-year survival around 11%. Standard of care are modified FOLFIRINOX and gemcitabin + albumin-bound paclitaxel regimens, postulated on the basis of PRODIGE 4 and MPACT clinical trials. For all metastatic patients next generation sequencing should be done and offered participation in clinical trials. Patients with germline mutations in BRCA1/2 genes have benefit of maintenance treatment with PARP inhibitors. POLO trial demonstrated improvement in PFS when olaparib was given after induction platinum-based chemotherapy.

Some emerging treatment options dominantly rely on targetable mutations such as RET gene fusions, NTRK gene fusions, NRG1 gene fusions, BRAF alterations and are under development. 90% of PDAC has oncogenic KRAS mutations which seem to be a promising therapeutic target. The most researched mutation so far is KRAS G12C, present in 1-2% of patients, showing promising results with KRAS inhibitors.

Immunotherapy has a minor role in treatment of PDAC because they are so-called *cold* tumors. Efforts are being made to discover how to make cold tumors warm in terms of vaccine and adoptive cell therapy research.

In conclusion, pancreatic ductal adenocarcinoma is formidable disease to diagnose and treat with abysmal prognosis. There have been some improvements in therapeutic approach and molecular diagnostics but new efforts are crucial to ensure better otucomes with an optimum quality of life.

Keywords: pancreatic ductal adenocarcinoma; therapeutic approach; mutation status

S10 – PATENT BLUE V DYE IN BREAST CANCER SURGERY - RISK OF ANAPHYLACTIC REACTION AND ROLE OF PREMEDICATION

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The Patent Blue V (PBV) dye can provoke allergic reaction of varying degrees of severity. Most often these are mild reactions in the form of urticaria or erythema, but sometimes can cause severe life-threating anaphylactic reaction. Most patients have no past medical history of allergy. In most reported cases there was a lack of previous exposure to PBV dye injection. PBV is widely used agent in textile, paper, agriculture industries, cosmetic and medical products, as a food additive (E131), and this can explain prior sensitisation caused by repeated exposure to some products. There is evidence that about 2,7% of the population would be allergic to blue dye. Probably, that number will increase in the future.

The incidence of anaphylactic reaction of any severity, associated with PBV dye is about 0.1%–2.8%. There is no relationship between PBV dose and severity of the allergic reaction. The median time to anaphylaxis was 20–30 min with a range of 0–90 min, up to 180 min. Immediate anaphylaxis is uncommon. Severe and potentially life-threating anaphylactic shock is rare, with an incidence of 0.06%. Cardiac arrest is infrequent and there are no cases of death described due to an allergic reaction to the PBV.

In the retrospective analysis from 2020 to 2023 at the University Hospital for Tumors, out of a total of 2,220 patients with breast cancer surgery with the use of PBV dye for the identification of sentinel lymph nodes, 11 patients had an anaphylactic reaction to PBV, with an incidence of 0.5%. An atypical anaphylactic reaction was described immediately after PBV injection in one patient, with cardiac arrest and prolonged refractory hypotension, without signs of skin rash, making the diagnosis and management of such cases challenging.

Although anaphylaxis usually presents as an acute episode, the mast cell can release mediators and support anaphylaxis for hours, causing a biphasic or late phase reaction in up to 10%, 6-8 h after the initial event. Patients should be monitored in the PACU or ICU during this period, even if hemodynamically stabile.

There is no unified consensus/guidelines for premedication plans to prevent perioperative anaphylaxis to PBV. It was found that pre-operative antiallergic medications do not significantly decrease the incidence of overall anaphylactic reactions, but markedly reduce the severity of adverse events. In high-risk patients (allergic diathesis) preventive anti-allergic medications should be applied before PBV injection. A preoperative regimen consisting of a glucocorticoid plus a histamine receptor blocker given intravenously, continues to be routinely recommended by many providers in all patients before PBV injection to prevent potentially life-threating anaphylactic reaction. Physicians must remain constantly vigilant with patients undergoing procedures using the PBV injection.

Keywords: patent blue V; anaphylactic reaction; breast cancer

S11 – COMPLICATIONS AFTER RADICAL VULVECTOMY AND INGUINAL LYMPHADENECTOMY

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Complications following radical vulvectomy, a surgical procedure primarily for treating advanced vulvar cancer, are multifaceted and can significantly impact patient recovery and quality of life. These complications can be categorized into early postoperative issues and long-term sequelae. Early postoperative complications include wound infections, hematomas, and seromas, which may necessitate further surgical intervention or prolonged hospital stay. Additionally, patients often experience significant pain and mobility challenges due to the extensive nature of the surgery. Long-term complications are substantial and include lymphedema, urinary and fecal incontinence, sexual dysfunction, and psychological distress. Lymphedema results from disruption of lymphatic drainage pathways, leading to chronic swelling

and discomfort. Incontinence issues arise from nerve damage and structural changes in the pelvic region. Sexual dysfunction, both physical and psychological, is prevalent due to anatomical changes and body image concerns. Effective management of these complications requires a multidisciplinary approach, including surgical expertise, nursing care, physical therapy, and psychological support, to improve overall outcomes and patient quality of life. Continued research into minimally invasive techniques and enhanced recovery protocols is essential to mitigate these adverse effects.

Keywords: radical vulvectomy; inguinal lyphadenectomy; complicarions

S12 – GASTRIC TUMORS – HAVE WE PROGRESSED?

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Introduction: Gastric cancer remains a significant global health challenge with high morbidity rates and mortality. It is the sixth most common cancer in the world and the third leading cause of cancer-related deaths. Despite the advances in last decades, the prognosis for patients with advanced disease remains poor. In recent years we are witnessing significant progress in understanding the biology of gastric cancer, which has led to the development of new treatment strategies aimed at improving patient outcomes.

Aim: To show progress in the treatment of gastric cancer over time, from ancient times to the present day.

Methods: Historically available data and large world databases were used.

Results: Early 20th century to mid-20th century: Initially, surgery was the only available treatment, and gastrectomy was the standard procedure. Outcomes were generally poor, with high rates of perioperative mortality and low survival rates, primarily due to late diagnosis and limited surgical techniques. The 5-year survival rate for stomach cancer was very low, often in the single-digit percentages for all phases together. Late 20th century: Advances in surgical techniques (more extensive lymph node dissection) and perioperative care significantly reduced mortality associated with surgery. Introduction of adjuvant chemotherapy and radiotherapy improved survival rates by reducing the risk of recurrence (clinical trial INT-0116 published in the late 1990s). Until the 1980s and 1990s, the 5-year survival rate for all stages combined was generally below 20% in many western countries (in countries with screening programs 50% and above). Global survival rates for gastric cancer have varied widely, reflecting differences in access to health care care, screening practices and availability of treatment. 21st century: The approval of trastuzumab in 2010 marked the introduction of targeted therapies in the treatment of gastric cancer. Better chemotherapy combinations and the use of neoadjuvant chemotherapy have improved response rates and survival for some patients. Minimally invasive surgery is used. Approval of immune checkpoint inhibitors, such as pembrolizumab and nivolumab, showed improved results for patients with PD-L1 positive tumors. We are in the era of precision medicine.

Conclusions: In conclusion, significant progress has been made in the treatment of gastric cancer, driven by advances in molecular biology, precision medicine, immunotherapy and targeted therapy.

Despite the progress achieved, several challenges remain in clinical practice, including those in treatment efficiency optimization, overcoming resistance mechanisms, reducing toxicity associated with treatment, differences in access to medical care, and limitations of health infrastructure.

Keywords: gastric cancer; treatment; molecular biology; precision medicine

S13 – IMAGING DIAGNOSIS OF PANCREATIC CANCER

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Diagnostic imaging plays a crucial role in early diagnosis and adequate staging of pancreatic tumors, before and after surgery or chemotherapy.

While dual-phase CT is a standard imaging modality, several other diagnostic imaging methods (MR, PET-CT, PET-MR and UZV) can be used to complement it. In some cases, complementary use of different imaging modalities can lead to a more accurate diagnosis.

Being aware of possibilities and limitations of different imaging modalities is essential for their proper indication.

Adequate indication and application of various imaging modalities according to existing guidelines as well as personalized approach to each individual patient may improve cure rates and reduce treatment-related morbidity.

The aim of this presentation is to provide a review of possibilities and limitations of standard and advanced diagnostic imaging modalities and compare measurement properties of different imaging modalities.

Keywords: pancreatic cancer; imaging; staging

S14 – NEUROENDOCRINE TUMORS – MULTIDISCIPLINARY TEAM

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Introduction: Neuroendocrine tumors (NET) are neoplasms that arise from neuroendocrine cells. These group of tumors are classified together because they share similar behavior and common microscopic features (secretory granules, production of biogenic amines and polypeptide hormones). Neuroendocrine cells are not present not only in the endocrine glands, but also in all other tissues of the body.

Aim: To show specificities of neuroendocrine tumors and the therapeutic options that are possible, as well as to clarify the role of the multidisciplinary team in the decision-making.

Methods: International guidelines for the treatment of neuroendocrine tumors are presented, as well as clinical practice in Croatia.

Results: In the treatment of NETs there are several possible options. The choice of therapy depends on the results of the initial diagnosis and disease stage. Analogues of somatostatin, chemotherapy (regimens CAPTEM, PE...), targeted therapy (everolimus, sunitinib...), and peptide receptor radionuclide therapy (PRRT) are possible therapeutic options.

Conclusions: Given the specificity of the disease and the large number of subtypes, it is necessary to treat NETs in a high-volume centers with the participation of a multidisciplinary team.

Keywords: neuroendocrine tumors; MDT; therapeutic options

S15 – NEW POSSIBILITIES IN HYBRID MOLECULAR IMAGING DIAGNOSTICS OF PRIMARY AND SECONDARY TUMORS IN THE ABDOMEN AND PELVIS

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Introduction: In the Special Hospital Radiochirurgia Zagreb, in addition to PET/CT diagnostics with low-dose CT and CT with the use of intravenous contrast, with our new Siemens Biograph Vision 600 device with ultra HD ("high definition") PET detectors – HDMSCT Definition Edge 128/384 layers ("high resolution, high count rate" PET/Edge CT), it is possible to perform exceptionally sophisticated PET/CT scans with extremely high spatial and temporal resolution which cannot currently be realized in other institutions in the Republic of Croatia that deal with PET /CT diagnostics.

Aim: The aim of the introduction of new PET/CT methods is to enable, primarily for oncologic patients, the best possible diagnosis of primary tumors, determination of the degree of extension and activity of malignant diseases, detection of local recurrence and distant metastases, determination of the type of treatment and monitoring of the effect of treatment, but now with additional possibilities of clear differentiation of inflammatory from malignant lesions, the best possible functional and morphological evaluation of tumor lesions with a minimal dose of radiation both for patients and staff, and adequate, ultra-precise planning of radiosurgery procedures, all with the help of five different types of radiopharmaceuticals.

Methods: In the period from October 2023 to March 2024, we performed UHD PET/DE (*dual energy*) CT in 65 patients with malignant tumors, fusion UHD PET/MR 3T in 60 patients with malignant tumors, and PET for biologically guided (eng. Bg SABR, *biology guided stereotactive ablative radiation therapy*) in 56 oncology patients, with the use of 18F FDG (radioactive fluorine-labeled fluorodeoxyglucose), 18F FET (fluoroethyltyrosine) and 18F FCH (fluorocholine).

Results: UHD PET/DECT is extremely effective in differentiating the character of the lesion in terms of malignant or inflammatory, necrotic and fibrotic, scarring changes, by simultaneously analyzing the metabolic characteristics of the lesions and assessing their angiogenesis by quantifying the concentration of iodine in the regions of interest as an indirect indicator of the degree of vascularization of the tumor.

Fusion UHD PET/MR 3T enabled the best possible functional and morphological assessment of tumor lesions, especially in anatomical regions where MR has an advantage over CT, while achieving high resolution and contrast between pathologic and healthy tissue, with significantly less exposure to ionizing radiation. Biologically guided radiosurgery is the latest painless, non-invasive method of surgery that is planned using PET/CT or fusion PET/MR, i.e. targeted accumulation of radiopharmaceuticals in tumor tissue during radiosurgery. The goal of the treatment is to increase precision and apply a higher dose of radiation to the tumor tissue while reducing side effects. Our Siemens Biograph Vision 600 UHD PET/CT device is also an intelligent molecular simulator/navigator, which with its exceptional precision and ability to visualize metabolically active lesions of only 2 mm in size, enables maximum successful treatment of primary tumors and extended oligometastatic and polymetastatic disease. The use of PET/CT or fusion PET/MR in the planning of a radiosurgery procedure clearly confirms or possibly changes the indication for a radiosurgery procedure, considering the very detailed determination of metabolic activity even in very small lesions, by simultaneous imaging of the whole body, which additionally confirms, evaluates and increases the justification of such therapy.

Conclusions: In contrast to the already existing PET/CT centers in the Republic of Croatia, the mentioned PET/CT device enables the performance of the completely new diagnostic procedures for the detailed analysis of tumors, in order to differentiate them more easily from inflammatory and fibrotic changes, at the same time with a detailed and ultra-precise metabolic and morphological assessment of tumors, faster imaging, reducing the dose of ionizing radiation, increasing comfort for patients and using an intelligent molecular simulator for planning and performing advanced radiosurgery and radiotherapy. The installation of this technology enables precise monitoring of all forms of treatment, surgical, radiotherapy and radiosurgery, as well as chemotherapy and immunotherapy. The mentioned diagnostic methods represent a new step forward in Croatian medicine, and the technology used to perform them is the latest step in the evolution of diagnostic oncology and is currently available only in the world's leading medical institutions and only in a few of the largest European hospitals, which is a guarantee that the mentioned procedures bring new quality and diagnostic and treatment options for Croatian patients in our common fight against cancer.

Keywords: tumors of abdomen and pelvis; imaging; PET/CT; UHD PET/DECT

S16 – SURGICAL APPROACH TO THE TREATMENT OF HILAR CHOLANGIOCARCINOMA

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Introduction: In this review paper on Klatskin's tumor, the mentioned pathology is presented, from nomenclature, etiology, pathology, classification, diagnostics to treatment modality. At the end of the paper, a personal series of six patients with Klatskin's tumor is described, along with a detailed presentation of the one patient's case, which is interesting because of the very thorough and comprehensive preoperative diagnostics.

Aim: To emphasize the complexity of the surgical problem of hilar cholangiocarcinoma, which is one of the biggest technical challenges for HPB surgery. Define treatment options with an emphasis on liver transplantation in eligible patients who have undergone neoadjuvant treatment according to the Mayo protocol.

Methods: Literature review and retrospective study of a personal series of patients with Klatskin's tumor operated on in the last four years at UHC Zagreb.

Results: In a series of six patients, the longest survival was observed in a patient with negative lymph nodes and R0 resection (44 months). The fatal outcome in the postoperative period (POD 16) occurred in a patient with right hepatectomy, after dysfunctional preoperative biliary drainage and preoperative cholangitis, and was a consequence of the patient's posthepatectomy liver insufficiency. There is a high proportion of R1 resection (5/6) despite declared R0 resection at intraoperative pathological findings in these same patients, and survival in this group is from 3 to 15 months. Concomitant venous (portal) resection was performed in 2 out of 6 patients as part of the left hepatectomy, while arterial resection was not necessary in this group of patients ("arterial disvestment" was performed in one patient). Two right, three left hepatectomies and one extended left hepatectomy were performed. Reoperations were necessary in four patients.

Conclusions: Radical R0 resection, with microscopically negative margins, is a prerequisite for longer survival in patients with Klatskin's tumor. Very detailed preoperative radiological and gastroenterological treatment and preoperative biliary drainage are necessary as a basis for reducing postoperative complications, reducing morbidity and mortality. It is necessary to start the Mayo protocol in UHC Zagreb and treat patients with hilar cholangiocarcinoma who meet the criteria with liver transplantation as a treatment modality with long postoperative survival and a reduction in the frequency of disease recurrence.

Keywords: Klatskin's tumor; surgical approach; R0 resection