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ABSTRACT BOOK

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Indhold

Clinical epidemiology and database research:

Poster #1-38

Clinical epidemiology and database research

#1: Reporting colon cancer staging using a template

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Abstract
Introduction
The purpose of this study was to evaluate the effect of completeness of the radiological reports in primary local staging colon cancer when using a template.

Materials and methods
The study used primary staging reports retrieved from the departments RIS/PACS. Five key tumour descriptors were evaluated within each report: tumour morphology (polypoid or annular), information on tumour breach of the colon wall (≥ T3), tumour out-growth in mm, nodal status and TNM in conclusion. The failure to provide a description of the presence or absence of a feature in a report counted as 'not reported'. To allow comparisons between reporting styles, the template or free-text style of reporting was also recorded.

Results
During a two year period, a total of 666 patients CT reports were evaluated at the colorectal center mul- tidisciplinary team (MDT) conference. In 200 of these reports a template was used. Information on tumour mor- phology (polypoid or annular) was present in 81% of the template reports vs 9% in free-text style. The figures in percentage for information on tumour breach of the colon wall (≥ T3) were 93% vs 48 %, tumour out-growth in mm: 51% vs 17%, nodal status: 99% vs 86% and TNM in conclusion: 98% vs 51%. $P < 0.0001$.

Conclusion
The present study provides additional support for the routine use of template reports to improve imaging reporting standards in colonic cancer.

Clinical epidemiology and database research

#2: Surgery of the primary tumour in 201 patients with high-grade gastroenteropancreatic neuroendocrine and mixed neuroendocrine-non neuroendocrine neoplasms

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Abstract
Introduction
The benefit of surgery in high-grade gastroenteropancreatic neuroendocrine neoplasms (GEP NEN) and mixed neuroendocrine-non neuroendocrine neoplasms (MiNEN) is uncertain. The aim was to investigate outcomes after tumour surgery in patients with high-grade (Ki-67>20%) GEP NEN or MiNEN stage I-III or stage IV.

Materials and methods
Analysis of data from patients treated in the period 2007-2015 at eight Nordic university hospitals. Overall survival (OS) and progression free survival (PFS)/disease free survival (DFS) were analysed by Kaplan- Meier estimates. Prognostic factors were evaluated using Cox regression.

Results
We included 201 surgically resected patients, 143 stage I-III and 58 stage IV with 68% having neuroendocrine carcinoma (NEC), 23% MiNEN, 5% NET G3 and 4% uncertain NEN G3. Primary tumours were located in colon/rectum (52%), esophagus/cardia (19%), pancreas (10%), stomach (7%), jejunum/ileum (5%), duodenum (4%), gallbladder (2%) and anal canal (1%). For patients with stage I-III, median DFS was 12 months (95% CI 5.5-18.5) and median OS was 32 months (95% CI 24.0-40.0). For patients with stage I-III and an R0 resection, median DFS was 21 months (95% CI 4.9-

37.1) and median OS was 39 months (95% CI 25.0-53.0). For patients with stage IV, median PFS/DFS was 4 months (95% CI 1.9-6.1) and median OS was 11 months (95% CI 4.8-17.2). For patients with stage IV and an R0 resection, median DFS was 6 months (95% CI 0-16.4) and median OS was 32 months (95% CI 25.5-38.5). Performance status >1 and colorectal primary were associated with poor prognosis. There was no difference in survival between patients with high-grade GEP NEN and MiNEN.

Conclusion
Surgery of the primary tumour in patients with loco-regional high-grade GEP NEN or MiNEN led to good long-term results and should be considered if an R0 resection is deemed achievable. Highly selected patients with stage IV disease may also benefit from surgery.

Clinical epidemiology and database research

#3: Distant metastases in squamous cell carcinoma of the pharynx and larynx: A population-based DAHANCA study

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Abstract
Introduction
In head and neck cancer, distant metastases may be present at diagnosis (M1) or occur after treatment (DM). It is unknown whether M1 and DM follow the same clinical development and share prognosis, as population-based studies regarding outcome are scarce. Therefore, we investigated the incidence, location of metastases and overall survival of patients with M1 and DM.

Materials and Methods
Patients diagnosed with squamous cell carcinoma of the pharynx and larynx in Denmark 2008-2017 were identified in the Danish Head and Neck Cancer Group (DAHANCA) database. We identified 7300 patients, of whom 197 (3%) had M1 and 498 (8%) developed DM during follow-up.

Results
The 5-year cumulative incidence of DM was 8%. One- and two-year overall survival for DM (27% and 13%) vs. M1 (28% and 9%) were equally poor. There was no significant difference in location of metastases for M1 and DM and the most frequently involved organs were lungs, bone, lymph nodes and liver, in descending order. In oropharyngeal squamous cell carcinomas, the location of metastases did not differ by HPV-status. For HPV-positive patients, 21% of DM occurred later than three years of follow-up compared to 7% of HPV-negative patients.

Conclusion
Incidence, location of metastases and prognosis of primary metastatic (M1) or post-treatment metastatic (DM) disease in head and neck squamous cell carcinoma are similar.

Clinical epidemiology and database research

#4: Differences in work participation between incident colon and rectal cancer patients – a ten-year follow-up study with matched controls

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Abstract
Introduction
Work-related issues have become increasingly relevant for colorectal cancer (CRC) patients, since the cancer is detected at an earlier age due to screening. The aim was to evaluate work participation up to ten years after colon or rectal cancer diagnosis compared between diagnosis and to a matched cancer-free population. Materials and methods
In this national register-based cohort study all first-time CRC patients in the period 2000-2015 with no previous cancer, between 20 and 60 years, were identified in the Danish Cancer Registry. A control group with no previous cancer was matched on gender, age, education, and income. For each year a mean Work Participation Score (WPS) was calculated (a percentage of weeks working) for individuals part of the labour market.

Results
A total of 5,625 colon cancer patients and 3,856 rectal cancer patients and 25,341 and 17,256 matched controls were included in the study, respectively.
The WPS increased for colon cancer patients from 45.69% after one year to 83.94% after four years, while rectal cancer patients had a score of 38.07% after one year and 80.07% after four years. The WPS was lower for cancer patients compared to controls, but the difference decreased after four years.

Conclusions
CRC patients had a lower work participation up to ten years after diagnosis compared to controls, while rectal cancer patients had a lower participation the first seven years after diagnosis compared to colon cancer patients. Work-related issues should be considered in the early stage of rehabilitation to increase work participation and thereby improve quality of life.

Clinical epidemiology and database research

#5: Parenthood among men diagnosed with cancer in childhood and early adulthood – trends over time in a Danish national cohort

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Abstract
Introduction
The number of children and young adolescents who survive cancer has steadily increased over the past decades, with a current 5-year survival rate of approximately 80%. Consequently, life circumstances after cancer have gained increasing importance, including the desire to have children. This study wants to explore the rate of fatherhood among men diagnosed with cancer in childhood and early adulthood compared to men without cancer and to show the trends over time.

Materials and methods
This study is a national, register-based cohort study. Men diagnosed with cancer in childhood and early adulthood (<30 years of age) were registered in the Danish Cancer Register in 1978-2016. At time of diagnosis, each cancer-diagnosed man was randomly matched with 150 undiagnosed men from the background population within the same birth year. The men were followed in national registers until death, migration or end of study. Cancer diagnosis were categorized as central nervous system (CNS), haematological cancers or solid cancers. Death was incorporated as a competing risk in all analyses.

Results
Men surviving CNS cancer had the lowest hazard ratio of fatherhood compared with the age-matched comparison group (HR= 0.67, 95% CI 0.57-0.79), followed by survivors of haematological cancers (HR= 0.90, 95%CI 0.81-1.01) while the highest chance of fatherhood was slightly increased among survivors of solid cancers (HR= 1.16, 95%CI 1.12-1.20). The hazard ratio of becoming a father increased over time. From the first decade to the last decade 30 years later, the hazard ratio of becoming a father increased for all three cancer groups. Also, men diagnosed with cancer when aged 20-29 years more likely became fathers over time compared to the age-matched comparison group.

Conclusion
Men diagnosed with cancer had significantly reduced rates of fatherhood compared with undiagnosed men, and rates of fatherhood among the cancer survivors increased markedly over time.

Clinical epidemiology and database research

#6: Hyponatremia is a prognostic marker in lung cancer. A Danish population-based cohort study of 8,166 lung cancer patients.

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Abstract
Introductions
Hyponatremia is a common electrolyte disorder in lung cancer patients, especially in patients with small- cell lung cancer (SCLC). It has been proposed as a prognostic indicator of higher mortality; however, data have been conflicting. Here, we determine the incidence and prognostic impact of pretreatment hyponatremia in a large Danish registry-based cohort of lung cancer patients.

Material and methods
Data on lung cancer patients diagnosed from January 2009 to June 2018 in The Central Denmark Region were extracted from the Danish Lung Cancer Registry and combined with data on the pretreatment sodium level extracted from the clinical laboratory information system. Hyponatremia was defined as a sodium level <135 mmol/l. Cox proportional hazard models assessed the prognostic value of hyponatremia on overall survival (OS) in patients with non-small cell lung cancer (NSCLC) and patients with SCLC.

Results
A total of 6,995 patients with NSCLC and 1,171 with SCLC were included. The hyponatremia incidence was 16 % among patients with NSCLC and 26 % among patients with SCLC. Hyponatremia was associated with an inferior OS in patients with NSCLC (<135 mmol/l: median 0.46 years (95 % CI: 0.41- 0.51) vs. ≥ 135 mmol/ l: median 1.05 years (95 % CI: 1.00–1.11)), p < 0.001; adjusted hazard ratio (HR) = 1.45 (95 % CI: 1.34-1.56)) as well as in patients with SCLC in (<135 mmol/l: median 0.67 year (95 % CI: 0.58- 0.73) vs. ≥ 135 mmol/l: median 0.73 years (95 % CI: 0.67-0.78); p = 0.0035; adjusted HR = 1.21 (95 % CI: 1.04- 1.41)).

Conclusion
The incidence of pretreatment hyponatremia is high in patients with SCLC as well as with NSCLC. Hyponatremia seems to be an independent predictor of inferior survival in lung cancer patients, especially in patients with NSCLC.

Clinical epidemiology and database research

#7: First worldwide database on Pressurized Intra-Peritoneal Aerosol Chemotherapy (PIPAC) directed treatment of peritoneal metastasis (PM)

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Abstract
Introduction
Phase-II trials have documented the favorable safety profile and promising clinical results of Pressurized Intra-Peritoneal Aerosol Chemotherapy (PIPAC) directed treatment in peritoneal metastasis (PM). Until results of randomized trials are available, the quality of documentation, benchmarking and acceptance by the users may be improved through a worldwide registry.

Materials and Methods
In 2019 the International Society for the Study of Pleura and Peritoneum (www.ISSPP.org) decided to create a worldwide PIPAC database, and Odense PIPAC Center was designated to this task. Selected data covering the first 6 months since launching of the ISSPP PIPAC Database are presented.

Results
The ISSPP PIPAC online database has six key elements (Patient, Consent, Treatment, Complications, Response evaluation and Follow-up). Ten international high-volume PIPAC centers included 459 PIPAC procedures in 181 patients during the first six months. The majority had gastric, colonic, pancreatic or ovarian cancer and approximately half of the patients had synchronous PM. Seventy percent had oncological treatment prior to the first PIPAC procedure and 24% had systemic therapy between PIPAC procedures (bidirectional treatment). The median number of PIPAC procedures per patient was 2 (1-8) with a non-access rate of 13% at first PIPAC. Median PCI score at first PIPAC was 17 (0-39). Only one grade 3 surgical complication was registered (0.2%) and adverse events according to CTCAE were all ≤ 2.
The preliminary analysis illustrates that the patients recorded in the ISSPP PIPAC Database mirror the general experience with PIPAC as presented in the literature.

Conclusions
The first worldwide PIPAC database has been implemented at Odense PIPAC Center (www.PIPAC.dk) under the auspices of ISSPP. Future steps include merging data on rare peritoneal diseases treated by PIPAC. The database holds great potential for international benchmarking and future collaborative scientific studies.

Clinical epidemiology and database research

#8: Direct costs of antineoplastic and supportive treatment for progressive multiple myeloma in a tax-based health system

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Abstract
Introduction
The prognosis for patients with multiple myeloma (MM) has significantly improved over the past decade, but new expensive drugs and multiple lines of treatment has dramatically increased the costs of care. Treatment plans are adjusted for individual patients depending on response and side effects, making it complex to estimate costs and provide evidence-based policy and clinical decision-making. Thus, our objective was to generate an up-to-date estimate of drug cost variation for progressing MM patients in a public health care system.

Materials and Methods
We included 41 MM patients from a personalized medicine study (2016-2019) at the department of Hematology, Aalborg University Hospital. Detailed information on antineoplastic and antibiotic treatment, in- and out-hospital visits, blood transfusions, and autologous stem cell transplantation were collected from individual patient journals and the hospital pharmacy registry. Costs associated to radiation and surgery were not included. Drugs were priced using billing data from the hospital pharmacy, while costs related to procedures and treatments other than antineoplastic and antibiotic drugs were estimated according to the Danish diagnosis-related group (DRG) system, which gives the average costs for various hospital procedures in Denmark. Mean costs from right-censored data were estimated using inverse probability weighting.

Results
The total observed (censored) costs for the 41 patients was €8.84million during 125 treatment years, with antineoplastic drugs as the main cost driver (€5.6million). Individual costs showed large variation between patients. The mean three-year cost per patient from first progression was €182,103 (€131,800 - €232,405)

Conclusion
The direct cost of treating MM patients reaches a sizeable sum. The large between-patient variation complicates prediction of real-world costs. Micro-costing analyses are needed for budgeting and real-world evaluation of cost-effectiveness.

Clinical epidemiology and database research

#9: Efficacy of PD-1 inhibition in recurrent Head and Neck cancer. A national DAHANCA cohort study.

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Abstract
Introduction
PD-1 inhibitors are well established in the treatment of recurrent or metastatic head and neck squamous cell carcinoma (rmHNSCC). These data come from randomized trials in selected patient populations. The aim was to investigate real- life efficacy of PD-1 inhibitors among an unselected and unbiased national cohort of rmHNSCC to determine its actual benefit.

Materials & Methods
Patients (pts) were eligible if they had received PD-1 inhibition in treatment of rmHNSCC. Patient and treatment- related data were collected prospectively from patient files at the five head and neck cancer centers and from the DAHANCA-database.
Endpoints were median overall survival (OS) and median progression-free survival (PFS), calculated from start of treatment to date of event or censoring. Survival was estimated by the KM-method. All analyses were two-sided and p-values <0.05 were considered significant.

Results
In total 201 pts were identified 2017-2020. Of these 144 (72%) were male, median age of 63 years [range 34-88] and 141 (70%) had metastatic disease while 60 (30%) had locally advanced disease. Median number of treatment cycles was 4 [range 1-54]. RR was 15.4%, OS 10.5 months [range 8.7-12.2] and PFS 5.1 months [range 3.8-7.1].
OS was significantly correlated to WHO PS ($p<0.0001$, HR=2.9 [95% CI: 2.0-4.0]). Both OS and PFS was 37.1 within PS=0. With PS=1, OS and PFS were 9.4 and 4.2 months respectively and 4.8 and 2.3 months for pts with PS≥2.
Concomitant treatment using steroids proved to be significantly correlated to a lower OS by comparing pts who had received steroids for ≥50% of the duration of their PD-1 treatment time to pts who had received it for <50% ($p<0.0001$ HR=3.7 [95%CI: 1.9-7.2]). The same pattern was seen for PFS.

Conclusion
This study showed acceptable efficacy with one fourth of pts surviving more than one year. Although a non-toxic treatment, response seems to be affected by poor performance and the need for steroid treatment during PD-1 therapy.

Clinical epidemiology and database research

#10: Prediagnosis epilepsy and survival in patients with glioma: a nationwide population-based cohort study from 2009-2018

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Abstract
Introduction
Considering that epilepsy is common, and knowledge is lacking on its role especially for the prognosis of high-grade gliomas, the purpose of this study was to investigate the association between epilepsy prior to glioma diagnosis and survival among glioma patients.

Materials and Methods
In a nationwide population-based cohort study, we included 3,763 adult glioma patients diagnosed between 2009-2018 according to the Danish Neuro-Oncology Registry. Information on epilepsy was redeemed through Danish Neuro-Oncology Registry, National Patient Registry, and National Prescription Registry. Cox proportional hazards models with 95% confidence intervals (CIs) were applied to examine hazard ratios (HRs) for the association between epilepsy (< 1 year prior to glioma including epilepsy at onset; 1-10 years prior to glioma; no prior epilepsy) and risk of death, and whether it differed according to tumor grade and size, performance status, and treatment modalities.

Results
A 32% decreased risk of death in patients with epilepsy within 1 year prior to glioma compared to no prior epilepsy was found (HR=0.68; CI 0.63-0.75). A favorable prognosis was seen for epilepsy in all glioma grades: II (HR=0.55; CI 0.39-0.77), III (HR=0.59; CI 0.48-0.73), and IV (HR=0.85; CI 0.77-0.94).

Conclusions
Patients with epilepsy within 1 year prior to glioma diagnosis had significant survival benefits compared to patients with no prior epilepsy. This association was significant for both low-grade gliomas (grade II) and high-grade gliomas (grade III and IV). Survival benefits in glioma patients with epilepsy at onset are possibly primarily attributable to tumor-specific histopathology, molecular biomarkers, and early diagnosis.

Clinical epidemiology and database research

#11: Influence of Hormone Treatment on Bladder Cancer Incidence and Prognosis

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Abstract
Introduction
Bladder cancer (BC) is one of the most commonly diagnosed cancers in the world. However, there are significant gender differences regarding incidence and prognosis. Males have a 4:1 higher risk of BC, whereas females often experience more advanced and progressive disease. Many explanations have been suggested, one involves the role of steroid hormones and their receptors. Androgen receptor and estrogen receptor-beta expression are shown to promote urothelial oncogenesis, whereas estrogen receptor-alpha seems protective against the disease. Currently, there are drugs available which can suppress these receptors and decrease their expression, however the application of these drugs in BC is only vaguely investigated.

Materials and Methods
A prospective cohort study with data collected from The Danish Cancer Registry, The Danish National Patient Registry, Cause of Death Registry, Danish Prescription Registry, Pathology Registry and Central Person Registry is conducted. The case-population includes all males and females with a diagnosis of prostate cancer, endometrial cancer or breast cancer in the period of 2002-2018, with no previous history of other cancers. The control population is a 1:10 group of individuals, matched on age, gender and residence. The study cohort is stratified according to gender and hormonal treatment. The primary outcome of investigation is incident urinary bladder cancer (BC) and secondary outcomes are stages of BC and prognosis.

Results
The project is still collecting data and results are currently pending. The hypothesis to be tested is a protective effect of hormonal therapy against incident bladder cancer.

Conclusions
To our knowledge, this will be the largest cohort study on the influence of hormones in Bladder Cancer today. Positive results may lead to a potential new target approach in BC. Furthermore, this study might reveal new answers to the gender difference that exist in urothelial BC.

Clinical epidemiology and database research

#12: The role of overweight and obesity in premenopausal ovarian and breast cancers

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Abstract
Introduction
Female obesity is associated with increased risk for some cancers, though the risk may vary according to menopausal status. We estimated the association between higher than normal BMI and incidence of premenopausal ovarian cancer and breast cancer according to receptor status.

Materials & Methods
Using Danish nationwide registries, we conducted a prospective cohort study with 464 971 women registered in the Danish Medical Birth Registry with BMI ≥18.5 kg/m2, and without a history of cancer. We used Cox proportional hazards regression models to estimate the hazard ratios (HRs) with 95% confidence intervals (95% CIs) of premenopausal invasive ovarian cancer, breast cancer, estrogen receptor positive and negative, HER2 positive and negative breast cancers according to BMI with age as the underlying time scale. We followed women until outcome, death, emigration, 50 years of age or end of follow-up (01-01-2020).

Results
Compared with normal weight, obesity was associated with higher rates of premenopausal ovarian cancer (HR=1.79, 95% CI 1.14-2.81) when adjusted for parity, use of hormonal contraception, family history of ovarian and/or breast cancer, and calendar year.
Obesity was associated with lower rates of premenopausal breast cancer (HR=0.75, 95% CI 0.66-0.85) when adjusted for parity, use of hormonal contraception, family history of ovarian and/or breast cancer, calendar year, smoking, and highest achieved education. The associations were strongest with estrogen receptor positive premenopausal breast cancers. Results according to HER2 status were similar to overall results for premenopausal breast cancer.

Conclusions
Obesity increased the incidence of premenopausal ovarian cancer and decreased the incidence of premenopausal breast cancer, especially estrogen receptor positive.

Clinical epidemiology and database research

#13: Intensified induction chemotherapy for locally advanced and synchronous metastatic squamous cell carcinoma of the anus – nationwide retrospective data and a prospective study (DACG-III) from the Danish Anal Cancer Group

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Abstract
Introduction
Locally advanced squamous cell carcinoma of the anus (LASCCA) have high risk of treatment failure calling for intensified treatment. Standard of care in the metastatic setting is palliative chemotherapy, however, selected patients with synchronous metastatic squamous cell carcinoma of the anus (mSCCA) could potentially be treated with induction chemotherapy (ICT) as part of a curative treatment strategy. We present a nationwide cohort of LASCCA and selected synchronous mSCCA treated with intensified ICT prior to definitive treatment (the DACG-B study).

Materials and Methods
The DACG-B study included all patients with LASCCA (T3-T4N0 or T1-T4N+) or synchronous mSCCA treated with intensified ICT consisting of cisplatin, ifosfamide, leucoverin and 5-flourouracil. Data were collected from medical records.

Results
A total of 184 patients with LASCCA, including 18 patients with synchronous mSCCA, treated with at least one cycle of intensified ICT were identified. Complete response of primary tumour after ICT was observed in 15%, with an overall response rate of 77%. In the LASCCA group the 3- and 5-year overall survival (OS) and disease-free survival (DFS) were 76% and 67%, respectively and 70% and 67%, respectively. In the mSCCA group 3- and 5-year OS and DFS were 71% and 52%, respectively and 50% and 44%, respectively. Of the 18 patients with mSCCA 15 completed a curative treatment strategy.

Conclusions
We present the largest cohort worldwide of LASCCA treated with intensified ICT and observed favourable outcome for these high-risk patients (manuscript ready for submission). We present proof of principle for a curative treatment strategy in the subgroup of patients with synchronous mSCCA (manuscript in preparation). Consequently, we have designed a national prospective phase II and biomarker study (DACG-III) ready to include. The aim is to validate ICT and biomarkers for patient selection.

Clinical epidemiology and database research

#14: Who are the vulnerable lung cancer patients at risk for not receiving first-line curative or palliative treatment?

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Abstract
Introduction
To identify vulnerable lung cancer patients in need for more comprehensive support we examined the association between factors related to not receiving first-line curative or palliative treatment.

Materials and methods
In a nationwide population-based study, we identified 14,996 patients diagnosed with non-small-cell lung cancer with performance status <3 during 2013-2018 in the Danish Lung Cancer Registry. Multivariate logistic regression models were used to estimate Odds Ratios (ORs) and 95% confidence intervals (CIs) for receipt of first-line treatment or palliative treatment, respectively according to vulnerability factors including stage, comorbidities, age, performance status, long distance to hospital, cohabitation status, education and alcohol abuse.

Results
During the study period, 21% lung cancer patients eligible for curative treatment did not receive the intended treatment while 10% did not receive treatment at all. At least three vulnerability factors were present among 17% of patients diagnosed with stage I-IIIA and 51% of patients diagnosed with stage IIIB-IV. Vulnerability factors associated with reduced likelihood of receiving first-line curative treatment included: advanced stage (OR=0.47; 95% CI=0.44-0.51), age > 80 years (OR=0.36; 95% CI=0.30-0.42), performance status=2 (OR=0.29; 95% CI=0.25-0.35), living alone (OR=0.81; 95% CI=0.70-0.92) and long distance to hospital (OR=0.89; 95% CI=0.75-1.06). Results were similar for palliative treatment.

Conclusions
Vulnerable lung cancer patients at risk for not receiving first-line curative or palliative treatment are characterized by being diagnosed with a high disease stage and performance status, above the age of 80 years, living alone and far from the hospital. Efforts should be made to develop support for vulnerable lung cancer patients to improve adherence to first-line treatment recommendations.

Clinical epidemiology and database research

#15: Socioeconomic status and prognosis in premenopausal breast cancer: A population-based cohort study in Denmark

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Abstract
Introduction
To investigate how socioeconomic status (SES) influences the effectiveness of cancer-directed treatment in premenopausal breast cancer patients in terms of breast cancer recurrence and mortality.

Materials and Methods
We assembled a cohort of all premenopausal women aged 18–55 years diagnosed with non-metastatic breast cancer and prescribed docetaxel-based chemotherapy in Denmark during 2007–2011. Population-based administrative and medical registries provided data on SES: marital status (married/registered partnership or single/divorced/widowed), cohabitation (cohabiting or living alone), education level (low, intermediate or high), income (low, medium or high), and employment status (employed, unemployed or health-related work absenteeism). Follow-up started six month after sugery, and continued until recurrence, death, emigration, 10 years, or 31st December 2016. For each SES measure, we computed incidence rates, cumulative incidence proportions and used Poisson regression to compute incidence rate ratios and associated 95% confidence intervals of recurrence and death. We stratified on ER status/ tamoxifen to evaluate interaction.

Results
Our cohort included 2,616 women; 286 (13%) women experienced recurrence and 223 (11%) died during follow-up (median 6.6 and 7.2 years, respectively). Women with low education, low income, unemployment or health-related work absenteeism had increased risk of mortality, but notably no increased risk of recurrence. Single women had both increased risks of recurrence and mortality. These findings were especially evident among women with ER+ tumors prescribed tamoxifen.

Conclusions
Low SES in premenopausal women with non-metastatic breast cancer was associated with increased mortality, but not always recurrence. This suggests underdetection of recurrences in deprived groups. Poor prognosis in women with low SES, especially single women, may partly be explained by tamoxifen adherence.

Clinical epidemiology and database research

#16: The Danish Myelodysplastic Syndromes Database: Patient characteristics and validity of data records

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Abstract
Introduction
The Danish Myelodysplastic Syndromes Database (DMDSD) comprises nearly all patients diagnosed with myelodysplastic syndromes (MDS) in Denmark since 2010. The DMDSD has, however, never been used for epidemiological research and the quality of registered variables remains to be investigated.
Objectives: To describe characteristics of the patients registered in the DMDSD, and to calculate predictive values and the proportion of missing values of registered data records.

Materials and methods
We performed a nationwide cross-sectional validation study of recorded disease- and treatment data on MDS-patients during 2010-2019. Patient characteristics and the proportion of missing values were tabulated. A random sample of 12% was drawn to calculate predictive values with 95% CIs of 48 variables using information from medical records as a reference standard.

Results
Overall 2284 patients were identified (median age:76 years, men 62%). Of these, 10% had therapy-related MDS, and 6% had an antecedent hematological disease. Hemoglobin level was less than 6.2 mmol/L for 59% of patients. Within the first two years of treatment, 59% received transfusions, 35% received erythropoiesis-stimulating agents, and 15% were treated with a hypomethylating agent. For the majority of variables there were no missing data. A total of 260 medical records were available for validation. The positive predictive value of the MDS diagnosis was 92% (95% CI: 88-95). Predictive values ranged from 64% to 100% and exceeded 90% for 36 out of 48 variables. Stratification by year of diagnosis suggested that the positive predictive value of the MDS diagnosis improved from 88% before 2015 to 95% after.

Conclusion
In this study, there was a high accuracy of recorded data and a low proportion of missing data. Thus, the DMDSD serves as a valuable data source for future epidemiological studies on MDS. Funding: This study was funded by the Danish Acute Leukemia Group and COMPAS.

Clinical epidemiology and database research

#17: Mortality after late breast cancer recurrence in Denmark

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Abstract
Introduction
Breast cancer (BC) recurrences continue to occur long after primary diagnosis. Late recurrence (i.e., 10 years or more after primary diagnosis) may have a more favorable prognosis than earlier recurrence. We, therefore, investigated the risk of BC-specific death and all-cause mortality after late recurrence and identified prognostic factors. Furthermore, we compared survival between late and early recurrence .

Materials and methods
Using the Danish Breast Cancer Group database and a previously validated algorithm, we identified all women with early or late BC recurrence during 2004-2018, who were alive and available for follow-up 6 months after recurrence. We followed them until BC death, death from other causes, emigration, ten years after recurrence or 31/12/2018. We calculated mortality rates (MRs) per 1000 person-years (PY) and cumulative BC mortality stratified by time of recurrence and by patient- and tumor characteristics of the primary tumor and of the late recurrence. Using Cox regression, we calculated adjusted hazard ratios (HRs) for BC death accounting for competing risks.

Results
Among 2,004 patients with late recurrence, 721 died of BC (MR= 84.8 per 1000 PY, 95%CI= 78.8-91.2; 10-year cumulative mortality=50%). Among 1,573 patients with early recurrence, 1,092 BC deaths occurred (MR= 173.9 per 1000 PY, 95%CI= 163.9-184.5; 10-year cumulative mortality=72%). Patients with a late recurrence had a lower 10-year risk of BC death compared with those with early recurrence (HR=0.73; 95%CI=0.61-0.87). Advanced stage at primary diagnosis and distant metastases were associated with increased mortality, while breast-conserving surgery at primary diagnosis, loco-regional recurrence and recurrence surgery were associated with lower mortality.

Conclusions
Patients with a late BC recurrence had a more favorable prognosis than patients with an early recurrence. The localization of recurrent disease was the main prognostic factor for BC death.

Clinical epidemiology and database research

#18: Nonplatinum-based therapy with Paclitaxel and Capecitabine for advanced squamous cell carcinomas of the anal canal: A population-based Danish Anal Cancer Group study (DACG)

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Abstract
Introduction
Squamous cell carcinomas of the anus (SCCA) is considered a rare malignancy. Chemoradiotherapy is a well-established curative treatment for locoregional disease which provides good local control and survival rates. However, some will experience locoregional failure or distant metastasis with an overall poor prognosis.
First-line platinum-based therapy for advanced SCCA implies a risk of substantial side effects and data on second-line treatment options are limited.
Paclitaxel and Capecitabine is a well-known regimen with a moderate toxicity profile. In Denmark, the combination has been administered for patients with advanced SCCA either as first-line therapy for the elderly and/or fragile patients or as second-line treatment after failure to endure or after progression on a platinum-based agent. However, its efficacy in SCCA has not been evaluated.

Materials and Methods
We conducted a retrospective study using Danish Hospital Registers of patients treated with
Paclitaxel and Capecitabine for inoperable, recurrent, or advanced metastatic SCCA in Denmark, between January 2000 - July 2018.

Results
A total of 52 patients met the eligibility criteria. Median age was 60.7 years (range 42–83). An overall response rate in patients receiving first-line (n = 28) and second-line (n = 23) Paclitaxel and Capecitabine of 39.3% (2 with complete responses) and 17.4% was observed, respectively. Median progression-free survival (PFS) was 4.5 months (95% CI 3.3–5.9) and 3.8 months (95% CI 2.4–5.5) with OS of 6.7 months (95% CI 5.9–8.5) and 5.9 months (95% CI 3.9–14), respectively. Performance status ≥2 and neutrophil to lymphocyte ratio ≥4 were significantly associated with a poorer PFS.

Conclusion
This study recognizes Paclitaxel and Capecitabine as a potential regimen for advanced SCCA, when recommended first-line therapy is not feasible or as a potential second-line treatment after failure of platinum-based chemotherapy. (Article currently in press: CancerMedicine)

Clinical epidemiology and database research

#19: Labor market attachment is associated with clinical- and sociodemographic factors two years after colorectal cancer surgery

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Abstract
Introduction
The rising prevalence of colorectal cancer (CRC) survivors diagnosed in the working age calls for an increased focus on labor market attachment. Previous studies have identified factors associated with labor market attachment among CRC survivors, but few have investigated the association with clinical factors such as type of surgery.
The aim of this study was to investigate the association between clinical/sociodemographic factors and the probability of being attached to the labor market 2 years after surgery (2YAS).

Materials and methods
National registries were used to form a dataset consisting of clinical-, sociodemographic- and work-related data from all 20-60 years old CRC patients diagnosed in 2001-2014, undergoing surgery, and attached to the labor market at time of surgery. Multiple logistic regression analysis was used to investigate associations between demographic/clinical variables and labor market attachment 2YAS.

Results
Data from 5,755 CRC patients were included. Overall, 59.9 % were working 2YAS. Among patients not working 2YAS, 49.0% had died or retired, while 51.0% were on temporary benefits, sick leave or disability pension. Factors significantly associated with higher probability of working 2YAS were younger age, male gender, higher educational level, no comorbidity, working at time of surgery, lower UICC stadium, and undergoing surgery in the most recent of four time periods. The probability of working 2YAS was significantly higher for left- vs. right-sided hemicolectomies, higher for LAR/high tumor vs. LAR/low tumor, and higher for LAR/low tumor vs. permanent colostomy.

Conclusions
Sixty percent of the included patients were working 2YAS. Sociodemographic- and clinical factors were associated with the probability of being attached to the work market. This knowledge can be used to inform patients and target interventions at patients with low probability of working after CRC.

Clinical epidemiology and database research

#20: Use and diagnostic outcomes of cancer patient pathways in Denmark – is the place of initial diagnostic work-up an important factor?

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Abstract
Introduction
The cancer patient pathway (CPP) for non-specific symptoms that can be cancer (NSSC-CPP) has been implemented in Denmark with great differences between and within the Regions. The diagnostic work up (often including a blood test and a CT scan) is in some places initiated by general practitioners (GPs) and in others by diagnostic units at hospital level. These variations may imply differences in the use of CPPs and NSSC-CPPs, and ultimately an overuse of health care resources or a delay in cancer diagnosis. Therefore, the aims of this study were 1) To describe the use of CPPs and NSSC-CPPs in people receiving an initial CT scan and 2) To describe the diagnostic outcomes of these two CT scanned groups six months and mortality one year after CT scan.

Material & Methods
A nationwide population-based study including citizens with a first CT scan between 2013-2016, either referred from GPs or hospitals. The outcome measures were: use and order of CPPs and NSSC-CPPs, cancer- diagnoses, selected non-cancer diagnoses and total- and cancer specific mortality. We calculated odds ratios (OR) from a multivariable logistic regression model.

Results
Individuals with a GP issued CT were more likely to start a NSSC-CPP (4.1 [3.9-4.2]) or a CPP (OR 2.3[2.2-2.3] than individuals with a CT scan from hospitals. Compared to one NSSC-CPP, individuals with a GP issued CT scan were less likely to have the following combinations of CPPs: NSSC-CPP+NSSC-CPP (OR 0.7 [0.6-0.8]), CPP+NSSC-CPP (OR 0.6 [0.5-0.7]) and CPP+CPP (OR 0.5 [0.5-0.5]) than individuals with hospital issued CT scans. Analysis on the diagnostic outcomes is ongoing and will be presented at the meeting.

Conclusion
This study will contribute with descriptions concerning the use of CPPs and NSSC-CPPs and the following diagnostic outcomes in Denmark. Our study is important when evaluating the benefits and harms of the different implementations of the pathways.

Clinical epidemiology and database research

#21: Treatment with triplet chemotherapy: Cisplatin, Ifosfamide and 5-Fluoruracil for Advanced Anal Squamous Cell cancer – A nationwide retrospective data analysis from the Danish Anal Cancer Group

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Abstract
Introduction
Squamous cell carcinomas of the anus (SCCA) are relatively rare malignancies with an incidence between 0.5-1.7 per 100.000 per year in the western countries. The incidence is currently increasing. Because of low incidence of SCCA and even lower incidence of advanced disease, there is limited knowledge on treatment options and clinical effect. Combination therapy with Carboplatin and Paclitaxel or Cisplatin and 5-fluorouracil are internationally recommended as first-line therapy for metastatic or inoperable SCCA. However, complete remission is rare and the prognosis poor with median survival of approximately 12 months.
The combination of Cisplatin, Ifosfamide and 5-Fluoruracil (CILF) represent an intensified treatment option and has been used for advanced SCCA in Denmark for several years, but its efficacy has not yet been evaluated which was the aim of the present study.

Materials and Methods
We conducted a retrospective study using Danish Hospital Registers, of all patients treated with CILF for metastatic or inoperable recurrent SCCA in Denmark, between October 2003 – October 2019.

Results
A total of 48 patients met the eligibility criteria. Median age at diagnosis was 57.4 years (range 41-75). Efficacy was observed, with an overall response rate of 35.5% (17 patients), of which three (6.3%) received a complete response. Median PFS was seven months (95% CI 3.4-8.6). Median OS was 13.3 months (95% CI 10.4-16.3).

Conclusions
This retrospective analysis indicates that CILF is a relevant treatment for advanced SCCA with respect to PFS and OS. Evaluation of toxicity calls for a prospective trial.

Clinical epidemiology and database research

#22: Risk of new primary cancer in patients with posterior uveal melanoma. A national cohort study

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Abstract
Introduction
Prior studies on incidence of new primary cancer in patients with posterior uveal melanoma (PUM) have produced conflicting results and the role of socioeconomic factors have not previous been investigated. The objective of this study was to utilize the unique Danish registries to determine the risk of new primary cancer in PUM patients.

Materials and methods
A total of 2,179 patients diagnosed with PUM from 1968 through 2016 and no prior history of cancer were matched on gender and birthdate with 22,717 non-cancer comparisons in a population-based matched cohort study.
Incidence of new primary cancer among patients with PUM and matched comparisons were described by crude incidence rates and the Cox regression model with time dependent hazard ratio. This allowed for adjustment of age, gender, calendar year at diagnosis/index date and socioeconomic factors. To address the skewed incidence of death in the two cohorts we applied cumulative incidence functions, by means of plots and Fine-Gray regression model to take death as a competing risk into account.

Results
Patients with PUM had a higher crude incidence of new primary cancer, RR 1.21 (95%CI: 1.08;1.35). From extended Cox model the rate of new primary cancer among patients was significantly increased 2-5 years (HR 1.49 (95%CI:1.23; 1.80)) and 11-15 years (HR: 1.49 (95%CI: 1.12; 1.99)) following the diagnosis of PUM and the estimate remained significant after adjusting for socioeconomic factors (HR 1.35 (95%CI:1.20; 1.55)). Patients with American Joint Committee on Cancer (AJCC) stage I showed an increased cumulative incidence of new primary cancer throughout the study, while the same trend could not be observed in stage II and stage III-IV due to the high cumulative incidence of death.

Conclusions
Patients with PUM have an increased risk of new primary cancer independent of socioeconomic factors. The distribution of cancertypes were similiar among PUM patients and matched comparisons.

Clinical epidemiology and database research

#23: Cancer risk in patients with warm autoimmune haemolytic anaemia - a nationwide cohort study

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Abstract
Introduction
Warm autoimmune haemolytic anaemia (wAIHA) is an acquired blood disorder characterized by autoantibodies directed against RBCs and can be primary or due to an underlying disease such as cancer. The association between wAIHA and some cancers has been established, but accurate risk estimates are missing. We investigated the cumulative incidence (CI) of cancer following a diagnosis of primary or secondary wAIHA, which we aimed to investigate.

Methods
Patients with wAHIA diagnosed 1980-2016 were identified in the nationwide Danish Haemolysis Cohort. Each patient was age-sex-matched with up to 50 comparisons from the general population. We identified cancer diagnoses using the Danish Cancer Registry. Any cancer diagnosis registered before index-date + 30 days were considered prevalent, while all cancer diagnoses thereafter were defined as incident. We calculated CIs of cancer after 1, 5, and 10 years.

Results
We identified 2,700 patients with wAIHA and 133,730 age-sex-matched comparisons. Among patients with wAIHA, 1,589 (58.9%) were primary, and 1,111 (41.1%) were secondary wAIHA – most frequently due to haematological cancers.
Our preliminary analyses of the CIs indicated that haematological and solid cancer were more common amongst patients diagnosed with wAIHA vs. comparisons. For all haematological cancers, the CIs remained higher in wAIHA vs. comparisons. The cumulative incidence at 5 year for patients with AIHA was 7.0 % (6.0-8.1). For comparisons, the CI at 5 year was 0.5 % (0.5-0.6). For all solid cancers, the CIs were higher the first 10 years following wAIHA diagnosis vs. comparisons. The CI for solid cancer in patients with wAIHA at 5 years was 8.6% (7.5-9.8) . For comparisons the CI at 5 years was 6.9% (6.8-7.1).

Conclusion
Patients with wAIHA have a higher risk of developing malignancies after wAIHA diagnosis. The increased risk for subsequent cancer development after wAIHA-diagnosis is most prominent for haematological cancers.

Clinical epidemiology and database research

#24: Regional variation i overlevelse for patienter med Non-Small-Cell Lung Cancer i Danmark, 2014-2018

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Abstract
Introduktion
Hver af de fem danske regioner varetager det samlede sundhedstilbud til deres borgere. Nærværende analyser undersøger en eventuel regional variation i overlevelse efter en lungekræftdiagnose i Danmark i perioden 2014-2018.

Materialer og Metoder
Der er udtrukket patienter fra DLCR for perioden 2014-2018, hvor patienterne er allokeret efter deres bopælsregion. Den regionale variation i overlevelse vurderes ved KM-kurver og Cox-regression, samt en sensitivitetsanalyse til at belyse mulige årsager til evt. forskelle.

Resultater
Undersøgelsen viser for populationen af non-small-cell lung cancer (NSCLC) patienter en øget dødelighed i Region Sjælland og en reduceret dødelighed i de tre vestdanske regioner, Region Nordjylland, Midtjylland og Syddanmark i forhold til Region Hovedstaden. HR varierer fra 0.88 for Region Nordjylland til 1.06 for Region Sjælland. En sensitivitetsanalyse viser, at disse forskelle delvist kan forklares af en mere favorabel stadiefordeling i de vestdanske regioner og af forskelle i kurativ behandlingsstrategi. For Region Nordjylland af en højere resektionsrate (35%), for Region Syddanmark af hyppigt anvendt stereotaktisk strålebehandling (13%) og for Region Sjælland af en lavere resektionsrate på 22%.

Konklusioner
For NSCLC patienter observeres der en øget dødelighed i Region Sjælland og en reduceret dødelighed i Region Nordjylland, Midtjylland og Syddanmark i forhold til Region Hovedstaden. Analysen peger på et muligt forbedringspotentiale, hvis andelen af patienter, der tilbydes kurativt intenderet behandling (resektion eller stereotaksi), kan øges i regioner, hvor raten var lav. Undersøgelsen giver ikke mulighed for at udtale sig om, hvilken behandlingsstrategi der er mest fordelagtig, hvad angår valg af resektion kontra stereotaktisk strålebehandling, men de gode resultater for Nordjylland med en høj resektionsrate har givet anledning til yderligere undersøgelse.

Clinical epidemiology and database research

#25: Obesity, type 2 diabetes, and breast cancer prognosis

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Abstract
Introduction
The prevalences of obesity, type 2 diabetes (T2D), and breast cancer (BC) are on the rise. According to previous studies, both obesity and T2D are associated with advanced stage and impaired prognosis in BC patients. However, the associations, including biological explanations, remain incompletely mapped. The objective of this study is to advance knowledge regarding the interplay between obesity, T2D, and BC investigating circulating levels of obesity- and T2D-related biomarkers (e.g. fibroblast growth factor 21, CRP, and TNF-α) at the time of BC diagnosis.

Materials and methods
All female BC patients (stage I-III) seen at the Dept. of Plastic and Breast Surgery, Aarhus University Hospital (AUH) between March 1st, 2010 and August 31st, 2020 were invited to participate (N=4,190). Blood samples were ascertained at diagnosis and stored at the regional biobank. We have retrieved all samples for analysis of baseline levels of potential prognostic biomarkers. Baseline and prospectively collected follow-up data will be ascertained from medical records and the Danish Breast Cancer Group (DBCG) database. Patients with a history of cancer or co-existing cancer will be excluded. We will examine the association of each biomarker with disease-free and overall survival.

Results
After enrolment, 851 patients were excluded. Four patients withdrew their consent, 194 are not registered in DBCG, 283 presented with carcinoma in situ only, 90 had a previous cancer history/co-existing cancer and 280 were registered in DBCG before March 1st, 2010. In total, 3,339 patients constitute the final cohort. Further preliminary results will be presented at the Danish Cancer Research Days.

Conclusions
We anticipate that this study will enhance the knowledge of the association between obesity, T2D, and BC. The study is expected to promote identification of the patients likely to have an inferior prognosis, who may benefit from heightened clinical care and possibly intervention.

Clinical epidemiology and database research

#26: Socioeconomic inequality in survival after oropharynx cancer according to HPV status: the impact of stage, smoking and comorbidity – a nationwide study from DAHANCA

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On behalf of the Danish Head and Neck Cancer Group (DAHANCA)

Abstract
Introduction
The socioeconomic inequality in survival after cancer is particularly pronounced for head and neck squamous cell carcinoma (HNSCC). The gap in HNSCC survival between affluent and deprived patients has increased concurrently with notable changes in the epidemiology of HNSCC, driven by increasing number of HPV-positive oropharyngeal squamous cell carcinoma (OPSCC). We investigate the impact of stage, smoking and comorbidity on the socioeconomic inequality in overall survival separately for patients with HPV-positive and HPV-negative OPSCC.

Materials and methods
Clinical information on all OPSCC patients who were diagnosed in Denmark between 2008-2019 and registered in the nationwide clinical database Danish Head and Neck Cancer Group (DAHANCA) with a known HPV-status (n=2526 HPV-positive, n=1465 HPV-negative) were linked to nationwide, administrative registries, to obtain information on socioeconomic position (education, income, cohabitation status), comorbidity and vital status. Cox proportional hazards models by HPV-status were used to investigate the impact of stage, smoking and comorbidity on the socioeconomic inequality in survival in confounder-adjusted models with and without adjusting for these mediating factors.

Results
The five-year all-cause mortality were significantly increased for patients with short education (HR: 2.3 (1.9-3.4), 1.5 (1.2-2.0)), low income (HR: 1.8 (1.4-2.3), 1.4 (1.1-1.7)) or living alone (HR: 2.1 (1.7-2.5), (1.4 (1.2-1.6)), for HPV-positive and HPV-negative OPSCC, respectively. Adjusting for differences in stage, smoking and HN-CCI explained a minor part of the socioeconomic differences in HPV-positive OPSCC survival, but had virtually no impact on the estimates for HPV-negative OPSCC.

Conclusions
Despite taking into account differences in HPV-status, stage at diagnosis, smoking status and comorbidity, we observe a significant socioeconomic inequality in survival after OPSCC, particularly within HPV-positive OPSCC.

Clinical epidemiology and database research

#27: Genetisk disposition for brystkræft – en retrospektiv kvalitetsgennemgang af patienter i Region Sjælland

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Abstract
Introduktion
Kontrolforløb for patienter, der er familiært eller genetisk disponeret for brystkræft, er fastlagt i henhold til gældende nationale retningslinjer og afhænger af alder, genprofil og kalkulerede risiko for at udvikle brystkræft. Risikoen for at udvikle brystkræft estimeres ved udredning på landets kliniske genetiske afdelinger, som henviser patienterne til relevant radiologisk surveillance.
I 2020 blev der i Region Sjælland foretaget et 360 graders kvalitetseftersyn af vejledninger, retningslinjer og arbejdsgange på brystkræftområdet. I forbindelse med eftersynet blev det besluttet, at identificere og gennemgå en historisk kohorte af patienter med øget familiær eller genetisk disposition for brystkræft og behov for radiologisk surveillance. Dette for at identificere patienter, der ikke er blevet tilbudt korrekt radiologisk surveillance i Region Sjælland i perioden 2008-2020.

Metode
Studiet er gennemført som et retrospektivt kvalitativt studie med audit af historiske patientforløb i OPUS journal, Sundhedsplatformen (SP) og Sundhedsjournalen. Kohorten er selekteret ud fra henvisningsdiagnosekoder og afdelings-SKS-koder fra OPUS (feb. 2008 til nov. 2017) og SP (nov. 2017 til juni 2020).

Resultater
I alt 1081 unikke patienter, for hvem en journalaudit var relevant, blev inkluderet i studiet. Ved journalaudit identificerede vi 21 patienter med mangelfuld radiologisk surveillance. Datoen for sidste rettidige radiologiske surveillance, var overskredet med gennemsnitligt 24 måneder.

Konklusion
Kvalitetsgennemgang af patienter i Region Sjælland, der er familiært eller genetisk disponeret for brystkræft, viste, at 98% af patienterne er korrekt udredt, vurderet og inkluderet i relevant forløb. 21 patienter med mangelfuld radiologisk surveillance vil blive kontaktet og tilbudt forløb i Region Sjælland.

Clinical epidemiology and database research

#28: Healthcare seeking and diagnostic evaluation of lung cancer symptoms – a population-based study

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Abstract
Introduction
The social inequality in lung cancer prevalence, stage at diagnosis and mortality rates are persistent. A high proportion of the inequality is related to smoking. In general, smokers report more lung cancer symptoms (LCS) than never smokers but are less likely to seek healthcare. To improve timely diagnoses of lung cancer, knowledge about social inequality and factors affecting healthcare seeking (HCS) and diagnostic evaluation of LCS are needed.
The overall aim of this Ph.D. study is, through five sub studies, to explore factors affecting the healthcare seeking behaviour and the diagnostic evaluation of LCS. In all sub studies the effect of smoking status and socioeconomic status is evaluated.

Material and methods
In 2012 a total of 100,000 individuals 20 years or older randomly selected in the general population were invited to fulfill an online survey on symptoms and HCS. Nearly 50,000 individuals answered the questionnaire. In 2022 a follow-up will be conducted. Data from both 2012 and 2022 will form the basis of this study. Variables included from the questionnaires are self-reported barriers for HCS, concerns about the LCS, influence on daily activity and health literacy. Data will be linked to national registers providing us with information about the diagnostic radiological evaluation.

Results
Results of the first sub study are currently being analysed. Preliminary results show that smokers are more embarrassed and worried about their LCS than never smokers. Additional results and hypotheses for the remaining sub studies will be presented at the conference.

Conclusion
To improve timely diagnosis and decrease social inequality in lung cancer an enhanced understanding of individuals in risk of postponing relevant HCS and knowledge about the diagnostic evaluation is crucial. This study will provide knowledge which is directly implementable in the healthcare system by reducing barriers for HCS and support the pathway from symptoms to diagnosis.

Clinical epidemiology and database research

#29: Uptake of influenza vaccination in cancer patients – preliminary results from a Danish register-based cohort study

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Abstract
Introduction
Since 2007, influenza vaccination has been free-of-charge for Danish residents aged ≥65 years or persons with acquired immune defects, which may include cancer patients if they have hematological cancers and/or receive chemotherapy or other immunosuppressive treatments. We aimed to describe the uptake of influenza vaccination in Danish cancer patients.

Materials and Methods
We included patients registered in the Danish Cancer Registry with a diagnosis of incident cancer from 1/10/2002 to 1/10/2017 and aged ≥18 years at diagnosis. We followed all patients for 5 years in Danish national registries to obtain influenza vaccination status at the end of each influenza season, cancer type, age at the beginning of each season, and administration of anti-cancer medical therapies (including chemotherapy, targeted therapies, and immunotherapy) from three months before the influenza season to the end of the season.

Results
Our study population included 306,717 cancer patients. The overall uptake of the influenza vaccination increased from 28.6% (95%CI: 28.3-29.0) in the 2007/2008 influenza season to 36.2% (95%CI: 35.9-36.5) in the 2017/2018 season. In 2017/2018, the uptake was 51% in patients aged ≥65 years, 13% in those <65 years, 45% in patients with hematological cancer, and 35% in those with solid tumors. The overall uptake was similar between patients receiving medical therapy (37%) and those not receiving (36%). The uptake was not associated with medical therapy in the following subgroups: hematological cancers, solid tumors, and age ≥65 years. For those <65 years the uptake was 21% in those receiving medical therapy and 12% in those not receiving.

Conclusions
Overall, the uptake of the influenza vaccination increased from 2007/2008 to 2017/2018. The uptake was higher in patients with hematological cancer compared with those with solid tumors. Receipt of medical therapy was not associated with higher vaccination uptake except in those aged <65 years.

Clinical epidemiology and database research

#30: Routes to diagnosis and the association with age in patients with cancer in Denmark

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Abstract
Introduction
This study intends to investigate the relationship between Routes to Diagnosis (RtD) – i.e. where in the healthcare system cancer patients present – and patients' age.

Materials & Methods
We conducted a population-based national cohort study in Denmark. We categorised each patient into one of eight specified RtD: death certificate only (DCO), screening, cancer patient pathway (CPP) from primary care, CPP from secondary care, unplanned admission, planned admission, other outpatient, and unknown. We described the proportions of patients with cancer diagnosed by different RtD, and examined associations between RtD and age categories using multinomial logistic regression controlling for sex, region of residence, year of diagnosis, diagnosis group, and multimorbidity.

Results
We included 144,632 cancers diagnosed in 139,013 patients in 2014-2017. The proportion of patients diagnosed through each RtD were: DCO (0.4%), screening (7.5%), CPP from primary care (45.9%), CPP from secondary care (20.0%), unplanned hospital admission (15.8%), planned admission (1.0%), other outpatient (6.3%), and unknown (3.1%). Elderly cancer patients were more likely to get diagnosed via unplanned admission and less likely to come through CPP from primary care compared to patients aged 50-79; e.g. 40.7% (95%CI: 23.9-26.9) of patients aged 90 years or more were diagnosed via an unplanned admission vs. 15% (95%CI: 14.5-15.6) of patients aged 50-59 years.

Conclusions
Across all age groups the majority of cancer patients were diagnosed through a cancer patient pathway. However, compared to middle aged cancer patients, elderly patients were less likely to get diagnosed via a CPP from primary care and more likely to get diagnosed via an unplanned admissions.

Clinical epidemiology and database research

#31: Early mortality risk prediction after curative-intent radiotherapy for head and neck squamous cell carcinoma

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Abstract
Introduction
Among patients with head and neck squamous carcinoma (HNSCC), curative-intent radiotherapy (RT) and chemoradiation (CRT) are associated with substantial acute morbidity and 5–10% of patients die within the first 180 days of treatment initiation. A large proportion of these deaths occur in the absence of known HNSCC recurrence or progression and may therefore to some extent be preventable. We developed a predictive model to estimate the risk of non-HNSCC mortality within the first 180 days after RT/CRT.

Materials and methods
Patients with HNSCC treated at Rigshospitalet or Herlev Hospital 2010–2017 were identified. Model predictor variables were chosen a priori based on a previously established impact on mortality risk. These included age, stage, performance status, subsite including p16-status, comorbidity, smoking and pre-treatment albumin levels. The 180-day non-HNSCC mortality risk was estimated by combining two cause-specific cox models; one with 180-day mortality as endpoint and another with HNSCC recurrence or progression as endpoint.

Results
We included 2209 patients. The 180-day non-HNSCC mortality rate was 4.4%. Almost one third of non-HNSCC deaths were caused by pneumonia. A bootstrap optimism-corrected estimate of the model's discriminative capacity was AUC = 0.743 (95% CI: 67-80.7) and the model appeared well calibrated for risk predictions up to 20%.

Conclusion
We developed a prediction model to estimate the risk of 180-day non-HNSCC mortality and plan to publish it as an online interactive tool. The model can be used to select high-risk patients for supportive interventions during and immediately following RT/CRT, which may potentially reduce early mortality rates.

Clinical epidemiology and database research

#32: A population-based survey of patients' experiences with teleconsultations in cancer care in Denmark during the COVID-19 pandemic

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Abstract
Introduction
During the COVID-19 pandemic, some cancer departments replaced selected outpatient visits with teleconsultations (TC). Our aim was to examine patient-related and cancer-specific characteristics associated with experiences with TC among patients with cancer during the COVID-19 pandemic.

Materials and methods
This population-based electronic survey included all patients with breast, lung, gastrointestinal, urological and gynaecological cancers having appointments in the outpatient clinics, Department of Clinical Oncology and Palliative Care, Zealand University Hospital, in March-April 2020. We used multiple logistic regression models to examine associations between patients' characteristics and their experiences with TC.

Results
Among the 2119 invited patients, 1160 (55%) participated. Two thirds of patients had one or more consultations with a physician replaced by TC. Patients who were male, aged 65-79 years and having TC for test results were statistically significantly more comfortable with TC, more confident that the physician could provide information and assess symptoms/side effects by TC and had a perceived better outcome of TC. Having breast cancer, high level of anxiety, low health literacy or TC for a follow-up consultation were associated with less positive experiences with TC. Living alone, short education, disability pension and comorbidity were associated with anxiety and low health literacy.

Conclusion
The majority of patients reported positive experiences with TC, however, with particular exception of patients with anxiety and low health literacy, who were also the patients with fewest socioeconomic resources and health competences. Use of TC in standard clinical practice should be carefully planned to meet patients' different information needs in order not to increase social inequality in cancer.

Clinical epidemiology and database research

#33: Routine PET-CT scans provide early and accurate recurrence detection in asymptomatic stage IIB-III melanoma patients.

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Abstract
Introduction
The use of routine imaging with 18F-FDG PET-CT (PET-CT) in melanoma surveillance is debated and evidence of its diagnostic value and yield in asymptomatic patients is limited. Denmark introduced nationwide routine surveillance with PET-CT in high-risk patients in 2016. The aim of this study was to examine the sensitivity, specificity, negative and positive predictive values, numbers-needed-to-scan and clinical impact of routine PET-CT in the surveillance of asymptomatic stage IIB-III melanoma patients.

Materials and methods
Data was retrieved from the population-based Danish Melanoma Database and patient records. All patients diagnosed with stage IIB-III melanoma at two University Hospitals in 2016 and 2017 were included. Patients underwent surveillance with clinical examinations and PET-CT scans at 6, 12, 24 and 36 months.

Results
In 138 patients, 243 routine PET-CTs were performed within a median follow-up time of 17.7 months. Routine PET-CT detected recurrence at least once in 25 patients (18.1%), including distant recurrence in 19 patients (13.8%). Stage IIB patients had the lowest recurrence rate (11.1%). Numbers-needed-to-scan to detect one distant recurrence was 12.8 patients and median time-to-recurrence was 6.8 months. Sensitivity was 100%, specificity was 94.7% and negative and positive predictive values were 100% and 74.4%, respectively. False positive findings prompted 22 additional investigations (of which ten invasive) in 17 patients (12.3%).

Conclusion
Routine PET-CT has a high sensitivity and specificity when used in high-risk melanoma surveillance. Time-to-recurrence and stage-specific recurrence rates indicate high gain of early routine imaging at six months especially for stage IIC and III patients.

Clinical epidemiology and database research

#34: Trends in postoperative chemoradiotherapy for glioblastoma patients: a Danish cohort study

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Abstract
Introduction
Postoperative chemoradiotherapy (CRT), using conventional radiotherapy (convRT), has a key role in the treatment of glioblastoma (GBM) patients supported by level 1A evidence. In the past decade, evidence supporting hypofractionated RT (HFRT) has emerged. The aim of this Danish cohort study was to evaluate the utilisation of postoperative CRT for real-world GBM patients over time.

Material and Methods
All adults with newly diagnosed GBM (histology confirmed) between 2011 and 2018 were identified via the Danish Neuro-Oncology Registry, which was furthermore used to extract all data. Patients were grouped per year of diagnosis. RT was classified as convRT (≤2 Gy/fr, dose 44-66 Gy) or HFRT (>2 Gy/fr, dose 34 or 40 Gy). Utilisation of CRT was measured by planned treatment. Multivariable logistic regression was used to analyse the association of relevant clinical variables with convRT or HFRT.

Results
The cohort consisted of 2153 patients, of whom 1743 patients were planned to start RT: average utilisation of 81% per year (range 77-84%, no trend over time).
ConvRT was planned in 1428 patients (66%), with a steadily decreasing utilisation from 73% in 2011 to 52% in 2018. In this subgroup, the utilisation of concomitant CRT was 86% (range 80-93%, no trend).
HFRT was planned in 315 patients (15%), with a utilisation of up to 26% in 2018, after a more pronounced increase since 2014. In this subgroup, the utilisation of concomitant CRT was 33% (range 0-47%, no trend).
The utilisation of HFRT compared with convRT, was significantly associated with higher age, poorer PS before RT, multifocal tumour, less extensive surgery, less concomitant CT, one hospital, and more recent diagnosis years.

Conclusion
The increased utilisation of HFRT is in line with emerging evidence during the cohort period. However, while HFRT was developed as a more convenient schedule, the overall utilisation of postoperative CRT did not increase in real-world Danish GBM patients.

Clinical epidemiology and database research

#35: Characterization of high-cost patients in systemic anti-cancer treatment: Evidence from a tax-based healthcare system from 2008 to 2019

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Abstract
Introduction
Expenditures on medicine for systemic anti-cancer therapy (SACT) have seen large increases within recent years, but little is known about the distribution of costs among treated patients. Within healthcare, expenditures are known to be skewed with a substantial share of the spending used on a small percentage of the patients. Knowledge about this group is crucial to understand what drives costs and to potentially initiate interventions.

Materials and methods
We defined high-cost cancer patients, exclusively based on SACT medicine costs, as the top 2.5% most expensive. Patient-level pharmaceutical costs were calculated using registrations of SACT usage for 12.589 patients in the North Denmark Region from 2008-2019 combined with billings from the hospital pharmacy of EUR 142.1 million. This allowed us to individually price 260.834 treatments. Accumulated 3-year costs were investigated for association to clinical variables using Poisson regression.

Results
High-cost patients accounted for 28.8% of the SACT expenditures and were observed across all major cancer groups, except for pancreatic cancer. The risk of becoming a high-cost patient was higher for younger age groups, i.e. 18-44 and 45-64 years, patients with BMI ≥ 25 and patients with multiple cancer diagnoses, while no significantly altered risk were observed with respect to gender and the number of comorbidities at first treatment. Changes in characteristics of high-cost patients across time were found with an increased risk of becoming high-cost for respectively elderly and lung cancer patients in recent years.

Conclusions
A small fraction of patients receiving SACT claims a large part of the expenditures. From a policy point of view, recognition that a relatively small group of individuals receiving treatment account for a large fraction of costs and understanding of what characterizes this group, can aid in devising more focused cost-containment strategies.

Clinical epidemiology and database research

#36: Circulating Lipids and Breast Cancer Survival in the Malmö Diet and Cancer study

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Abstract
Rationale
Overweight and obesity are associated with inferior prognosis in breast cancer. The explanation is considered multifactorial, and dyslipidemia may be a contributing factor. The purpose of this study was to examine the association between circulating lipids and breast cancer outcome in patients enrolled in the Malmö Diet and Cancer Study (MDCS) cohort.

Patients and methods
Circulating lipid levels were measured upon enrollment in the MDCS. We identified all MDCS participants with incident invasive breast cancer between 1991-2014. Follow-up time began at breast cancer diagnosis and continued until the first of invasive breast cancer recurrence, death, or five years of follow-up. We estimated incidence rates of recurrence at five years and fit Cox regression models to compute crude and adjusted hazard ratios (HRs) with 95% confidence intervals (95% CI) of recurrence-free survival and overall survival according to cohort-specific tertiles of Apolipoprotein A-1 (Apo A-1) and Apolipoprotein B (Apo B).

Results
We enrolled 850 eligible patients. During the five years of follow up, there were 90 invasive recurrences over 3,806 person-years. In multivariable analyses, high levels of Apo B were associated with an increased rate of recurrence (tertile 3 vs. 1, HR= 2.06 [95% CI: 1.02-4.15]). However, high levels of Apo B were not associated with overall survival (tertile 3 vs. 1, HR= 1.07 [95%CI: 0.59-1.97]). We observed no associations between high levels of Apo A-1 and recurrence (tertile 3 vs. 1, HR= 1.05 [95%CI: 0.59-1.86]) or overall survival (tertile 3 vs. 1, HR=1.19 [95%CI: 0.66-2.16]).

Conclusion
High pre-diagnostic level of Apo B was associated with an increased risk of recurrence among breast cancer patients. Circulating Apo A-1 was not associated with breast cancer outcome. The results warrant further investigation into the importance of lipid-regulation in breast cancer patients.

Clinical epidemiology and database research

#37: Risk of tumors of the central nervous system among women treated with fertility drugs: a population-based cohort study

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Abstract
Introduction
Hormonal factors have been suggested to affect the risk of central nervous system (CNS) tumors. Very few epidemiologic studies have examined the association between hormonal drugs used for fertility treatment (fertility drugs) and risk of CNS tumors, and the results have been inconclusive. Using data from a large population based cohort of women with fertility problems in Denmark (The Danish Infertility Cohort), we examined the association between use of fertility drugs and subsequent risk of CNS tumors.

Materials & Methods
The study population included 148,016 Danish women with fertility problems aged 20-45 years and living in Denmark from January 1995 to December 2017. Information on use of fertility drugs [clomiphene, gonadotropins, human chorionic gonadotropin (hCG), gonadotropin-releasing hormone (GnRH) modulators and progesterone], CNS tumors, vital status and covariates was extracted from the Danish health registers. Cox proportional hazard models with adjustment for confounders were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for gliomas, meningiomas and benign tumors of the spinal cord and cranial nerves.

Results
During a median follow-up of 11.3 years, 52 gliomas, 152 meningiomas and 117 benign tumors of the spinal cord and cranial nerves were diagnosed. Use of hCG was associated with an increased risk of gliomas, although the association did not reach statistical significance (HR=2.13; 95% CI 0.90-5.01). In contrast, use of hCG was associated with a statistically significant decreased risk of meningiomas (HR=0.49; 95% CI 0.28-0.87). No strong associations were observed with meningiomas, gliomas or benign tumors of the spinal cord and cranial nerves for the other types of fertility drugs.

Conclusion
The use of most types of fertility drugs did not increase the risk of CNS tumors, but an increased risk for gliomas and a decreased risk for meningiomas was observed after use of hCG.

Clinical epidemiology and database research

#38: Social vulnerability index for advanced cancer patients: a COMPAS study – Danish Research Center for Equality in Cancer

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Abstract
Introduction
Social vulnerability appears to be influencing cancer trajectories. This has led to a hypothesis that socially vulnerable patients with advanced cancer might use rehabilitation and/or palliative care initiatives to a lesser extent than socially advantaged patients. Identifying socially vulnerable patients is crucial but challenging because of the complexity of social vulnerability. Social vulnerability is multifactorial, and therefore socially vulnerable patients cannot be identified only by including one factor.
The aim of the study is to develop a social vulnerability index based on administrative data in a population-based cohort of advanced cancer patients.

Materials and Methods
The index is developed using a cohort of cancer patients, who died from cancer within five years after the diagnosis. Through the Danish health registries information about social factors and health data were extracted. The registries used are The Danish Civil Registration System, The Danish Register of Causes of Death, The Danish National Patient Registry, DREAM database, and registers of income. The factors are weighted differently to form the index, and appropriate cut-off values are evaluated.

Results
The cancer cohort consists of 44,187 patients identified from The Danish Cancer Registry. All patients were diagnosed and died in the period from 1 January 2013 to 31 December 2018 with maximum five years from diagnosis to death. The patients had a mean age of 71.4 years and the majority were men (54 %). Most frequent cancer types were lung (28 %), upper gastrointestinal (19 %), and lower gastrointestinal (13 %). The index development is still in progress.

Conclusion
Development of a social vulnerability index for advanced cancer patients is needed. The index must capture social vulnerability in entirety and may work better as predictive factor than individual factors in identification of patients who are underserved regarding rehabilitation and palliative care.

Clinical Trials:

Poster #39-85

Clinical trials

#39: DAHANCA 38: Systematic use of patient reported outcome during radiotherapy for head and neck cancer (NCT03918382)

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Abstract
Introduction
The national DAHANCA 38 trial compares systematic use of Patient Reported Outcomes (PRO) during radiotherapy for head and neck squamous cell carcinoma (HNSCC) with standard clinical counseling. The hypothesis is that active use of PRO during radiotherapy (RT) will lead to improvements in the patients' quality of life, based on more precise monitoring and management of side effects. We here present the study protocol.

Material/methods
The trial is designed as a prospective nationwide, sequential cohort study, clinicaltrials.gov ID No. NCT03918382, DAHANCA 38 protocol.
The study includes patients ≥ 18 years diagnosed with HNSSC and planned for RT (primary or postoperative) at the University Hospitals of Aalborg, Aarhus, Herlev, Naestved, Odense and Rigshospitalet.
In the first phase, 97 patients will be included in the control group. In the second phase 194 patients will be included in the PRO group. The intervention is active use of electronic PRO. Patients in the PRO group report their symptoms on a tablet at baseline, weekly during RT until week 2 after RT completion. The PRO answers will be presented graphically and used as part of the consultation. The PRO questions consist of HNC relevant items from PRO-CTCAE™ and EORTC item library. QoL (EORTC QLQ-C30 and EQ-D5-L5) questionnaires will be answered in both groups at baseline, week 4 of treatment, at completion of RT and 2 months after RT completion.

Results
Primary endpoint is health-related quality of life at end of RT. Data on secondary endpoints will include time to start opioid treatment, time to tube-feeding/other feeding, weight loss, DAHANCA toxicity and compliance to treatment.

Conclusion
In collaboration with DAHANCA a national study on active use of PROs during RT for HNSSC has been established. The results will generate evidence on the use of PROs versus standard counselling during RT.
The study is expected to end inclusion early 2022.

Clinical trials

#40: A phase II-study of electroporation potentiated immunotherapy in liver metastatic pancreatic cancer (EPIC-1)

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Abstract
Introduction
Pancreatic cancer (PC) is the fourth leading cause of cancer death. This is largely due to late diagnosis, aggressive tumor biology and resistance to chemotherapy. Immune checkpoint inhibitors (ICI) have shown impressive results in several tumor types, but not in PC. Animal trials have, however, shown that concurrent ablation of a tumor lesion using irreversible electroporation (IRE) can stimulate a universal anti-cancer immune response. Immunological studies of IRE treated patients suggest that this effect could be translated to humans. The aim of this trial is to examine the efficacy and safety of combined pembrolizumab and IRE ablation in metastatic PC.

Materials & Methods
Sixteen patients (PS 0-1) with progression on or intolerance to first or subsequent lines of chemotherapy will be included at Aalborg University Hospital. Patients must have 1 liver metastasis suitable for IRE ablation and ≥1 separate measurable lesion for response evaluation. Patients will receive 400mg of pembrolizumab on day 1 and are treated with IRE on day 10. Pembrolizumab is administered every 6 weeks for up to 6 months. Response evaluation (RECIST 1.1) will be performed every 2 months. Blood and tumor immune cell composition is examined by flow cytometry and by immunohistochemistry before pembrolizumab initiation, before IRE and after IRE. Changes in tumor gene expression is examined by NanoString™ RNA sequencing.

Results
The primary outcomes are objective response and rate of serious adverse events. Secondary outcomes include overall survival and changes in parameters associated with antitumor immunity.

Conclusions
This study in progress will for the first time access the feasibility, efficacy and safety of combined treatment of ICI and IRE in metastatic PC.
The study is supported by a grant from the Danish Cancer Society.

Clinical trials

#41: COLONIC RESECTION FOR CANCER AS DIABETOGENIC RISK FACTOR - A Study of the Pathophysiological Effects of Colon Resection on Glucose homeostasis (The COLECDIAB study)

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Abstract
Introduction
Colon cancer (CC) survivors have an increased risk of developing T2D. A recent study revealed that the surgical procedures per se may be causally involved. Hence, left-sided colon resections increased the risk of developing T2D. In addition, treatment with chemotherapy may play a role in the pathogenesis. Given the steadily improving survival rate after a CC diagnosis, prevention of secondary diseases such as T2D is important to improve quality of life in these patients and to reduce socioeconomic expenses.
This study aims to elucidate the effect of resection of tumors located in the left part of the colon on pathophysiological intermediates, which may lead to T2D 12 months post-surgery or later. The physiological mechanism might be a changed postprandial secretion of gut hormones including glucagon-like peptide-1 (GLP-1) secreted from L-cells in the left part of the colon. We will investigate changes in primarily glucose homeostasis as well as in gastrointestinal hormones, microbiota, visceral fat accumulation and markers of low-grade inflammation in CC survivors who underwent a left hemicolectomy or sigmoidectomy.

Material and Methods
60 patients will be included in this explorative clinical study. Patients will be divided into 4 groups depending on surgical procedure and treatment with chemotherapy. In the group of patients undergoing left hemicolectomy or sigmoidectomy ± treatment with chemotherapy 2 x 15 patients will be included, and in the group of patients scheduled to undergo right hemicolectomy ± treatment with chemotherapy another 2 x 15 patients will be included. During the 3 study visits (before surgery, 3-4 weeks post-surgery and 12 months post-surgery) the following tests will be performed: An oral glucose tolerance test, blood and fecal sampling, a DXA scan and an ad libitum meal test.

Status
At the end of January 2021, we have included 10% of the patients.

Clinical trials

#42: Municipal return to work management in cancer survivors: a controlled intervention study.

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Abstract
Introduction
Resuming work during or after cancer treatment has become an important target in cancer rehabilitation. The aim was in a controlled trial to study the return to work (RTW) effect of an early, individually tailored vocational rehabilitation intervention targeted to improve readiness for RTW in cancer survivors.

Materials and methods
Participants diagnosed with breast, cervix, ovary, testicular, colon-rectal, and head-and-neck cancers as well as being employed were allocated to a vocational rehabilitation intervention provided by municipal social workers (n:83) or to usual municipal RTW management (n:264). The intervention contained three elements: motivational communication inspired by Acceptance and Commitment Therapy by which RTW barriers were addressed, municipal cancer rehabilitation and finally employer and workplace contact. RTW effect was assessed as relative cumulative incidence proportions (RCIP) in the control and intervention group within 52 weeks of follow-up, estimated from the week where treatment ended at the hospital. RCIP was interpreted and reported as relative risk (RR) with 95% confidence intervals (CI) adjusted for gender, age cancer diagnosis, education, comorbidity, and sick leave weeks.

Results
Across cancer diagnoses 69 (83.1%) and 215 (81.4%) returned to work in the intervention and control group, respectively. No statistical effect was seen (RR 1.08 (95% CI 0.98–1.19)). Repeating the analyses solely for participants with breast cancer (n¼290) showed a significant effect of the intervention (RR 1.12 (95% CI 1.01–1.23)).

Conclusion
More than 80% returned to work in both groups. However, no statistical difference in RTW effect was seen across cancer diagnoses within one year from being exposed to an early, individually tailored vocational rehabilitation intervention compared with usual municipal RTW management.
Trial registration number: ISRCTN50753764

Clinical trials

#43: Quantitative measurements of adaptive bone remodeling around the Cemented Zimmer® Segmental stem after tumor resection arthroplasty using dual-energy X- ray absorptiometry.

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Abstract
Introduction
Limb salvage surgery is currently offered to more than 90% of patients with bone or soft tissue sarcomas and to a greater extent also to patients with metastatic bone disease. The aim of the present study was to evaluate the adaptive remodeling of the periprosthetic cortical bone after insertion of a tumor prosthesis with a cemented stem.

Material and Methods
A prospective study of 21 patients (F/M=12/9), mean age 55 years (range 15-81) with metastatic bone disease (n=9), sarcomas (n=8) or aggressive benign tumors (n=4) who underwent bone tumor resection and reconstruction with a tumor prosthesis (Zimmer® Segmental 130 mm straight fluted cemented stem with trabecular metal (TM) collars) in the proximal femur (n=10), distal femur (n=9) or proximal tibia (n=2) . Measurements of bone mineral density (BMD) were done postoperatively and after 3, 6, and 12 months of the periprosthetic bone and in both ankles by using dual-energy X-ray absorptiometry. BMD (/g/cm2) was measured in 4 regions of interest around the cemented stem and in one region of interest 1 cm proximal from the ankle joint. Repeated measures ANOVA and students paired t-test was used to evaluate BMD changes over time.

Results
At 1-year follow-up, BMD compared to the postoperative value was seen in all 4 regions of interest with a statistically significant bone loss of 8-15%. The bone loss was most pronounced (14-15%) in the 2 regions of interest closest to the TM collar and lowest (8%) adjacent to the tip of the stem. We found the largest reduction in BMD around proximal femoral stems (11%-18%). After 1 year the decrease in BMD of the ankle on the affected extremity was 9% and the ankle on the contralateral extremity was close to baseline.

Conclusion
The periprosthetic BMD around the cemented 130 mm Segmental stem decreased significantly during the first postoperative year and is considered caused by a combination of stress shielding and immobilization.

Clinical trials

#44: Predictive biomarkers of response to Mitomycin C - A randomized controlled trial in non-muscle invasive bladder cancer

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Abstract
Introduction
Short-term intensive chemoresection with Mitomycin C can potentially spare patients with chemosensitive tumours from surgery. However, no research exists on biomarkers of response in non-muscle invasive bladder cancer (NMIBC) patients treated with Mitomycin C. The main objective was to identify and validate predictive biomarkers to chemoresection.

Materials and methods
A randomized, controlled trial was conducted between January 2018 and June 2019 in two urological departments in Denmark. Patients had a history of Ta low-grade/high-grade NMIBC and were included upon recurrence. The intervention group (58 patients) received chemoresection with Mitomycin C followed by surgery only in patients with incomplete response. Tumour and reference germline DNA from the intervention group were analysed by whole-exome sequencing. Predictive biomarkers were validated in the context of Ta low-grade tumours from the UROMOL study and a muscle-invasive bladder cancer cohort treated with neoadjuvant chemotherapy (NAC).
The main outcome was a direct response to chemotherapy in the intervention study.

Results
In the intervention group, 57% of patients had chemosensitive tumours and complete response. Chemoresistant tumours were associated with mutations in SPTAN1, APC and a high APOBEC signature contribution. Chemosensitive tumours were associated with FGFR3 wild-type and mutations in PARP4, PTEN, ZFHX3 and AFDN. Validation showed concordance with FGFR3, ZFHX3, PARP4 (UROMOL cohort) and with APOBEC signature (NAC cohort). Main limitations include no biopsy immediately prior to chemoresection and the partially unmatched validation
cohorts.

Conclusions
More than 50% of patients treated with chemoresection with Mitomycin C could avoid surgery. The combination of five candidate genes and the level of APOBEC signature contribution correctly categorized the treatment response in 79% of the patients.

Clinical trials

#45: DBCG RT Natural trial: Partial versus no breast radiation therapy for women ≥ 60 years operated with breast conservation for a relatively low risk early breast cancer, a clinically controlled randomized trial

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Abstract
Introduction
Since April 2016 partial breast irradiation (PBI) has been DBCG (Danish Breast Cancer Group) standard for selected low risk breast cancer patients operated with breast conservation. This is based on results from the UK
IMPORT LOW trial and from the DBCG PBI trial. The 5-year risk of local recurrence after PBI is 0.5% compared with a 2% risk of contralateral new breast cancer. Data from randomized trials on gain from radiation therapy (RT) indicates a risk reduction of local recurrence from RT by 2/3. Thus, omission of PBI may increase the 5-year risk of local recurrence to 1.5-2%, i.e. to the level of a contralateral new primary. In the DBCG RT Natural trial the DBCG RT Committee tests if omission of PBI in selected patients is possible without causing an unacceptable local recurrence rate.

Material/Methods
Patients ≥60 years operated with breast conservation for a low-risk breast cancer (non-lobular, pT1, pN0, ER+, grade 1-2, HER2-, margin ≥2mm) are randomized ± PBI, where PBI is based on 3DCRT 40 Gy/15 fr. Strata are institution and endocrine therapy. The study will randomize 926 patients 1:1. The primary endpoint is 5-year invasive local recurrence. Secondary endpoints are local morbidity, fear of cancer recurrence and pattern of recurrences. NCT 03646955.

Results
Accrual was initiated Oct 2018, and as of April 2021, 366 patients were included, 253 randomized and 113 opted for no PBI. The trial is active in RT departments in Denmark (n=7), Norway (n=6), Sweden (n=4), and Chile (n=1).

Conclusion
The DBCG RT Committee constantly aims to optimize the indication for adjuvant breast radiation therapy to ensure a balance between gain and harm. The DBCG RT Natural trial is part of that strategy.

Clinical trials

#46: The DBCG RT Proton trial: Adjuvant breast proton radiation therapy for early breast cancer patients, a clinically controlled randomised phase III trial

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Abstract
Introduction
The prognosis of breast cancer (BC) has improved over decades, thus long-term morbidities increasingly play a role. Serious late effects (LE) from radiation therapy (RT) are second cancer and heart disease. RT improves the prognosis, but must be balanced with risk of RT induced LE. Proton therapy (PT) causes lower dose to organs at risk. The hypotheses of this phase III randomised trial are that compared to photon RT 1) the risk of cardiac disease is lower using PT, 2) the risk of second cancer is reduced using PT, and 3) the risk of distant failure and death from BC is reduced by using PT.

Material/Methods
The selection criteria for the trial were based on a planning study on 180 RT plans collected from 18 hospitals. Using DBCG criteria for optimal dose coverage of targets may lead to a high dose to the heart/lung. If the mean heart dose (MHD) is ≥4Gy and/or the V20 lung is ≥37% the patient is eligible. The primary endpoint is heart disease 10 years post RT, risk of lung cancer, recurrence and loco-regional morbidities. The power calculation is based on a 5-yr freedom from heart disease of 94.2% for a non-irradiated woman 60 years of age, 93.7% for a PT patient with MHD 0.5 Gy, and 89.8% for at photon treated patient with MHD 4 Gy. Thetrial will accrue 1502 patients. The follow-up evaluations are in harmony with other DBCG RT trials and international PT trials. A subset of the patients will have extensive cardiac evaluations including heart-CT, echocardiography and PET scans.

Results
The randomised trial was initiated June 2020 at AUH and 30 patients have been randomized. Due to the COVID-19 pandemic, initiation of the remaining Danish centers was delayed. All Danish centers are expected to start inclusion of patients early 2021.

Conclusion
PT for BC is introduced as a new treatment option for selected patients with high RT dose to heart and/or lung. PT is expected to reduce the risk of serious RT associated late effects and improve disease control.

Clinical trials

#47: Partial versus whole-breast irradiation for early breast cancer patients in the phase III randomized DBCG PBI trial

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Abstract
Purpose
Based on low risk of local recurrence (LR) in selected breast cancer (BC) patients (pts), the Danish Breast Cancer Group initiated the randomized DBCG Partial Breast Irradiation (PBI) trial (NCT00892814). The radiotherapy (RT) was external beam 40 Gy/15 fr. The hypothesis was that PBI did not increase the risk of grade 2-3 breast induration compared with whole breast irradiation (WBI).

Methods
880 pts ≥60 years operated with breast conservation for BC (non-lobular unifocal pT1N0, ER+, HER2-, grade 1-2, margin ≥2mm) were randomized WBI vs. PBI during 2009-16. The primary endpoint was grade 2-3 induration.

Results
866 pts were eligible from 5 centers. Median age was 66 years. Median follow up was 6.7 years. The 3-yr rate of induration was 9.9% (WBI) and 5.4% (PBI), p=0.017. Irradiated volume was associated with induration with a 3-year incidence in large-breasted pts of 13% (WBI) and 6% (PBI) versus 6% (WBI) and 5% (PBI) in small-breasted pts. All RT associated morbidities were similar or better with PBI.
As first event, 15 pts (1.7%) had a loco-regional recurrence (4 WBI, 11 PBI), HR 2.35 (95% CI 0.72, 7.62), p=0.16, and 13 of these were LR. Five were new primaries (1 WBI and 4 PBI), the rest were true LR (3 WBI and 5 PBI). Contralateral BC was detected in 18 pts (2.1%). Distant recurrence as first event was seen in 3 pts, and simultaneous with loco-regional failures in 3 pts. Non-breast second cancer was diagnosed in 62 pts (7.2%), no difference between the groups. In all, 70 pts (8.1%) died, five from BC, 33 from second cancers, two from cardiac disease (both WBI left-sided) and 30 from other causes. The 9-year overall survival was 89.3% (WBI) versus 86.5% (PBI), p=0.37.

Conclusion
External-beam PBI 40Gy/15 fr for low-risk BC pts did not result in more induration compared to WBI.
Irradiated volume was a risk factor for induration. Few loco-regional recurrences were detected and not related to PBI.
Updated results with longer follow-up will be provided.

Clinical trials

#48: The DBCG RT Skagen Trial 1: Hypo- vs normofractionated loco-regional radiation of early stage breast cancer in a randomized trial

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Abstract
Introduction
Based on poor results using hypofractionated adjuvant radiotherapy (RT) of breast cancer (BC) 50 Gy/25 fr. has been Danish Breast Cancer Group standard for loco-regional RT since 1982. Results from the DBCG HYPO trial stimulated a renewed interest in hypofractionation, and the non-inferiority DBCG SKAGEN TRIAL 1 was initiated. The hypothesis is that 40 Gy/15 fr does not result in more arm lymph oedema than 50 Gy/25 fr 3 years post RT. If boost is indicated, this is provided as simultaneous integrated boost.

Material/Methods
Since 2015, patients (pts) ≥18 years operated for BC with an indication for loco-regional RT are randomized 1:1 to 50 Gy vs. 40 Gy. The primary endpoint is ipsilateral arm lymph oedema 3 years post RT. Oedema is present if the circumference of the ipsilateral arm is 10% higher compared with the other arm. The RT planning is based on the ESTRO consensus for target volume delineation. Participating Danish centers submit all treatment plans to the National Dose Plan Bank. Non-Danish participating centers submit few plans for quality assurance of the planning. It is expected that 10% of pts treated with 50 Gy will have arm lymph oedema 3 years after RT. To rule out an increase by
5% using 40 Gy, 1012 patients with 3 years morbidity evaluation will be included. Accrual remains open until 3-year morbidity information has been collected in 1012 pts. NCT02384733.

Results
The trial is open for accrual in 7 countries, and as of April 2021, 2832 pts are accrued. Extensive quality assurance of the RT planning demonstrated high compliance with DBCG guidelines.

Conclusion
With the current accrual rate it is estimated that the DBCG SKAGEN TRIAL 1 will close with almost 3000 pts in 2021, thus providing statistical power for analyses of the importance of fractionation in different subgroups. The DBCG RT Committee will decide what is the future standard fractionation for loco-regional radiation therapy when the trial closes.

Clinical trials

#49: DANERA: External radiation therapy in neuroendocrine neoplasms: A nationwide Danish study. Trial in progress.

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Abstract
Introduction
The incidence of rare cancers such as neuroendocrine neoplasms (NEN) increases without significant improvements in the outcome either in Denmark or worldwide as NEN management is not standardized to date. The value of external beam radiation (EBRT) and chemoradiotherapy (CRT) approaches in NEN treatment, both with palliative and especially curative intents, is still unknown and never examined in prospective trials. No studies of dose- response relationships in NEN with different histopathological and/or tumour-specific genetic characteristics exist.

Materials and methods
This is a national multicenter Phase II parallel non-randomized and observation prospective study, which will be conducted across 3 Danish NET centres. The study will prospectively evaluate the efficacy of the EBRT/CRT on local-regional tumour control and disease, progression-free and overall survival in two independent NEN patient cohorts of broncho-pulmonary and gastroenteropancreatic origins, respectively. The efficacy of EBRT on symptom relief and improvement of quality of life will be evaluated in an observational cohort of incurable NEN patients. Furthermore, these studies will also evaluate the combination of histopathological, biochemical, and tumour- specific genetic markers, which may provide an assessment for the proper selection of NEN patients for curative treatment.

Conclusion
This is a National study initiated and run by the Danish Neuroendocrine Tumor Society. This study is an important pioneering project that could help better understand the impact of EBRT/CRT in managing this rare disease. Ultimately, this study may provide guidance to identify NEN patients who could prognostically benefit from EBRT/CRT strategies, thereby avoiding unnecessary side effects in the radioresistant subgroup of NEN patients.

Clinical trials

#50: NOAC 9 - A Phase II Randomised Nordic Anal Cancer Group Study on plasma HPV guided Follow-Up - a trial in progress

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Abstract
Background
Anal Cancer (AC) is a rare disease with increasing incidence. Curative chemoradiotherapy implies a good prognosis, but structured follow-up is needed to detect early recurrence to allow for curative salvage treatment or early palliative care. Most AC are HPV associated. HPV is integrated into the tumor DNA and can be detected in the plasma as circulationg tumor DNA, which has a half life of 2 hours. ctDNA should not be present in patients cured for their cancer. By a highly sensitive multiplex ddPCR we detect all relevant HPV types for AC. Our pilot data showed a significant lead time to clinically detected recurrence in cases from our Danish patients in the DACG-I (PLAN-A study).
The purpose of NOAC 9 is to investigate if circulating pHPV can improve the detection of early treatment failure or recurrence and hereby assist in increasing the potential for cure from chemoradiotherapy for anal cancer.

Materials and methods
A prospective Phase II randomised Nordic multicenter trial comparing standard follow-up with ctDNA guided imaging after SCCA. Inclusion criteria comprise patients with AC eligible for (chemo)radiotherapy,≥ 18 of years, written and oral consen. Randomisation 1.1 to A SOC follow-up, and sampling for biobank or B a pHPV test every 3-4 months. pHPV positive result lead to extra imaging with PET-CT. Negative results lead to SOC program and continued pHPV test. The primary endpoint is the disease-free survival requiring 298 patients. More than 10 Nordic centers in Norway, Sweden, Finland and Denmark are collaborating. Secondary endpoints will provide data on late toxicity, Qol, and a Nordic biobank.

Results
We expect to start inclusion during summer 2021, funded by the DCCC and the Nordic cancer union. The trial will be presented at the International Multidicplinary Anal Cancer Conference (IMACC2021) in Århus, DK.

Conclusion
NOAC9 will show proof-of principle of pHPV guided follow-up after AC and other HPV related cancers.

Clinical trials

#51: Prognostic Relevance of Geriatric assessment and Onco-geriatric Screening In cancer patients age Seventy or more - A randomized controlled trial study protocol (PROGNOSIS-RCT)

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Abstract
Introduction
Frailty in older cancer patients affects quality of life, physical function, and survival. The aim of this study is to evaluate the effect of Comprehensive Geriatric Assessment (CGA) based interventions in older cancer patients screened frail with the G8 screening tool (G8).

Materials and methods
A randomized controlled trial including newly diagnosed patients age 70+ years with solid carcinomas. Patients will be screened for frailty with the G8 at the Department of Oncology at Odense University Hospital. Frail patients (G8≤14) will be randomized 1:1 to either CGA-based interventions or standard of care, along with standardized antineoplastic treatment. Patients are randomized into two separate groups with different primary endpoints depending on initiation of palliative or curative intended antineoplastic treatment.
A geriatrician led CGA with corresponding interventions and clinical follow-up will be conducted at initiation of antineoplastic treatment. The CGA will be a multidisciplinary assessment covering multiple geriatric domains: Medication review, comorbidity, nutritional status, physical function, functional status, cognition, mood, fall risk, and social support. The CGA will be conducted using a standard set of validated assessment tools.
Primary endpoints are physical function at 3 months measured with the 30-sec Chair-Stand-Test (palliative setting) and unplanned hospital admissions at 6 months (curative setting). Additional outcome measures include Quality of Life, treatment toxicity and adherence, and 1 year survival.

Results
Inclusion began November 1st, 2020 and is ongoing. 134 (palliative) and 188 (curative) patients will be enrolled, of which 37 and 29 patients have been recruited April 15th, 2021.

Conclusion
This study will provide knowledge concerning the role of CGA as a supplement treatment for frail older patients with cancer and may contribute towards developing national guidelines for incorporating CGA in oncology settings.

Clinical trials

#52: Intraoperative digital breast tomosynthesis (DBT) of lumpectomy and its impact on reoperation rate in breast conserving surgery

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Abstract
Introduction
Breast cancer is the most common type of cancer among women in Denmark, and most of the patients are treated surgically with breast conserving surgery (BCS). The main challenge during BCS is to remove the invasive breast cancer, obtaining negative resection margins, and at the same time maintain cosmesis. Consequently, 17%-30% of the patients will need a repeat surgery due to positive margins with invasive tumor or Ductal Carcinoma in Situ (DCIS) at final histopathology. We aim to evaluate the resection margins with a new radiological method, Digital Breast Tomosynthesis (DBT) that performs 2D imaging with a series of 1 mm thin slices of the lumpectomy. Our primary outcome is to investigate, if DBT can improve the likelihood of obtaining negative resection margins during BCS and thereby reduce the need of repeat surgery. The secondary outcome is to evaluate the diagnostic accuracy of DBT predicting resection margin status during BCS.

Materials and methods
We are recruiting 250 breast cancer patients in a randomized study at a breast care unit at Aarhus University Hospital. Patients are randomized preoperatively to receive either DBT or standard one view radiography of the lumpectomy. During BCS, a breast radiologist will evaluate if the resected margins are positive or negative. Radiological data will be compared to final histopathology as a reference. The re-operation rate in the DBT- and the radiography group of patients will subsequently be compared.

Results
As of 23rd April 2021, we have included 112 primary breast cancer patients. Data collection is ongoing and under evaluation.

Conclusions
Repeat breast surgery is associated with high surgical risks, poorer cosmetic outcome, and increased psychological and economic burden. The need for re-resection is determined post-operatively from the final histopathological findings. Describing a robust radiological method during BCS that predicts accurate resection margin status is therefore desirable.

Clinical trials

#53: ProWide - Patient reported outcomes used for weekly internet-based detection of progressive disease in lung cancer: preliminary findings of an ongoing national randomized controlled trial

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Abstract
Introduction
Remote symptom-monitoring may improve clinical outcomes in patients with lung cancer. We hypothesise that a proactive approach to patient-reported outcomes improves symptom-control and timely detection of disease progression. In a national randomised controlled trial, we aim to evaluate if remote electronic symptom-monitoring improves overall survival in a Danish context.

Materials and methods
Eligibility criteria are lung cancer, stage III-IV disease treated with palliative intent, performance status ≤2, internet access and non-progressive disease after completed induction treatment. Maintenance therapy is allowed. Patients are randomised to weekly symptom-monitoring as a supplement to standard of care follow-up (intervention arm) or standard of care follow-up (control arm). In the intervention arm, patients weekly complete a 14-item questionnaire on a homepage. The software is programmed to notify a nurse when a symptom exceeds a predefined severity threshold. If symptoms indicate disease progression, a CT scan is performed as soon as possible. Supportive care is adjusted according to the symptom reports. Primary outcome is overall survival.

Results
Since September 2018, 437 patients have been enrolled (target sample=492). Eight of ten Danish oncology departments participate. Most common reason for not meeting inclusion criteria is insufficient access to IT solutions (n=122, 46%). Recruitment rate is 73%.
Of 203 patients allocated to the intervention arm, 193 (95%) started the intervention. In total, 18 (9%) patients have prematurely left the trial. In the intention-to-monitor population, overall weekly compliance is 80% and biweekly 84% resulting in a total of 5,630 completed symptom reports.

Conclusions
The study set-up is feasible. The intervention has the potential for improved follow-up of patients with lung cancer and will provide the base for a possible future implementation of PRO-based symptom-monitoring. Final results are awaited in 2022.

Clinical trials

#54: DBCG-IMN: Long-term survival gain with internal mammary node irradiation to breast cancer patients

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Abstract
Introduction
The Danish Breast Cancer Group Internal Mammary Node study (DBCG-IMN) demonstrated improved 8-year overall survival with internal mammary node irradiation (IMNI) in patients with early node-positive breast cancer. Here, we present long-term results from the DBCG-IMN cohort.

Patients and methods
This nationwide, prospective cohort study allocated patients with early, node-positive breast cancer to adjuvant radiotherapy +/- IMNI depending on cancer laterality. Patients with right-sided cancer received IMNI. Patients with left-sided cancer were treated without IMNI due to risk of radiation-induced heart disease. Other treatment was independent of laterality. The primary study end-point was overall survival. Secondary end-points were distant recurrence and breast cancer mortality. Analyses were by intention to treat.

Results
During 2003-2007, 3,089 women were allocated to IMNI (right-sided, n=1,491) or no IMNI (left-sided, n=1,598). With 14.8 years median follow-up, 589 patients with and 701 patients without IMNI had died. The corresponding 15-year OS rates were 60.1% and 55.4%. The adjusted hazard ratio (HR) for death was 0.86 (95% CI, 0.77 to 0.96; P = 0.007) in favor of IMNI. The 15-year risk of developing distant recurrence was 35.7% (526 recurrences) and 38.6% (602 recurrences) with vs. without IMNI (adjusted HR 0.88 (95% CI, 0.79% to 1.00%; P = 0.04)). The 15-year breast cancer mortality with IMNI was 31.7% (467 deaths from breast cancer) compared to 33.9% (537 deaths from breast cancer) without IMNI (adjusted HR, 0.88 (95% CI, 0.78% to 1.00%; P = 0.05)). The distribution of other deaths was similar across groups.

Conclusions
In patients with node-positive early breast cancer treated with IMNI or not depending on breast cancer laterality, IMNI reduced the risk of distant recurrence and death from breast cancer, thereby improving long-term survival.

Clinical trials

#55: Impact of integrative open dialogue about complementary alternative medicine. A phas II randomized controlled trial

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Abstract
Introduction
Increasing rates of cancer patients use complementary alternative medicine (CAM) as an adjunct to conventional treatment. CAM may reduce the symptom burden of antineoplastic treatment but also cause new side effects and non-adherence to conventional treatment. To ensure patient safety and high quality care, it is crucial to integrate open dialogue about CAM between health professionals and patients in daily oncology care. The best method for integrating open dialogue about CAM is, however, not established. Thus, we investigated the impact of an integrative open dialogue about CAM (IOD-CAM) on patients´health, quality of life and well-being.

Material and Method
This phase II, parallel group, randomized controlled trial compared IOD-CAM with standard care (SC). Patients were randomly assigned to standard care (SC) plus IOD-CAM or SC alone. A nurse specialist facilitated IOD-CAM in 1or 2 sessions. Primary endpoint was frequency of grade 3-4 adverse events (AE) eight weeks after enrollment. Secondary endpoints were frequency of grade 1-4 AE, quality of life, psychological distress, perceived information, attitude towards and use of CAM 12 and 24 weeks after enrollment. Survival was analyzed post-hoc. The study was prospectively registered with ClinicalTrials.gov (NCT03857776).

Results
Fifty-seven patients were randomized to IOD-CAM and 55 to SC. No significant difference in frequency of grade 3-4 AEs was shown 8 weeks after enrollment. The same applied to grade 1-4 AE and quality of life, psychological distress, and perceived information 12 and 24 weeks after enrollment. A tendency towards better emotional quality of life, improved survival, and lower level of anxiety was found in the IOD-CAM group.

Conclusion
IOD-CAM is not superior to SC in reducing frequency of AE. It may reduce psychological stress, and improve quality of life and overall survival. Further research on the effect of IOD-CAM on emotional well-being and overall survival is warranted.

Clinical trials

#56: DaBlaCa-16: Randomized controlled trial with a modified urinary conduit to lower strictures after radical cystectomy – the MOSAIC-study

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Abstract
Introduction
In Denmark, 400 patients undergo a cystectomy annually. In connection with the cystectomy, a urinary diversion is constructed; most often using an ileal segment.
Long-term complications after cystectomy and urinary diversion are increasing due to improved cancer care and higher survival rates. A total of 15% of cystectomized patients experience strictures of the ureteroenteric anastomosis, which leads to an increased risk of infections, loss of renal function, and repeated surgical interventions. The left ureter is affected in 70% of all the incidents, presumably due to the typical ileal conduit with retrosigmoid transposition of the left ureter.
A new modified ileal conduit has been compared with the conventional diversion 'ad modum Bricker' in two small retrospective studies. The modified conduit is constructed with prolongation of approximately 5 cm of ileum compared to the typical diversion. This allows the conduit to be extended in a retrosigmoid fashion from the left to the right side of the abdomen. Thus, the left ureter is less mobilized and the distal part of the ureter is resected more, which is thought to be important to prevent stricture formation.

Materials and methods
This study is a randomized controlled trial where patients undergoing cystectomy are randomized between the modified conduit and the conventional ileal conduit 'ad modum Bricker'. The study will include 300 patients from all five centers performing cystectomy in Denmark. Primary endpoint is the rate of ureterenteric strictures, and secondary endpoint is both surgical complications and renal function within 24 months.

Results
We hypothesize a decrease of left sided ureteral strictures from 15% to 5%, but results are still pending.

Conclusion
If our hypothesis is confirmed, the modified urinary diversion would lead to lower rates of benign ureteral strictures following radical cystectomy for bladder cancer with huge benefits for the clinician and more importantly, the patients.

Clinical trials

#57: Adjuvant Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) during laparoscopic resection of high-risk gastric cancer: Preliminary results of a multicentre phase-I study (PIPAC-OPC4)

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Abstract
Introduction
Patients with gastric adenocarcinoma (GAC) are often diagnosed with advanced disease with poor prognosis even after curative treatment. The peritoneum is the most frequent site of metastases/recurrences, but only a small fraction of systemic chemotherapy reaches the peritoneum. Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) delivers chemotherapy directly into the abdominal cavity as aerosol under pressure and the response in patients with peritoneal metastases is encouraging. We hypothesize that PIPAC may also be effective in the adjuvant setting. The aim of this study is to investigate the feasibility and safety of PIPAC after resection in high-risk GAC patients.

Materials and Methods
20 patients with high-risk GAC are included at Odense University Hospital and Karolinska University Hospitals to a prospective, multicentre, non-randomised, non-blinded, open-label, phase-I study. Primary outcome is the number of patients with medical adverse events (AEs) according to Common Terminology Criteria for Adverse Events (CTCAE) and surgical complications according to Dindo-Clavien, evaluated 30 days after surgery. PIPAC is considered safe and feasible if <20% of the patients have serious complications (Dindo-Clavien≥3b or CTCAE≥4). PIPAC
is performed with cisplatin and doxorubicin directly after the completion of the laparoscopic D2 gastrectomy. Peritoneal lavage cytology is done before and after gastrectomy / PIPAC.

Results
10 GAC patients were included from Feb. 2020-March 2021. Six patients were excluded due to peritoneal metastases found during surgery. Four patients completed neoadjuvant chemotherapy, surgery, PIPAC and follow-up. The patients were discharged after 6 days (range 6-7) and no surgical or medical complication occurred.

Conclusion
Preliminary data imply that adjuvant PIPAC during laparoscopic resection of high-risk GAC is safe and feasible. The study's relevance is emphasized by the fact that 60% had peritoneal metastases at the time of surgery.

Clinical trials

#58: PROPHYLACTIC AND THERAPEUTIC BREAST RECONSTRUCTIVE PROCEDURES A prospective study on optimization of breast reconstruction and quality of life

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Abstract
Introduction
Complication rates related to breast reconstruction are as high as 40%. However, these rather high rates of complications may be considerably lowered by applying newer imaging modalities such as Indocyanine Green Angiography (ICG-A). Surgical complications can delay adjuvant treatment, which may be associated with decreased survival.
The present PhD-study aims to prospectively study a new imaging modality´s impact on breast reconstruction and how this approach may reduce and prevent the incidence of per- and postoperative complications.

Methods
Three prospective studies investigating breast reconstructive surgery using peroperative ICG-A and the clinical impact of real-time tissue perfusion. Primary outcomes: localizing source vessels in the breast reconstructive tissue. Incidence of surgical complications and time to uneventful healing. Secondary outcomes: Patient satisfaction and quality of life, scar assessment, timely administration of adjuvant therapy and risk of developing lymphedema.

Results
We enrolled 94 patients. All patients attended followed-up 4 weeks, 4-6 months and 12 months postoperatively, conducting >200 visits in the outpatient clinic. A systematic review and meta-analysis on the primary research in question and a narrative review on the intraoperative use of ICG-A was completed and published.

Conclusion
This PhD-study will add significantly to the current knowledge optimizing surgical treatment of breast cancer at the Department of Plastic Surgery and Department of Breast Surgery Rigshospitalet. The results may also provide the breast cancer patients with evidence-based new treatment modalities preventing late-effects of the treatment and institute adjuvant therapy within the appropriate time frame. In time, the results from the present studies will yield valuable information regarding the possible benefits of breast reconstructive procedures in a truly multidisciplinary setting, including all aspect of breast cancer treatment.

Clinical trials

#59: Can 15O-H2O PET/MR and circulating tumor DNA safely select bladder cancer patients for a bladder sparring approach?

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Abstract
Introduction
The standard treatment of muscle invasive bladder cancer (MIBC) is cystectomy. Recent results regarding the current Danish practice with 4 series of neoadjuvant chemotherapy (NAC) have shown that 50¬–60% of all MIBC patients undergoing NAC before cystectomy are histopathological without residual tumor in the cystectomy specimen. Currently, there is no optimal method to evaluate whether the patient is T0 or has residual tumor in need for consolidating radical treatment.
This study aims to investigate if a combination of 15O-H2O PET/MR and urine circulating tumor DNA (ctDNA) measurements can predict complete response to NAC in patients with MIBC and thereby identify potential candidates for organ preservation.

Materials and methods
This is a prospective, explorative, single arm, non-randomized clinical trial that will enroll 54 patients from AUH with localized MIBC and fit for NAC and cystectomy. Prior to cystectomy, patients will undergo one 15O-H2O PET/MR scan before NAC and one after completion of 4 series of NAC.
Before, during, and after NAC, consecutive blood and urine samples will be analyzed for presence and changes in ctDNA levels by exome sequencing and digital droplet PCR. Results obtained from 15O-H2O PET/MR, ctDNA analysis, and pathological and clinical outcome data will be correlated.
We expect that 50% of all patients will have complete local response estimated by histopathology. In these patients, we expect 15O-H2O PET/MR to identify 90% of all as complete response based on reduction in tumor blood flow and structural changes. We expect 50% of patients without complete local response, to have positive ctDNA following NAC.

Results
Start of recruitment: May 2020 – status: 16/54 pts.

Conclusions
This study will be the first to use 15O-H2O as tracer in bladder cancer. If proven efficient, evaluation of patients undergoing NAC with 15O-H2O PET/MR and ctDNA could potentially safely select patients for a true bladder sparring approach.

Clinical trials

#60: Sentinel lymph node mapping in early-stage cervical cancer – a national prospective multicenter trial on accuracy and late effects (SENTIREC CERVIX)

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Abstract
Introduction
Sentinel lymph node (SLN) mapping may replace staging radical pelvic lymphadenectomy in women with early-stage cervical cancer. In a national multicenter setting, we evaluated SLN mapping in women with early-stage cervical cancer and investigated the accuracy of SLN mapping in tumors >20 mm. Further, we evaluated the rate and severity of lymphedema using patient-reported outcome measures (PROMs).

Materials & Methods
We prospectively included women with early-stage cervical cancer from Mar 2017-Jan 2021 to undergo SLN mapping. Women with tumors >20 mm underwent completion pelvic lymphadenectomy. We determined SLN detection rates, the incidence of nodal disease, sensitivity, and negative predictive value (NPV) of SLN mapping. The rate and severity of lymphedema were evaluated using four validated PROMs before surgery and three months postoperative.

Results
We included 245 women, and 38 (15.5%) had nodal metastasis. The SLN detection rate was 96.3% (236/245), with 82.0% (201/245) bilateral detection. In a stratified analysis of 103 women with tumors >20 mm, 27 (26.2%) had nodal metastases. The sensitivity of SLN mapping adhering to the algorithm was 96.3% (95% CI 81.0-99.9%) and the NPV 98.7% (95% CI 93.0-100%). A total of 200 women completed the baseline and the three-month questionnaires. The rate of lymphedema was 7.3% in 111 women who underwent SLN mapping alone and 31.8% in 89 women who underwent completion pelvic lymphadenectomy ($p < 0.001$). Lymphedema was significantly associated with a lower quality of life (QoL) three months postoperative in nine of 24 QoL domains.

Conclusions
Our results suggest that SLN mapping is a reliable method in women with early-stage cervical cancer. However, until oncological safety is established, we recommend completion pelvic lymphadenectomy in women with tumors >20 mm. SLN mapping alone leads to a significantly lower rate of lymphedema, and lymphedema is associated with lower QoL in several domains.

Clinical trials

#61: Prospective Surveillance for Breast Cancer-Related Lymphedema: A Multicenter Randomized Controlled Trial

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Abstract
Introduction
Breast cancer-related lymphedema (BCRL) continues to be a major problem which negatively impacts survivors' mental and physical well-being. In Denmark, there is no streamlined approach for measurement and management of BCRL likely due to a paucity of evidence into effective, scalable and accessible surveillance programs. This trial will establish the efficacy of prospective surveillance and early intervention on the development of chronic BCRL.

Material and methods
This is a multicenter trial of patients at high-risk for BCRL comparing the outcomes of the prospective surveillance program (PS) vs usual care (UC). All patients booked for breast cancer surgery are screened for eligibility. Patients with axillary lymph node dissection (ALDN) are at high-risk for BCRL and randomized to PS or UC, while patients without ALND form a low risk cohort. All participants are assessed with bioimpedance spectrography and self-measured arm circumference (CIR) at pre-surgery and 24 months post-surgery. In addition, the PS group perform self-measured arm CIR at home every three months. When ≥6% arm volume increase or symptoms of BCRL is evident, PS participants are referred to lymphedema therapists and provided with at fitted compression garment. The primary outcome is prevalence of chronic BCRL at 24-months post-surgery.

Results
Recruitment is ongoing at the University Hospitals in Aarhus, Odense, Roskilde, Herlev and Rigshospitalet. Since January 2021, a total of 148 patients have been included. Of these, 14 and 14 are randomized to PS and UC, respectively.

Conclusion
Development and testing of evidence-based self-management programs is imperative to reduce the number of women who develop chronic BCRL. It has significant value to identify BCRL early and thereby potentially prevent the progression to avoid irreversible changes that require life-long management with the subsequent physical, emotional, and financial impact.

Clinical trials

#62: Association between Health-related Quality of Life and Completion of First-line Treatment among Lung Cancer Patients - a PACO 2 study

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Abstract
Introduction
Studies have shown that QOL is associated with cancer survival and many experts recommend including an assessment of patients QOL in the diagnostic evaluation. We investigated the association between QOL and lung cancer-related symptoms with the completion of planned first-line oncological treatment among newly referred lung cancer patients.

Materials and methods
Newly referred lung cancer patients from the Oncology Department at Herlev University Hospital, Denmark, participated in the PACO 2 study. Information about completion of planned first-line treatment and clinical variables such as stage and comorbidity was obtained from medical records. QOL and lung cancer-related symptoms was assessed using self-reported EORTC quality of life (QLQ-C30) questionnaire and the associated lung cancer module (QLQ-LC13). Logistic regression analysis was used to test the association between QOL and completion of first-line treatment.

Results
A total of 137 patients, of whom 71 (52 %) were men, participated in the study. The mean age was 69 years, most patients were married (62 %), earlier smokers (73 %) and 43 % of the patients had two or more comorbidities. Most patients had a medium (36 %) or long education (38 %). About half of the patients (54 %) completed the first-line treatment as planned. Patients with higher physical function (OR 5.00; 95% CI: 1.80-15.46), role function (OR 4.40; 95% CI: 1.66-12.84), emotional function (OR 3.77; 95% CI: 1.42-10.55) and social function (OR 2.97; 95% CI: 1.03-9.18), as well as patients with less fatigue (OR 6.53; 95% CI: 2.32-21.03), pain (OR 5.45; 95% CI: 1.53-23.72), appetite loss (OR 3.67; 95% CI: 1.09-13.78) and dyspnea (OR 3.09; 95% CI: 1.06-9.60) were more likely to complete first-line treatment.

Conclusion
QOL and cancer-related symptoms were associated with completing first-line treatment. An assessment of QOL should be part of the diagnostic evaluation of lung cancer patients.

Clinical trials

#63: First results from NIMBUS: the Danish network for quality assurance of MR images used in radiotherapy

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Abstract
Introduction
It is known that MRI is not as geometric accurate as CT. In MRI-guided RT, this can have implications for the accuracy of dose delivery. MRI is available in all RT facilities in Denmark and to monitor image quality, a national network for QA of MR images in RT (NIMBUS) was founded in 2018. The network aims to assess and improve image quality across all centers and to secure image quality in national clinical trials. In this study, the geometric accuracy of different MR scanners in eight centers was evaluated.

Materials and methods
Centers were contacted through the first NIMBUS MRI QA workshop. A general MRI sequence (3D T1W GRE) was used to test geometric accuracy, with adjustments to accommodate field strength differences at each center. A large field of view phantom (Magphan RT 820) was used in a traveling-phantom audit for all acquisitions. Distortion analysis of the MRI scans was performed with web-based software (Smári). The analysis output was distortions as a function of distance to iso-center as well as max distortions.

Results
Seven of eight RT centers and one radiological department participated in this study. In total, eight MRI scanners and two MR-linacs were evaluated.
All max distortions were below 0.43 mm within 200 mm from the iso-center of the scanner and below 1.2 mm within 350 mm, except for one 1.5 T MRI scanner with levels of 1.8 and 6.4 mm, respectively. No dependency on field strength was seen for the reported distortions.

Conclusion
In general, nine of ten scanners showed acceptable max distortions below 0.5 mm within 200 mm from the iso-center of the scanner. The reason for the high level of distortion of the MRI scanner at one center has not yet been found, but the detection of an outlier proves the value of the national collaborative MRI quality assurance network. The next steps include analysis of clinical MRI sequences, other image quality metrics, and a web-based QA system for monitoring.

Clinical trials

#64: Navigate – Improving survival in vulnerable lung cancer patients through nurse navigation: a multicenter randomized controlled trial

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Abstract
Introduction
Comorbidity, poor physical health and limited psychosocial resources may challenge treatment adherence and contribute to social inequality in lung cancer survival. In this study we test the effect of the Navigate intervention on one-year overall survival, treatment adherence and health-related quality of life among vulnerable lung cancer patients.

Materials and methods
In a multicenter two-armed randomized (1:1) controlled trial, we will evaluate the effect of the Navigate intervention comprising nurse navigation, systematic monitoring of patient-reported outcomes (PROs) and exercise therapy compared with standard care. The nurse-navigator will support patients in treatment adherence and exercise therapy using motivational interviewing and initiate appropriate actions to key alert PROs. Eligible patients must fulfill criteria for vulnerability according to a study specific screening instrument. Inclusion will begin September 2021 and we aim to enroll 518 vulnerable lung cancer patients >18 years diagnosed with non-small cell lung cancer (all stages) and performance status <2. The primary outcome, one-year overall survival and the secondary outcomes, treatment adherence, and health-related quality of life will be evaluated at 12 months using Cox proportional hazards models and mixed-effects models respectively.

Results and conclusions
This is the first RCT to test the effect of an intervention specifically targeting vulnerable lung cancer patients. If the results are positive, Navigate will provide a new model for patient-centered care for vulnerable lung cancer patients. We hope to take the first important steps towards reducing inequality in lung cancer care by giving vulnerable lung cancer patients a greater possibility to achieve similar treatment outcomes as more resourceful patients.

Clinical trials

#65: DaBlaCa-15: SURVEILLANCE OF HIGH GRADE NON-MUSCLE INVASIVE BLADDER CANCER USING XPERT® BLADDER CANCER MONITOR – SEALS XPERT

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Abstract
Aim
To investigate if the urinary biomarker 'Xpert® Bladder Cancer Monitor' can replace cystoscopy in the follow-up of patients with non-muscle invasive bladder cancer (NMIBC)

Background
The gold standard of follow-up of NMIBC is urine cytology and cystoscopy, but this is expensive, can lead to urinary tract infections, and is in itself an unpleasant investigation. Methods of detecting cancer molecules in urine samples as a non-invasive and comfortable alternative are currently being developed. In order not to miss recurrences, a urinary biomarker test needs a high sensitivity and negative predictive value. The 'Xpert® Bladder Cancer Monitor' is a urinary biomarker that detects five mRNA targets often expressed in NMIBC. The test has shown promising results in preclinical trials.

Materials and method
Patients are included in a multicentre two-arm randomized non-inferiority clinical trial at 7 Danish urological outpatient clinics. Patients with previous high-grade NMIBC undergoing cystoscopy and cytology in an outpatient setting and with no recurrence of NMIBC will be randomized 1:1 in the trial arms. Patients in the interventional arm will have cystoscopies replaced with the 'Xpert® Bladder Cancer Monitor' test. Patients in the control arm will follow the clinical guidelines for follow-up of NMIBC. The primary outcome of interest is recurrence-free survival and secondary outcomes are progression-free survival, quality of life, and health care cost.

Results
Currently, 255 patients out of 392 patients have been included and randomized (trial started in November 2019). The interim safety analysis is planned to be finished early summer 2021 after 1 year follow-up of the first 120 patients.

Conclusion
Conclusions are pending further results.

Clinical trials

#66: DACG II - Bone-sparing chemoradiotherapy for anal cancer - A prospective phase II trial.

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Abstract
Background
Chemoradiotherapy (CRT) is the primary treatment modality for anal cancer (AC) and implies a high dose to the primary tumor and lymph node areas in the pelvis. Treatment planning is guided by prioritizing the target and constraints to the organs at risk (OAR), traditionally dose levels to the bowel, bladder and femoral heads. Although it has been observed that the pelvic bones react to radiotherapy, there is a lack of data on the consequences of pelvic insufficiency fractures (PIF), and subsequent limited focus on protecting the bone structures.
This study is a prospective clinical trial of bone sparing treatment planning in AC patients. We seek to lower the risk of PIF, while adhering with the constrains to the bowel, bladder and other conventional OAR, and finally to describe the fraction of PIFs in patients treated with IMRT or VMAT techniques.

Materials and methods
Study design: A prospective phase II Danish multicenter (Århus, Herlev and Vejle) trial
investigating the optimal bone-sparing CRT option for patients with localized AC. The calculated sample size is n=85.
Inclusion criteria: Patients with biopsy verified localized AC eligible for definitive CRT, ≥ 18 years, written and oral consent. Exclusion criteria: previous pelvic radiotherapy, previous systemic therapy with severe bone marrow suppression or haematological diseases, hip-replacement, contraindications to magnetic resonance imaging (MRI) scan.
Objectives and endpoints: The primary objective is a reduction of PIF from 50% to 35%. The primary endpoint is rate of MRI proven PIF at 1 year. Multiple secondary endpoints include rate of PIF at 3 years, late toxicity to normal tissue in the pelvic area, quality of life and patient reported outcomes, and biomarkers.

Results
The study is a trial in progress, with expected start of inclusion during summer 2021.

Conclusion
DACG II will hopefully lead to a new standard in planning bone-sparing radiotherapy for patients with anal cancer.

Clinical trials

#67: Value of regular endosonography and [18F]fluorodeoxyglucose PET-CT surveillance after surgery for gastro-oesophageal junction, stomach or pancreatic cancer

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Abstract
Introduction
Most patients undergo follow-up after surgery for cancers of the gastro-oesophageal junction, stomach or pancreas, but data to support which modalities to use and the frequency of investigations are limited.

Methods
As part of the EUFURO study, 183 patients were randomized to either visits to the outpatient clinic at 3, 6, 9, 12, 18, and 24 months after surgery (standard), or to the addition of [18F]fluorodeoxyglucose PET/CT and endosonography (EUS) with fine-needle aspiration biopsy to clinical assessments (intervention). Data from the intervention arm were used to analyse the diagnostic performance of EUS or PET/CT in detecting recurrences.

Results
During the scheduled follow-up, 42 (47%) of 89 patients in the intervention arm developed recurrence; PET-CT and EUS in combination detected 38 (90%) of these recurrences. EUS detected 23 (55%) of the 42 patients with recurrent disease during follow-up and correctly diagnosed 17 (89%) of 19 locoregional recurrences. EUS was able to detect isolated locoregional recurrence in 11 (85%) of 13 patients. In five patients, EUS was false-positive for isolated locoregional recurrence owing to missed distant metastases. PET-CT detected 33 (79%) of the 42 recurrences, while locoregional recurrence where detected in 12 (63%) of 19 patients, and isolated locoregional recurrence in only seven (54%) of 13. 23 falsepositive PET/CT led to 44 futile procedures. Detection of asymptomatic isolated locoregional recurrence led to 9 (69%) patients were treated with secondary curative attempt with either high dose radio- chemotherapy (>50Gy) in five patients, or chemotherapy followed by re-resection in four.

Conclusion
Accuracy in detecting recurrences by concomitant use of PET-CT and EUS was high (90%). PET-CT had moderate to high sensitivity for overall recurrence detection, but low specificity. EUS was superior to PET-CT in the detection of locoregional and isolated locoregional recurrences.

Clinical trials

#68: Conventional skeletal survey versus Whole-body CT for osteolytic lesions in multiple myeloma - a prospective study.

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Abstract
Introduction
Multiple Myeloma (MM) is a bone marrow cancer with frequent osteolytic disease. Evaluating bone involvement is essential as it is an important criterion for starting treatment. For many years conventional skeletal survey (CSS) has been used but based on retrospective data The International Myeloma Working Group now recommends using Whole Body CT (WBCT). This study compares CSS to WBCT at baseline and prospectively for finding progression of bone involvement.

Materials and methods
96 MM patients at Odense University Hospital and Stavanger Hospital were followed for up to
4 years. Patients were scanned every year for the first 2 years and every 6 months thereafter or if suspicion of bone disease was raised. progressive bone disease was defined as new lesions of at least 5 mm or growth of lesions by at least 5 mm. For evaluation paired t-test and McNemars exact test was used.

Results
534 investigations (267 pairs) were evaluated. WBCT consistently found more bone lesions pr patient 8.2 CI (6.8;9.6) vs CSS 3.6 CI (2.7;4.5). The additional lesions found by WBCT were primarily in the axial skeleton while there was no difference, in the skull. In the extremities a few more lesions were found on CSS 0.40 CI (0.2-0.5) vs WBCT 1.80 CI(1.1;2.4). 23.6% CI (20.6;26.6) of patients had a negative CSS and a positive WBCT (P<0.0001)
Over the period a total of 19 cases of progressive bone disease (PBD) was found with 20 new lesions and 3 growing lesions found on WBCT vs 8 cases with 8 new lesions on CSS (P<0.001). The cases not found on CSS were primarily in the spine, sternum, and pelvic region. There were no cases of PBD on CSS not found on WBCT.

Conclusions
WBCT consistently outperformed CSS for finding osteolytic lesions. This supports the current recommendation for using WBCT for skeletal evaluations. Significantly more new lesions were found during follow-up by WBCT compared to CSS suggesting that using only CSS is likely to underestimate progression rates.

Clinical trials

#69: DAHANCA 33: A phase II, multi-center study of dose escalated radiotherapy guided by functional imaging for patients with hypoxic head and neck squamous cell carcinoma

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Abstract
Introduction
Hypoxic cancer cells within a tumor have been shown to be resistant to radiation. This could lead to an increased risk of treatment failure in tumors treated with primary radiotherapy (RT). Hypoxic tumor areas can be visualized with PET imaging and hypoxia-sensitive tracers e.g. 18F-flouroazomycin arabinoside (FAZA). These resistant cancer cells can be targeted by increasing the dose to tumor volume.
The main purpose of the study is to demonstrate improved curability with dose escalated radiotherapy in locally advanced HNSCC patients identified by hypoxic FAZA PET scans.

Methods
The study is an open, prospective, experimental single-arm, phase II multi-center study with a planned inclusion of 60 patients with stage III-IV squamous cell carcinoma of the larynx, pharynx or oral cavity. Inclusion only of p16-negative tumors, if originating from the oropharynx. Patients must be eligible to undergo treatment with hyperfractionated, accelerated radiotherapy (HART: 76 Gy in 56 fractions, 2 fractions daily), concomitant hypoxic cell sensitizer nimorazole with or without low-dose cisplatin. A FAZA PET scan is carried out as part of radiotherapy planning. Patients with PET-visualized hypoxia within the primary tumor receive dose escalated, intensified radiotherapy with HART, nimorazole and weekly cisplatin. The dose is escalated to the entire target volume.
The primary endpoint of the study is locoregional failure defined as persistent or recurrent disease in the tumor or regional lymph nodes. Elective neck dissection is not allowed. Secondary endpoints are: overall survival, disease-specific survival, acute and late treatment-related morbidity.

Preliminary results
As per April 28th 2021, a total of 45 patients are enrolled, and a hypoxic sub-volume is identified within tumors of 71% of patients. The study continues to actively recruit patients.

Trial registration: Registered on ClinicalTrials.gov with Identifier NCT02976051.

Clinical trials

#70: Pre- and on-treatment target volume variations for tumor and involved lymph nodes in rectal cancer patients.

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Abstract
Introduction
Developments in rectal cancer treatment has increased the demands on treatment delivery accuracy. While day-today variation in tumour position has been studied, corresponding data are needed for individual involved lymph nodes (GTV-N). This study examined variations in the position of the GTV-T and GTV-N on repeat MRI-scans before and during RT.

Materials and methods
The study was based on interim data from an ongoing clinical trial (AMPERE, NCT03619668), where patients are MRI scanned three times before RT (on separate days) and three during RT (after one, two and four weeks of RT). GTV-T and one GTV-N were delineated on all scans. The scans were co-registered (rigid bone match) to the first pre-treatment MRI (baseline). We calculated the center-of-mass (COM) position for each GTV-T and GTV-N, and the distance between COM on each MRI relative to the baseline. Furthermore, the distance between the GTV-T and GTV-N was calculated and compared to the distance on the baseline scan.

Results
The patient population consisted of 10 patients with locally advanced rectal cancer, treated with long course RT (50.4 Gy in 28 fractions). GTV-T was located in the lower rectum in 8/10 patients (two in mid-rectum) and GTV-N within the mesorectum. The mean COM position relative to baseline was 0.33 cm (SD 0.22; range 0.03 – 1.14) for the GTV-T and 0.33 cm (SD 0.20; range 0.06 – 1.00) for the GTV-N. The mean difference in distance from GTV-T to GTV-N relative to baseline was -0.16 cm (SD 0.30; range -0.85 – 0.58); which was numerically larger during treatment compared to pre-treatment (p=0.02). No significant difference was found in the variation of COM for GTV-N compared to GTV-T, nor for pre-treatment versus on-treatment scans.

Conclusions
While both GTV-T and GTV-N exhibited considerable variation in position relative to baseline, this did not differ between the volumes. Shift of GTV-N relative to GTV-T was larger during treatment compared to pre-treatment.

Clinical trials

#71: DACG-I: Towards Improved Chemoradiotherapy for Anal Cancer - Results from the national Plan-A study

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Abstract
Introduction
Anal cancer (AC) is a rare disease with around 200 new cases per year in Denmark. Primary treatment with chemoradiotherapy (CRT) is effective, but to optimize outcome and reduce side effects there is an urgent need for tailored treatment options. The aim of this study was to report the incidence of treatment related side effects and to identify potential predictive and prognostic molecular biological features in AC.

Material
A prospective collection of clinical data including toxicity (NCI-CTCAE v.4.0) and patient reported outcome (PRO) (EORCTQoL-C30, CR29, CX24 and LARS) and a biobank with tissue and blood, collected at baseline, during therapy and at 1, 3 and 5 years follow up from patients treated with CRT in Denmark 2016-2021. The study was conducted with support from DCCC-RT, the Danish Bio-and Genome Bank, and the Danish Cancer Society.

Results
A total of 314 patients were included in the data collection and 88 patients in the biobank collection. Published data on side effects include high acute PRO scores with weak agreement to CTCAE (Kronborg, Radiother Oncol. 2018). One-year PROs captured more symptoms than CTCAE (Kronborg, ESTRO 2020 and WGI 2020) and detected a high incidence of symptomatic, MR verified pelvic insufficiency fractures (Kronborg, ESTRO 2021). The analysis of total level of circulating DNA proved the ability to use a simple method to obtain important patient- and tumor information from the blood (Lefevre, Radiother Oncol. 2020), whereas measurement of HPV tumor DNA during CRT detected clinically relevant elimination patterns with potential to support tailored CRT (Lefevre, submitted 2021). Long term outcome and toxicity data will be mature for evaluation ultimo 2021.

Conclusion
The DACG-I study has provided important information for future tailored treatment in AC. Results will be further investigated in the DACG-II study investigating a bone-sparing treatment planning strategy, and further biomarker studies.

Clinical trials

#72: OPTIMISE - OPTIMIzation of treatment SElection and follow up in oligometastatic colorectal cancer - a ctDNA guided phase II randomized approach

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Abstract
Background
In oligometastatic colorectal cancer (CRC) there is a curative potential from treating a single or few local metastases. Some patients obtain long-term survival, whereas others show an aggressive biological behavior with early recurrence and systemic dissemination despite the use of adjuvant chemotherapy (CT). Due to limited evidence, there is no clear consensus on the use of CT in relation to local treatment. A pilot study demonstrated, that presence of ctDNA in plasma after curative treatment for oligometastatic CRC indicates a poor prognosis. The aim of this study is to investigate the clinical utility of ctDNA analysis to guide treatment decisions in oligometastatic CRC.

Materials and methods
An open label 1:1 randomized phase II exploratory study investigating use of ctDNA-guided therapy compared to standard of care after local treatment for metastatic CRC. Circulating cell free DNA will be analyzed for CRC specific KRAS, NRAS and BRAF mutations by a digital droplet PCR panel and for hypermethylation by a methylation assay. ctDNA positivity will lead to escalation of CT consisting of 4 months of FOLFOXIRI followed by 2 months of 5FU monotherapy. ctDNA negativity will based on shared decision making lead to de-escalation i.e. less or no CT. The study will run in two Danish centers (AUH and Vejle) and be expanded if feasibility criteria are met.

Results
This study will demonstrate the feasibility of patient inclusion, rate of imaging detected residual disease, rate of ctDNA positivity and shared decision making in ctDNA-guided therapy for oligometastatic CRC. It will lead to a larger multicenter, phase II randomized study, investigating the clinical utility of ctDNA-guided treatment.

Conclusion
Oligometastatic CRC can be cured, but with a high risk of recurrence. Currently, clinical indicators for optimal selection of post-treatment CT are missing. In the present study, we investigate ctDNA-guided treatment to optimize use of CT and hereby outcome.

Clinical trials

#73: Can we reduce known BCG side effects by reducing BCG dwell time? A Nordic randomized clinical trial

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Abstract
Introduction
Non-muscle invasive bladder cancer (NMIBC) accounts for the majority of newly diagnosed bladder cancers. Adjuvant treatment in high risk NMIBC is 6 weekly instillations in the bladder with Bacillus Calmette Gurién (BCG) with 9 additional maintenance instillations over the following 12 months. BCG causes a local immune reaction in the bladder where activation of the immune cells kill the tumor cells and prevents recurrence and progression. However, studies indicate that approximately 70 % of all BCG-treated patients experience side effects(SEs). Because of SEs, some patients terminate their planned instillations which can lead to a higher risk of progression.
Previous studies have tried to overcome this barrier by reducing the concentration of BCG with conflicting results. Reducing the time of exposure, “dwell time”(DT), is another theoretical way to reduce SEs. DT has not been systematically investigated before in regards to potential reduction of SEs.

Materials and methods
This project will recruit 314 patient through a Nordic collaboration in four countries. The patients will be randomized 1:1 into an intervention and a control group. All SEs will by registered each day during the instillation weeks with daily questionnaires send on SMS to the patient. Before each instillation, an evaluation is performed, based on the past weeks reported SEs. The first DT for instillation is 2 hours. Hereafter, DT is reduced to 1 hour or 30 minutes for patients in the intervention group that experience SEs, depending on the SEs. Whereas DT in the control group is 2 hours throughout the study.

Results
Inclusion started in March 2021 and so far, 13 of the 314 patients have been included.

Conclusions
We aim to investigate whether reducing DT in patients with SEs will decrease severity of SEs caused by BCG instillations and thereby increase the number of patients completing all planned instillations, postponing and potentially reduce the need for cystectomy.

Clinical trials

#74: DAHANCA 37:Gen-bestråling af hoved-halskræft med proton-strålebehandling (NCT03981068).

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Abstract
Introduktion
Hvis man én gang er strålebehandlet mod hoved-halsområdet er det problematisk at give en ny strålebehandling for et tilbagefald eller en ny kræftknude, pga. risikoen for alvorlige, inklusiv livstruende, bivirkninger. Hvis genbestråling er patientens eneste mulighed for at blive rask, kan strålebehandling med protoner nedsætte den samlede stråledosis til patienten, og måske nedsætte risikoen for alvorlige bivirkninger.

Materialer og metoder
DAHANCA (den Danske Hoved-Halskræft Gruppe) har startet en fase II genbestrålingsprotokol med vide inklusionskriterier. Den oprindelige stråleplan skal være til rådighed således at man kan lave en samlet dosisplan for både den oprindelige og den aktuelle dosisplan. Patienterne diskuteres på en national videokonference før henvisning. Egnede patienter vil blive tilbudt hyperfraktioneret accelereret strålebehandling med 60 Gray på 50 behandlinger, 10 behandlinger om ugen. Det primære endepunkt er alvorlige bivirkninger (CTC grad ≥ 3). Vigtige sekundære endepunkter bliver tumorkontrol, patient rapporterede symptomer og livskvalitet. Det er planlagt at inkludere 20 patienter.

Resultater
Fem patienter, 47-87 år, er behandlet i protokollen siden 1. kvartal 2020. Fire mænd, alle p16 negative, tre stadium IV. Tre yderligere patienter blev diskuteret på videokonference og blev ikke tilbudt behandling i protokollen. Der er ikke rapporteret alvorlige bivirkninger til behandlingen endnu. Generelt er der henvist færre patienter til protonstrålebehandling i 2020 end forventet, og det gælder også denne protokol.

Konklusion
Med de tilgængelige samlede dosisplaner og adgang til strålebehandling med protoner mener vi at kunne tilbyde patienten skånsom strålebehandling. De tidligste erfaringer viser at det er produktivt at diskutere patienterne nationalt, og udvikle mere ens kriterier for patient udvælgelse. Med studiet får vi ny viden om de forventede bivirkninger og den optimale udvælgelse af patienterne.

Clinical trials

#75: Ultralyd elastografi i diagnostiseringen af endetarmskræft – foreløbige data

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Abstract
Introduktion
Kræft i endetarmen er en hyppig forekommende kræftform i Danmark. Ligeledes er der sket et stigning i antallet af tidligere stadier, samt komplekse polypper. Trods fremskridt i diagnosticeringen af endetarmskræft, er det fortsat en vanskelig opgave.
Formålet med dette studie er derfor at undersøge om ultralyd elastografi (hårdhedsmåling) kan benyttes i diagnostiseringen af kræft i endetarmen.

Materialer og metoder
Under udredning for komplekse polypper samt kræft i endetarmen, udføres en transrektal ultralyd. Et nyligt supplement til denne undersøgelse, er elastografi, hvor vævets hårdhed kan måles.
Igennem en 1-årig periode er der indsamlet data fra 89 patienter, der i forbindelse med udredningen af en forandring i endetarmen, har fået foretaget 6 elastografimålinger. Patologisvar er gold-standard. ClinicalTrials.gov Identifier: NCT04409990.

Resultater
Histopatologi identificerede 42 adenomer og 48 adenocarcinomer. Gennemsnitsalderen var 70 år og 60 % var mænd. Elastografi var predictiv for malignitet (P = 0,027). En ROC curve, med en AUC på 0,85, gav en cut-off værdi på 75,5 kPa, med sensitivitet, specificitet samt accuracy på henholdsvis 0,74, 0,90 og 0,82.

Konklusioner
Foreløbige data tyder på at ultralyd elastografi kan hjælpe til diagnosticering af advancerede polypper og kræft i endetarmen.

Clinical trials

#76: Doseescalated pencil beam proton therapy for re-irradiation of pelvic recurrences from rectal or anal cancer - The ReRad II and III studies.

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Abstract
Introduction
The primary treatment of pelvic recurrences from rectal or anal cancer is surgery, and outcome is highly dependent on radical resection.
Re-irradiation can be used either pre-operatively or as a definitive treatment for un-resectable recurrences. To maintain acceptable summed doses to organs at risk (OAR), the most frequent re-irradiation dose is app. 40 Gy. However, for both cancers doses above 50 Gy is associated to better pathological response.
Comparative planning was done to determine if dose escalation with pencil beam proton therapy was feasible for pelvic recurrences.

Materials and methods
Patients included in the ReRad I study (Rectal cancer recurrences, 40.8 Gy, (1.2 Gy BID) were selected for comparative planning, with photons (1 or 2 arc VMAT, Eclipse) and protons (3 posterior field robust IMPT planning, Eclipse v13.7) to 40.8, 55 or 65 Gy(RBE).
Dose to OARs were compared for photon vs. proton plans. Wilcoxon's signed rank test was used for comparison. A p-value≤0.05 was considered statistically significant.

Results
Eight patients were included. Time to re-irradiation was 4.1 years (range: 2.2-6.9) and CTVs ranged from 84 cm3 to 1080 cm3.
Mean Dose to all OARs was lower with 40.8 Gy(RBE) proton vs. 40.8 Gy photon plans. Comparing 55 Gy and 65 Gy(REB) proton plans to the 40.8 Gy photon plan, mean dose to bowel loops and femoral heads was significantly lower despite dose escalation, all $p<0.01$. Mean bladder dose was lower with dose escalations, but only significantly for 55 Gy, $p=0.04$ and $p=0.055$. Mean sacral dose was similar with protons, $p=0.17$ and $p=0.05$.

Conclusions
Dose escalation to 55 or 65 Gy(RBE) for re-irradiation of pelvic recurrences is possible while keeping mean doses to OARs at lower or same levels as 40.8 Gy photon plans. Dose escalated re-irradiation with pencil beam proton therapy will be applied in two prospective phase II trials: ReRad II for rectal cancer recurrences and ReRad III for anal cancer recurrences.

Clinical trials

#77: Effect of patient-reported outcomes as a dialogue-based tool in cancer consultations on patient self-management and health-related quality of life: a clinical, controlled trial

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Abstract
Introduction
With increased survival among patients with metastatic melanoma and limited time with health care providers, patients are expected to become active and thereby develop the knowledge, skills, and confidence to make effective solutions to self-manage health. The use of patient-reported outcomes (PRO) could have the potential to enhance patient activation. However, PRO-based interventions that facilitate an activation in patients with metastatic melanoma are lacking.

Material and methods
In this prospective, non-randomized, controlled, clinical trial, Danish patients with metastatic melanoma were assigned to either the intervention (systematic feedback and discussion of PRO during each consultation for a year) or the control group (treatment as usual) based on geographical affiliation. The primary outcome was the patient activation measure (PAM), which reflects self-management. Secondary outcomes were health related quality of life (HRQoL), self-efficacy, and patient-physician interaction. Outcomes were measured at baseline, and after three, six, and 12 months. The analysis of the effect over time from baseline to 12 months employed mixed-effects modeling.

Results
Between 2017 and 2019, patients were allocated to the intervention group (N=137) or the control group (N=142). We found no significant difference in patient activation between the two groups over time. The course of HRQoL was statistically significantly improved by the intervention compared to the control group over time. The other secondary outcomes were not improved by the intervention.

Conclusion
The intervention did not improve knowledge, skills, and confidence for self-management for patients with metastatic melanoma. Neither did it improve coping self-efficacy nor perceived efficacy in patient-physician interaction. However, the results suggest that the intervention can have a significant impact on HRQoL and in particular social and emotional well-being among the females.

Clinical trials

#78: Feasibility of local proton-photon plan comparison for selection of patients for a national proton trial in head and neck cancer (DAHANCA 35)

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Abstract
Introduction
Proton therapy offers theoretical advantages in reducing morbidity from head and neck cancer radiotherapy compared to standard radiotherapy. However, study designs are challenging as not all patients may benefit from proton treatment. The Danish Head and Neck Cancer Group (DAHANCA) has prepared a randomised trial in an enriched population of head-neck cancer patients aimed at reducing the risk of late dysphagia and xerostomia. The enrichment lies in the plan comparison, where only patients with a normal tissue complication probability (NTCP) reduction in favor of protons can be randomised. The ability to select and refer patients were tested in a feasibility study.

Methods
From June 2019 to December 2020, selected patients with squamous cell carcinoma of the pharynx or larynx at all six Danish head-neck cancer centers were offered proton-photon plan comparison. In case of a pre-specified NTCP reduction in favor of proton treatment for dysphagia (6 months) ≥ grade II (DAHANCA toxicity score) or xerostomia (6 months) ≥grade II (EORTC HN35), the patient was offered proton treatment in Aarhus.

Results
Proton-photon plan comparisons were performed in 141 patients and 71 (50%) patients achieved an NTCP reduction above the clinical goal. In general, most patients were selected based on a reduction in the risk of dysphagia.

Of the 71 patients, 55 (77%) accepted referral to proton treatment. In these 55 patients, the median time from radiotherapy decision to the first proton fraction was 19 calendar days (interquartile range 18-23) and from referral to the national proton therapy center to first proton fraction 9 days (interquartile range 8-11). All patients started proton treatment within the time limits set by the Danish national integrated cancer pathways.

Conclusion
Proton-photon plan comparisons with NTCP modelling at local head and neck cancer centers can be used to select patients for a national proton trial without exceeding time limits.

Clinical trials

#79: Tumor reactivity for patients treated with Nivolumab and Bevacizumab for recurrent Glioblastoma

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Abstract
Introduction
Glioblastoma multiforme (GBM) is an aggressive brain tumor with a median survival is 14.6 months [1]. Novel treatments are necessary to improve survival and especially quality of life.

Methods
We present our translational study; a phase II open label, two-armed translational study of Nivolumab and Bevacizumab for recurrent GBM, who have failed Stupp's regime [1]. Patients are included in two arms depending on the possibility of salvage neurosurgical resection. Both arms receive Nivolumab and Bevacizumab administrated every second weekend, and the surgical arm also receive Nivolumab 7 days prior surgery in order to obtain post-surgical specimens for analysis. Forty-four patients were included by January 2021; 20 in each arm (four screen-failures). In the surgical arm, 20 fresh tumor samples as well as paired tissue from primary tumor were available. Tumor infiltrating lymphocytes (TILs) and tumor digest were produced in vitro from recurrent settings. Young TILs were expanded from fresh tumor fragments after minimal-culture, whereas rapidly expanded TILs (REP TILs) were obtained after massive expansion [2].

Results
We investigated by intracellular cytokine staining the TIL reactivity after exposure to autologous tumor digest in order to evaluate whether the TILs were tumor-reactive or bystanders. Material from 19 patients was analyzed (one out of the 20 collected biopsies was limited in size, and no tumor digest could be produced). Four out of 19 TIL samples showed tumor reactivity after exposure to the autologous tumor digest. Though meaning that 15 patients showed no tumor reactivity.

Conclusions
Tumor reactivity was ranged between 2 tox% in CD8+ TILs and from 10 to x% in CD4+ TILs. Tumor reactivity data from the surgical arm will be further analyzed in relation with the available WES and RNAseq data from biopsies collected before and after Nivolumab. However, these analyses are pending.

Clinical trials

#80: Stereotactic radiosurgery for brain metastases - exploring the limits

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Abstract
Introduction
A 4-year research program within the DCCC Oligo Work Package is underway. We aim to answer key questions including: How effective is stereotactic radiosurgery (SRS) in achieving intracranial disease control? How to deal with recurrent brain metastases (BM)? How to differentiate recurrent BM from treatment related changes? How does BM disease differ across various types of cancer?

Materials and methods
A retrospective database containing all patients treated with SRS for BM between 2008-2019 at Rigshospitalet and Herlev Hospital is being built. Characteristics of patients, BM (including number, size, location, previous surgery) and radiotherapy are registered as well as survival times, patterns of recurrence and salvage treatments. Collaboration with other groups allowing for disease specific in-depth analysis is welcomed.

A national prospective clinical trial named Re-TREAT examining repeated SRS for recurrent BM has been initiated. The primary endpoint is local control, but toxicity and exploratory outcomes including results of advanced imaging (dynamic magnetic resonance imaging (MRI) and positron emission tomography (PET)) will be examined. Forty-four patients will be accrued in a two-year period. Participating centers are Rigshospitalet and the University Hospitals of Herlev, Odense, Aarhus, and Aalborg.

Results
Currently, 1180 patient cases (out of appprox. 1850) have been entered into the database. Non-small cell lung cancer (51%), breast cancer (13%) and metastatic melanoma (7%) were the most prevalent diagnoses. Forty-four percent of patients had proven intracranial relapse following SRS and 20% underwent >1 course of SRS.
The study protocol for Re-TREAT has been approved by the authorities and will open for accrual in May 2021.

Conclusions
Updated results from the database including analyses of efficacy of SRS, survival times and recurrence patterns will be presented. Status of the Re-TREAT trial including case examples will be given.

Clinical trials

#81: Feasibility of three exercise-based randomized controlled trials in older patients with cancer

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On the behalf of the GEPOC, BREACE and PACE-Mobil project groups.

Abstract
Introduction
Exercise in older adults is beneficial for functional independence and quality of life. However, evidence of the effect of exercise and its feasibility in older patients with cancer is scarce. Furthermore, recruiting older patients for exercise-based trials during their cancer treatment may be difficult. The study aim was to investigate preliminary findings on feasibility of an exercise-based intervention for older patients undergoing treatment for cancer.

Materials & methods
Older patients (+65 years) with newly-diagnosed cancer were included in three randomized controlled trials; PACE-Mobil: patients with advanced pancreatic, biliary tract or non-small cell lung cancer in palliative settings; GEPOC: patients with localized colorectal cancer after resection (+/- adjuvant treatment); BREACE: patients with breast cancer in (neo)adjuvant or palliative settings.
For all groups, the intervention comprised a 12-week supervised group-exercise program in hospital setting 2x/week including warm-up, balance and flexibility and progressive resistance training. Adherence to exercise was calculated as the percentage of attended sessions divided by planned sessions.

Results
Median age was 70, 72 and 79 years, for BREACE, PACE-Mobil and GEPOC, respectively. Recruitment rates varied between the studies; PACE-Mobil: 84 of 269 (31%) eligible patients were randomized (study completed); GEPOC 45 of 83 (54%) and BREACE 34 of 110 (31%) eligible patients were included (studies ongoing). Frequent reasons for declining participation were: feeling stressed/weak, transportation challenges or preferred exercising in other settings. Adherence ranged from 67 to 72%. Eight patients experienced adverse events due to exercise, only one hindering completion of the program. Dropout rates in the studies ranged from 16 to 26%.

Conclusions
Engaging older patients in exercise interventions is challenging. However, adverse events were rare and adherence to the exercise intervention was high.

Clinical trials

#82: DAHANCA 30: Et randomiseret non-inferiority studie af hypoxi-profilvejledt nimorazolbehandling i forbindelse med primær strålebehandling af planocellulære hoved-halskarcinomer

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Abstract
Introduktion
Hypoxi er en kendt årsag til stråleresistens ved behandling af hoved-halskræft med stråleterapi. Dette resulterer i dårligere outcome for iltfattige kræftknuder. Nimorazol er en hypoxisk radiosensitizer, som, givet konkommitant med stråleterapi, er vist at reducere stråleresistensen og dermed forbedre stråleeffekten i iltfattige kræftknuder. Præparatet gives i dag til de fleste strålebehandlede patienter med hoved-halskræft, velvidende at det formentlig kun er virksomt hos undergruppen med de mest ilt-fattige svulster. Denne gruppe patienter har man hidtil ikke været i stand til særskilt at identificere. Med en udviklet hypoxi gen-profil tyder det på, at såvel de iltfattige svulster (respondere), som de iltrige svulster (non-respondere) kan udpeges. Ved at undlade brug af nimorazol hos gruppen af non-respondere kan disse patienter spares for bivirkninger til præparatet som hovedsageligt er kvalme og madlede. Formålet med studiet er, at eftervise, hvorvidt gen-profilen kan udpege patienter som skønnes ikke at have gavn af nimorazol under strålebehandling.

Materiale og metoder
Patienter med hoved-halskræft, hvor der i henhold til DAHANCA's retningslinjer er indikation for nimorazol under primær strålebehandling kan inkluderes. Studiet er et randomiseret non-inferiority studie med planlagt
1262 inkluderede og randomiserede patienter. Hos inkluderede patienter foretages hypoxisk profil på deres diagnostiske biopsi. Hvis denne tyder på en iltrig kræftknude, randomiseres til stråleterapi/kemostråleterapi +/- nimorazol. Hvis profilen tyder på en iltfattig kræftknude får patienten standard behandling, dvs. incl. nimorazol.

Resultater
Ultimo 2020 er der 759 inkluderede patienter, hvoraf 536 er randomiserede. Inklusionen i studiet er stigende.

Konklusion
Studiet fortsætter som planlagt. Der er til dato ikke set uventet toksicitet hos de patienter der indgår i studiet.

Clinical trials

#83: Effects of Hyperbaric Oxygen Therapy on soft-tissue mass and lymphatic clearance in patients with breast cancer-related lymphedema

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Abstract
Introduction
Breast cancer-related lymphedema (BRLE) has negative consequences for quality of life and physical function. We aimed to test if Hyperbaric Oxygen Therapy (HBOT) could reduce early stage BRLE.

Materials and Methods
Participants were recruited from a randomized controlled trial (n=158) examining the effect of resistance training after breast cancer surgery in women at high-risk for lymphedema. Participants who experienced BCRL 1 year after surgery, they were invited to participate in a one-arm explorative clinical trial of HBOT. Participants received 40 sessions of 90-minute pressure exposures at 2,4 Bar while breathing 100% oxygen. Lymphedema was measured as inter-limb soft-tissue mass by Dual Energy X-Ray Scans (DXA) and inter-limb lymphatic clearance by lymphoscintigraphy. Patient-reported outcomes for symptoms and function were assessed by validated scales. Statistical analyses included univariate mixed effects models for repeated measurements.

Results
Fifty women from the RCT were eligible, 19 accepted participation and all 19 completed follow-up. Results of analysis on DXA data showed no significant change in arm inter-limb soft-tissue mass (β=2.3 %, 95% confidence interval (CI) -0.23; 4.82). Furthermore, lymphoscintigraphy measures showed no change in inter-limb lymphatic clearance (β=8%, CI -13; 30). We found overall significant and clinically relevant improvements in patient-reported outcomes for symptoms and function.

Conclusions
This explorative trial examined if treatment with HBOT could reduce early stages of BCRL. Preliminary analysis did not show an objectively measured reduction of limb volume or improvement of lymphatic clearance with time in the study, but participants experienced a lower burden of symptoms and less functional limitation after HBOT.

Clinical trials

#84: Circulating tumor DNA for early detection of recurrence and risk-stratification in melanoma

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Abstract
Introduction
This project assesses circulating tumor DNA (ctDNA) for stratification of risk of recurrence and for early detection of recurrence in Danish patients treated for melanoma. We compare ddPCR based ctDNA detection of melanoma specific mutations in plasma, with current gold standard methods for staging and surveillance, including tumor histopathology, sentinel node biopsy and whole-body 18F-FDG PET-CT.

Methods
Study 1: Examines melanoma patients from three hospitals in Denmark, who have a high risk of recurrence and who undergo regular clinical examination and PET-CT scans. Blood sampled at every clinical visit will be examined for ctDNA using ddPCR. Correlation with recurrence or metastasis, detected clinically or with PET-CT will be analyzed.
Study 2: Examines patients from three hospitals in Denmark, newly diagnosed with melanoma in all clinical stages. ctDNA will be measured pre-operatively and 30 days post-operatively. Results will be analyzed for correlation between measurable ctDNA and tumor characteristics, sentinel node status and other known prognostic markers. Economic evaluation will be conducted in order to establish the cost-effectiveness of ctDNA compared to current practice in both studies, should it be shown capable of replacing one or more current methods.
Expected outcome
Study 1: Tests the hypothesis that ctDNA monitoring of high-risk patients results in earlier detection of recurrence at reduced costs compared to PET-CT scans, that entail the use of intravenous contrast agents and ionizing radiation. Study 2: Explores the feasibility of 1) ctDNA based risk evaluation prior to surgery, potentially removing the need for sentinel node biopsy, and 2) ctDNA based detection of minimal residual disease (MRD) following surgery, improving recurrence risk stratification and identifying patients that might further benefit from adjuvant therapy. Economic evaluation will inform whether the use of ctDNA could be cost-effective on a national level.

Clinical trials

#85: OptimalTTF-2: Optimering af Tumor Treating Fields behandling til patienter med første progression af glioblastom med kraniemodelerende kirurgi. Et nationalt, randomiseret og igangværende fase 2 studie

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Abstract
Introduktion
Glioblastom (GBM) er den hyppigste og mest dødelige form for hjernekræft. I Danmark er der ca. 280 nye tilfælde om året. På trods af optimal behandling med kirurgi, stråle- og kemoterapi er sygdommen uhelbredelig og progression er næsten uundgåelig. Gennemsnitsoverlevelsen for ny diagnosticeret GBM og ved første progression (rGBM) er hhv. 14-16 måneder og 6-9 måneder. Der er derfor brug for nye og kreative behandlinger.
Tumor Treating Fields (TTFields) er en ny behandling, hvor elektroder sættes på skalpen og via et bærbart batteri dannes et ufarligt elektrisk felt, der hæmmer kræftcellernes vækst. TFFields har i studier vist lovende effekt på GBM med ~30% øget overlevelse på selekterede patientgrupper med GBM. Vi har udviklet en ny kirurgisk teknik "kraniemodellerende kirurgi" (KM-kirurgi) til at forbedre effekten af TTFields. Ved nøje placering af fem små borehuller i kraniet, kan effekten af TTFields øges med op til 100% da modstanden fra kraniet mindskes. KM-kirurgien laves samtidigt med tumorfjernelsen. Vores fase 1 studie (2016-2019) på rGBM konkluderede, at denne kombination var sikker med en gennemsnitsoverlevelse på 15,5 måneder.

Metode
OptimalTTF-2 er et prospektivt, investigator-initieret, nationalt, randomiseret 1:1 fase 2 forsøg. Vi ønsker at afklare om TTFields og KM-kirurgi, i tillæg til nuværende behandling, øger overlevelsen for voksne patienter med rGBM. Randomiseringen består i hvorvidt der udføres KM-kirurgi.
Forsøget startede november 2020 med en forventet varighed på 3 år. Der forventes inklusion af 70 patienter. Primære endepunkt er 12-måneders overlevelse. Der udføres en interimsanalyse efter de første 52 patienter er blevet fulgt i 12 måneder og forsøget stoppes, hvis KM-kirurgi gruppen ikke lever længere end kontrolgruppen.

Konklusion
OptimalTTF-2 er et igangværende nationalt fase 2 forsøg som undersøger en ny og kreativ behandling for rGBM, med potentiel øget overlevelse.

Emerging Treatments:

Poster #86-99

Emerging treatments

#86: Drug repurposing screen reveals glioblastoma cell line susceptibility to statins

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Abstract
Introduction
The standard therapy for glioblastoma patients is tumor resection followed by radiotherapy and temozolomide chemotherapy. Although glioblastoma has been extensively molecularly profiled along with other cancers, this knowledge has not yet been translated into improved survival outcomes. We used a bioinformatics approach to identify potential novel therapeutic strategies for glioblastoma.

Methods
Comprehensive online datasets which have assessed up to 1376 cancer cell lines in multiple ways were interrogated to identify potential drug candidates for glioblastoma. Datasets included were from the cancer cell line encyclopedia (mRNA expression), the Achillies project (cell viability following Crispr-Cas9 knockout) and PRISM (drug treatment). A t-test comparing cell viability of glioblastoma cell lines versus other cancers was used to identify potential drug candidates, followed by the use of multiple statistical tools to investigate potential mechanism of action and status of biomarkers.

Results
Fluvastatin, pitavastatin and atorvastatin produced the most significant effects in glioblastoma cell lines, with both fluvastatin and pitavastatin being particularly potent. The anti-cancer properties of statins have previously been attributed to the inhibition of HMG-Coa reductase. Here, we found their effects correlated with erastin, an enhancer of ferroptosis and with gene knockout of UBIAD1, which participates in non-mitochondrial ubiquinone synthesis. These effects were both found in glioblastoma cells and other cancers with a mesenchymal-like phenotype.

Conclusion
Statins appeared to be especially effective against glioblastoma lines and the effect could be linked to ferroptosis and inhibition of UBIAD1. In vitro validation of this finding is ongoing.

Emerging treatments

#87: Penetration depth and tissue concentrations of cisplatin and carboplatin in a HIPEC procedure - assessment in a novel experimental porcine model.

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Abstract
Introduction
Peritoneal dissemination from intraabdominal cancers is associated with poor prognosis and a rapid disease progression. Hyperthermic Intraperitoneal Chemotherapy (HIPEC) treatment has been used for the last 10-15 years with an increased overall survival period and recurrence-free time, yet no studies have investigated the local drug concentrations and drug penetration depth. The aim of this study is to develop a novel, reproducible and valid large porcine HIPEC model to dynamically assess local concentrations of cisplatin and carboplatin, simultaneously in various target tissues by means of microdialysis in two separate studies.

Materials and methods
Cytoreductive Surgery will be performed on the animals and microdialysis catheters will be placed for sampling of drug concentrations in different depths in the peritoneum, intestines, liver, and the hepatoduodenal ligament. Treatment time for the HIPEC procedure will be standard duration of 90 min at a temperature of 41°C. Cisplatin will be administered in a concentration of 75 mg/m2 and carboplatin of 800 mg/m2. During and after the HIPEC procedure microdialysates will be obtained. Blood samples will be drawn simultaneously to assess the systemic cisplatin and carboplatin absorption. Concentrations of cisplatin and carboplatin from the samples will be quantified using ultra-high-performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS).

Results
Pharmacokinetic data of cisplatin and carboplatin will be performed by non-compartmental analysis. Plasma and tissue concentrations will be plotted as a function of time. The first results will be presented at the conference.

Conclusion
We propose a new HIPEC porcine model for future research, with the potential to assess and optimize the HIPEC procedure by evaluation of basic key elements of the treatment. This has the potential to improve patient treatment with increased survival and less side effects.

Emerging treatments

#88: The role of stereotactic body radiotherapy (SBRT) in neuroendocrine neoplasms

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Abstract
Introduction
The role of SBRT in the treatment of neuroendocrine neoplasms (NEN) remains undetermined. To date, no studies of SBRT efficacy in different histopathological subgroups of NEN exist. This study reviewed our institution's experience using SBRT in treating well (WD)- and poorly differentiated (PD) NEN of both localized and oligometastatic disease.

Material and methods
Data from NEN patients treated with SBRT between 2013 and 2020 were retrospectively collected from medical records and the radiotherapy treatment planning system. Local tumour control (LTC), patterns of progression, and clinical outcome were analyzed using descriptive statistic.

Results
Thirteen patients (a total of 15 sites) were treated with SBRT. The median Ki67% -index was 15 (range, 1-80). The majority of the patients had WD broncho-pulmonary NEN (61.5%). Of these patients, three (23%) received SBRT of the primary tumour site. Ten patients (77%) received SBRT at one or more metastatic sites (eight liver, one lung, three in the brain). The median SBRT dose was 45 Gy (range, 20-67,5 Gy) in 1-8 fractions depending on localization, size and motion. The median BED10 was 112,5 Gy (range 60-219 Gy). Most patients experienced distant progression after SBRT.
The 6-months and 1-year LTC rates were 73% and 60%, respectively. The median PFS was six months (range 1-63). Local in-field failure was observed in three patients (five sites), two with WD and one with PD. All of these patients were treated at metastatic sites, three liver and two brain metastases. The median time to local progression for all patients was 51 months (range 6 to 78). Median OS was 25 months (range 2-198).

Conclusions
SBRT is a promising non-invasive treatment modality that could provide LTC of primary and metastatic sites in NEN patients. A further comprehensive evaluation of the efficacy and toxicity of SBRT in NEN of different origins, various differentiations and grades is warranted.

Emerging treatments

#89: Repositioning of drugs for rectal cancer applying reversal global gene expression analysis

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Abstract
Introduction
Rectal cancer is a common disease with a high mortality rate. The treatment options are limited and comprise combinatory neoadjuvant chemoradiotherapy and surgery. Here we combined gene expression data of rectal cancer patients with drug-induced gene-expression profiles of cancer cell lines to identify drug candidates for repositioning.

Material and Methods
We generated six gene expression signatures using publicly available datasets (468 tumors and 374 normal tissues). Next, we matched these six signatures to 66,612 drug-induced gene expression profiles (71 cell lines and 12,442 drugs) from the Library of Integrated Network-based Cellular Signatures (LINCS) L1000 dataset using the workspace Open Cancer TherApeutic Discovery (OCTAD). To validate our findings, we tested the sensitivity of 33 colorectal cell lines (Cancer Dependency Map - DepMap) to drugs showing high potency to reverse the rectal cancer-specific expression signatures.

Results
We found that the differentially expressed genes in each signature are mainly associated with colorectal cancer, cell cycle, ATR signaling pathway, E2F transcriptional factor networks, and CXCR chemokine receptor binding. We detected 372 genes deregulated in all rectal cancer signatures, which were consistently co-expressed with CDK1, BUB1, AURKB, PBK, and MELK kinase found in RNA-seq data from 100,131 human samples (ARCHS4 database). Our OCTAD-based approach generated a final consensus list of 64 drugs with high potential to reverse the gene expression profile of rectal cancer. Finally, we found that drugs targeting CDK1 (alvocidib, purvalanol-a, PHA-793887, and JNJ-7706621) or AURKB (danusertib and JNJ-7706621) effectively inhibited the growth of colorectal cancer cell lines with similar signatures of rectal cancer cohort.

Conclusions
The computational drug repositioning approach identified drugs that potentially reverse rectal cancer signatures and inhibited the growth of colorectal cancer cell lines.

Emerging treatments

#90: Treatment of malignant pleural effusion with Pressurized Intrathoracic Aerosol Chemotherapy (PITAC)

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Abstract
Introduction
Patients with malignant pleural effusion often need repeated pleural drainage. Its etiology is multifactorial. Pressurized Intrathoracic Aerosol Chemotherapy (PITAC) is a new treatment option, where standard chemotherapeutics are aerosolized under pressure within the pleural cavity during a thoracoscopy. PITAC may reduce the amount of malignant pleural effusion.

Material and Methods
Retrospective analysis of prospectively collected data from Odense PIPAC Center, Odense University Hospital. No formal in- and exclusion criteria, but patients should have malignant pleural effusion, a performance status of 0-1 and no solid organ metastases. PITAC was performed in general anesthesia with two standard trocars. Pleural effusion was removed or pleural lavage cytology was performed. If possible, also pleural biopsies were obtained, and cisplatin 7.5 mg/BSA followed by doxorubicin 1.5 mg/BSA was aerosolized within the affected pleural cavity.
Patients were discharged after 24 hours of recovery. Adverse events were recorded according to Common Terminology Criteria for Adverse Events (CTCAE) v. 4.0.

Results
Two patients were treated with PITAC from February 2018 to June 2019. A 67 years old woman with platinum resistant ovarian cancer with pleural and peritoneal metastases had two PITACs. There was no pleural effusion at the second PITAC and no CTCAE>2, but treatment was stopped due to general disease progression. The second patient was 56 years old and had breast cancer with pleural and peritoneal metastases. She had three PITACs. No CTCAE>2 was recorded. There was no reduction of pleural effusion, but cytology prior to PITACs 2 and 3 was negative. A CT showed disease progression and treatment was stopped.
Both patients had synchronous Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) treatment due to peritoneal metastasis.

Conclusions
PITAC seems feasible and should be evaluated in prospective clinical trials.

Emerging treatments

#91: Immunological targeting of the immunosuppressive tumor microenvironment with TGF-β-derived peptide vaccination in in vivo murine tumor models.

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Abstract
Introduction
The efficacy of cancer immunotherapy can be strongly impaired by immunosuppression in the tumor microenvironment (TME). A key player in the development of an immunosuppressive TME is Transforming growth factor-β (TGF-β). The aim of this project is to evaluate the anti-tumor effect of immune-modulating cancer vaccines with TGF-β-derived peptides in murine tumor models.

Materials and Methods
C57BL/6 mice were subcutaneously (s.c.) inoculated with 0.5 million tumor cells. Two syngeneic tumor models were used: MC38 (colon adenocarcinoma) and Pan02 (pancreatic adenocarcinoma), representing hot and cold tumors, respectively. Tumor volume was measured using a digital caliper. Mice were s.c. vaccinated every 7 days with either 50 or 100 µg per peptide adjuvanted with Montanide ISA 51VG. Vaccinations were initiated on day 0 or 10 post- inoculation. For studies with anti-CTLA4, 350 µg of antibody were injected intraperitoneally every 7 days starting on day 0. The presence of vaccine-induced TGF-β-specific T cells was assessed by ELISPOT.

Results
Vaccinations with an immunogenic MHC-II-restricted murine TGF-β-derived peptide significantly suppressed tumor growth in MC38 tumor-bearing mice. In addition, the combination with anti-CTLA4 treatment resulted in the infiltration of TGF-β-specific T cells in the tumor. Combination of MHC-I and MHC-II-restricted TGF-β-derived peptide vaccination resulted in a significant reduction in tumor growth in Pan02 tumor-bearing mice. We are working on elucidating the mechanism of action underlying the anti-tumor effect of TGF-β-derived peptide vaccinations by analyzing vaccine-induced changes in the TME by flow cytometry and gene expression analysis.

Conclusions
We have shown that TGF-β-derived peptide vaccination reduces tumor growth in syngeneic murine tumor models. Our findings support the feasibility and potential of TGF-β-derived peptide vaccination as a novel immunotherapeutic approach to target immunosuppression in the TME.

Emerging treatments

#92: Canine cancer patients - a clinical translational model for investigating efficacy and adverse effects of FLASH radiotherapy

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Abstract
Introduction
FLASH radiotherapy (RT) is a novel technique that delivers RT in a fraction of a second, and is proposed to have efficacy similar to conventional RT with fewer adverse effects. However, more research is needed before FLASH RT can be applied in large scale human cancer trials. Accordingly, the overall focus of the current project was to accelerate the process leading to human clinical trials by gaining knowledge from canine cancer patients. The primary aim was to investigate feasibility and toxicity of FLASH RT, while a secondary aim was to evaluate treatment response.

Materials & Methods
Canine cancer patients with spontaneous solid malignant tumors were enrolled if radiotherapy was part of their optimal treatment plan. Included dogs were treated with a single fraction of FLASH RT at Skåne University Hospital. Tumor size and adverse effects were documented at the initial visit, on the treatment day and on day 7, day 30, 3 and 6 months post therapy, together with a Quality of Life (QoL) questionnaire filled out by the owners.

Results
So far, 15 dogs with a total of 17 tumors have been successfully treated with FLASH RT. Tumor types included were mast cell tumors (n=7), sarcomas (n=5), carcinomas (n=2), malignant melanoma (n=2) and plasmacytoma (n=1), either in a macroscopic setting (n=10) or post-surgery (n=7). One patient (intranasal carcinoma) experienced a grade 3 moist desquamation of the nasal plane following 35 Gy. Otherwise, adverse effects were grade 1 or none. Tumor responses ranged from complete response to short or long-term stable disease. Owners generally felt their dog had a good QoL following treatment.

Conclusion
FLASH RT can be used safely to treat spontaneous solid tumors in canine cancer patients, representing a relevant clinical cancer model. The dogs treated with FLASH RT in this study generally experienced clinical benefit and no or low grade toxicities. This will help form the basis for establishing future human clinical trials.

Emerging treatments

#93: Toxisitet og morbiditet ved behandling med laparoskopisk hypertermisk intraperitoneal kemoterapi i kombination med standardbehandling for lokal avanceret ventrikelcancer: ProPEC-I trial.

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Abstract
Introduktion
Trods prognostiske fremskridt ved behandling af ventrikelcancer (VC), dør fortsat 400 mennesker årligt i Danmark. Sygdommen er aggressiv og diagnosticeres ofte sent. Blandt den 1/3 af patienterne, der kan tilbydes kurativt intenderet behandling, progredierer 10-15% præoperativt, primært i peritonealkaviteten hvor systemisk kemoterapi har dårlig penetrans. Ved spredning til peritoneum er medianoverlevelsen ubehandlet 3,1 mdr., med pallierende kemoterapi 6-14 mdr., mens 2-og 5-årsoverlevelsen er hhv. 11% og 0%.
Vi undersøger en ny behandling til forebyggelse af progression under præoperativ kemoterapi (POC). Studiet introducerer laparoskopisk administreret HIPEC forud for standardbehandlingen for lokalavanceret VC. Vi ønsker at afklare, om behandlingen er gennemførlig og sikker.

Materialer og Metoder
Randomiseret kontrolleret feasibility studie, inkluderende 14 patienter randomiseret 1:1 til HIPEC/No-HIPEC. Kontrolgruppen modtager standardbehandling med POC herefter standard D1+ gastrektomi. Interventionsgruppen modtager ProPEC-I regimet, bestående af en cyklus laparoskopisk administreret HIPEC med 100 mg/m2 cisplatin ved 40°-41° C, givet ved diagnostisk laparoskopi. Herefter følges standardregimet. End-points er toxisitet- og morbiditetsrater og patientrapporteret Quality of Life (QoL). Patienterne følges mhp. 3-års progressionsfri overlevelse samt 5-års overlevelse.

Resultater
Syv patienter er inkluderet, 4 har gennemført 1 års follow-up. De 3 patienter, der har gennemført ProPEC-I regimet, har påbegyndt standardbehandlingen uden forsinkelser.

Konklusioner
Dette studie er det første i verden til at undersøge profylaktisk laparoskopisk HIPEC før standardbehandlingen for VC. Studiet undersøger primært, om ProPEC-I er sikkert, samt om regimet giver forsinkelser ift. opstart af standardbehandlingen. Yderligere studier vil være nødvendige til vurdering af muligheden for at forebygge peritoneal progression, og dermed øge overlevelsen for VC.

Emerging treatments

#94: Suppression of tumor-associated neutrophils by lorlatinib attenuates pancreatic cancer growth and improves treatment with immune checkpoint blockade

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Abstract
Introduction
Pancreatic ductal adenocarcinoma (PDAC) patients have a 5-year survival rate of only 8% largely due to late diagnosis and insufficient therapeutic options. Neutrophils are among the most abundant immune cell type within the PDAC tumor microenvironment (TME), and are associated with a poor clinical prognosis. However, despite recent advances in understanding neutrophil biology in cancer, therapies targeting tumor-associated neutrophils are lacking. The non-receptor tyrosine kinase FES is expressed in neutrophils and we have identified FES as a possible target to suppress neutrophils and prevent PDAC progression. Lorlatinib is an FDA approved, third-generation, ATP-competitive small-molecule tyrosine kinase inhibitor that was recently shown to potently inhibit FES.

Materials and Methods
Kinase profiling measurements were performed on a PamChip Kinase Profiling Microarray System. Animal studies were carried out with either KPC or C57BL/6 mice. Orthotopic- tumor and metastasis models were established with injections of KPC mT4 cells into either the pancreas or the spleen. Tumor and metastasis burden were assessed by weight of either the pancreas or liver relative to mouse weight. Flow cytometry analysis of tumor, metastasis and bone marrow were carried out on a BD FACSAria III.

Results
Lorlatinib suppresses neutrophil development and recruitment from the bone marrow and indirectly suppress the growth of PDAC primary and metastatic sites. Furthermore, we find that lorlatinib improves the response to immunotherapy in PDAC tumors.

Conclusions
We demonstrate that lorlatinib indirectly suppresses the growth of PDAC at primary and metastatic sites by suppressing neutrophil development in the BM and modulating tumor-promoting neutrophil functions within the TME.
This is the first study to identify an effect of lorlatinib in modulating tumor-associated neutrophils, and to demonstrate the potential of lorlatinib to treat PDAC.

Emerging treatments

#95: Thiopurines: Increasing tumour mutational burden to improve immune and checkpoint blockade response within tumours.

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Abstract
Introduction
Immunotherapies, such as immune checkpoint inhibitors, have revolutionised the treatment of cancer, for example anti-PD-1 therapy in melanoma. Two positive indicators of tumoral response to immunotherapy include an immunologically "hot" phenotype and a high tumour mutational burden. However, many types of cancer remain resistant to immunotherapy due to absence of these indicators. Therefore, this project aims to improve the immune response to these therapy-resistant tumours and the tumour's response to the immune checkpoint inhibitors through the use of the thiopurine drug, 6-thioguanine (6-TG). Thiopurine-based therapy is currently used as a treatment for patients suffering from Acute Lymphoblastic Leukaemia, and has been shown to reduce relapse rates in these patients when used as low-dose maintenance therapy. Here, in the pre-clinical setting, we investigate the impact of 6-TG on tumour-infiltrating lymphocytes, and the tumour's response to the immune checkpoint inhibitors, as proof-of-concept prior to progression into clinical trials.

Materials & Methods
We use in vitro and in vivo murine models of melanoma to investigate dose-response, thioguanine nucleotide integration into DNA (DNA-TGN) (mass-spectrophotometry), tumour mutational burden (Whole Genome Sequencing), and neoantigenicity (RNA sequencing). Flow cytometry is used to assess immune cell levels in peripheral blood and their infiltration into the tumour.

Results
Our in vitro results show we have identified a dose of 6-TG which allows clinical-grade integration of DNA-TGN. Our in vivo results show delayed growth of 6-TG treated tumours compared to control, which we attribute to improved immune response to the tumour.

Conclusions
While our research is still on-going, our initial results are promising. After confirming these results, we will introduce immune checkpoint inhibitor therapy to make our final conclusions, before the projects proceeds to clinical trials involving patients.

Emerging treatments

#96: Ultra-fast scintillator-based dosimeter for pencil beam scanning proton FLASH therapy

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Abstract
Introduction
FLASH is a novel radiotherapy modality where the radiation dose is delivered with ultra-high dose rates (>40Gy/s). Pre-clinical FLASH studies have shown remarkable normal tissue sparing, with unaltered tumor response, when compared to conventional dose rates. Proton FLASH is currently being investigated. Dose rate monitoring with a high temporal resolution is essential to validate that the treatment is delivered under FLASH conditions. In this project, a novel ultra-fast dosimetry system for pencil beam scanning (PBS) proton FLASH therapy was developed and used in pre-clinical FLASH mouse studies at our institution.

Materials and Methods
The dosimetry system uses fiber-coupled scintillating ZnSe:O crystals of sub-millimeter dimensions to sample the dose rate in single points at 50kHz. In PBS delivery, the detector signal consists of distinct plateaus corresponding to the individual spots. The signal height depends on the instantaneous dose rate at the detector position. The length of each plateau represents the spot duration. The individual spot durations for single-layer FLASH fields were measured in a phantom study and compared with treatment log files. In vivo dosimetry was implemented in a pre-clinical FLASH mouse study by placing a single detector on the exit side of the mouse leg. The field mean dose rate was determined from the integrated signal and the total irradiation time and compared with the log-file determined values.

Results
The phantom time measurements showed that the total duration of an uninterrupted spot sequence was 0.251±0.003ms longer than the logged duration. This discrepancy was mainly due to too short logged duration for the first spot in the sequence. The measured dose rates agreed with log files with an RMS difference of 0.92Gy/s.

Conclusion
A scintillator dosimeter was developed and successfully used during pre-clinical proton FLASH studies. The measured spot duration and dose rates were in excellent agreement with log files.

Emerging treatments

#97: Experimental setup for demonstration of pencil beam scanning proton FLASH in a mouse model

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Abstract
Introduction
Radiotherapy causes less normal tissue damage when delivered with ultra-high dose rates (FLASH, >40Gy/s) than with conventional dose rates. This FLASH effect has mainly been investigated with electron beams, but proton FLASH would have broader clinical perspectives for treatment in all tumor depths. We recently demonstrated a clear skin sparing effect of pencil beam scanning proton FLASH in mice (Danish Cancer Research Days 2021, submitted abstract). Here, we thoroughly characterize the experimental setup used for this demonstration of proton FLASH.

Methods
The right hind leg of the mice was submerged in water and irradiated with a 2cm x 3cm field using either FLASH (250 MeV, 138 mice, 31.7-54.4 Gy) or conventional dose rate (244 MeV, 154 mice, 24.1-40.7Gy). The field profiles were measured with radiochromic films. The absolute dose was measured with an ionization chamber (IC, Advanced Markus) and alanine pellets. For FLASH, a daily dose calibration routine based on IC was established and benchmarked against calorimetry. In vivo dosimetry was performed for all FLASH mice with alanine in the beam entrance and a scintillator crystal near the mouse leg.

Results
Dose inhomogeneities at the entrance caused by the relatively large spot spacing were washed out at the mouse leg depth. IC and alanine doses agreed within 4% for FLASH and 1.5% for conventional dose rate. The IC based dose calibration for FLASH agreed with calorimetry within 0.1%. The dose rate was 0.4 Gy/s for CONV and 80Gy/s (range 69-90 Gy/s) for FLASH. The alanine in vivo FLASH dose differed up to 12% from the planned dose, but agreed better with the scintillator in vivo doses.

Conclusion
An experimental setup to demonstrate the FLASH effect for proton pencil beam scanning was established and thoroughly characterized. Dose variations observed with alanine in vivo dosimetry were confirmed with an independent in vivo dosimeter and thus interpreted as true variations in the delivered dose.

Emerging treatments

#98: Implementation of standardized minimally invasive restorative rectal cancer resection – The Delaney-Package. A prospective single center cohort study

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Abstract
Introduction
Anastomotic leak is a feared complication after restorative rectal resection (RRR) in rectal cancer patients. Several surgical initiatives with standardization of specific surgical steps have been implemented to decrease the risk of anastomotic leakage after RRR. However, studies have not described whether a full implementation was possible in case the standardization included a number of surgical steps. The aim of this study was to evaluate the implementation of a standardized technique for all rectal cancer patients undergoing RRR with intended minimal invasive approach. Furthermore, to evaluate the risk of AL during the implementation.

Materials and methods
Rectal cancer patients undergoing intended minimal invasive RRR at Aarhus University Hospital between 2017 and 2020. Six standardized surgical steps (the "Delaney-package") directed to improve anastomotic healing were mandatory for all RRR. Additional changes were made during the period with prohibition of Dexamethasone and limiting the use of endoscopic stapling technique.

Results
Use of the full Delaney-package, including all six surgical steps, increased from 40.3% (95% CI, 0.28-0.54) to 86.2% (95% CI, 0.68-0.95). The risk of AL decreased from 21.0% (95% CI, 0.12-0.33) to 6.9% (95% CI, 0.01-0.23)

Conclusion
It was possible to implement the full Delaney-package for rectal cancer patients undergoing RRR with a robot-assisted approach. The risk of AL decreased during the study period. Other colorectal centres can easily adapt this standardized approach.

Emerging treatments

#99: Proton FLASH as normal tissue sparing radiation therapy in a mouse model

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Abstract
Introduction
Preclinical studies indicate a normal tissue sparing effect using ultra-high dose rate (FLASH) radiation with comparable tumor response. This differential response has promising perspectives for improved clinical outcome. Most data so far are based on electron beams with limited utility for clinical use. Clinical proton therapy facilities can deliver FLASH dose rates at depths that provide access to all tumor sites, but preclinical data of the effect of proton FLASH are still very scarce.
The aim of this study was to demonstrate the effect of proton FLASH delivered with a scanning pencil beam in a mouse leg model, and to quantify the normal tissue sparring factor, the FLASH factor.

Materials and Methods
The right hind limb of CDF1 mice were irradiated with a single fraction of protons at either conventional or FLASH dose rate in the entrance plateau of a pencil beam scanning proton beam. Conventional dose rate was 0.4 Gy/sec (field dose rate) 244 MeV. FLASH dose rate was 69.7-88.7 Gy/s (Field dose rate), 250 MeV. In total,
292 mice were irradiated in four separate experiments. The endpoints were the level of acute moist desquamation to the skin of the foot within 25 days post irradiation
.
Results
Full dose response curves for five levels of acute damage to skin for both conventional and FLASH dose rate were obtained. A distinct normal tissue sparing effect was observed in the FLASH arm of the study. This effect was similar across all scoring levels with a weighted mean value of 1.46.

Conclusions
This study demonstrates a normal tissue sparing effect of proton FLASH when delivered with pencil beam scanning. Full dose response curves for acute skin damage in a mouse leg model were obtained, which enabled the quantification of the normal tissue sparing factor for proton FLASH. A 41-55% higher dose was required to give the same biological response when using FLASH dose rates compared to the conventional dose rates.
This study was supported by Varian.

Palliation and Psychosocial Support: Poster #100-110

Palliation and psychosocial support

#100: Struggling to Eat to Survive Cancer - Lived Experiences of Eating among Adolescents and Young Adults Undergoing High-Emetogenic Chemotherapy

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Abstract
Introduction
Eating difficulties; changes in taste, poor appetite, nausea and vomiting are closely linked to reduced food intake and poor QOL. This study focusses on adolescents and young adults with cancer (AYAs) receiving high-emetogenic chemotherapy (HEC). Despite anti-emetogenic medication, the prevalence of nausea and vomiting is more frequently reported among AYAs than among the adult population.
To date, little is known about how eating as a phenomenon is disrupted by cancer and its treatment. Such knowledge will critically inform the understanding of eating difficulties and improve AYAs' eating possibilities. Therefore, the purpose of this study was to provide an in-depth understanding of AYAs' lived experiences with eating at home between HEC sessions.

Materials & Methods
Eligible AYAs were 15-29 yrs., diagnosed with oncological or haematological cancer, treated with HEC and Danish speaking, recruited from three university hospital departments. Thirteen AYAs, aged 17-29 yrs. were included. Data were collected by in-depth interviews. Data analysis was guided by van Manen's hermeneutic-phenomenological methodology.

Results
The essential meaning of the phenomenon of eating can be characterized by the overarching theme ´Struggling to eat to survive' and unfolded through the following three themes: ´Cooperating with a deceiving body´, ´Capturing moments of eating opportunities´ and ´Being loved and cared for ´at home´.

Conclusions
Struggling to eat was essential for survival and a fundamental existential challenge that required reflection and consciousness. AYAs experienced their deceiving bodies as a major concern, which challenged their ability to eat and forced them to develop eating strategies. AYAs kept hold of doing ´something´ to maintain control of their own lives and thereby assist clinical outcomes and cure. It is highly relevant for healthcare professionals to acknowledge that eating is individual in nature and affects AYAs entire lifeworld.

Palliation and psychosocial support

#101: Research protocol: "Resilient Caregivers" – A randomized controlled trial of a resilience-based intervention for psychologically distressed partner caregivers of cancer patients

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Abstract
Introduction
Intimate partners of cancer patients often experience significant psychological distress, but there is a lack of psychological interventions that specifically target this population. "Resilient Caregivers" is a novel resilience-based group intervention for distressed partner caregivers of cancer patients. The intervention was developed according to a resilience framework focusing on meta-reflective skills, coping strategies and value clarification. The aim of this study is to evaluate the effectiveness of this intervention in a randomized controlled trial (NCT04610034).

Materials and methods
We will recruit participants (n = 80) through the Oncology Department at Herlev Hospital,
randomized to either the intervention or usual care. The intervention takes place at the Danish Cancer Society's counselling center in Herlev. Participants are eligible if they are partners of patients diagnosed with Stage I-III cancer and experience distress (> 4 on the Distress Thermometer). "Resilient Caregivers" consists of seven group sessions of approximately two-and-a-half hours each, focusing on resilience in relation to being a partner caregiver of a cancer patient. The primary outcome is symptoms of anxiety as assessed by the Generalized Anxiety Disorder scale. Secondary outcomes include distress, depression, resilience, metacognitive beliefs, valued living and coping strategies. Outcomes are assessed at baseline, and at 3, 6 and 12 months follow-up. Data will be analyzed using mixed models for repeated measures.

Results
Recruitment began in April 2021. We will present preliminary data regarding recruitment and if available, data on satisfaction from the first groups.

Conclusions
If shown to be efficacious, the novel "Resilient Caregivers" program has the potential to improve the lives of both partners and cancer patients. The manualized group format supports cost-effective implementation in a range of therapeutic settings.

Palliation and psychosocial support

#102: Improvement of pain management in a comprehensive cancer center: A comparison of two cross-sectional studies 8 years apart.

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Abstract
Introduction
In 2011 a multidisciplinary palliative team (MPT) was established at Rigshospitalet (DK) and a cross-sectional survey in inpatients was carried out at the Departments of Hematology and Oncology. High symptom burden, high prevalence of pain (64 %) and insufficient analgesic treatment was demonstrated. In 2019 a similar survey was carried out.

Materials and methods
This study compares prevalence of symptoms including pain and analyzes analgesic treatment of adult in-patients in a comprehensive cancer center.
Two cross-sectional studies (May-Jun 2011; Feb-Sep 2019). Inclusion criteria: malignant diseases, age≥18y, able to understand Danish. EORTC QLQ-C30 and Brief Pain Inventory (BPI) were applied.

Results
134 and 183 inpatients included in 2011 and 2019, respectively. In 2019 more oncological in-patients had advanced disease (P=0.0096), and in-patients had generally a lower performance status (P=0.0028), and were more often on a palliative treatment plan (P=0.0034). Unchanged high prevalence of impairments and symptoms on EORTC; however, significant increase in severe pain (P=0.0143). In 2019, pain relief was 22 percentage points (pp) higher (P=0.0010) and patients with untreated pain was 35 pp lower (P<0.0001). Overall, opioid prescription increased 24 pp (P<0.0001). In patients having pain, opioid prescription increased 37 pp (P<0.0001). Fifteen pp increase in combined around-the-clock and on-demand opioids (P=0.00015). Prevalence of neuropathic pain mechanism increased 43 pp (P<0.0001) and use of adjuvant analgesics in that group increased 19 pp (P=0.0716).

Conclusion
Although, in-patients of the 2019 survey were older, more fragile and more often on a palliative treatment plan than in 2011 an overall unchanged high symptom burden was observed. However, significant improvement of pain management was observed in 2019. The establishment of a MPT may possibly have contributed to improved pain management.

Palliation and psychosocial support

#103: Peer support – a new model for psychosocial supportive care in a hematological clinical care setting

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Abstract
Introduction
Treatment with intensive chemotherapy for a malignant hematological disease increases the risk of a significant symptom burden and psychological distress in patients and their caregivers. The limited resources in health care and the shift toward outpatient care make it important to find new approaches to strengthen the available support systems. Peer support is a method with the potential to rethink supportive care with the use of voluntary resources. Therefore, we investigated the feasibility of peer support interventions in patients and caregivers.

Methods
Two single-arm feasibility studies including either newly diagnosed patients (n=36) with acute leukemia or caregivers (n=26) of newly diagnosed patients with hematological malignancies were designed. The interventions consisted of 12 weeks of support for patients or caregivers provided by ambassadors who were either former patients (n=25) or former caregivers (n=19). During the intervention, ambassadors provided one-on-one individual support by face-to-face meetings, telephone, or e-mail contact. The ambassadors attended a preparatory course and were offered group and individual supervision during the intervention.

Results
Peer ambassador support was feasible and safe in both patients, caregivers, and their ambassadors who reported high satisfaction with the individually adjusted support. Patients improved in psychosocial outcomes over time. Ambassadors maintained their psychosocial baseline level, with no adverse events, and used the available supervision to manage challenges and to exchange experiences with other ambassadors.

Conclusions
Peer ambassador support was feasible and has the potential to be a new model for care incorporated in the hematology clinical care setting, creating an active partnership between peers. Thus, it is recommended to offer individual peer support to all adult members of the family during the disease trajectory.

Palliation and psychosocial support

#104: How does the COVID-19 pandemic affect the quality of life reportings of Danish patients with multiple myeloma?

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Abstract
Introduction
Patients with multiple myeloma (MM) have increased risk of dying if infected with COVID-19, and the pandemic has changed standard of care towards extended use of oral regimens and limiting hospital visits. We aimed to analyze patient-reported quality of life (QoL) in Danish patients with MM pre-COVID and during-COVID.

Materials and Methods
The study was a natural experiment using a cross-sectional study design. Data originates from the ongoing survey "Quality of life in Danish patients with MM" (QoL-MM) and is collected at 12 follow-up time points over a two-year period. Twenty-five QoL domains are included, assessed by the EORTC QLQ-C30, the MM module QLQ-MY20, the Chemotherapy-Induced Peripheral Neuropathy module and the Short-form health survey version 2. The QoL data was analyzed using mixed effects linear regression, with a year-period-interaction. Pre-COVID versus during-COVID QoL mean score difference was considered evident, if the difference was both statistically significant (p-value <0.05) and clinically relevant.

Results
In the study, 616 patients were included with a mean age of 68.2 years. Completion rates were 96%, and 2,576 completed sets of questionnaires were included. No deterioration in QoL was reported during the 1. or 2. wave of the COVID-19 pandemic compared to one year earlier. The patients under 65 years of age reported improved physical functioning (p-value 0.016), decreased fatigue (p-value < 0.001), less insomnia (p-value 0.002) and improved role functioning (p-value <0.001) during the 1. wave. This effect was not evident during the 2. wave.

Conclusion
Based on our data, the pandemic has no negative affect on the reported QoL in patients with MM. Patients under 65 years of age might have experienced relief due to a slower paced life during the 1. wave lockdown. A limitation, however, may be that the questionnaires used are not validated to capture psychosocial health during a pandemic.

Palliation and psychosocial support

#105: Stå Sammen – en digital dyadisk intervention til yngre brystkræftpatienter og deres partnere

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Abstract
Introduktion
I Danmark får over 800 yngre kvinder mellem 25 og 49 hvert år brystkræft. Kræft påvirker ikke kun patienten, men også den syges partner og børn. Partnere til kræftpatienter er ofte lige så psykisk belastede som patienter selv, og deres børn er i øget risiko for psykiske udfordringer. Der er derfor behov for støttende indsatser som er målrettet parrets fælles håndtering af livet med kræft. For yngre familier med kræft adskiller tilværelsen med mindre børn og en aktiv karriere sig markant fra tilværelsen for den gennemsnitlige brystkræftpatient på 60+. Derfor imødekommer eksisterende tilbud om støtte ofte ikke de udfordringer man som ung familie står med.

Materialer og metoder
Vi vil i dette studie udvikle og pilotteste en digital intervention skræddersyet til yngre patienter med ny diagnosticeret brystkræft og deres partnere. En fleksibel digital levering gør det muligt for parret at gennemføre interventionen når det passer dem. Gennem en række moduler til mobiltelefon, bestående af videoer og interaktive øvelser, får parret mulighed for at lære nye måder at håndtere de udfordringer der opstår ifm. et kræftforløb. Modulerne dækker emner som samarbejde, stress-håndtering, intimitet og kommunikation. Formålet er at styrke parrets evne til at indgå i gensidig støtte og problemløsning, for at mindske kræftens belastende indflydelse.
I et pilot-studie med 20 yngre brystkræftpatienter og deres partnere, vil vi teste om interventionen 1) er acceptabel for parrene 2) gennemføres som tiltænkt, og 3) viser en foreløbig effekt på parrenes fælles stresshåndtering og mentale helbred.

Resultater
Baseret på interviews med tidligere patienter og review af nyeste litteratur, er vi i gang med at udvikle og usability-teste interventionen. Vi forventer at kunne vise de første færdige moduler i sensommeren.

Konklusioner
Hvis pilot-studiet viser sig acceptabelt er målet at påvise interventionens effekt i en stor lodstrækningsundersøgelse.

Palliation and psychosocial support

#106: ConquerFear-Group: Development and preliminary efficacy of a psychological intervention for fear of cancer recurrence delivered in groups

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Abstract
Introduction
Fear of cancer recurrence (FCR) is a prevalent and debilitating reaction to cancer diagnosis and treatment. Our objectives were to adapt ConquerFear, an individually delivered psychological intervention for FCR, into a group format, ConquerFear-Group, and to evaluate its preliminary efficacy.

Materials and methods
Eligible patients had completed treatment for breast cancer 3 months to 5 years previously, were ≥18 years, and scored ≥22 on the Fear of Cancer Recurrence Inventory-Short Form (FCRI-SF). The manual was first evaluated with seven patients (Pilot 1), adjusted in accordance with feedback provided by therapists, patients, and the original ConquerFear developers, further evaluated with eight patients (Pilot 2), and again adjusted. The preliminary efficacy of the final manual was evaluated with 27 patients, randomized in blocks to ConquerFear-Group or active control (AC) (relaxation training) (Pilot 3). The primary outcome was the FCRI total score completed at baseline, post-treatment, and 3 and 6 months follow-up.

Results
Adjustments of the original ConquerFear manual (Pilot 1 and 2) included changes in the order of treatment components, simplified exercises, and shortened homework. Compared with ACs, ConquerFear-Group participants experienced reductions in FCRI total scores from baseline to post-treatment (p=.004, Hedges's g=0.59), to 3 months (p=.026, g=0.50), and to 6 months later (p=.043, g=0.93), with effects corresponding to medium-to-large effect sizes (Pilot 3). Although non-significant, compared with AC, ConquerFear-Group was also associated with larger reductions in general distress and maladaptive metacognitions, corresponding to small-to-medium effect sizes (g=0.40–0.61).

Conclusions
ConquerFear is feasible and efficacious in a group format. The preliminary results need to be confirmed in a larger randomized trial.

Palliation and psychosocial support

#107: Cannabis among patients with cancer receiving palliative care - A cross-sectional survey

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Abstract
Introduction
Self-medication with cannabis is common practice among patients with cancer. Absence of quality control and guidance by health care professionals (HCP) may expose patients to medical, safety and legal uncertainties. We aimed to investigate the extent and perception of cannabis use in patients with cancer receiving palliative care.

Material and methods
A cross-sectional survey was conducted between June 2019 and January 2021 at the Unit of Palliative Care at North Denmark Regional Hospital. Eligible patients (adult patients with cancer, excluding patients that were moribund or suffering from brain damage, dementia or delirium) who gave informed consent, filled in a questionnaire.

Results
With a response rate of 66% (34 % declined), 160 patients completed the questionnaire. Median age was 73 years (range 19 to 96) and 54% were female. Lung cancer was the most common diagnosis (23%). History of cannabis treatment was reported by 39 (24%) patients and 121 (76%) were cannabis naïve. Among the experienced patients 64% had discussed cannabis with the HCP versus 28% of naïve patients ($p<0.01$). Regarding belief in cannabis for therapeutic control of cancer disease the figures were 51% versus 21%, respectively ($p<0.01$). Likewise, the figures were 87% versus 61%, respectively, ($p=0.056$) regarding belief in cannabis for symptom relief.
Cannabis on a prescription would be preferred to non-prescription cannabis by 82% experienced and 98% naïve patients ($p<0.01$).

Conclusions
Among the majority of patients with cancer receiving palliative care, cannabis is perceived effective, either for control of the cancer disease and/or relief of symptoms, and prescription cannabis would be preferred to self-medication by most patients.

Palliation and psychosocial support

#108: The effects of long-term opioid treatment on the endocrine system in patients with cancer-related pain: A systematic review

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Abstract
Introduction
Opioids' analgesic effect for cancer pain is undeniable; however, questions regarding side effects related to long-term opioid treatment (L-TOT) as suppression of endocrine system have being raised. This systemic review aimed at investigating effects of L-TOT on the endocrine system in patients with cancer-related pain.

Materials and methods
A systematic search on MEDLINE, EMBASE and Web of Science databases for clinical studies was performed. Inclusion criteria were studies that assessed endocrine measures in adult patients with cancer-related pain in L-TOT (≥4 weeks). Outcomes (hormones and comorbidities) and quality of evidence were assessed.

Results
A total of 240 studies were identified; out of which 235 studies were excluded (189 abstracts, 38 duplicates, five other outcomes and three non-opioid interventions) and five cross-sectional studies were included and analyzed. Comparisons between patients in L-TOT and patients without opioid treatment were associated with lower levels of testosterone and free testosterone in males, luteinizing hormone in both sexes and follicular stimulating hormone in females. Moreover, associations between higher MEDD (morphine equivalent daily dose) and higher levels of cortisol and prolactin in both sexes and higher MEDD and lower levels of testosterone and free testosterone in males were observed. All five studies had limitations that reduce the level of evidence (low/very low).

Conclusion
The few studies found demonstrated that patients with cancer-related pain on L-TOT may have gonadal hypofunction and possibly correlated with dose level. However, the evidence is weak and further research is required.

Palliation and psychosocial support

#109: Ændringer i patienters opfattelse af helbredsrelateret livskvalitet gennem behandling for myelomatose

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Abstract
Introduktion
Myelomatose er en uhelbredelig hæmatologisk kræfttype, hvor patienter rapporterer høj symptombyrde og nedsat helbredsrelateret livskvalitet (HRQL). Ændringer i HRQL hos patienter med myelomatose er primært undersøgt med gentagne patient-reported-outcomes (PRO) målinger over tid. Validiteten ved direkte sammenligninger af HRQL scorer indsamlet ved gentagne PRO målinger kan påvirkes, hvis patienter ændrer deres opfattelse af HRQL over tid, kaldet response shift. Formålet med studiet var at undersøge om patienter med myelomatose ændrer deres opfattelse af HRQL over tid.

Materialer & metoder
Studiet er et longitudinelt semi-struktureret interviewstudie baseret på den teoretiske model, Quality of Life Appraisal, som er udviklet til at belyse opfattelser af HRQL. Patienter blev inkluderet på tidspunktet for behandlingskrævende sygdom (nydiagnostiseret eller relaps) og interviewet ved baseline og seks måneder. Interviews blev analyseret ved brug af Systematisk Tekstkondensering af Malterud. Ændringer i patienternes opfattelse HRQL blev identificeret.

Resultater
14 patienter blev inkluderet. De samme fire temaer som belyser HRQL blev identificeret ved baseline og seks måneder senere, men der fremtrådte forskeligheder inden for temaerne; Tilpasning til stigende grad af symptomer og nedsat funktion i hverdagen var blevet en anvendt copingstrategi. Genovervejede værdier og prioriteringer i livet udtrykt ved stigende behov for social støtte og øget fokus på opretholdelse af et meningsfuldt liv. Sygdomsstatus og fremtidsperspektiverne blev en større del af opfattelsen af HRQL.

Konklusion
Studiet viste at patienter med myelomatose ændrer deres opfattelse af HRQL igennem et behandlingsforløb, hvilket kan påvirke PRO scorer. Dette betyder at gentagne PRO målinger ikke kun afspejler en ændring i HRQL som følge af behandling, men også interne psykologiske processer, som patienterne gennemgår. Dette kan påvirke data og bør inddrages i tolkningen af gentagne PRO data.

Palliation and psychosocial support

#110: Identifying, organizing, and prioritizing content for a rehabilitation program among young adult cancer survivors: A Group Concept Mapping study

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Abstract
Introduction
Despite research showing that young adult cancer survivors (YACS) (18-39 years) face multidimensional challenges regarding participation in everyday life, there is a lack of knowledge about how a rehabilitation programme can strengthen their participation in everyday life from the perspective of the end-users. Hence, this study aims to involve YACS, their families, and professionals in identifying and prioritizing relevant ideas for content to include in a rehabilitation program to strengthen YACS' participation in everyday life.

Material and methods
Group Concept Mapping, a mixed-methods participatory approach, was conducted among YACS, their families, and professionals. In three phases, participants brainstormed, sorted, and rated the importance of the ideas online, respectively. Hierarchical cluster analysis and multidimensional scaling were applied to produce a Cluster Rating Map, which was validated face-to-face by participants. In the last phase, a conceptual model was developed.

Results
Through brainstorming, 59 participants identified 149 ideas. Of the 59 participants, 27 sorted the ideas while 26 participants rated the ideas. Four YACS and four professionals validated the Cluster Rating Map resulting in a conceptual model depicting eight topics relevant to include in a rehabilitation program: (1) Treatment and possibilities within the social and health care system, (2) Rights and Finance, (3) Education and Work, (4) Psychological problems, (5) Body and Everyday life, (6) Peer to peer, (7) Sexuality and Relationships, and (8) Family and Friends. All topics were rated highly and equally important.

Conclusion
YACS, their families, and professionals identified and prioritized a span of highly relevant topics to include in rehabilitation programs aiming to strengthen participation in everyday life for YACS. This will inform the future development of an age-appropriate rehabilitation program for YACS.

Patient Involvement:

Poster #111-128

Patient involvement

#111: Feasibility of monitoring cancer patients with a smart t-shirt: Protocol for the OncoSmartShirt study

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Abstract
Introduction
Studies have shown that there may be a dissimilar perception on symptoms between cancer patients and health care professionals, which may cause that patients with symptoms notify the clinic irregular or not at all. Wearables may help identifying symptoms earlier.
A new design of a wearable is a smart t-shirt, which has sensors embedded.
The purpose of this study is to evaluate the feasibility of using a smart t-shirt for remote monitoring of biometric sensor data in adolescent and young adult (AYA) and elderly patients during cancer treatment.

Materials and Methods
Twenty Danish cancer patients ≥18 years in antineoplastic treatment at Department of Oncology Rigshospitalet Denmark will be recruited continuously, whether patients are in curative or palliative care.
10 cancer patients under 39 years defined as adolescents and young adults (AYA) and 10 cancer patients over 65 years defined as elderly. Inclusion in the study will have no interference with the treatment.
The OncoSmartShirt study is an explorative study investigating the feasibility of using the ChronolifeTM Smart t-shirt during cancer treatment. This smart T-shirt is designed with multiple sensors and electrodes fully embedded which engender 6 different measurements flow continuously.
The intervention being studied is: to wear a smart t-shirt throughout the day (minimum 12 hours pr day) for 3 weeks. Secondly qualitative interviews will be carried out and patients will be asked to fill in a questionnaire concerning their experience with wearing the shirt.

Results
Start-up of the trial and inclusion of patients will begin in June 2021.

Conclusion
The study will assess the feasibility of using the ChronolifeTM smart T-shirt for home monitoring of vital parameters in cancer patients during their treatment, and bring new insights to how wearables and biometric data can be used as part of symptom recognition in cancer patients in the quest of increasing patients' quality of life.

Patient involvement

#112: Sexual Counselling in Patients with Late Side Effects after Cancer in the Pelvic Organs

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Abstract
Introduction
Studies show, that 35-50% of survivors after pelvic cancer experience disease or treatment related sexual dysfunction. Besides physical problems, patients experience body image problems, relationship problems, anxiety, feelings of disappointment, and grief. These consequences potentially have a negative effect on sexual health and quality of life. Aim of the study is to estimate the impact of pelvic cancer on sexuality and to assess the need for and effect of sexual counseling and treatment.

Materials and Methods
The study started in November 2018 and proceeds over a 5-year period. If patients declare any sexual dysfunction after cancer treatment, they can – if desired – be referred to sexual counselling at either the two centres at Aarhus University Hospital or at Sexological Centre, Aalborg University Hospital.
Patients are assessed using different validated PROMs with focus on quality of life, sexual distress, and sexual functioning, with assessment before commencing sexual counsellingt, and 3 and 12 months follow-up.

Results
By April 2021, 65 patients have been referred to sexual counselling and 58 patients have ended a course of treatment at either one of the three centres. About 2/3 of the referred patients are males. The majority of patients (74%) had rectal cancer. Among male patients, 83% had erectile dysfunction as the primary diagnosis at referral. Among female, the primary diagnoses were dyspareunia (56%), lack of desire (19%) and body image problems (19%).
Most male patients were treated with PDE-5 inhibitors, while female patients' estrogenic suppositories, hyaluronic gel, and dilation treatment.

Conclusion
This study will provide knowledge about the effect of sexual counselling on cancer related sexual dysfunction. With more data, we will be able to measure different outcomes prospectively, and record the need for and direct effect of professional treatment of any sexual dysfunction.

Patient involvement

#113: En antropologisk undersøgelse af implementering af fælles beslutningstagning i "Sammen om Valg – Et trygt forløb for den gynækologiske kræftpatient"

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Abstract
Introduktion
Fælles beslutningstagning (FB) kan bidrage til større involvering af patienter i kræftbehandling. Implementering af en ny praksis er imidlertid vanskelig. Projektet Sammen om Valg blev gennemført med det formål at understøtte et paradigmeskift og implementere FB i forbindelse med behandling af kvinder med recidiv af æggestokkræft. Indsatsen omfattede bl.a. udarbejdelse af to beslutningsstøtteværktøjer (BESLUTNINGSHJÆLPERTM).
Et kvalitativt, antropologisk studie havde til formål at afdække hvordan FB kom til udtryk blandt de sundhedsprofessionelle, samt hvilke faktorer i den kliniske praksis, der henholdsvis fremmede og hæmmede implementering af FB.

Materialer & Metoder
En antropologisk undersøgelse omfattede 16 dages feltstudier i 2019 i hver af de onko-gynækologiske ambulatorier i Århus, Odense og Vejle. Noter og lydfiler fra deltagerobservation, 17 semistrukturerede interviews med overlæger, afdelingslæger, yngre læger og sygeplejersker samt uformelle samtaler blev transskriberet og efterfølgende tematiseret som en del af den induktive metode.

Resultater
Der fremkom tre overordnede temaer; lægerne og FB, Beslutningshjælperen og sygelejerskerne og FB. Synlig ledelsesopbakning blev nævnt som en vigtig facilitator for FB, mens afdelingernes behandlings- og flowkultur virkede hæmmende. Kontinuitet og tillid mellem læge og patient kunne både fremme og hæmme implementering af FB. Nogle klinikeres frygt for patientens reaktion, hvis de blev præsenteret for Beslutningshjælperens statistikkort udgjorde en barriere for anvendelse. Sygeplejerskernes rolle i FB blev tydelig, når patienten havde brug for støtte i den nye rolle som aktiv beslutningstager.

Konklusion
På alle afdelinger herskede en "behandlings- og flowkultur", som kan hæmme implementering af FB, hvorimod forudsigelighed og synlig ledelsesopbakning faciliterer. Undersøgelsens resultater blev udmøntet i folderen '10 gode råd til implementering af FB' som siden er anvendt i de kliniske afdelinger.

Patient involvement

#114: Nurse-led consultations based on ePRO among women with gynecological cancer – design of a multidisciplinary study

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Abstract
Introduction
Electronic patient-reported outcome (ePRO) can facilitate appropriate and continuous symptom monitoring reported by the patient. An evidence-based approach to systematically monitor symptoms and communication with the patients to increase self-management is required. The purpose of this study is to develop a model of care for systematic nurse- led consultations based on ePRO and to investigate how these can be introduced into a multidisciplinary treatment regimen for patients with ovarian- and endometrial cancer.

Materials and methods
The study design is a quasi-experimental four-phase, sequential cohort research design with comparisons between non-equivalent groups. Women with ovarian- and endometrial cancer will be recruited before they receive first-line chemotherapy. This study will examine; 1) The frequency and severity of the management of symptoms in standard physician counseling (standard care), 2) Development of a new model of care, 3) A feasibility study testing nurse-led consultations based on ePRO, 4) Estimate the effect of nurse-led counseling based on ePRO compared to standard care. Patients in the intervention group will respond to a disease-specific PRO questionnaire once a week until treatment cessation. Patients in both groups will answer questionnaires (EORTC QLQ-C30, OV-28/EN-24, HADS, and SES6G) at baseline, 3,6, and 9 months.

Results
The primary outcome is health-related quality of life (EORTC QLQ-C30) at 9 months. Secondary outcomes will be the disease-specific quality of life (EORTC OV-28/EN-24), frequency and severity of physician/nurse-reported symptoms and adverse events (CTCAE), levels of anxiety, and depressive symptoms (HADS), and self-efficacy (SES6G).

Conclusions
We assume that proactive use of ePRO in nurse-led consultations may contribute to enhanced symptom management, self-management, and an improved CONNECTion between patients and healthcare professionals. The results of this study will be presented in 2024.

Patient involvement

#115: THE COST OF LIVING WITH CANCER DURING THE SECOND WAVE OF COVID-19: A MIXED METHODS STUDY OF DANISH CANCER PATIENTS´ PERSPECTIVES

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Abstract
Introduction
Being exposed to a threat like Covid-19 must be overwhelming for patients with cancer. Surveys have shown a high degree of concern. However, only a few qualitative studies exist, primarily from the first wave of Covid-19.
This study investigated experiences and levels of distress and resilience among Danish cancer patients during the second wave of the COVID-19 pandemic.

Material & Methods
The mixed methods design included a subset of cancer patients who had responded to a cross-sectional survey in May 2020. Data were collected through telephone interviews from September to November 2020. The National Comprehensive Cancer Network Distress thermometer (NCCN DT), and Connor-Davidson-Resilience Scale (CD-RISC2) were used to measure distress and resilience. Data were analysed by thematic analysis and descriptive statistics.

Results
Forty patients with lung, breast, colorectal and skin (melanoma) cancer were included; 65% were women. Mean age 62.2 years (standard deviation [SD], 13.2). Most patients had curable disease (65%); 50% were in active treatment and 50% in post-treatment follow up.
The interviews revealed four themes: 1) the cost of living with cancer during COVID-19, 2) changes in cancer care delivery, 3) particularly vulnerable 4) importance of family support. Mean NCCN DT score 2.3 (SD, 2.6). Mean CD-RISC2 score 7.25 (SD, 1.1).

Conclusion
Patients took many precautions, resulting in comprehensive limitations in daily and family live. Having cancer was still their primary concern. Cancer care delivery was often changed with telephone consultations. This was mostly accepted. Patients worried that COVID-19 would put a strain on the health system, indirectly resulting in poorer cancer care. Active treatment, comorbidities or older age increased feelings of vulnerability. Family support was essential, and the health system must find ways to include family virtually, especially during acute illness or important medical consultations.

Patient involvement

#116: Development of item set to evaluate acute patient-reported treatment toxicity to pelvic online magnetic resonance-guided radiotherapy

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Abstract
Introduction
The MR-linac provides online magnetic resonance-guided radiotherapy (MRgRT) that combines real-time visualization of the tumor and surrounding tissue with radiotherapy (RT) to deliver treatment more accurately. Patient-reported outcomes (PRO) add the patient perspective to evaluating treatment toxicity related to new technology. The objective of this mixed-methods study was to develop and explore the content validity of a set of PRO items to evaluate acute pelvic toxicity including online MRgRT.

Materials and methods
A literature review and chart audit were conducted to identify symptomatic adverse events (AEs) to be selected from the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) library and European Organisation for Research and Treatment of Cancer (EORTC) item library. To validate the content, the item set was applied in a prospective pilot cohort of patients referred for pelvic RT with curative intent. Patients reported symptoms weekly during RT and the subsequent four weeks. Follow-up reports were collected at 8, 12, and 24 weeks after RT. To ensure symptom coverage clinician-reported toxicity and individual patient interviews were obtained. The symptomatic AEs were included in the final item set if ≥20% of patients reported them.

Results
18 acute symptomatic AEs were selected for the initial item set. 40 patients (32 prostate cancer, 8 cervical cancer) were included in the analysis of the pilot study. Both patient groups reported all 18 acute AEs except for vomiting not being reported by >20% of patients thus excluded from the item set. Adding a few diagnosis-specific AEs was required for both prostate and cervical cancer patients.

Conclusions
An item set was developed for prostate and cervical cancer patients to assess the most common acute symptomatic AEs related to primary pelvic RT including online MRgRT. Capturing all patient-reported symptoms required adding diagnosis-specific items.

Patient involvement

#117: The iBlad App - a tool for patient involvement and symptom tracking in bladder cancer

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Abstract
Introduction
Thirty percent of all bladder cancer patients receive chemo- or immunotherapy for muscle-invasive and/or metastatic disease, resulting in a vast burden of symptoms. Knowledge about symptoms and quality of life (QoL) may improve management and supportive care. Results from the iBLAD study show that the patients are willing to participate in PRO-research, have high rates of hospitalization and low rates of treatment completion, due to potentially preventable symptoms. Moreover, they have an overall good compliance with ePRO. The aim of this project is to develop and implement a national application (app) for patients with bladder cancer that builds upon knowledge from the iBLAD study.

Methods and materials
The tailored symptom questionnaire, developed in the iBLAD study be integrated into the app and the patients´ reports used actively. If the patients report a symptom, they will receive self-management advice or be told to contact the hospital, depending on the severity. The patients will also complete QoL questionnaires (QLQ-C30 and QLQ-BLM30). Moreover, the patient reporting can be used as a dialogue tool during the clinical encounter. Thus, the app will enable regular symptom tracking, feedback to patients and QoL reporting to achieve earlier symptom management and improved supportive care.

Results
Implementation will take place at six hospitals across Denmark, the goal being to make the app a part of routine care. Development and implementation will be carried out in close cooperation with the patient organization for bladder cancer, the multidisciplinary cancer group and the Danish national clinical database. The aggregated data can be used for research in the future.

Conclusion
In this study, a national app will be developed and implemented, enabling monitoring of symptoms and QoL among bladder cancer patients. In addition, self-management advice will be provided to patients and the app will serve as a dialogue tool in the clinical encounter.

Patient involvement

#118: Etablering af PRO forløb og App for patienter med prostatakræft i Aktiv overvågning.

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Abstract
Introduktion
Patienter diagnosticeret med prostatacancer, der behandles med Aktiv Overvågning, modtager meget forskelligartet opfølgning afhængig af kontaktlæge og bopæl. Manglende evidens for den bedste standardbehandling, kan mistænkes at bidrage til ulighed i sundhed
Vi ønsker at forbedre kvaliteten af behandlingstilbuddet Aktiv overvågning. Derfor udvikles en PRO intervention, stærkt inspireret af de erfaringer vi har fra 2500 patienter, som har været gennem andre PRO forløb i afdelingen. Formålet er at øge patientinddragelsen og bedre behandling og derved skabe de bedste rammer for patientens oplevelse af tryghed og overskuelighed. Interventionen er udviklet med hensigt at sikre, at vi kommer bedre omkring sygdom og symptomer ved alle patienter. Samtidig skabes der et sikkerhedsnet under deres behandling, i forhold til kontrol og opfølgning, dette har ikke har været standardiseret praksis tidligere.
PRO bidrager med viden om, hvordan prostatacancer påvirker patienternes livskvalitet, og lære patienterne at være opmærksomme på egne symptomer. Kontinuerlig dokumentering af livskvalitet i spørgeskemaet, vil bidrage til fokus på ændringer i deres symptomer.

Materialer & metoder
I dette studie udvikles en PRO App med det formål at styrke patientinddragelsen. Udgangspunktet er den eksisterende App: MitSygehus. App'en skaber et transparent forløb, så patienter og pårørende føler sig bedre støttet, med lettere adgang til informationer samt dialog med de fagprofessionelle.
Desuden udvikles en patientskole, med tilbud om introduktion til deres behandlingsplan samt viden om deres sygdom.
4 patienter har deltaget i udviklingen af forløbet og app modulet, for at sikre relevans af indholdet.
De 10 første deltagere i studiet inddrages til evaluering af det færdige indhold i App'en via kvalitative interview.

Resultater
Projektet er igangværende, med pågående dataindsamling. 90% af ny diagnosticerede patienter gennem 12mdr. forventes at deltage. Evaluering efter 6 og 12 mdr.

Patient involvement

#119: Udvikling af beslutningsstøtteværktøj til patienter med hoved-halskræft med formål at reducere barrierer til forskningsforsøg vedrørende protonterapi

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Abstract
Introduktion
Danskere har lige adgang til sundhedsydelser, men til trods for det, er der påvist social ulighed til bl.a. kræftbehandling. For patienter med hoved-halskræft er forskellen betydelig og har konsekvenser for overlevelsen.
I et nuværende forskningsforsøg afprøves, hvorvidt senfølger til strålebehandling af hoved-halskræft kan reduceres med protonterapi. I Danmark tilbydes protonterapi kun på Aarhus Universitetshospital.
Patienter med hoved-halskræft er hyppigere lavere uddannede, og kan have udfordringer med at forstå information om forskningsforsøg, samt forhold der gør sig gældende relateret til behandlingsforløbet med protonterapi. Eksempelvis den geografiske afstand til behandlingsstedet.
Dette projekts formål er at generere viden om faktorer og barrierer med betydning for patientens indgang i forskningsforsøg samt accept af behandling med protonterapi. På baggrund heraf udvikles et beslutningsstøtteværktøj, som bidrag til, at patienter tilegnes nødvendige forudsætninger for at kunne indgå i en beslutningsproces vedrørende forsknings- og behandlingstilbud af hoved-halskræft.

Metode
1. Tværsnitsstudie, hvor sammenhænge mellem socioøkonomiske – og geografiske faktorer, livskvalitet samt sundhedskompetence undersøges i forhold til deltagelse i forskningsforsøg.
2. Barrierer og facilitatorer til patientens indgang i forskningsforsøg samt accept af centraliseret protonterapi identificeres ved deltagerobservation i henvisende stråleklinikker samt interviews med patienter og læger.
3. Udvikling af beslutningsstøtteværktøj til patientens og lægens fælles beslutningsproces vedrørende forskningsforsøg og centraliseret protonterapi. Patienter og læger involveres som partnere gennem hele udviklings- test- og implementeringsprocessen.
Projektets vejledergruppe er Professor Cai Grau, Professor Susanne Dalton, Overlæge Kenneth Jensen samt Klinisk Sygeplejespecialist og antropolog Annesofie Lunde Jensen.

Resultater og konklusioner
Foreligger endnu ikke.

Patient involvement

#120: The DBCG RT SDM trial: Shared Decision Making with Breast Cancer Patients

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Abstract
Introduction
Implementation of shared decision making (SDM) with all cancer patients has been part of the Danish, national strategy for oncology care since 2016. One method of facilitating SDM is the use of a patient decision aid (PtDA), which present evidence-based options in a clear, neutral way and facilitate clarification of the patient's preferences. For the present study, a generic PtDA has been adapted to the clinical decision whether or not to have adjuvant whole breast radiotherapy. The hypothesis is that SDM supported by a PtDA will increase patient-reported engagement in the decision making on adjuvant radiotherapy.

Materials and Methods
This study is a multicenter, cluster-randomized phase III trial. At study start-up, physicians are randomized 1:1 to usual practice (arm A) or SDM supported by the PtDA (arm B). Physicians in arm B will use the PtDA during their consultations with the patients in the trial. Eligible participants are women above 18 years of age with histologically verified breast cancer (T1-2, N0-Nmi, M0) or ductal carcinoma in situ, who are offered adjuvant whole- breast RT 40 Gray/15 fractions (+/- boost) after breast-conserving surgery according to DBCG guidelines. The trial will include 662 patients in total. The primary endpoint is patient-reported engagement in radiotherapy decision making. Secondary endpoints are patient-reported fear of cancer recurrence, decisional conflict, decision regret, patient engagement, knowledge about radiotherapy, health-related quality of life, and oncologist-reported patient engagement. NCT 04177628.

Results
Accrual was initiated March 2020. As of April 2021, 228 patients were included, 130 of them in arm B. The trial is including at four Danish radiotherapy departments.

Conclusions
The gained evidence and practical experience from this trial are likely to facilitate further implementation of SDM in oncology practice and other medical specialties.

Patient involvement

#121: Oncology patients support the cardiopulmonary resuscitation (CPR) conversation: an exploratory mixed method study of CPR preferences

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Abstract
Introduction
Often, health care professionals struggle to discuss CPR preferences with advanced cancer patients. We aimed to study the views of oncology patients on the subject of CPR as well as the timing of a CPR conversation.

Materials and methods
We performed an exploratory qualitative study in the emergency function at the department of Oncology. All admitted patients were presented with a questionnaire concerning their views and thoughts on CPR. The association between patient characteristics and responses were analysed using multivariable multinomial logistic regression. After discharge from the hospital, semi-structured telephone interviews were conducted with a random subset of the study population and were analysed using qualitative descriptive method.

Results
114 patients completed the questionnaire. 73 patients (64%) had considered whether they wanted CPR in case of cardiac arrest. Specifically, 30 patients (26%) did not want CPR performed. Of these, six patients (20%) had a recorded do-not-resuscitate (DNR) order. 13 patients (11%) had made a living will. 53 patients (47%) had discussed CPR with others. 15 patients participated in the telephone interviews. The vast majority of the interviewees (14 patients) stated that the CPR conversation was important and natural. Regarding the timing of the discussion both early and late in the course of treatment were suggested. Some patients preferred a continuous discussion. Five patients stated that they preferred to talk to a physician they felt familiar with.

Conclusions
Most patients had contemplated CPR, but few patients had made a living will. Most interviewees supported a CPR conversation, however, the majority of patients who refused CPR, did not have a recorded DNR order. Further studies on the individualization and timing of the CPR discussion as well as the barriers of the health care professionals are needed.

Patient involvement

#122: Viden om kvalitet i kræftpatientforløb

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Abstract
Introduktion
For at sikre høj og ensartet kvalitet samt bedst mulig brug af ressourcerne i kræftpatientforløbet, er det essentielt at følge kvaliteten af de sundhedsfaglige indsatser på kræftområdet og handle, hvor der er potentiale for forbedringer. Det kræver viden om kvaliteten i hele forløbet.
Vi har undersøgt, hvad der definerer god kvalitet i kræftpatientforløbet, om sundhedsvæsenet har de nødvendige data til at måle kvaliteten, om der findes offentligt tilgængelig viden om kvalitet på kræftområdet, og hvem der har ansvaret for at måle og følge kvaliteten i det samlede forløb.

Materialer & Metoder
Undersøgelsen baserer sig på a) en gennemgang af rapporter, videnskabelig litteratur, hjemmesider samt lovgivning og retningslinjer på kræftområdet, b) interviews med repræsentanter fra sundhedsfaglige institutioner og organisationer, c) observationer i klinisk praksis og d) workshop med repræsentanter fra sundhedsfaglige organisationer og institutioner.

Resultater
Vi finder, at den eksisterende viden om kvalitet primært stammer fra den del af kræftpatientforløbet, der varetages af sygehuset, mens der er alt for lidt viden om kvaliteten af indsatser, der varetages af almen praksis og kommunerne. Der mangler viden om den del af det diagnostiske forløb, som ligger før kræftpakkeforløb, om diagnostiske undersøgelser og MDT-konferencer, samt om den del, der typisk følger efter behandlingen – bl.a. komplikationer, senfølger, rehabiliteringstilbud og basale palliative indsatser. Den eksisterende viden er spredt på mange aktører og i mange forskellige rapporter, som giver et fragmenteret billede af kvaliteten.

Konklusioner
Vi anbefaler, at der på nationalt niveau foretages en løbende systematisk monitorering af hele kræftpatientforløbet, og at der årligt offentliggøres en kvalitetsopfølgning på kræftområdet med fokus på, hvor der er forbedringspotentiale. Opfølgningen skal være rettet mod både sundhedsvæsenet og offentligheden, herunder patienter og pårørende.

Patient involvement

#123: 'I feel reassured but there is no guarantee'. How do women of childbearing age respond to conservative management of precancer? A qualitative study

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Abstract
Introduction
From previous studies, we know that many women experience discomfort, worry and anxiety when they are examined for and diagnosed with abnormal cytology. However, we have limited and contradictory knowledge about how a conservative treatment of cervical intraepithelial neoplasia (CIN) may affect women of childbearing age emotionally or how it may affect pregnancy plans.

Design/method
Twenty women of childbearing age who were diagnosed with CIN2 and managed conservatively with colposcopy, biopsy, and smear every 6 months, were interviewed. The interviews were audiotaped and transcribed verbatim. A thematic analysis was performed using a phenomenological approach.

Results
All participants experienced getting nervous and anxious when they initially were diagnosed with CIN2.
However, most women reported that they carried on with their everyday lives with only minor occasional worries about CIN2, often prompted just before check-up. The women did not postpone their plans for pregnancy due to CIN2, but experienced the worries and the check-ups associated with CIN2 as disruptive elements in their family planning. Various factors influenced the women's emotional well-being: coping strategies, life circumstances, information needs, mental and physical discomfort during gynecological examination with biopsy.

Conclusions
Our results indicate that for most younger women with CIN2, worries were prominent upon the first message about CIN2 and still present in the women's consciousness on occasion. Some women were particularly nervous and found the period between check-ups frustrating and challenging. This finding may provide a framework for CIN2 management for younger women of childbearing age. Responsive and prompt health care services that employ relational coordination, provide patient-centred information, and prepare women for living with uncertainty could ease and support women's emotional responses, when diagnosed with CIN2 and treated conservatively.

Patient involvement

#124: Living with CCUS and the increased risk of hematological malignancy – a qualitative study of patients' perspectives

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Abstract
Background
Studies have shown that patients in a genetic risk group experience psychological and emotional effects. The healthcare system's awareness of how information about genetic mutations is given to the patients and how the knowledge affects the patients play a significant role in the way knowledge of genetic mutations is handled by the patients.

Patients referred for long-term cytopenia would previously be informed that it was either due to immune destruction or decreased blood cell production. Next Generation Sequencing (NGS) allows many of these patients to be identified as having the premalignant condition Clonal Cytopenia of Undetermined Significance (CCUS), which means that they have acquired mutations in genes that are also known to be mutated in myeloid cancer. Some CCUS patients are at increased risk of developing aggressive myeloid cancer within 1-10 years. There are around 250 new cases in Denmark pr. year.

Since CCUS is a relatively novel diagnostic entity, it is of interest to investigate how such a premalignant diagnosis and consequently increased risk of developing cancer affects the patients' everyday life.
This study will provide hitherto new qualitative information on how CCUS patients experience and cope with genetic testing. It may also give perspective on how the information is perceived, whether patients achieve a full understanding of the meaning of having mutations and whether this understanding benefits the patients.

The aim is to investigate:
- how the awareness of having a premalignant diagnosis may influence patients' everyday life
- how the patient perceives the information giving by the doctor at diagnosis

Materials and methods
An exploratory and longitudinal qualitative study using individual interviews with 20 patients based on a semi- structured interview guide. It will be conducted twice, i.e., at study entry and one year after.

Results and Conclusions
Results from the first interviews will be presented at the meeting.

Patient involvement

#125: SELMA – Self management in chronic hematological disease.

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Abstract
Introduction
This is an ongoing study, which explores how quality of life, mental health and lifestyle is influenced when a follow-up program is terminated in a population of low risk hematological patients including both cancer survivors and patients with chronical hematological diseases.

Material & Methods
Between January 2020-2021, a total of 508 patients at the Clinic of Hematology, had their follow-up terminated. The information was provided via e-Box in a letter signed by the head of clinic. Approximately, one year after (spring 2021) we contacted all 508 persons in order to obtain information concerning symptoms of anxiety and depression, health related quality of life, health behavioral changes and health care utilization. Further we measured self-efficacy, health literacy and uncertainty intolerance. For cancer patients, we also assessed fear of cancer recurrence. We included treatment information from medical records and in the Hospital Discharge Register we identified information on comorbidity.

Expected results/Perspectives
Due to the exponential increase in longevity and improvements in cancer prognosis, routine follow-up applying standard protocols to all cancer survivors is continuously discussed. We aim to present data from a group of low-risk patients, who experience self-management compared to scheduled follow-up. The data presented will shed light on the psychological and behavioral consequences of terminating follow-up routine programs and switching to self- management for patients with low-risk hematological disease.

Patient involvement

#126: Esophageal and gastric cancer follow-up in Denmark: A critical evaluation of current practice with patient involvement and a framework for future follow-up

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Abstract
Introduction
Patient's quality of life (QoL) is affected following diagnosis and treatment of esophageal and gastric cancer, due to extensive treatment and a massive symptom burden.
Esophageal and gastric cancer survivors have reported a need for clear information of the disease and what to expect, as well as support to handling nutritional problems, psychosocial distress and to navigate in the healthcare system. This work presents the first steps in the process of developing a national follow-up model for esophageal and gastric cancer patients, aiming at improved support for symptoms and distress, followed by a positive impact on quality of life.

Materials and Methods
The study was designed as a case study for Denmark, providing a systematic effort to describe current quality of follow-up on a national level and to identify factors of importance for improvement of follow-up.
The process was based on comprehensive involvement og patients and health professionals from all treating centers in Denmark, and a scoping review of the literature.

Results
A patient advisory board was established and involved at a consultation level. Main outcomes from the patients were: sufficient access to help and support is conditioned by clear access to 'the system'; higher availability of peer support is requested, and information preferences differ immensely between patients.
There was marked variation between the departments, in particular with regard to the responsible health professional in consultations.
Of the 188 selected references, 12 were included in the review, describing interventions spanning from educational methods and symptom-specific interventions, to well-defined follow-up models.

Conclusions
Involvement of patients and health care professionals, along with identified literature led to constructive feedback on quality of current follow-up and elaborated factors of importance for improved practice, forming the basis for a future, national follow-up model.

Patient involvement

#127: Kræftpatienters oplevelser af telefonkonsultationer under corona-pandemien

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Abstract
Introduktion
Under corona-pandemien i foråret 2020 blev konsultationer på Klinisk Onkologisk Afdeling og Palliative Enheder på Sjællands Universitetshospital i videst muligt omfang ændret til telefonkonsultationer. For at belyse hvordan kræftpatienterne oplevede at være patient under corona-pandemien og ændringen til telefonkonsultationer, blev der gennemført en kvalitativ interviewundersøgelse.

Materialer og metoder
Der blev udvalgt 15 patienter fra afdelingen, som havde haft telefonkonsultation med lægen i foråret 2020. Blandt de interviewede var der patienter med tarmkræft, gynækologisk kræft, brystkræft, lungekræft og prostatakræft. Interviewene blev gennemført i juni og juli 2020, som semistrukturerede telefoninterviews. Interviewene blev optaget, ordret transskriberet og tematisk analyseret.

Resultater
Der fremkom fem temaer: Accept og forståelse for situationen, telefonkonsultationer tillægges mindre betydning, pårørendes deltagelse, konsekvenser af corona-pandemien, begrænsninger ved telefonkonsultationer og telefonkonsultationer fremadrettet.

De interviewede havde en forståelse for situationen, og telefonkonsultationer var bedre end ingenting. Telefonkonsultationerne blev tillagt mindre betydning, og patienterne antog en positiv besked, når pårørende ikke var inviteret med. Emotionel, kognitiv og praktisk støtte fra pårørende var essentiel. Der var en oplevelse af dobbeltbelastning i form af generelle bekymringer for kræftsygdommen og specifikke bekymringer for større sårbarhed ved covid-19. Manglende ansigtsudtryk, sprogbarrierer, færre nuancer og spørgsmål kunne være en udfordring ved telefonkonsultationer. Videokonsultationer, forberedelse og opfordring til deltagelse af pårørende på medhør blev foreslået til fremtidige telefonkonsultationer.

Konklusioner
Ved fremtidige telefonkonsultationer er det vigtigt, at formålet er tydelig, at patienterne ved hvad der forventes, og at pårørende inddrages for at sikre det bedste udbytte.

Patient involvement

#128: Capturing issues that matter the most to patients with metastatic melanoma to discuss with their physician

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Abstract
Introduction
Patient-reported outcomes (PROs) are increasingly being used to support patient-physician communication. However, systematic and evidence-based knowledge about issues that matters the most for patients with metastatic melanoma to discuss with their physician is scarce. We aimed to identify such issues and to explore the applicability of PRO-based dialogue tools to facilitate a focus on these issues.

Material and methods
In this exploratory study, 144 patients with metastatic melanoma were asked to complete a PRO-based dialogue tool before every planned consultation with a physician for a year. The dialogue tool consisted of the European Organization for Research and Treatment of Cancer-Core Quality of Life Questionnaire, the Hospital Anxiety and Depression Scale, and an open-ended question where the patients' three most important issues to discuss with the physician was to be reported. Data from this open-ended question was analyzed through qualitative content analysis and frequency and patterns were examined using descriptive statistics.

Results
In total, 1107 dialogue tools were completed. On average, patients completed the tool 5.5 times. Despite the completion of the tool, the open-ended question was not always completed. Side effects and symptoms were the most reported issues. No obvious pattern was found regarding age, sex or time. Five overriding themes emerged from the content analysis of the reported issues. These were only partly captured by the ordinary PRO measures.

Conclusion
The use of PRO measures in clinical communication is no guarantee of capturing all that matters to patients with metastatic melanoma to discuss with their physician. A more flexible and tailored approach than ordinary PRO measures is needed to capture what is most important to discuss. The addition of an open-ended question elucidating important issues can be beneficial. Further research is needed in sustainable PRO-based dialogue solutions.

Personalised Medicine, Biomarkers & Diagnostics: Poster #129-169

Personalised medicine, biomarkers & diagnostics

#129: Dissection of mantle cell lymphoma bone marrow B lymphocytes on the single-cell level with focus on clinical markers and SOXC family members

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Abstract
Introduction
Mantle cell lymphoma (MCL) is a B cell lymphoma with lymph node (LN), and often bone marrow (BM) involvement. Here, we study the transcriptome of BM MCL cells to provide insight into the complex and diverse molecular architecture of MCL.

Methods
CD19+ cells from diagnostic BM of 8 MCL patients (pts.) with LN and BM involvement and Cyclin D1 (CCND1)+SOX11+, was used for single cell mRNA sequencing (ScRNA-seq) with 10x Chromium and Illumina NovaSeq 6000. Data was analyzed with Cell Ranger (10x Genomics) and R (Seurat 3.2).

Results
ScRNA-seq revealed transcriptional inter-tumor heterogeneity, while healthy pre-pro/pro-B cells displayed similar expression across pts. MCL cells had enrichment of genes involved in key pathways related to B cell cancers such as PI3K/AKT/mTOR and NFκB.
Generally, the cells were transcriptionally defined as CD20+CD45+CD5low/-CD19 low/-CD23 low/-CD27 low/-. While the light chain (LC) restriction was overall concordant with clinical laboratory analyses, 9.5%(0.1–24.4%) of LC+ cells were both κ and λ +. A subset of SOX11+ MCL cells were CD23+(1.45–9.29%) supporting previous findings. While 85% of all SOX11+ cells were IgM+(35–98%) and 17% IgD+(1–43%), all pts. had SOX11+ cells expressing IgA(2–47%) and IgG(1–15%), suggesting that some MCL cells may be antigen-experienced although expected to originate from naïve B cells. Of all cells, 4.49% expressed SOX4, a marker of immature B cells, and 3.07% co-expressed SOX11. Not surprisingly, expression of MCL markers such as SOX11, CCND1, CD5 and CD20 were highly correlated (p=0.02, ρ=0.99).
A blastoid MCL case had a subset of cells co-expressing SOX11, SOX4 and FAT1 (20% of SOX11+). FAT1 is a marker of ALL, and SOX4 play a role in survival of malignant lymphoblasts, posing these for further investigation.

Conclusion
Our study demonstrates inter-tumor heterogeneity, characterizes MCL-specific expression profiles and provides insight into clinical markers at single-cell mRNA level.

Personalised medicine, biomarkers & diagnostics

#130: AHRR (cg5575921) methylation safely improves specificity of lung cancer screening eligibility criteria

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Abstract
Introduction
We tested the hypothesis that AHRR (cg05575921) methylation improves specificity of lung cancer screening eligibility criteria.

Materials and methods
9,206 individuals from a general population cohort, the 1991-94 examination of The Copenhagen City Heart Study were followed in the health registries for vital status and lung cancer within 5 years after baseline examination. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and number of eligible individuals per incident lung cancer for seven lung cancer screening eligibility criteria (DANTE, DLCST, ITALUNG, LUSI, NELSON, NLST and PLCO) were evaluated. AHRR (cg05575921) methylation extent at different cut points was added and results compared. The model with the lowest number of eligible individuals per 5-year lung cancer was validated within 5,370 individuals from the 2001-03 examination.

Results
The seven eligibility criteria, identified risk-groups ranging from 3,182 (DANTE) to 1,641 (ITALUNG) individuals. The PPV was highest for the PLCO criteria (3.2 %), while DANTE showed the highest NPV (99.7%). Adding AHRR (cg05575921) methylation led to much higher specificities for all criteria. Number of eligible individuals per 5-year lung cancer varied from 38 (NELSON) and to 27 (NLST) with AHRR (cg05575921) methylation <55%. This last model led to a reduced screening burden of 21.9 % and an increased ($p<0.05$) specificity to 84.0%. These findings were reproduced among the 5,370 individuals of the 2001-03 examination.

Conclusions
Adding AHRR (cg05575921) methylation on top of current eligibility criteria for lung cancer screening improves specificity by excluding those individuals with the lowest risk.

Personalised medicine, biomarkers & diagnostics

#131: Effect of radiation therapy on cerebral cortical thickness in glioma patients

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Abstract
Introduction
One of the side effects of radiation therapy (RT) is thinning of the cerebral cortex, which may contribute to cognitive impairment. In this study, we assessed the effect of RT on the thickness of the cerebral cortex in regions that have previously been found susceptible to dose-dependent cortical thinning .

Materials and methods
Six adult lower grade glioma patients were included in this study. Clinical CTs and MRIs were collected and co-registered before RT and one year post-RT. Changes in cortical thicknesses for selected regions were correlated to local dose. Spearmans' correlation was used to test for significant dependence between change in thickness and radiation dose. P-value <0.05 was considered significant. Bonferroni correction was applied for multiple testing (N=7).

Results
The mean changes in cortical thickness and corresponding dose in the supramarginal region were 0.04±0.05 mm and 16.9±17.0Gy, respectively. In the inferior parietal region, the values were 0.02±0.03 mm and 11.2±11.5Gy. In the superior parietal region, the values were 0.02±0.04 mm and 14.9±15.9Gy. In the superior temporal region, the values were 0.01±0.06 mm and 11.9±11.6Gy. In the posterior cingulate region, the values were -0.06±0.11 mm and 31.9±21.4Gy. In the paracentral region, the values were -0.02±0.07 mm and 26.3±24.6Gy. In the lateral orbitofrontal region, the values were 0.04±0.06 mm and 23.1±17.6Gy. Only the posterior cingulate region showed significant correlation between cortical thinning and local dose with a Spearmans' correlation coefficient of ρ=-0.93.

Conclusion
Of the previously reported dose dependent cortical thinning only the posterior cingulate region could be verified in the current patient population. For our population, the local dose values in this posterior cingulate region was higher that the remaining regions and it is likely that a population with a different distribution of regional doses would result in different cortical thinning.

Personalised medicine, biomarkers & diagnostics

#132: Standard versus delayed FDG-PET/CT imaging regarding detection of lymph node metastasis in patients with invasive bladder cancer scheduled for curative intended treatment

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Abstract
Introduction
In Denmark, 2-[18F]-Fluoro-2-deoxy-D-glucose (FDG)-positron emission tomography/computed tomography (PET/CT) is standard for detection of metastasis in patients with invasive bladder cancer (BC) before curative intended treatment (CIT).
The aim of this study is to examine if the difference in the standardized uptake value (SUV) between 60 minutes (standard imaging (SI)) and 180 minutes (delayed imaging (DI)) post FDG injection is a better predictor of pelvic lymph node (LN) metastasis than the current SI.

Material and Methods
A total of 220 patients diagnosed with invasive BC evaluated for CIT were examined with duel FDG-PET/CT. All patients had SI and an additional DI low dose scan of the pelvic region performed. Pathology for biopsied or removed LNs were registered. Scans were evaluated by two experienced nuclear medicine specialists blinded to the final pathological outcome. SUVpeak and SUVmax were registered for all pelvic LNs with FDG uptake at both scan time. Receiver operating characteristic (ROC) curves were calculated with regards to metastasic prediction from difference in SUVpeak and SUVmax. ROC curves were used to determine the optimal cut-off, with sensitivity and specificity, for the percentage change in SUVpeak and SUVmax respectively.

Results
Fifty-two patients had 72 pelvic LNs with FDG uptake on both scans with known histology. Of the 72 LNs, 49 (68%) were negative for metastasis and 23 (32%) were positive for metastasis. A 16% increase from SI to DI in SUVpeak was optimal cut-off with a sensitivity of 54% and a specificity of 74% with AUC of 0.66 (95% CI: 0.52-0.79). For the SUVmax the optimal cut-off was a 37% increase from SI to DI with a sensitivity of 55% and a specificity of 70% with AUC of 0.59 (95% CI: 0.45-0.73).

Conclusions
We found that an increase in SUVpeak or SUVmax from SI to DI could be a potential predictor of LN metastasis in patients with BC where LNs with increased FDG uptake are identified on FDG-PET/CT.

Personalised medicine, biomarkers & diagnostics

#133: Scrotal Paget's disease associated with metastatic carcinoma with apocrine features and ERBB2-amplification/HER2 overexpression responding well to weekly paclitaxel combined with trastuzumab and pertuzumab. A case report.

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Abstract
Introduction
Extramammary Paget's disease might be associated with underlying malignancy.
Cutaneous apocrine carcinoma is a rare type of sweat glands neoplasm, usually localized in the axillary or anogenital regions.Metastatic cases are diagnostic and therapeutic challenges. In some cases, human epidermal growth factor receptor 2 (HER-2) is overexpressed.

Materials and Methods
We report on a patient with a scrotal Paget's disease and primary disseminated carcinoma with apocrine features who was offered personalized treatment.

Results
A 65-year-old man presented with an erythematous, ulcerative and painful area at the scrotal skin and palpable lymph nodes in the left groin. An FDG-PET-CT scan showed bilateral PET-positive enlarged inguinal and iliac lymph nodes and FDG-accumulation in 6th cervical vertebrae, with a bone metastasis confirmed by a supplementary MR scan. A punch biopsy from the scrotum showed Paget's disease with microscopically invasive foci of carcinoma. Histological features were not specific, but immunoprofile was suggestive of apocrine carcinoma with HER-2 overexpression. The genomic profile showed ERBB2-amplification, a tumor-associated TP53 mutation and likely pathogenic SETD2 mutation. The tumor was microsatellite stable (MSS). After discussion of the case at the national tumor board, the patient was offered treatment with weekly paclitaxel combined with trastuzumab and pertuzumab every third week.After 3 series a CT-scan showed complete regression of the enlarged lymph nodes and sclerosing of corpus of the 6th cervical vertebrae. On inspection, the tumor area on scrotum decreased dramatically in size and the patient no longer experienced pain. The patient continues to have deep partial response.

Conclusion
Personalized treatment showed convincing radiological and clinical activity of this unusual case.

Personalised medicine, biomarkers & diagnostics

#134: Tumor mikromiljø i stadium II colon cancer

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Abstract
Introduktion
Patienter med stadium II colon cancer (CC) behandles primært med operation efterfulgt af adjuverende kemoterapi til udvalgte patienter med høj recidivrisiko. Værdien af de nuværende selektionskriterier er omdiskuteret og gevinsten af adjuverende kemoterapi kan ikke sikkert eftervises.
Projektet har til formål at finde biomarkører ved den invasive tumorfront i det tumoromgivende stroma, der kan anvendes prognostisk og identificere patienter med høj recidivrisiko, så kemoterapi kan målrettes denne gruppe patienter.

Materialer & metoder
Der etableres en moderne, screenet patientkohorte behandlet efter opdaterede kirurgiske og onkologiske principper inkluderende st. II CC patienter operativt behandlet i Region Syddanmark i perioden 2014-2016. Alt udtaget og arkiveret tumorvæv indhentes og en biobank med vævssnit fra den dybeste nedvækst i tarmvæggen indsamles. På disse vævssnit vil vi kortlægge mikromiljøet omkring tumor og karakterisere samt kvantificere forskellige tumorassocierede immun- og stromaceller (T-lymfocytter herunder regulatoriske T-lymfocytter samt cancer-associerede fibroblaster) og karakteristika omkring tumor (tumor-stroma ratio og tumor budding). Evalueringen foregår dels ved mikroskopi af HE- samt immunhistokemisk farvede vævssnit og dels ved digital mikroskopi, hvor vi udvikler en app-baseret billedalgoritme som kvantificeringsværktøj. Den prognostiske værdi af biomarkørerne vurderes ved at sammenholde med recidiv og overlevelsesdata, der indhentes fra den elektroniske patientjournal COSMIC med en follow-up tid på mindst 5 år efter operation.

Resultater
521 patienter er inkluderet i kohorten. En mikroskopisk gennemgang af alt tumorvæv fra tarmresektaterne er pågående og forventes afsluttet august 2021. Herefter påbegyndes evalueringen af de enkelte biomarkører.

Konklusion
Studiet forventes at klarlægge den prognostiske værdi af biomarkører i tumors mikromiljø i en velkarakteriseret og screenet kohorte af st. II CC patienter.

Personalised medicine, biomarkers & diagnostics

#136: Prevalence of HER2 overexpression and amplification in squamous cell carcinoma of the esophagus: A systematic review and meta-analysis

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Abstract
Introduction
The prevalence of HER2 positivity in esophageal and gastric adenocarcinoma (ADC) has been studied extensively and the benefit of HER2 directed therapy is well established in ADC. In contrast, accurate data on HER2 in esophageal squamous cell carcinoma (ESCC) is lacking and there is no published clinical data on HER2 targeted treatment for ESCC.
The objective of this study was to assess prevalence of HER2 positivity in ESCC, in order to evaluate feasibility of initiating a phase 2 trial of HER2 targeted treatment in ESCC patients.

Methods
We conducted a systematic review and meta-analysis examining the prevalence of HER2 in ESCC. Data on in situ hybridization (ISH) and immunohistochemistry (IHC) were extracted to derive pooled prevalence estimates and characteristics of the studies were extracted for subgroup analysis.

Results
Eighteen studies were identified with a total of 1505 patients. HER2 gene amplification by ISH were prevalent in 10 % (95 % CI 6.9 %–15 %) of ESCC patients. The prevalence of HER2 overexpression (IHC3+) and borderline HER2 expression (IHC2+) were 6 % (95 % CI: 3.5 %–8.7 %) and 10 % (95 % CI: 6.0 %–17 %), respectively. An estimated 8.6 % (95 % CI: 5.5 %–13 %) of ESCC patients were HER2 positive using initial IHC followed by reflex ISH confirmation of borderline HER2 expression.

Conclusion
Estimated prevalence of HER 2 positivity in ESCC were 10% assessed by ISH and 8.6% assessed by initial IHC followed by ISH. This warrants further investigation and we are planning to conduct a national retrospective analysis of ESCC tissue to evaluate for HER2 overexpression and amplification. As well as conducting a national phase 2 trial of trastuzumab in combination with chemotherapy and pembrolizumab as first line treatment in metastatic HER2 positive ESCC patients.

Personalised medicine, biomarkers & diagnostics

#137: Circular RNA as a prognostic biomarker in stage II colon cancer

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Abstract
Introduction
The current treatment of stage II colon cancer faces major challenges as 10-20% of patients suffer from relapse despite surgical treatment and adjuvant chemotherapy. This situation calls for new approaches as we do not have any good methods of eminent selection of patients with high risk of recurrence, in addition, chemotherapy is not very efficient and has considerable toxic side effects. The aim of this study is to divide patients into groups with a low-risk and a high- risk of disease relapse by evaluating the biomarker potential of circular RNA (circRNA). circRNA has until recently been seen as a product of erroneous splicing, but studies about the functions and importance in cancer development has now begun to emerge. The fact that the circRNAs does not have any free ends makes it an extremely stable molecule that is preserved and measureable on formalin-fixed paraffin-embedded (FFPE) tissue. The current known functions of circRNA, includes but are not limited to sponging of tumor suppressing micro RNA, protein sponging and gene expression regulation.

Methods and materials
On a discovery cohort of fresh frozen colon cancer tissue, we will perform a broad RNA expression analysis, by using RNA sequencing. Subsequently we will investigate the most promising candidates in a large danish cohort. We will develop highly sensitive and specific assays with clinical applicability using the nCounter SPRINT platform from NanoString Technologies that are capable of measuring circRNA on FFPE tissue, making it highly clinically relevant. Lastly, we will identify the cellular origin of these candidates by using in situ hybridization and compare the expression pattern with data on tumor stroma interaction.

Results
We expect that our results will contribute to the selection of patients with stage II colon cancer with high risk of disease recurrence.

Conclusions
We expect the study will discover the potentials of circRNA as a biomarker in colon cancer.

Personalised medicine, biomarkers & diagnostics

#138: Validation of SFRP1 Promoter Hypermethylation in Plasma as a Predictor of Survival and Gemcitabine Efficiency in Patients with Stage IV Pancreatic Adenocarcinoma

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Abstract
Introduction
No reliable predictive blood-based biomarkers are available for determining survival from pancreatic cancer. This combined explorative and validation study examines promoter hypermethylation of Secreted frizzled- related protein 1 (phSFRP1) in plasma-derived cell-free DNA as a predictive marker for survival and gemcitabine effectiveness in patients with stage IV pancreatic adenocarcinoma.

Materials and Methods
This work consists of an explorative study and a validation study. Patients were included prospectively. Blood samples were drawn before diagnostic workup and treatment. We conducted methylation-specific polymerase chain reaction analysis of the promoter region of the SFRP1 gene, based on bisulfite treatment. Survival
was analyzed with log-rank test and Cox proportional hazard regression. The adjusted model included the variables age>65, WHO Performance Status, and gender.

Results
The explorative study included 40 patients. Patients not receiving chemotherapy (n=15) had a mOS of 2.0 months. Among patients who received gemcitabine (n=25), patients with phSFRP1 had a shorter median overall survival (4.4 months) than the unmethylated group (11.3 months). This difference was significant in adjusted cox-regression with a HR of 4.8 (95% CI; 1.5-15.3). The validation study included 58 patients who received gemcitabine. Patients with phSFRP1 had a shorter median overall survival (3·2 months) than the unmethylated group (6.3 months). This difference was significant in adjusted cox-regression with a HR of 3.5 (95% CI; 1.8-6.7).

Conlusions
In both the explorative and the validation study, phSFRP1 was associated with poorer survival in stage IV pancreatic cancer patients receiving gemcitabine treatment. This may indicate that SFRP1-positive tumors are more aggressive and less sensitive to gemcitabine treatment than tumors without SFRP1 hypermethylation. This knowledge may facilitate tailored treatment of patients with stage IV pancreatic adenocarcinoma.

Personalised medicine, biomarkers & diagnostics

#139: CLINICAL USE OF CIRCULATING TUMOUR DNA IN METASTATIC ALK-TRANSLOCATED LUNG CANCER

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Abstract
Introduction
Metastatic non-small cell lung cancer (NSCLC) is a clinical challenge because of its poor prognosis. The discovery of oncogenic drivers in metastatic NSCLC has improved survival with the development of oncogene directed targeted therapy. The EML4-ALK (ALK) translocation is an oncogenic driver found in approx. 5% of all NSCLCs. The standard treatment for patients with incurable ALK-translocated NSCLC is ALK-inhibitors. However, the clinical efficiency varies greatly among patients. Moreover, acquired treatment resistance is inevitable and little is known about its underlying mechanisms.

Aim
To investigate if circulating tumour DNA (ctDNA) from blood samples can be used to evaluate treatment response and detect resistance mechanisms in patients with metastatic ALK-translocated NSCLC.

Materials & Methods
This is a multinational, prospective project. Patients with ALK-translocated metastatic NSCLC treated with ALK-inhibitors as part of routine clinical practice are included. Blood samples are collected at each routine outpatient visit. The ctDNA is extracted from plasma and analysed by next generation sequencing (NGS) analysis. NGS analysis is performed at baseline before treatment start, at 14 days after treatment start and at clinical progression or death.

Results
The study is ongoing. We are currently starting to analyse the baseline and the first blood samples after treatment start. Our preliminary results show that the ALK translocation in the blood disappears after commencement of ALK-targeted treatment. We will continue to assess the effect of treatment and correlate it with ctDNA dynamics, and we will investigate resistance mechanisms.

Conclusions
We hope that this project can identify ctDNA as a tool for optimising future targeted treatment of ALK-translocated NSCLC. This project has the potential to help select the right patient at the right time for the right treatment.

Personalised medicine, biomarkers & diagnostics

#140: Deeper insight into intratumoral heterogeneity by MRI and PET-guided stereotactic biopsies from glioblastoma patients

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Abstract
Introduction
Glioblastoma is one of the most aggressive cancer and its molecular evolution is not fully understood. We used PET imaging combined with deep sequencing of glioblastoma biopsies at both the RNA and DNA levels to get a deeper insight into molecular evolution. In the clinical setting, PET imaging provides information about metabolically active tumor areas, but the genetic signature are unclear. Our primary objective was to perform an intratumoral spatial comparison of biopsies from potentially aggressive and less aggressive areas in glioblastomas according to PET scans.

Materials and methods
We used MRI, 11C-methionine(MET) PET, and 18F-FDG PET in combination to obtain a series of neurosurgical stereotactic biopsies from tumor areas with high MET and 18F-FDG uptake (hotspot), low MET and 18F-FDG uptake (coldspot), as well as tumor periphery of six glioblastoma patients that were processed for whole genome, exome, and transcriptome sequencing.

Results
Differential gene expression and gene ontology analysis showed that hotspots were enriched in gene sets associated with DNA replication, cell cycle, and ligand receptor interaction. Genome and exome analysis suggested hotspots and coldspots to have similar mutational profiles. However, a limited number of hotspot-specific mutations and novel fusion transcripts indicated that hotspot associated tumor cells developed from coldspot associated tumor cells and point at the potential role of hotspot driver genes in glioblastoma evolution.

Conclusion
Our findings reveal that hotspots in glioblastomas represent a more advanced stage of molecular evolution than coldspots.

Personalised medicine, biomarkers & diagnostics

#141: Diffusion kurtosis imaging and white matter damage after radiotherapy of adults with brain tumours

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Abstract
Background
Radiotherapy (RT) is crucial in the treatment of adults with lower-grade gliomas (LGG), but may cause delayed and late toxicity with severe impact on patients' cognitive functioning and quality of life. A novel method, diffusion kurtosis imaging (DKI) may be able to detect microstructural white matter (WM) changes and thus serve as an early biomarker of radiation induced toxicity to healthy brain.

Materials and methods
Eleven adult LGG patients referred to postoperative RT were included. The MRI protocol consisted of pre- and post-contrast 3D T1W, axial T2 FLAIR, sagittal T2 and diffusion-weighted (DW) sequences including a fast, three minutes DKI sequence. Patients were scanned before RT and 3 and 12 months after the end of RT. WM and grey matter (GM) were segmented on the pre-treatment T1W MRI and rigidly co-registered to radiation dose distributions and follow-up scans. Mean diffusivity (MD) was calculated from the DKI scan in WM and GM for voxels receiving radiation dose between 0 and 45 Gy.

Results
Six patients (oligodendroglioma grade 2 (n=2), anaplastic oligodendroglioma (n=2), diffuse astrocytoma (n=1) and anaplastic astrocytoma (n=1)) were available for analysis. The median age was 52.5 years (33-64 years). The most common tumour location was frontal lobe (n=5) and the remaining was parietal lobe (n=1). Patients were treated with photons (n=3) or protons (n=3) to a prescribed dose of 50.4 Gy (n=3) and 59.4 Gy (n=3) using a relative biological effect of 1.1 in the proton plans. Pre-treatment median MD for GM and WM was 1.35 (1.18 - 1.47) µm2/ms and 1.01 (0.96 - 1.05) µm2/ms, respectively. The respective median MD increased to 1.44 (1.33-1.68, p=0.03) µm2/ms and 1.04 (0.98-1.15, p=0.03) µm2/ms for GM and WM at 12 months post RT.

Conclusion
Mean diffusivity may detect RT induced microstructural damage of WM and GM in LGG patients. Further validation on a larger patient population and assessment of the clinical relevance is ongoing.

Personalised medicine, biomarkers & diagnostics

#142: Combining artificial intelligence and patient reported outcome (PRO) for bleeding risk assessment in patients with cancer

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Abstract
Introduction
The strongest risk factor for bleeding episodes is previous bleeding. Therefore, detailed knowledge about bleeding history is important to stratify patients with cancer needing specialized care due to increased bleeding risk. Information on bleeding episodes can be found manually in the electronic health record (EHR), but it is a time-consuming cumbersome process. Further, the patient can provide supplementary knowledge about bleeding history, e.g. from outpatient episodes, but obtaining a detailed bleeding history is time-consuming. By combining an artificial intelligence (AI) algorithm for identifying bleeding episodes in the EHR and a patient administrated questionnaire on bleeding symptoms (self-ISTH-BAT), we aim to establish decision-support tools for bleeding risk assessment in cancer patient.

Method
An AI algorithm for identifying bleeding episodes in the EHR has been developed at our department. Our current AI algorithm has a 90% sensitivity and 90% specificity for detecting bleeding episodes in EHR. The algorithm will be applied on the EHR of all patients diagnosed with cancer in the region of southern Denmark from 2015 to 2020. Initially, the algorithm will be trained on patients with urogenital cancer. We expect the performance can be enhanced to >98% sensitivity and >98% specificity. Concurrent with the AI project, we have translated and validated a Danish self-ISTH- BAT, which prospectively will be applied to all patients before urogenital cancer surgery at Odense University Hospital. We will evaluate feasibility, user perspective and clinical usability of self-ISTH-BAT.

Result
As the project began Marts 2021, no data is available. We expect the projects will provide effective tools to risk stratify and handle patients with bleeding episodes and patients with cancer. Both the AI algorithm and the self-ISTH-BAT, can be incorporated in the EHR, and therefore be implemented in clinical settings immediately after success, probably nationwide.

Personalised medicine, biomarkers & diagnostics

#143: Immune evasion in Lynch syndrome associated epithelial ovarian cancer

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Abstract
Introduction
Lynch syndrome is a multi-tumor syndrome characterized by mismatch repair deficiency (MMR-d), microsatellite instability (MSI), and increased tumor-infiltrating lymphocytes (TILs) making these tumors candidates for treatment with immune checkpoint inhibitors. However, response may depend on tumor-induced immune evasion mechanisms, e.g. loss of Beta-2-Microglobulin (B2M) or up-regulation of programmed death 1 ligand (PD-L1). We investigated the immune response and B2M and PD-L1 expression in Lynch syndrome-associated ovarian cancers.

Material and methods
We successfully analyzed 30 Lynch syndrome-associated epithelial ovarian cancers collected through the Danish Hereditary Non-Polyposis Colorectal Cancer (HNPCC) register. MMR-d, MSI, immune response (CD3, CD8, and CD68), and immune evasion mechanisms (B2M and PD-L1) were investigated. Statistical associations between these markers were evaluated in addition to survival in relation to B2M/PD-L1.

Results
Of the 29 evaluable tumors, 27 were MMR-d (93.1%), while 14 of 26 evaluable tumors were MSI (53.8%). MMR- d/MMR-proficiency associated with MSI/MSS in 60.0%. Half of the ovarian tumors presented with high levels of TILs. Loss of B2M expression was observed in 46.7% of the tumors, while expression of PD-L1 was seen in 28.0% of the cases. There was no association between B2M/PD-L1 or MSI/TILs/survival. Loss of B2M was often seen in tumors with low TILs ($p = 0.056$ or $p = 0.059$ for CD3 and CD8 positive cells, respectively).

Conclusions
MMR-d, MSI, and TILs were also seen in Lynch syndrome-associated ovarian cancers making these potential candidates for checkpoint-based immunotherapy. Immune evasion through B2M may correlate with resistance but this needs to be investigated further in larger cohorts.

Personalised medicine, biomarkers & diagnostics

#144: MRI staging of colon cancer - a prospective blinded study

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Abstract
Introduction
Magnetic Resonance imaging (MRI) scanning is performed on almost all patients with rectal cancer. The main purpose was to assess the diagnostic accuracy of MRI staging in colon cancer.

Material and Methods
Patients had a computed tomography (CT) scan with multi-slice technique. For the MRI scan, a 3 Tesla MRI unit was used. Experienced radiologists reported the scans in a blinded setup. The CT and MRI scan results were presented at the multidisciplinary conference (MDT), where the blinding was lifted. Surgery was performed within a median of 7 days after the MDT. The endpoint of the study was the histopathological surgical specimen.

Results
From 2018 to 2020, 134 patients were included in the study. CT detected 118 of the 134 tumors, whereas MRI detected all tumors. Overall, for detecting bowel wall penetration CT had a sensitivity of 75.5% and specificity of 75.0%. MRI had values of 59.6% and 88.6% giving a positive predictive value of 93%. For discriminating T3ab and T3cd cancers CT had a sensitivity and specificity of 33.3 % and 77%, whereas MRI had higher values with 55.6% and 100%. CT could detect 31.3% and MRI 46.4% of all pT4 tumors, with a specificity of 89.1% and 95.3% respectively
The CT had a sensitivity and specificity in lymph node involvement of 59.0% and 56.3%. The same values for MRI were 57.4% and 54.2% respectively. For the evaluation of extra vascular involvement, CT had a sensitivity of 33.3% and specificity of 84.4 %. Whereas MRI had higher values with a sensitivity of 54.1% and specificity of 77.1%
Tumors containing mucin had less diffusion restriction with an ADC on 1.08 vs 0.767 ($p < 0.001$).

Conclusion
In general, colon tumors were 12 % less detectable at CT compared to MRI. MRI and CT had similar accuracy in detection of bowel wall penetration and lymph node involvement. MRI had higher positive predictive value in detecting advanced T3 and T4 tumors compared to CT. We found MRI promising in the preoperative staging.

Personalised medicine, biomarkers & diagnostics

#145: Beskrivelse af den nationale MDT konference for pancreascancer: deltagelse og tilbud om operation

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Abstract
Introduktion
I august 2018 iværksatte Sundhedsstyrelsen initiativet National MDT konference ved kræft i bugspytkirtlen. Ved den nationale MDT vurderes resektabiliteten af tumorer hos patienter uden metastatisk sygdom.
Undersøgelsen beskriver henvisningsandel og operationsandel for patienter, som er henvist til den nationale MDT konference.

Materialer & Metoder
Datakilder er journalnotater og henvisningsskemaer fra den nationale MDT ved Rigshospitalet, samt data fra Dansk Pancreas Cancer Database (DPCD). Studiepopulationen omfatter alle henviste patienter til den nationale MDT i perioden august 2018 – september 2020 (n=262). Der anvendes en referencepopulation af patienter med pancreascancer med diagnosedato i 2018 (N=1096) fordelt på bopælsregion ved diagnose. Udfald er estimeret henvisningsandel og operationsandel per bopælsregion, samt samlet opgørelse af resektionsandel.

Resultater
Fra august 2018 – september 2020 blev 262 patienter henvist til vurdering ved den nationale MDT, og heraf er 67 (26%) patienter blevet tilbudt et operativt indgreb. Region Midtjylland og Nordjylland henviste svarende til det skønnede forventede antal patienter uden fjernmetastatisk sygdom (115% og 107%, respektive). For Region Syddanmark var henvisningen lavere end det anslåede forventede antal (66%), og for Hovedstaden og Sjælland var det observerede antal henviste patienter betydeligt lavere end det forventede (17%). Resektionsandelen var 13% (34 af de 262 patienter).

Konklusioner
Fra august 2018 til september 2020 var der variation i henvisningsandelen til den nationale MDT mellem de fem danske regioner. I alt 26% af de patienter der blev evalueret på den nationale MDT blev vurderet til at være potentielt resektable, og der var kun lille variation mellem regionerne. Af de 26% blev halvdelen efterfølgende opereret. Således har den nationale MDT konference potentiale til at bidrage til at ensarte behandlingstilbuddet for patienter med pancreascancer i Danmark.

Personalised medicine, biomarkers & diagnostics

#146: Deep learning for triage in Danish breast cancer screening: A retrospective multicenter study of diagnostic accuracy, feasibility and clinical attributes

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Abstract
Introduction
Screening mammograms of Danish women are read independently by at least two expert breast radiologists. Double reading as well as a not insignificant false positive rate is quite resource demanding. Deep learning (DL) based solutions have shown great potential for reducing false positives, earlier detection of interval cancer and improving efficiency in mammography screening. This study investigates if a DL model used as a triaging tool can optimize workflow while maintaining a non-inferior cancer detection performance. Furthermore, clinical differences between DL-detected cancers and screen-detected cancers are evaluated.

Materials and methods
Nearly 262.000 consecutive screening mammograms between 2014 to 2018 from the Region of Southern Denmark (RSD) are collected with a 2-year follow-up period. Data is retrieved from the Vendor Neutral Archive of RSD (VNA SYD), Danish Quality Database on Mammography Screening (DKMS) and Danish Breast Cancer Cooperative Group (DBCG) database. Eligible study cases are processed by a commercially available CE marked DL model. In a simulated triage workflow, mammograms identified as non-suspicious by the DL model go only to single reading, while the rest above a triage threshold score go to standard double reading. The metrics of performance are the area under the curve (AUC), recall rate and number of examinations needing radiologist interpretation. Clinical differences between DL-detected cancers and screen-detected cancers in terms of patient and tumor characteristics as well as cancer outcomes are evaluated.

Results
The study is still ongoing and data collection has nearly been completed.

Conclusions
This study is expected to provide important information on how a DL model can improve diagnostic quality and optimize workflow in breast cancer screening. Results from this project are expected to benefit future national and international recommendations on the integration of DL solutions for mammography screening.

Personalised medicine, biomarkers & diagnostics

#147: Cervical intraepithelial neoplasia grade 2 (CIN2) - exploring the value of biomarkers for triage

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Abstract
Introduction
Cervical intraepithelial neoplasia (CIN) specifies HPV associated cervical precancer lesions derived from the squamous epithelial cell line. CIN is graded by the level of severity in CIN1 (low), CIN2 (moderate), CIN3 (severe) respectively. CIN2 represents a heterogenic expression of both CIN1 like and CIN3 like evolving lesions which current methods do not allow to discriminate in risk of progression. A reliable diagnose is a paramount in clinical management of CIN2 to avoid risk of over- or undertreatment (surgical procedure or surveillance), thus, ongoing efforts to explore novel methods in risk-stratification of CIN2 lesions are highly important. The novel biomarker HPV E4 targets main steps in the pathological pathway of cellular transformation in HPV associated lesions such as CIN2. Prior research, show that the biomarker can discriminate CIN1 like from CIN3 like resembling lesions in CIN2, suggesting that HPV E4 may be a valuable marker in risk-assessment of CIN2. We lack knowledge on HPV E4 as predictor for CIN2 evolvement.

Aim
To examine the potential of HPV E4 in predicting the risk of CIN2 progression.

Materials and Methods
We will conduct a case-control study, matched 1:1 on age and calendar year of diagnose. The study population represents N=500 women, 23-40 years of age with an incidental CIN2 diagnose during 2000-2010, followed by two years surveillance. Exposure: HPV E4 negative (CIN3 like). Cases are specified as those progressing (CIN3 or cervical cancer) during the surveillance period and controls those who regress (CIN1 or normal). Statistics: Conditional logistic regression model (OR (95%CI)).

Conclusions
HPV E4 may act as significant predictor for CIN2 evolvement and reliable marker for risk-assessment of CIN2 lesions. This may strengthen the shared decision-making in the clinical management of women with CIN2, enabling targeted treatment of those in need.

Personalised medicine, biomarkers & diagnostics

#148: Metabolic [18F]FDG-PET parameters at diagnosis are prognostic for overall survival in pediatric sarcoma patients

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Abstract
Introduction
Pediatric sarcoma is a heterogeneous group of tumors, where osteosarcoma (OSS), Ewing sarcoma (ES) and rhabdomyosarcoma (RMS) constitute the most frequently occurring subtypes. [18F]FDG PET/CT is an integrated part of staging and monitoring disease, but the prognostic value of [18F]FDG-PET metabolic parameters is still debated.
The aim of this study was to investigate pretherapeutic [18F]FDG parameters - metabolic tumor volume (MTV) and total lesion glycolysis (TLG) for primary tumor (P-MTV and P-TLG) and whole-body tumor burden (Total-MTV and Wb-TLG) in regards to prediction of overall survival (OS).

Methods
Retrospective, single-center study of children diagnosed with OSS, ES or RMS in the period 2005-2020 with a pretheraputic [18F]FDG-PET/CT. Maximum standardized uptake value (SUVmax) and SUVpeak were measured in primary tumor and metastases. Semiautomatic volumes of interest (VOI) of
all tumor lesions were drawn using following SUV thresholds: SUV 2.0, SUV 2.5, SUV 40%max, SUV 60%max, SUVmean liver+1SD and SUVmean liver+2SD. P-MTV, P-TLG, Total-MTV and Wb-TLG were calculated for each threshold. Outcome data regarding OS were collected from the Danish register of pediatric cancer (DBCR).

Results
66 patients had pretherapeutic [18F]FDG-PET/CT (OSS:n=18, ES:n=24, RMS:n=24). Five-year OS was 74.2%. In univariate Cox regression analysis of Log2 transformed variables with OS as outcome, Log2-Total-MTVLiver1SD resulted in the highest hazard ratio (HR) of 1.45 (95% CI:1.15-1.82, P=0.002). Log2-Wb-TLG40%, Log2-Wb-TLGLiver1SD, Log2- Total-MTVLiver2SD, Log2-Wb-TLGLiver2SD were also significantly associated with OS (P <0.05).

Conclusion
This is the first study investigating [18F]FDG parameters including both primary tumor and metastases in pediatric sarcoma. We find Total-MTV and Wb-TLG based on SUV thresholds normalized to mean liver uptake are significantly associated with OS, suggesting these may be useful prognostic biomarkers in risk stratification.

Personalised medicine, biomarkers & diagnostics

#149: Single-cell analysis of tumor-associated microglia and macrophages from human glioblastoma

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Abstract
Introduction
Patients with glioblastoma, the most frequent and malignant primary brain tumor type, have a poor prognosis with a median survival of 14 months. A major therapeutic problem is chemoresistance. In surgically removed glioblastoma tissue, tumor-associated microglia and macrophages (TAMs) constitute up to 30 % of the cells. These cells are capable of secreting cytokines, chemokines and growth factors, thereby influencing the local microenvironment. However, the existence of different TAM subtypes and their role in glioblastoma is not fully comprehended and rarely considered therapeutically. This could explain why many clinical trials fail despite of promising preclinical results.
This project aims to interrogate the existence and characteristics of different TAM subtypes in human glioblastoma biopsies in order to identify novel subpopulations and therapeutic targets.

Materials and Methods
CD11b+ TAMs were isolated from patient glioblastoma tissue, and single-cell RNA sequencing was performed using the 10X Genomics Chromium platform for single-cell generation and an Illumina NovaSeq6000 system for sequencing.

Results
We have now sequenced 50,000 TAMs from three glioblastomas and 24,000 microglial cells from two normal brain biopsies. We were able to identify known TAM populations, but also subpopulations, which have not been described before. Analysis is ongoing.

Conclusions
We have detected a TAM population which is more complex than the established M1 and M2 phenotypes, constituting a novel TAM subpopulation. We are currently investigating this finding to validate specific markers associated with this subpopulation, and for identification of novel clinically relevant targets.

Personalised medicine, biomarkers & diagnostics

#150: DPYD-genotype bestemmelse før opstart af 5-fluorouracil, capecitabin, og tegafur.

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Abstract
Introduktion
DPYD-genet koder for enzymet dihydropyrimidindehydrogenase (DPD), som er det hastighedsbegrænsende enzym i nedbrydningen af fluoropyrimidiner (FP), som omfatter 5-fluorouracil, capecitabin, og tegafur. I Danmark behandles årligt omkring 4.500 patienter med FP, hvoraf størstedelen er patienter med gastrointestinale karcinomer. Patienter med nedsat DPD-aktivitet har markant øget risiko for alvorlig toksicitet, som inkluderer diarré, mucositis, febril neutropeni og i sjældne tilfælde død, ved standard dosering af FP. Den hyppigste årsag til nedsat DPD-aktivitet er enkeltnukleotidpolymorfier, i DPYD-genet. I litteraturen er der beskrevet 4 relativt hyppige mutationer i DPYD-genet med betydning for hyppigheden af alvorlig toksicitet. Ved at nedsætte startdosis med 50% hos patienter med nedsat DPD-aktivitet kan risikoen for alvorlig toksicitet således reduceres. EMA anbefalede i marts 2020 at teste for nedsat DPD-aktivitet før behandling med FP. Formålet med dette studie er at implementere DPYD-genotypen i standard klinisk praksis samt at registrere frekvensen af alvorlig toksicitet.

Materialer & Metoder
Siden juli 2020 har test af DPYD-genotypen været standard på OUH til patienter, der behandles første gang med FP. DPYD-genotypen analyseres to gange om ugen, og der undersøges for 4 mutationer i DPYD-genet.

Resultater
Siden d. 1/7/2020 har 579 patienter fået analyseret DPYD-genotypen på OUH. Der er fundet 9,3% (54/579) patienter, som var heterozygote for en af de undersøgte DPYD-varianter.

Konklusioner
Implementering af DPYD-genotypen er praktisk mulig. De foreløbige resultater tyder på, at forekomsten af kliniske betydende DPYD-varianter er højere i Danmark end andre steder i Europa. I større studier fra Frankrig og Holland har man fundet henholdsvis 4,7% og 7,7% som var heterozygote. Udover at undersøge forekomsten af DPYD-varianter i Danmark skal projektet undersøge, om anvendelsen af DPYD-genotypen reducerer forekomsten af alvorlig toksicitet.

Personalised medicine, biomarkers & diagnostics

#151: Whole Genome Sequencing of Circulating Tumor DNA (ctDNA) in MetastaticCastration Resistant Prostate Cancer

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Abstract
Introduction
Prostate cancer (PC) causes ~1200 deaths/year in Denmark, as advanced metastatic castration resistant PC (mCRPC) remains incurable. Genomic biomarkers that predict mCRPC progression and treatment response are urgently needed to facilitate personalized treatment. Plasma contains cell free DNA (cfDNA), a subset of which in cancer patients is tumor-derived (circulating tumor DNA, ctDNA). We previously investigated the biomarker potential of cfDNA low-pass (LP, ~0.5X) whole genome sequencing (WGS) and targeted sequencing, but the value of deeper and broader WGS in mCRPC patients is undescribed.

Materials and methods
In this pilot study, we performed WGS of plasma cfDNA and matched buffy coat (blood leukocytes) samples from 10 mCRPC patients previously analyzed by LP-WGS and targeted sequencing. In WGS data, single-nucleotide variants (SNVs) and indels were called with Mutect2, copy-number variants (CNVs) with ichorCNA, and structural variants (SVs) with BRASS.

Results
We sequenced the samples to a coverage of 20-28X (buffy coat) and 27-44X (cfDNA). Preliminary variant analysis identified a median of 19,646 SNVs/patient (range: 12,463-52,013) and 3270 indels/patient (range: 1871-104,084). SNV/indel rates were highest in intergenic regions (15.7 variants/Mb) and lowest in 5'-UTR regions (10.7 variants/Mb). Furthermore, a median of 50.4% of the genome was affected by CNVs (range: 17.5-78.9%). Common PC CNVs were observed, including gains at chromosome 8 (MYC) in 9/10 patients and at chromosome X (AR) in 3/10 patients. Finally, a median of 209 SVs (range: 88-554) were called in each patient. PC SVs often affect TMPRSS2, and this was observed in 3/10 patients. Onwards, we will run additional variant callers to strengthen our findings. We will also analyze kataegis, chromotripsis, chromoplexy, and mutational signatures in the data.

Conclusions
WGS of mCRPC cfDNA contributes to the identification of ctDNA variants that may serve as novel potential biomarkers.

Personalised medicine, biomarkers & diagnostics

#152: Serial analysis for methylated circulating tumor DNA enables early detection of recurrence in patients treated for colorectal cancer liver metastases

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Abstract
Introduction
Despite curatively intended surgery of colorectal cancer liver metastases (CRLM), the prognosis remains poor with nearly 50% recurring within two years. Due to lack of evidence, there is no international consensus of post-operative surveillance for CRLM patients. Here we evaluated the clinical pertinence of longitudinal circulating tumor DNA (ctDNA) as a prognostic marker of recurrence and compared it to standard-of-care surveillance.

Materials and methods
We recruited 96 patients treated for CRLM with curative intent. ctDNA was assessed every third month for up to three years using the multiplex droplet-digital PCR test “TriMeth”, which targets three colorectal cancer-specific DNA methylation markers. We retrospectively analyzed 499 plasma samples blinded for clinical outcome.

Results
TriMeth ctDNA status of post-operative blood samples collected before and after adjuvant chemotherapy (ACT), showed significant association to recurrence free survival (before ACT: HR=4.5, 95% CI: 2.1–9.5, P<0.0001; after ACT: HR=6.1, 95% CI: 2.5–15.4, P<0.0001). Overall, serial TriMeth analysis revealed sensitivity of 87% for recurrence detection. Notably, TriMeth identified molecular recurrence up to 17 months before radiologic recurrence (median 6.5 months, IQR: 3.8–9.8, P<0.0001). During surveillance, around 10% of CT scan results were inconclusive. TriMeth analyses at the time of inconclusive CT scans predicted recurrence with high positive and negative predictive values (PPV=100%, NPV=75%). Using serial ctDNA analysis, we assessed the ctDNA growth rate and discovered that fast growth was associated with poor overall survival (HR: 1.6, 95% CI: 1.1–2.2, P=0.0053).

Conclusion
Serial post-operative TriMeth ctDNA analysis has a strong prognostic value and is more sensitive for recurrence detection than CT imaging. The novel combination of ctDNA detection and CT scans provides unique opportunities for optimizing the post-operative surveillance of patients with CRLM.

Personalised medicine, biomarkers & diagnostics

#153: Overweight and prognosis in triple-negative breast cancer patients: a systematic review and meta-analysis

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Abstract
Purpose
To conduct a systematic review and meta-analysis evaluating the impact of overweight on prognosis in triple- negative breast cancer (TNBC) patients.

Methods
Systematic searches were conducted in PubMed and Embase using variations of the search terms triple- negative breast neoplasms (population), overweight and/or obesity (exposure), and prognosis (outcome). Data were extracted from longitudinal observational studies, which used survival statistics with hazard ratios (HRs) to examine disease-free survival and/or overall survival according to body mass index measured at the time of diagnosis of TNBC. Overweight was defined using the World Health Organization guidelines. Guided by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist, study data were extracted and study quality assessed with the Newcastle- Ottawa Scale independently by two authors. The effect sizes (HRs) were combined with random-effects models, and the results were evaluated and adjusted for possible publication bias.

Results
The study selection process identified 13 eligible studies of 8,944 TNBC patients. The pooled estimates indicated that, relative to non-overweight, overweight was associated with both shorter disease-free survival (HR=1.26; 95%CI: 1.09–1.46) and shorter overall survival (HR=1.29; 95%CI: 1.11-1.51). Supplementary Bayesian meta-analyses showed evidence for non-zero effects, with the alternative hypothesis being 7.4 and 9.9 times more likely than the null-hypothesis for disease-free survival and overall survival, respectively.

Conclusion
The available data suggest that overweight is associated with shorter disease-free and overall survival among TNBC patients. The results should be interpreted with caution due to possible publication bias.

Personalised medicine, biomarkers & diagnostics

#154: Validation of Updated Diagnostic Criteria: IDH-Wildtype Diffuse Astrocytoma with Molecular Features of Glioblastoma

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Abstract
Introduction
A committee by cIMPACT-NOW recently agreed on a panel of three molecular criteria, able to identify isocitrate dehydrogenase wildtype (IDHwt) diffuse astrocytic gliomas (DA) exhibiting a more aggressive clinical course with shorter survival, resembling glioblastoma WHO grade IV. The criteria are epidermal growth factor receptor amplification, telomerase reverse transcriptase promoter mutation and combined whole chromosome 7 gain and whole chromosome 10 loss. Only one molecular criteria is required to diagnose: "Diffuse astrocytic glioma, IDH wildtype, with molecular features of glioblastoma, WHO grade IV". The aim of this study was to validate the updated diagnostic criteria.

Materials and Methods
Patients diagnosed with DA from 2004-2018, at Aalborg University Hospital were included. Tumor samples from the time of diagnosis were examined for the molecular markers using Next Generation Sequencing, immunohistochemistry and fluorescence in situ hybridization. Crude and adjusted cox regression analyses, log-rank tests and Kaplan-Meier survival curves were used to compare survival.

Results
44 patients were included. Median follow-up was 9.1 years and shortest 1.1 years. The median overall survival of patients with IDHwt DA with or without one of the molecular criteria was 10 and 16.5 months, respectively (p=0.17). Cox regression analysis of the molecular criteria in the subgroup of patients with IDHwt tumors yielded a HR of 3.9 (95% CI; 0.49-31.3) and the adjusted model yielded a HR of 14.6 (95% CI; 0.76-277). An adjusted model including patients with both IDHwt and IDH-mutant tumors gave a HR of 3.89 (95% CI; 1.33-11.4).

Conclusions
The molecular criteria predicted a significantly poorer survival independent of IDH-status. In patients with IDHwt tumors, the molecular criteria trended towards poorer survival. Due to the limited sample size, we could not definitely validate the proposed model. A larger multicenter study is ongoing.

Personalised medicine, biomarkers & diagnostics

#155: Optimal modality of ultrasound guided biopsies for assessing suspected melanoma metastasis in subcutaneous tissue and lymph nodes

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Abstract
Introduction
Ultrasound-guided (US) fine needle aspiration cytology (FNAC) and core needle biopsy (CNB) enables minimally invasive assessment of suspected melanoma metastasis in lymph nodes and subcutaneous tissue. However, there is no consensus as to which modality that has the highest accuracy in different clinical scenarios, and which modality that renders the fewest non-diagnostic biopsy results.

Materials and methods
Using retrospective journal audit, we identified all patients followed for melanoma in our department, who had undergone either US guided FNAC or CNB due to suspicion of melanoma metastasis in the period December 2016 to June 2019. Biopsy results were classified as melanoma metastasis, other cancer, non-diagnostic or benign, and compared to a minimum of 6 months follow-up data for verification. Sensitivity, specificity, negative and positive predictive values of FNAC and CNB were calculated based on the location of the suspected metastasis, the way the suspicion was raised (clinical, PET-CT or US) and clinical stage at the time of biopsy. Differences in categorical variables between groups were compared using Fisher's exact test or Chi-square test.

Results
232 US guided biopsies in 164 patients were identified; 109 FNAC and 123 CNB. For FNAC, overall sensitivity was 83.3% (95% confidence interval: 69.2-92.0%) and negative predictive value was 88.4% (77.9-94.5%). For CNB, overall sensitivity was 92.4% (83.6-96.9%) and negative predictive value was 88.0% (75.0-95.0%). There were significantly fewer non-diagnostic results using CNB (n=11, 8.94%) than using FNAC (n=24, 22.0%) (P=.0095).

Conclusion
Results indicated no significant differences between FNAC and CNB accuracy based location, suspicion and clinical stage. CNB was significantly associated with fewer non-diagnostic results.
Further randomized studies with a larger study population could uncover the accuracy for each modality according to different clinical scenarios.

Personalised medicine, biomarkers & diagnostics

#156: Response evaluation in patients with colorectal liver metastasis using pre-and post-chemotherapeutic core needle biopsy

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Abstract
Introduction
Chemotherapy response evaluation by the standard unidimensional Response Evaluation Criteria In Solid Tumors (RECIST) is imprecise and inconsistently correlated to long-term survival. The aim of our study was to assess the safety and feasibility of a novel minimal invasive histological based chemotherapy response evaluation method in patients with unresectable colorectal liver metastases (CRLM).

Material and methods
Eight patients with unresectable CRLM were included. A laparoscopic ultrasound (LUS)-guided full core needle biopsy of a selected CRLM, was performed before initiation of chemotherapy. The procedure was repeated after two months of palliative chemotherapy.
Biopsies from CLRM were examined using the 5-tiered tumor regression grade (TRG).

Results
Seven patients completed both rounds of the study. TRG 5 was found in all eight pre-chemotherapy tumor specimens. In the post-chemotherapy specimen, histological features of response were found in six patients (TRG 2-4), while one patient had no histological response features (TRG 5). This patient had partial response when assessed by RECIST. No serious complications occurred.

Conclusion
We managed to establish a minimal invasive and histological based method for chemotherapy response evaluation in patients with unresectable CRLM. TRG evaluations could be performed on the specimens obtained by this method. We found a discrepancy between RECIST and TRG in one out of seven patients. The procedure proved feasible and safe. The clinical role of this histology-based response evaluation method remains to be elucidated in studies based on higher numbers of patients and including long-term follow-up.

Personalised medicine, biomarkers & diagnostics

#157: Integrative analysis of DNA methylation and gene expression profile in the neoadjuvant chemoradiotherapy response of locally advanced rectal cancer

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Abstract
Introduction
Neoadjuvant chemoradiotherapy and surgery is the standard treatment for locally advanced rectal cancer (LARC). Patients achieving complete pathological response (pCR, 15% to 30%) present better overall survival and lower recurrence rates than incomplete responders (pIR). A better understanding of the disease paves the ground to predict response and potential treatment options.

Materials and Methods
The DNA methylation and expression profile of pre-treatment LARC biopsies (N=32) and five normal rectal (NT) tissues were assessed using array-based technology. Differentially methylated (DM) probes (false discovery rate/FDR <5% and $|\Delta\beta|>0.15$) and genes (DEG – FDR < 5%) were identified using limma. Pearson correlation test (r values with $p<0.05$) was used to identify probes and genes with positive (r+) or negative (r-) correlation. Integrative gene-list enrichment analysis was performed using Enrichr.

Results
Most of the DM probes (66%) identified in pCR cases (N=11) presented a negative correlation with gene expression, while in pIR (N=21) the opposite scenario was observed (28% were r-). In both groups, most of the r- probes were mapped in the promoter regions (pCR = 64%, pIR = 53%). The genes regulated by methylation in pCR were associated with the PI3K-Akt signaling pathway (KEGG) and loss of function of SMAD2/3 and TGFBR1 (Reactome). Among the genes showing negative correlation, MIR1197 stands as a potential marker of pCR, with hypomethylation and increased gene expression. pIR altered genes were related to cell adhesion molecules (KEGG) and extracellular matrix organization (Reactome). The prediction of drugs acting on the expression of these genes revealed cisplatin and carboplatin as the most significant candidates.

Conclusion
The integrative analysis of DNA methylation and expression of LARC revealed markers of pCR and drugs that are more likely to act on pIR cases.

Personalised medicine, biomarkers & diagnostics

#158: Automated planning to balance coverage of potential microscopic disease with organ at risk dose in head-and-neck cancer.

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Abstract
Introduction
Laryngeal and pharyngeal cancer (LPC) patients treated with curatively intended radiotherapy often suffer from long-term side-effects due to high radiation doses to organs at risk (OARs). Our national treatment protocol defines three target levels: high (PTV1), intermediate (PTV2), and low risk (PTV3). Studies point at lower risk of subclinical disease in intermediate-risk volumes. We aimed to explore patient-specific trade-offs between dose to targets vs OARs.

Methods
Using in-house software for automated multi-criteria optimization, we created six sets of plans for 12 LPC patients. All planning objectives were fixed, except for the near-minimum dose (D99%) for PTV2/3, which was loosened in five trade-off plans (TPs). Coverage aims were:
-Baseline plan (BP): D99%≥95% for all targets
-TP2-90: PTV2 D99%=90%
-TP3-90: PTV3 D99%=90%
-TP2-85: PTV2 D99%=85%
-TP3-85: PTV3 D99%=85%
-TP23-85: PTV2&3 D99%=85%
Prescribed doses were 68, 60, and 50Gy for PTV1, PTV2, and PTV3. Mean OAR doses and PTV D99% were compared between each TP and the BP.
For each TP the distance to the PTV edge was found for all underdosed voxels and the 95th percentile value (ED95) was reported.

Results
We achieved substantial patient-specific lowering of OAR doses for all patients by allowing controlled coverage reductions for PTV2 and/or PTV3.
Maximum reductions in mean doses to OARs were 5.3/5.6Gy for ipsi/contralateral parotids, 11.1/9.0Gy for ipsi/contralateral submandibulars, 5.1Gy for oral cavity (all TP23-85), 5.6/7.9/8.0Gy for upper/lower (TP23-85) and mid (TP3-90) pharyngeal constrictors, 7.9/13.7Gy for supraglottic/glottic larynx (TP3-90/85), 7.9Gy for esophagus (TP3-90), and 7.3Gy for thyroid (TP3-85).
PTV2/3 D99% was reduced by max. 6.4/7.1Gy; 92% of TPs had ED95 < 4mm.

Conclusion
Automated multi-criteria optimization can be used to explore the patient-specific reduction in side-effect risk achievable by slightly lowering coverage of edges in intermediate and low-risk targets.

Personalised medicine, biomarkers & diagnostics

#159: Response monitoring in metastatic breast cancer: a comparison of survival times between FDG-PET/CT and CE-CT

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Abstract
Introduction
The choice of response monitoring approach in metastatic breast cancer (MBC) may affect clinical decision-making and patient survival. We compared overall survival for patients monitored with contrast-enhanced computed tomography (CE-CT), [18F]-fluorodeoxyglucose positron emission tomography/computed tomography (FDG- PET/CT), or a combination of them.

Materials and Methods
Patients with biopsy-verified MBC (recurrent or primary disseminated disease) who were treated at a single university hospital (Denmark) in 2004-2018 were included. The study was approved by the Danish Patient Safety Authority. Patients who were response-monitored with FDG-PET/CT, CE-CT, or a combination of these were followed until August 2019. Clinical, histopathological, and response monitoring data were analyzed in a multivariable Cox proportional-hazards regression model comparing survival for CE-CT and FDG-PET/CT groups.

Results
A total of 300 patients were included with CE-CT (n=144), FDG-PET/CT (n=83), and the combined group (n=73). Median survival was 30.0 months (95% CI: 25.5-36.0), 44.3 months (95% CI: 29.7-80.2), and 54.0 months (95% CI: 44.3-80.1), respectively. Five-year survival rates were comparable for the FDG-PET/CT group (41.9%) and combined group (43.3%), and both were significantly higher than for the CE-CT group (15.8%). Using the CE-CT group as reference, the hazard ratio was 0.44 (95% CI: 0.28-0.67, P=0.001) for the FDG-PET/CT group after adjusting for baseline characteristics. FDG-PET/CT detected the first progression 4.7 months earlier than CE-CT (9.3 vs. 13.6), leading to an earlier change in treatment.

Conclusions
Patients with metastatic breast cancer who were response-monitored with FDG-PET/CT alone or in combination with CE-CT had longer overall survival than patients monitored with CE-CT alone. This suggests that using FDG-PET/CT for response monitoring in patients with metastatic breast cancer improves clinical decision-making and patient survival.

Personalised medicine, biomarkers & diagnostics

#160: Dynamic rotational and translational motion-including dose reconstruction in a commercial treatment planning system

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Abstract
Introduction
Intrafractional motion during radiotherapy delivery can deteriorate the delivered dose. Dynamic rotational motion exceeding 38° has been observed during prostate cancer radiotherapy, but methods to determine the dosimetric consequences of dynamic rotations are lacking. Here, we create and experimentally validate a dose reconstruction method that accounts for dynamic rotations and translations in a commercial treatment planning system (TPS).

Methods
A 4D dose matrix was generated with 0.4s time resolution by splitting the original treatment plan into multiple sub-beams and recalculating the dose of the split plan in the TPS. Dose accumulation was performed via TPS scripting by querying the dose of each sub-beam in dynamically moving points, allowing dose reconstruction with any dynamic motion.
The dose reconstruction was validated with film dosimetry for two prostate dual arc VMAT plans with intra-prostatic lesion boosts. The plans were delivered to a pelvis phantom with internal dynamic rotational motion of a film stack (21 radiochromic films). Each plan was delivered without motion and with three prostate motion traces. Dose reconstruction was performed and compared with film dose measurements by 3%/2mm gamma failure rates (GFR) and DVH metrics. Finally, calculations were made with static average rotation.

Results
The TPS agreed well with film: mean (range) GFR difference for motion-induced dose errors for TPS and film (with static as reference in gamma calculation) was -1.8% (-3.2-0.0%); GFR for TPS and film doses (film as reference) was 1.7% (0.0-6.0%).
The dynamic dose reconstruction reliably reproduced large interplay effects (hot spots and cold spots in the measured dose), that were not revealed in calculations with static average rotation.

Conclusions
A method to perform dose reconstructions for any dynamic motion was developed and experimentally validated. It showed large differences in dose distribution between dynamic and static rotations.

Personalised medicine, biomarkers & diagnostics

#161: TOMBOLA – a national, ctDNA guided phase II intervention trial for early detection of metastatic relapse after cystectomy – DaBlaCa-14

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Abstract
Introduction
About 45% of patients with muscle-invasive bladder cancer (MIBC) experience metastatic relapse within 2 years after cystectomy (CX). Early detection of relapse and start of treatment may be crucial to improve outcome. To investigate the impact of early treatment of disseminated disease, we initiated this trial (TOMBOLA), where we measure circulating tumor DNA (ctDNA) in serial samples to monitor minimal residual disease.

Materials & Methods
~282 patients undergoing neoadjuvant chemotherapy (NAC) and CX. We estimate 127 will develope relapse. Immunotherapy (PDL-1 inhibitor Atezolizumab, up to 18 series) will be administered upon molecular relapse (ctDNA positivity). Sequencing of DNA from tumor/blood. Collection of ~20 serial blood samples per patient (80mL). ctDNA analysis by droplet digital PCR (ddPCR). QoL Quality of Life registration.
Endpoints: 1. Complete response after immunotherapy (negative ctDNA and negative CT scan) 2. progression free and overall survival; QoL.

Results
Infrastructure was establishment and enrollment of patients with MIBC, stage T2-4a, PET/CT N0M0 is ongoing at five clinical centers. Whole exome sequencing of primary tumor and paired germline from 30 patients is finished (mean target coverage 274x and 188x, respectively) and mutations are called. For each patient, serial plasma ctDNA samples are analyzed immediately using 4-6 personalized ddPCR assays targeting tumor-specific mutations. Currently, 15/30 patients have been cystectomized, 45% (7/15) were ctDNA positive at 3 weeks (n=3), 2 months (n=2), 3 months (n=1) and 4 months (1) post CX. No clinical relapse was detectable by simultaneous CT scan. The PI was informed within 2-9 days after sampling and immunotherapy was initiated.

Conclusions
We established the necessary infrastructures at 5 clinical centers in a National set-up. We are analyzing serial plasma ctDNA from 30 patients included so far, response and survival will be analyzed after enrollment of all patients.

Personalised medicine, biomarkers & diagnostics

#162: Emerging evidence for the application of FAK inhibitors in melanoma therapy

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Abstract
Introduction
Melanoma is the skin cancer causing the most deaths. If not treated early, melanoma can advance and metastasize to different body districts. At this stage, it becomes hard to treat and results in a very poor prognosis. Despite the successful application of immune and targeted therapies, the treatment of advanced melanoma as well as the molecular mechanisms underlying melanoma development and progression are still in need of further investigation. Recently, we have found a promising candidate for melanoma biology in the protein AMBRA1 (Activating Molecule for Beclin1 Regulated Autophagy1) whose function is required in regulating several cellular processes, such as autophagy, cell proliferation and cell death. In this project, we dissected the multifaceted role of AMBRA1 in melanoma development and explored its therapeutic relevance in melanoma treatment.

Materials and Methods
We took advantage of the preclinical mouse models of melanoma carrying BrafV600E mutation and Pten deletion (tamoxifen-inducible and syngeneic models) and a panel of human melanoma cells. In our study, we also applied the publicly available TCGA-SKCM and Leeds Melanoma Cohort datasets of melanoma patients.

Results
We found that the protein AMBRA1 is extremely crucial for a correct cell division and its absence induces melanomagenesis. We discovered that AMBRA1 deletion promotes melanoma growth and metastasis by hyperactivating the FAK (Focal Adhesion Kinase) signaling pathway, both in vivo and in vitro. Indeed, we also proved that low expression of AMBRA1 in human melanoma is associated with an invasive phenotype. Moreover, tumor growth and invasion are strikingly affected by FAK inhibition in murine melanoma depleted of Ambra1 and in human melanoma cells low expressing AMBRA1.

Conclusions
This study identifies AMBRA1 as novel tumor suppressor in melanoma and proposes the oncogenic FAK1 signaling to be exploited as therapeutic target in melanoma where AMBRA1 is hypo-expressed.

Personalised medicine, biomarkers & diagnostics

#163: Tumor Stage of Women with Primary Breast Cancer Before and After Covid-19 Lockdown

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Abstract
Introduction
It is debated whether a change of health behavior after covid19 lockdown leads to more advanced disease presentation among cancer patients. We wanted to explore this issue among Danish women with primary breast cancer.

Material and methods
The data used in this registry-based study were collected from the national Danish breast cancer database administered by the Danish Breast Cancer Group (DBCG). Since 1978, the DBCG has prospectively collected data on patients-, tumor- and treatment- characteristics of close to all Danish breast cancer patients.
By 1 February 2021, a total of 3,736 breast cancer patients were registered in the DBCG database, diagnosed in 2020. Patients receiving neoadjuvant treatment, and patients without information on tumor size, axillary nodal status, and whether they were diagnosed in the mammography screening program were excluded. The lockdown in Denmark was introduced on 11 March. We chose to assume that women where surgery was performed up to 15 April had started the diagnostic set up before lockdown. Thus the two time periods were 1 January – 15 April and 16 April – 31 December 2021.

Results
Tumor size was available among 3,105 patients. In the first period, the average tumor diameter was 18.0 mm / in the second period 18.5 mm. The difference was not significant (P=0.28). Nodal status was available in 3,041 patients. In the first period, the percentage of node-positive patients were 28.8% / in the second period, 31.6%. The difference was not significant (P=0.15). Among 3,691 with information on screening detection, 32.9% was screening detected in the first period / 29.5% in the second period. This difference was borderline significant (P=0.05).

Conclusions
We conclude that covid19 lockdown has had a minor influence on tumor stage among Danish women with breast cancer. The insignificant rise in tumor size and nodal status can be explained by the minor drop in mammography screening attendance.

Personalised medicine, biomarkers & diagnostics

#164: Does longitudinal Diffusion-Weighted MRI have the potential to carry biological information?

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Abstract
Introduction
Introduction of the hybrid MRI linear accelerator (MR-linac) has made longitudinal Diffusion-Weighted MR Imaging (DWI) more accessible. This allows studying temporal changes of quantitative DWI metrics such as Apparent Diffusion Coefficient (ADC), a promising biomarker for response prediction. Here, a semi-automatic computer-based tool for segmentation of dedicated ROIs for ADC measurement is tested for its capacity to detect potential biological changes.

Materials and Methods
Thirty patients with rectal cancer referred to radiotherapy (RT) were MRI scanned prospectively before treatment (baseline) and two weeks into RT (week 2). MRI protocol consisted of T2W imaging and repeated DWI (test-retest). A semi-automatic segmentation tool was implemented using in-house developed software. ADC values was measured using manual ROI delineation by a radiologist and semi-automatic ROI delineation with the tool. Correlation between the ADC values based on the two delineation methods was measured using Pearson's correlation coefficient. Image related ADC uncertainty was measured using test-retest data; the central 70% confidence interval was established using bootstrap of the observed non-normal distribution.

Results
At baseline, correlation between mean ADC values within manually and semi-automatically delineated ROIs was 0.89. ADC change between baseline and week 2 was measured using semi-automatic ROI delineation. The measured ADC change (-139*10-6 — 491*10-6 mm2/s) was larger than the image related ADC uncertainty (+/- 92.8*10-6 mm2/s).

Conclusion
Longitudinal ADC changes were larger than image related uncertainty, and thus potentially reflect treatment related biological changes. The presented semi-automatic segmentation for ADC calculation correlates well with manual delineation by a radiologist. The segmentation tool may be useful in other targets and may be well-matched for the MR-linac workflow.

Personalised medicine, biomarkers & diagnostics

#165: Pancreascyster i Region Nordjylland: en forskningsdatabase

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Abstract
Cyster i bugspytkirtlen påvises i stigende grad som følge af øget brug af billeddiagnostik. Visse cysteformer kan give en øget risiko for kræft i bugspytkirtlen og kræver ofte udredning af malignitets potentiale.
Der er gjort flere forsøg på at bestemme hyppigheden af bugspytkirtel cyster på befolkningsniveau. I et tysk studie blev 1077 undersøgt og 49.1 % havde cyster i bugspytkirtlen. Cyster i bugspytkirtel er derfor hyppigt forekommende.
På trods af de ret ekstensive udredningsprogrammer, der nu eksisterer på både nationalt og internationalt niveau, eksisterer der forsat ingen selvstændige danske eller nordiske opgørelser eller registre over omfanget af cysternes hyppighed eller belastning af sundhedsvæsnet. Der eksisterer en overordnet kodning (ICD-10-CM: K86.2), som ikke tillader detaljeret udtræk om cysternes karakteristika.
Korrekt håndtering indbefatter kontrolprogram og udvælgelse af patienter til kirurgisk forebyggende operation - et ekstensivt indgreb med risiko for morbiditet og mortalitet. Følgevirkningerne efter operationen er komplekse og ofte med behov for enzym og insulin substituering. Mod dette skal opvejes en fjernelse af risikoen for kræft i bugspytkirtlen. Betragtes det ekstensive udredningsprogram og risikoen for kræft med væsentlig sygdomsbyrde og høj risiko for tilbagefald, vil det være af væsentlig samfundsbetydning at belyse området, så sygehusforløb optimeres og patienterne får en korrekt forståelse af sygdommens natur.
I fire studier belyses forekomsten af simple og avancerede cysters forekomst og udvikling i en dansk repræsentativ region. Alle tilfælde registreres og følges i 10 år. Patienterne inviteres til at deltage i et opfølgningsprogram og biomarkørstudie med både blodprøvetagning og analyse af aspireret cystevæske.

Personalised medicine, biomarkers & diagnostics

#166: DBCG RT Nation – Developing breast cancer radiotherapy through big data analysis

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Abstract
Introduction
Every year, around 1,100 Danish patients are treated with loco-regional radiotherapy (RT) for high-risk breast cancer (BC) The aim of RT is to reduce the risk of recurrence and improve survival. However, there are also risks from RT, including radiation-associated heart and lung disease.
The Danish Breast Cancer Group (DBCG) has initiated the collection of all Danish RT treatment plans from high-risk BC patients treated 2008 to 2016, in total 9,861 patients, for large-scale investigations of radiotherapy effects.

Materials and methods
The patients were identified from the DBCG database. All DICOM files related to the treatment planning are being collected from the department where the treatment was administered. Due to the large number of patients, automatic solutions for data extraction are being implemented.
Two projects have been initiated to utilise the data.
1) The correlation between RT dose to the heart, coronary artery calcifications and risk of radiation induced heart disease will be explored. A phase IV study will report on the radiation dose the internal mammy lymph nodes. (Refsgaard)
2) Differences in delineation practices of target and risk organs will be mapped and correlated with RT dose distributions. Automated methods for both delineation and treatment planning will be investigated. (Skarsø)

Results
Presently, data from two departments have been collected, in total: 2,718 treatment plans. In our initial data analysis, we have observed effects of implementation of national guidelines on the delineated volume and radiation dose to the heart and internal mammary lymph nodes for one center over a nine-year period.

Conclusions
In conclusion, we were able to automatically retrieve most of the data (97.2% and 95.6%) from two out of seven departments. We were able to detect and report a clear effect of national guideline implementation on the clinical RT planning practice showing increased consistency in delineation and included volumes.

Personalised medicine, biomarkers & diagnostics

#167: Proteomic analysis of ovarian carcinoma tissue to reveal changes in expression of proteins involved in coagulation

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Abstract
Introduction
It is well recognized that cancer patients are at higher risk of developing a venous thromboembolic event (VTE) than other patients. The risk of VTE is influenced by person-, tumor-, and treatment related factors. Patients with some cancer types are at higher risk of VTE than others, ovarian cancer being one of them, especially if the histopathologic subtype is clear cell adenocarcinoma.
The aim of the study is to quantify a possible upregulation of procoagulant proteins in ovarian carcinoma tissue compared to normal tissue.

Materials & Methods
Tumor and normal tissue collected from patients included in a clinical trial at the Department of Gynecology and Obstetrics, Aalborg (from 2015-2018) is analyzed using mass spectrometry for proteome analysis. The patients had been followed with regularly clinical examination, blood sampling and compressive ultrasound scans for one year after admission for suspected ovarian cancer to investigate their risk of developing symptomatic and asymptomatic VTE. We supplemented the analysis with tissue from patients with ovarian clear cell carcinomas stored in the Danish Bio- and Genomebank.

Results
We analyzed tissue samples from 40 patients (10 patients with cancer and VTE, 20 patients with cancer and no history of VTE, and 10 patients without cancer and no VTE events).
Preliminary results from the proteome analysis indicate that a majority of proteins involved in the biological process 'blood coagulation' (Gene Ontology Term:0007596) are downregulated in carcinoma tissue compared to normal tissue.

Conclusions
Confirmation of the preliminary results is required and further analysis should be done to reveal possible differentiation in the downregulation of both proteins involved in coagulation and fibrinolysis to explain the proposed unbalance.
The study is supported by Heinrich Kopps Legat and Ebba og Aksel Schølins Fond.

Personalised medicine, biomarkers & diagnostics

#168: Drug resistance in patients with chronic lymphocytic leukaemia

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Abstract
Introduction
Chronic lymphocytic leukaemia (CLL), a B cell malignancy, is the most common type of leukaemia in adults. Promising drugs, such as Bruton's tyrosine kinase (BTK) inhibitor, ibrutinib, and the B-cell lymphoma-2 (BCL2) inhibitor, venetoclax, are now part of the treatment options for CLL patients. Although most patients respond well to these drugs, some patients also show or acquire resistance. This resistance may be explained by mutations in genes. About half of the venetoclax resistant cases have mutations in the BCL2 gene and 50–80 % of the ibrutinib resistant patients have mutations in the BTK and/or Phospholipase C Gamma 2 (PLCG2) gene.
The aim of this project, initiated August 2020, is to identify novel somatic mutations that can explain resistance to ibrutinib and venetoclax in CLL.

Materials and methods
Deep panel sequencing targeting rearranged B-cell receptor genes (LymphoTrack, Invivoscribe) will be used to identify patient-specific CLL clones in blood before ibrutinib or venetoclax treatment and subsequently quantify the residual disease during treatment. We plan to enrol 120 patients. Exome sequencing will be performed in the upper and lower quartile of the patient cohort showing best and poorest treatment response.

Results
In the preliminary data, we detected 2 clones in 4/5 patients at diagnosis using LymphoTrack. In the pilot study, we performed exome sequencing on 4 CLL patients that showed resistance to ibrutinib and did not harbour mutations in the genes BTK and PLCG2. However, we identified mutations in genes involved in the B cell signaling pathway and apoptosis (PTPN18 and SPEN) and the gene BIRC3, which has been associated with chemorefractoriness.

Conclusion
Our initial data identified potential candidate genes that might be involved in ibrutinib resistance. By enrolling a larger patient cohort in the ongoing study, we hope to gain novel and valuable information about the biology behind resistance to ibrutinib and venetoclax.

Personalised medicine, biomarkers & diagnostics

#169: Serial circulating tumor DNA analysis to assess recurrence risk, benefit of adjuvant therapy, growth rate and early relapse detection in stage III colorectal cancer patients

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Abstract
Introduction
Sensitive methods for risk stratification, monitoring therapeutic efficacy, and early relapse detection may have a major impact on treatment decisions, patient management, and outcomes for stage III colorectal cancer patients. We assessed the prognostic and predictive impact of serial circulating tumor DNA (ctDNA) measurements performed before, during and after adjuvant chemotherapy (ACT) and during surveillance.

Materials and methods
We recruited 168 stage III CRC patients treated with curative intent at Danish and Spanish hospitals between 2014-2019. To quantify ctDNA in plasma samples (n=1204), 16 patient-specific somatic single nucleotide variants were profiled using multiplex-PCR, next generation sequencing.

Results
Detection of ctDNA was a strong recurrence predictor, both postoperatively (HR=7.2, 95% CI 3.8-13.8, p<0.001), directly after ACT (HR=51, 95% CI 15-170, p<0.001), and when measured serially, after the end of treatment (HR=42, 95% CI 16-110, p<0.001). The recurrence rate of postoperative ctDNA-positive patients treated with ACT was 80% (16/20). All patients, who stayed ctDNA-positive during ACT, relapsed. Serial post-treatment measurements revealed two distinct rates of exponential ctDNA growths, SLOW (27% ctDNA-increase/month) and FAST (137% ctDNA-increase/month) (p<0.001). The rate was predictive of survival (HR=2.7, 95%CI 1.1-6.7, p=0.039). Serial ctDNA analysis every three months detected recurrence with a median lead-time of 9.8 months compared to standard-of-care computed tomography (CT). Restricting analysis to coinciding ctDNA and CT assessments showed a ctDNA lead-time, of up to 21.6 months, in 28% of cases.

Conclusion
Serial postoperative ctDNA analysis has a strong prognostic value, is more sensitive for recurrence detection than CT-imaging and enables tumor growth rate assessments. The novel combination of ctDNA detection and growth rate assessment provides unique opportunities for guiding decision-making.

Screening:

Poster #170-182

Screening

#170: Can biopsies be omitted after normal colposcopy in patients referred with low-grade cervical cytology

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Abstract
Introduction
The Danish national guidelines recommend four biopsies in all women who undergo colposcopy to avoid under-diagnosis of cervical intraepithelial neoplasia (CIN). Conversely, the American Society for Colposcopy and Cervical Pathology (ASCCP) does not recommend non-targeted biopsies for women referred for colposcopy at the lowest level of risk. The aim of this study was to investigate the value of taking biopsies in patients with less than high-grade squamous intraepithelial lesions (HSIL) cytology and a normal colposcopic impression.

Materials and methods
Between January 2017 and September 2020, women over 18 years old referred for colposcopic examination due to either an abnormal smear or follow-up after previous CIN were invited to participate in the study.
All study participants underwent colposcopic examination and had four biopsies taken. The biopsies were analyzed separately.

Results
In total, 1327 women with abnormal cervical cancer screening results or attending follow-up after a previous CIN diagnosis were enrolled in the study and examined by colposcopy. Of these, 173 were newly referred with low- grade squamous intraepithelial lesion/atypical squamous cells of undetermined significance (LSIL/ASCUS) cytology and had a negative colposcopic impression and four adequate biopsies. Overall, 56.1% of the women were diagnosed with dysplasia, and 22.0% were diagnosed with CIN grade 2 or worse (CIN2+). When combining the results of the four biopsies, we found a 100% relative increase in CIN2+ cases compared to using only one biopsy (from 11.0% to 22.0%, P=0.006).

Conclusion
In a population of women referred with low-grade cervical cytology and a normal colposcopic impression, we found that more than half had dysplasia, and that approximately one out of five were diagnosed with treatment- requiring dysplasia (CIN2+) when the results of four biopsies were combined. The detection of CIN2+ was doubled when four biopsies were used compared to one biopsy.

Screening

#171: Gaps between recommendations and their implementation: A register-based study of follow-up after abnormalities in cervical cancer screening

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Abstract
Introduction
Follow-up after screen-detected abnormalities is crucial for the success of cervical cancer screening programs but is usually not closely monitored in official screening statistics. We determined how the follow-up deviated from the recommendations in the Danish organized program.

Materials and methods
Using Danish nationwide population-based registers, the follow-up pathways of 60,199 women aged 23-59 with non-negative screening samples from 2012-2014 were mapped until end of 2018. We studied the timeliness and appropriateness of follow-up tests after cervical cytology screening and the total resource use in accordance with the national recommendations. Regression analyses were used to determine variations in adherence according to age, provider type, region, and history of abnormalities.

Results
Among women referred for immediate colposcopy, 91.3% (95% CI: 90.9%-91.6%) attended within four months, whereas up to about half of the women with a recommendation for a repeat test received this test either too early or very late. Overall, only 43% (95% CI: 42.9%-43.7%) of women with non-negative screening tests received the recommended follow-up, whereas 18 % (95% CI: 17.6%-18.2%) received more than was recommended, 35% (95% CI: 34.4%-35.1%) received some follow-up but less than recommended and 4% (95% CI: 3.9%-4.2%) were not followed up at all. These proportions varied by screening diagnosis, woman's age, type of health care provider, region, and history of abnormalities.

Conclusion
On average, women underwent more tests of each type than recommended by the guidelines. Deviations from follow-up recommendations are very frequent even in organized cervical screening programs and should be routinely monitored by screening program statistics.

Screening

#172: Rectal cancer patient's coping strategies and considerations regarding Low Anterior Resection Syndrome and its impact on quality of life – a qualitative interview study

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Absact
Introduction
The burden of Low Anterior Resection Syndrome (LARS) on the quality of life (QoL) of patients treated for low and mid rectal cancer is frequently underestimated. Studies indicate that LARS has a negative impact on patient QoL in up to 80%, with major alterations in 40%.
However, an ongoing PROM study investigating late sequelae after rectal cancer finds that a number of patients scoring major LARS experience none or poor impact on quality of life.
The aim of the study was to identify patient's considerations and coping strategies on why the burden of LARS has little or none influence on their quality of life.

Materials and Methods
The study is a qualitative interview study and a part of the Danish Cancer Society Centre for Research on survivorship and Late Adverse Effects after Cancer in the pelvic organs.
The data collection started in autumn 2020 and expected finished summer 2021. The data will be collected using telephone interviews. In all 20 patients treated for cancer in the pelvic organs will be included. Data will be analysed using a hermeneutic inspired thematic analysis.

Results
Narratives by the patients on their experiences living and coping with LARS after colorectal cancer.

Conclusion
This study will provide knowledge about understanding the discrepancy between having a high LARS score but little impact on quality of life, a knowledge with clinical relevance to health care professionals trying to enhance treatment adherence, reduce errors, improve outcomes and last but not least to improve quality of life in cancer survivors.

Screening

#173: Prognostic Relevance of Geriatric assessment and Onco-geriatric Screening In cancer patients age Seventy or more: Preliminary findings of a prospective cohort study (PROGNOSIS-G8)

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Abstract
Introduction
Older patients with cancer constitute a heterogeneous group with varying comorbidity; therefore, geriatric assessment with initial screening is recommended. The Geriatric 8 (G8) is a promising screening tool with good accuracy and a strong association with survival, however, evidence is sparse with regards to patient-centered outcomes. This study aims to address the prognostic value of the G8 with quality of life (QoL) as the primary outcome.

Materials and Methods
In an ongoing prospective cohort study (since June 1st, 2020), patients age ≥70 years with solid carcinomas are screened with the G8 at the Department of Oncology at Odense University Hospital prior to 1st line antineoplastic treatment. Participants are asked to fill out the EORTC QlQ-C30 and ELD-14 QoL questionnaires at baseline and at 3, 6, 9, and 12-month follow-up. Baseline data including G8 score, Charlson comorbidity index, performance status (ECOG-PS), cancer type, stage, and treatment intent are collected. Differences in QoL between frail (G8 score ≤14) and non- frail participants will be tested using the t-test (mean differences) or the Wilcoxon Rank Sum test (median difference) depending on distribution and adjusted for potential confounders.

Results
As of April 20th, 2021, 786 participants have been included, of whom 399 have contributed with baseline QoL data. 469 participants (59.6%) were frail. After 3 and 6 months 17.6% and 16.2% of baseline QoL participants were lost to follow-up.

Conclusions
Preliminary data suggests that the G8 can be used to identify a subgroup of frail older patients in an outpatient oncology setting and that the prevalence of frailty in older Danish patients with cancer, is in line with previous international reports.

Screening

#174: Low socioeconomic status is associated with increased odds of incomplete colonoscopy in the Danish colorectal cancer screening program

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Abstract
Introduction
In the Danish colorectal cancer screening program 8% of the colonoscopies are incomplete. We investigated the association between socioeconomic status (SES) and odds of incomplete colonoscopy (IC).

Materials and methods
In this register-based cohort study data was obtained from the Danish Colorectal Cancer Screening Database and combined with data from Danish national registers. SES was measured as income divided into quartiles from lowest to highest, and highest completed education categorized as basic school, high school/vocational education and higher education. Outcome was defined as complete or incomplete colonoscopy. 71,973 first round participants were included with follow-up colonoscopy done within 2014-2019. Multivariate logistic regressions were used. We adjusted for age, gender, civil status, comorbidity and use of peristalsis-affecting medicine.

Results
For ICs due to inadequate bowel preparation the level of income was associated with the risk of having an IC with an odds ratio (OR) of 1.67 (95% CI: 1.46;1.91) in 1st quartile, OR 1.38 (95% CI: 1.21;1.56) in 2nd quartile and OR 1.17 (95% CI: 1.03;1.33) in the 3rd quartile compared to 4th quartile. Educational level showed an OR for high school/vocational education of 0.87 (95% CI: 0.79;0.97) compared to higher education. No significant effect was seen for basic school education. Regarding ICs due to other causes than inadequate bowel preparation, income influenced the risk of IC in the 1st quartile with an OR of 1.19 (95% CI: 1.05;1.35) and in the 2nd quartile with an OR of 1.19 (95% CI: 1.06;1.34). For educational level no significant associations were seen.

Conclusions
SES estimated by income is associated with the probability of having an IC, however educational level does not show the same unambiguous association. Future studies should focus on screening participants with lower SES and how to reduce their risk of an IC.

Screening

#175: Balancing risks: Qualitative study of attitudes, motivations and intentions about attending for mammography during the COVID-19 pandemic

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Abstract
Introduction
When COVID-19 was declared a pandemic in March 2020, several countries paused their cancer screening programmes. In Denmark the population-based breast cancer screening programme remained open. The aim of this study was to explore attitudes, motivations and intentions about attending for mammography among women who cancelled or postponed breast cancer screening during and due to COVID-19.

Methods
A telephone interview study was conducted at the end of April 2020. A qualitative, phenomenological approach was chosen to identify themes and concepts and a semi-structured interview guide was developed. The analysis was structured according to constructs from the theory of planned behaviour, including attitudes to breast cancer screening, norms and motivations to comply with breast cancer screening, perceived control and anticipated regret.

Results
Interviews were carried out with 33 women aged 50–69 (mean 62) years. The women felt that screening was of secondary importance during the height of the pandemic and they felt low perceived control over transportation to the screening clinic and over the screening situation itself, where social distancing was impossible. They perceived messages from the authorities as conflicting regarding the request for social distancing and a lack of recommendations about using face masks at the screening clinic.

Conclusions
Women who postponed or cancelled breast cancer screening during the COVID-19 pandemic felt that public recommendations appeared contradictory. Uncertainty about the 'new norm(al)' of COVID-19 made them stay at home, although the screening clinics remained open. The findings point to the importance of addressing perceived inconsistency between recommendations from the World Health Organization and the national management of these recommendations, and to secure univocal information from the authorities about the recommended use of healthcare services in a time of crisis.

Screening

#176: Estimating the effect of FIT-based Colorectal Cancer screening on mortality using a Regression Discontinuity Design (ongoing study)

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Abstract
Introduction
The stool-test guiac fecal occult blood test (gFOBT) for colorectal cancer (CRC) screening has been evaluated in randomized trials and found to lower overall mortality. Since, the newer and more sensitive fecal immunochemical test (FIT) has been implemented in many national screening programs including the Danish. As national programs are in place, observational data is usually the only option to evaluate the effect of FIT screening. However, lack of suitable comparison groups impedes evaluation of the ultimate goal for screening to reduce mortality. The FIT result is a continuous measure of fecal hemoglobin, and a pre-specified cut-off determines colonoscopy referral. We propose that the regression discontinuity design (RDD) enables quasi-experimental evaluation and aim to estimate the effect of a positive FIT on mortality in a nationwide screening program, and thus being referred to colonoscopy.

Materials and Methods
We will use data from the Danish CRC Screening database, and link information from the National Patient Register, the registries of Statistics Denmark, and the Civil Registration Registry. We will include all screening participants invited from 2014 to 2019. We will employ a cohort design, and the study population will be followed from date of FIT result until emigration, death or 31/12/2020.
The RDD method can be utilized when a dichotomized cut-off is applied to a continuous variable to determine treatment or intervention. In the immediate area around the cut-off, the method assumes random assignment of a result to below or above the cut-off. If the intervention prompted by the cut-off has an effect, a discontinuity in the mortality rate will be observed at the cut-off.
Analysis includes fitting a cox regression model for two comparable groups below and above the cut-off, and estimating the hazard ratio at the cut-off.

Results and Conclusions
The study and data analysis is ongoing. We will present preliminary results at the conference.

Screening

#177: MANAGEMENT OF HPV POSITIVE WOMEN IN CERVICAL CANCER SCREENING: RESULTS FROM A DANISH PILOT IMPLEMENTATION

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Abstract
Introduction
Cervical cancer screening is offered to women aged 23–64 in Denmark. From Jan 2021, human papillomavirus (HPV) testing is gradually introduced as a new screening method for women aged 30–59 years. HPV testing is highly sensitive for detecting precancerous lesions. However, the best way to manage women with a positive HPV test at screening remains debated. The aim of this study was to inform screening strategies by estimating the risk of severe cervical precancerous lesions or cancer (CIN3+) among HPV positive women, according to HPV type and cytological status.

Materials/methods
During May 2017–Oct 2018, HPV-based screening was performed on 16,067 women aged 30–59 attending screening in the uptake area of the Dept. of Pathology, Vejle Hospital, Region of Southern Denmark. Women with HPV16/18, or other high-risk HPV types and abnormal cytology, were referred to colposcopy. We obtained information on screening results and subsequent CIN3+ diagnoses from the Pathology Databank. Kaplan-Meier's method was used to estimate the risk of CIN3+ within 12 months of referral, depending on HPV type (16/18 vs other types) and cytology status (high-grade abnormal, low-grade abnormal, normal cells).

Results
We included 1,433 HPV positive women, of whom 600 were referred to colposcopy. In women with HPV16/18 (n=343), the risks of CIN3+ were 90%, 26% and 17% in women with high-grade abnormal, low-grade abnormal and normal cytology, respectively. In women with other high-risk HPV types (n=257), the risk of CIN3+ was 67% in those with high-grade abnormal and 8% in those with low-grade abnormal cytology.

Conclusion
Women with HPV16/18 had high risk of CIN3+, irrespective of cytology status. Women with other HPV types and low-grade abnormal cytology may not need immediate referral, but could be offered repeat screening after a year. This could reduce immediate referrals by ≈30%. These findings can inform the design of HPV-based cervical cancer screening in Denmark.

Screening

#178: Research protocol: Can we kill three birds with one stone? A randomised controlled trial to increase participation in cervical and colorectal cancer screening.

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Abstract
Introduction
Organised, population-based screening is recommended for breast cancer, cervical cancer (CCU) and colorectal cancer (CRC). In Denmark, the three screening programmes have been implemented, but the participation rate in breast cancer screening considerably exceeds both CCU and CRC screening. The aim of this study is to evaluate effectiveness of an intervention offering home-based CCU and CRC screening to women when attending breast cancer screening, if they are not up to date with the screening programmes.

Materials and methods
A randomised controlled trial will take place in Central Denmark Region from September 2021. Breast cancer screening units will be randomised to serve as intervention unit or control unit on selected days. On intervention days, women aged 50-69 years attending breast cancer screening will be offered a check-up on her CCU and CRC screening status. If the woman is not up to date in CRC screening, she will be offered to receive a kit to obtain a Faecal Immunochemical Test (FIT). If she is not up to date in CCU screening and younger than 65 years, she will be offered to receive a home- sampling kit for Human Papillomavirus (HPV) screening. Based on power calculation with an allocation ratio of 1:4, 4565 women must be included in the study with 913 in the intervention group to detect an increase in participation from 60% to 65% with a power of 80%.

Results
Main outcome will be difference in proportion of women participating in CCU and CRC screening within 3 and 6 months after the intervention as compared to the control group.
Outcomes within the intervention group will be proportion of women accepting a check-up on screening status, proportion of women not being up-to-date, and proportion of women accepting home-sampling kits.

Conclusions
The study has potential to increase participation in CCU and CRC screening and thereby on the long term reduce morbidity and mortality by using a simple and easily scalable intervention.

Screening

#179: A Walk-In Clinic as an Alternative Approach to Reach Non-Attenders of the Cervical Cancer Screening Programme in the North Denmark Region – an Observational Study

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Abstract
Introduction
In Denmark, approximately 25 % of women do not participate in the cervical cancer screening programme and initiatives to increase participation are called upon. The primary aim of this study was to investigate if a walk-in clinic could attract previous non-attenders of the cervical cancer screening programme.

Materials & Methods
We designed a walk-in clinic that was open two days a week from 4 to 7 pm. The study period was five months. The clinic was situated in the departments of gynecology in the two main hospitals of the North Denmark Region. The main purpose of the clinic was cervical cancer screening. Women who were not eligible for screening or had other health complaints were referred to their general practitioner. Women, included in the study, filled out a questionnaire regarding educational and occupational status and their screening history was registered using data from the Danish Pathology Data Bank.

Results
In the study period, 255 women visited the walk-in clinic, 249 women met the inclusion criteria. Age range of the participants was 23 – 77 years, with a median age of 45 years. The majority of the participants were currently employed (81 %) or students (10 %), the remaining being retired (5 %) or unemployed (4%). Screening history showed that 138 (55.4 %) were on time or less than 6 months delayed compared to their recommended screening interval. 61 women (24.5 %) were delayed more than 6 months but less than 2 years. 50 women (20.1 %) had more than two years of screening delay of whom 8 women had never been screened. Of the remaining 42 women the median time since last screening was 8.2 years (range 5.0 – 25.3 years).

Conclusions
Women attending the walk-in clinic tended to be primarily actively working or students (91 %). All age groups in the screening population were represented. Screening history showed that 44.6 % had not followed the recommended screening programme.

Screening

#180: Clinical Features Affecting Prognosis in Non-Small Cell Lung Cancer Patients Receiving Immunotherapy

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Abstract
Introduction
Several clinical features may negatively affect immunotherapy outcomes in patients with lung cancer. Nonetheless, patients with baseline characteristics such as poor performance status (PS) and distant metastases are underrepresented in randomized controlled trials. The aim of this real-world study is to investigate clinical features affecting prognosis in lung cancer patients receiving immunotherapy as second line therapy and beyond.

Methods
Data from 222 consecutively treated patients with advanced non-small cell lung cancer (NSCLC) receiving nivolumab or pembrolizumab in second line and later were identified. Data were obtained from medical records at the Departments of Oncology, Copenhagen University Hospitals Herlev and Rigshospitalet, from 1st September 2015 to 1st of March 2019. Latest follow-up is 1st of July 2020.

Results
The median follow-up time was 27.4 months and the median overall survival (OS) of the entire population was 12.7 months. Baseline PS, liver metastases (LM) and bone metastases (BoMs) significantly affected OS. The median OS for PS 0, 1 and 2 were 21.7, 11.6 and 2.9 months, respectively ($p < 0.0001$). The median OS for patients without LM vs. with LM was 13.8 and 6.9 months, respectively ($p = 0.004$). The median OS for patients without BoMs vs. with BoMs was 14.0 and 7.3 months, respectively ($p = 0.0002$). In patients ≥ 75 years vs. < 75 years, there were no significant difference in median OS ($p = 0.89$). The multivariate analysis identified baseline PS, LM and BoMs as independent predictors of OS. The hazard ratios for PS 1, PS 2, LM and BoMs were 1.7 ($p= 0.007$), 3.6 ($p < 0.0001$), 1.7 ($p= 0.004$) and 1.5 ($p=0.02$), respectively.

Conclusion
In NSCLC patients receiving immunotherapy in 2nd line and beyond , poor PS, LM and BoMs prior to treatment had negative impact on survival time. Immunotherapy in patients ≥ 75 years had comparable effectiveness to patients < 75 years.

Screening

#181: Mental Illness and Participation in Colorectal Cancer Screening: A Review.

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Abstract
Introduction
Compared with the background population, persons with mental illness have increased cancer mortality, partly due to lack of treatment. Colorectal cancer (CRC) is one of the leading causes of death and CRC screening has increasingly been implemented around the world. Screening has the potential to alleviate the gap in cancer mortality due to mental illness, however, it is uncertain whether lack of participation in screening contributes to excess mortality. This review aims to summarize the literature on participation in CRC screening among persons with mental illness.

Materials and methods
We searched four databases (PubMed, PsychInfo, Embase and Cochrane Library) to identify published literature on mental illness and participation in CRC screening programs. We included full-text papers available in English and published before February 2021. Papers concerning intellectual and developmental disabilities, and dementia were excluded.

Results
In total, 12 studies were included. Overall, the studies do not show clear evidence that persons with mental illness participate less in CRC screening. However, persons with severe mental illness seem to participate less in CRC screening with e.g. one large cohort study reporting a hazard ratio of 0.88 [0.87; 0.88] of participation in CRC screening among persons with mental illness. Two studies showed that severe symptoms decreased participation. A survey surprisingly found that persons with depressive symptoms may participate more in CRC screening compared with persons without. Four of the studies had a small study population (n<250), while three studies lacked a comparison group. Overall, the existing evidence remains ambiguous. Strength of the associations and the direction was influenced by screening program design, participants selection, and the screening method.

Conclusion
An association between severe mental illness and lower participation in CRC screening is possible, but evidence is sparse.

Screening

#182: The effect of the Danish National colorectal screening program on detecting cancer for patients with diabetes

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Abstract
Background
Diabetes is associated to higher incidence of colorectal cancer (CRC)

Aim
To evaluate whether individuals with diabetes participate in the Danish National CRC screening program, and estimate the effect of screenings invitation on the number of CRC diagnoses for individuals with and without diabetes.

Material and Methods
Retrospective cohort study based on national health registers describing all residents in Denmark aged 50-72 years (N=1.273,094) linked with data from the National CRC screening programme. Individuals were randomly invited to the first round of screening between 2014-2017. In total, 665,266 Danes had received an invitation by May 1 2016, whereas 607,828 were invited later. The likelihood of participate were compared among those with and without diabetes adjusting for age and gender. The intention-to-treat effect of invitation was assessed by the likelihood of being diagnosed with CRC between invited and not yet invited individuals.

Results
In total, 1,273,094 were invited, of those 8.5% had diabetes. Participant rates were 57,4% in the diabetic and 65,7 % in non-diabetic population (adjusted risk difference 9.2% (95%CI, 8.8%-9.6%)).
In general, screening invitations increased the likelihood of being diagnosed with CRC by 1.5‰ (95%CI 1.3-1.6), and those with diabetes had an additional effect of 0.7‰ (95%CI, 0.1-1.2‰), when compared to the non-diabetic invited individuals.

Conclusion
Even though, individuals with diabetes had lower adherence (9%) to CRC screening, the proportion of diagnosed CRC was higher among invited persons with diabetes compared to those without diabetes. Studies on how to improve screening participation among individuals with diabetes are needed.

Treatment Morbidity and Late Effects:

Poster #183-200

Treatment morbidity and late effects

#183: En underlig fornemmelse – at leve med sensomotoriske forstyrrelser efter behandling med oxaliplatin for kolorektal cancer – et kvalitativt studie

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Abstract
Introduktion
Overlevelse efter behandling for kolorektal cancer er forbedret betydeligt med nuværende behandlinger, herunder behandling med det kemoterapeutiske lægemiddel oxaliplatin. Imidlertid kan oxaliplatin medføre kronisk perifer neuropati, der f.eks. kan påvirke overlevernes oplevelse af kropslig koordination, balance, bevægelse og finmotorik. Der mangler viden om betydningen af disse sensomotoriske forstyrrelser i hverdagslivet efter medicinsk kræftbehandling. Derfor er formålet med dette studie at undersøge hvordan overlevere oplever og giver mening til fænomenet kroniske sensomotoriske forstyrrelser i hverdagslivet efter oxaliplatin behandling.

Materiale og metode
Studiets design tog udgangspunkt i eksistentiel fænomenologi og beskrivende livsverdensforskning som den metodologiske tilgang. Data blev genereret via tegninger og semistrukturerede interviews med 8 overlevere med sensomotoriske forstyrrelser i mere end 1 år efter afslutning af adjuverende behandling med oxaliplatin. Data blev analyseret ved fænomenologisk refleksion.

Resultat
De sensomotoriske forstyrrelser blev oplevet som underlige fornemmelser, der var svære at beskrive. De optrådte som tvetydige fornemmelser i hænder og fødder, og medførte en fremmedgørelse af kroppen. Manglende sensorisk kontakt med fysiske overflader skabte afstand til verden, hæmmede finmotoriske aktiviteter og påvirkede sociale kontakter.

Konklusion
Kroniske sensomotoriske forstyrrelser efter oxaliplatin behandling havde vidtrækkende konsekvenser for udøvelse af hverdagslivets aktiviteter. Hverdagslivets ureflekterede og umiddelbare natur blev udfordret, idet overlevernes evne til at fornemme ting og deres forhold til andre mennesker var ændret. Tegninger kan understøtte interviewets verbale beskrivelser af sensomotoriske forstyrrelser, idet de bidrager til at visualisere, hvordan overlevere oplever deres krop og hjælpe både overlevere og sundhedspersonale til at opnå en ny forståelse af fænomenet og dets betydning.

Treatment morbidity and late effects

#184: Development of clinical guidelines for management of treatment-related sequelae following colorectal cancer

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Abstract
Introduction
Advancement of colorectal cancer treatment has resulted in an increasing number of colorectal cancer survivors. Mental and physical wellbeing after treatment is an important issue for survivors, who often experience treatment- related sequelae affecting quality of life. In a national multidisciplinary setting, we aim to develop a guideline facilitating identification - and possibly treatment – of these sequelae, supporting high quality cancer care across the Danish healthcare system.

Materials and methods
Guidelines were searched in 16 databases and relevant studies were systematically searched in 4 databases from inception to 2021. The guideline is developed by a panel of experts including oncologists, urologists, sexologists, stoma care specialists, gastroenterologists and surgeons using the levels of evidence and grades of recommendations according to the Oxford Centre for Evidence-based Medicine. The guideline content will be approved by the Danish Colorectal Cancer Group and the format by the Center for Clinical Practice Guidelines | Cancer.

Results
The search has yielded 13 guidelines and 886 abstracts of which 188 have been included for full text review. Sequelae are divided into bowel dysfunction, psychosocial aspects, pain/neuropathy, sexual- and urinary dysfunction. Multiple studies identify the extent of treatment sequelae and their impact on quality of life, however, fewer studies explore treatment options. Few clinical guidelines include recommendations for managing treatment-related sequelae or focus only on specific aspects.

Conclusion
Treatment-related sequelae following colorectal cancer are common and attention needs to be focused on identifying patients with unmet treatment needs and the development of evidence-based treatment algorithms. The guideline developed here will be designed as a practical guide to identify, diagnose and treat the most frequent and distressing sequelae after treatment for colorectal cancer.

Treatment morbidity and late effects

#185: Systematic screening for sexual dysfunction after treatment for rectal cancer

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Abstract
Introduction
Prevalence of sequelae after rectal cancer is high. A new modality for systematic screening as part of follow up is currently being tested in five surgical units in DK. This study aims to investigate the prevalence of sexual dysfunction and the impact of treatment, using short validated PROMs. Also, the study investigates the patients´ need for referral to sexual counseling.

Materials and Methods
Rectal cancer patients have been included in the survey since November 2018 and the study is ongoing. Patients complete questionnaires at 3, 12, 24 and 36 months after surgery.
The 5-item IIEF is used to measure sexual function in males, while in females, the 7-item Rectal Cancer Female Sexuality Score is used. Two extra items regards causes of disrupted sexual life and overall evaluation of sexual life.

Results
By April 2021, 248 patients have completed the survey at both 3 and 12 months. Mean age at surgery was 67 years (SD 11) and 62% were males.
73(29%) of the patients had radiotherapy and 136(55%) have a permanent stoma.
At 3 and 12 months, 71(46%) and 67(43%) of males considered their sexual functioning bad/very bad. Among females, 24(26%) were sexually active at 3 months, while 31(33%) were active at 12 months. Among the active females, 4(17%) and 3(10%) considered their sexual functioning bad or very bad at 3 and 12 months.
25 males and 5 females have been referred for sexual counselling.
A permanent stoma and radiotherapy is associated with bad sexual functioning after 3 months; adjOR 2.88 (ci 1.30-6.39) and adjOR 4.83 (ci 1.79-13.1).

Conclusion
Sexual dysfunction is common after rectal cancer surgery. However, only 12% have been referred for sexual counselling, mainly males. Despite sexual problems in females, most find their sexual functioning good or acceptable. Systematic screening can facilitate valid estimates of the impact of rectal cancer treatment, and ensure that sexual dysfunction is identified and treated in those who request it.

Treatment morbidity and late effects

#186: Impact of anti-cancer treatment on quality of life and physical function in older patients with hematological cancers: a systematic review

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Abstract
Introduction
Among older patients with cancer, preservation of quality of life (QoL) and physical function (PF) is essential. Older patients with hematological cancer may be eligible for systemic treatment, which may effect QoL and PF. However, this is sparsely investigated. Thus, we explore the impact of cancer treatment on QoL and PF during and after treatment in older patients with hematological cancer.

Materials and Methods
A systematic search of studies published from 2000 to October 2020 in six major databases was conducted. Eligible studies were prospective RCTs and non-RCTs including patients with: any type of hematologic cancer, aged ≥65 years, undergoing treatment, with data from baseline and at least one follow-up available. Primary outcomes were patient-reported global QoL and PF and objectively assessed PF, evaluated at 2-3 months (short-term) and 6 months (medium-term) months into treatment and 6 months after treatment (long-term).

Results
Eleven RCTs and five non-RCTs, comprising 3331 participants, mostly of good performance status were included. The most common cancers were multiple myeloma (n=2147), chronic lymphatic leukemia (n=572) and acute myeloid leukemia (n=343). Fifteen studies (n=3296) evaluated patient-reported QoL and PF. Two studies (n=50) assessed objective PF. Short, medium and long-term data was reported in 10, 11 and five of the 16 included studies, respectively. Patient attrition was frequent and complete case analysis was used in five out of the 16 included studies. Overall, patient-reported QoL and PF remained stable or improved over time. Objective PF remained stable at both short and medium follow-up.

Conclusions
Our review indicates that cancer treatment do not negatively impact QoL or PF in older patients with hematological cancer. However, cautious interpretation is needed due to methodological concerns. Also, the paucity of studies investigating treatment effects on objective PF needs to be addressed in future trials.

Treatment morbidity and late effects

#187: Pelvic insufficiency fractures detected by MRI one-year after Chemoradiotherapy for anal cancer.

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Abstract
Introduction
Pelvic insufficiency fracture (PIF) is a well-known late complication to pelvic radiotherapy (RT), which can cause pain and decreased mobility.
PIFs are described in 1.4-14% of anal cancers (AC) after RT. However, studies are retrospective and heterogeneous in definition, imaging, and follow up (FU).
The aim of this study was to determine incidence of PIF on bone specific MRI 1 year after RT, and correlate to sacral bone dose volume parameters.

Methods and materials
Patients were treated with 54-64 Gy to tumor and pathological lymph nodes and 48-51.2 Gy for elective nodal areas, all VMAT planned.
PIF identification on 1-year 1.5T MRI: High signal intensity changes in the bone marrow on Sagittal STIR (5 mm) and accompanying subtle linear, low signal intensity on coronal T1 (FSE 7mm of total bony pelvis and proximal femur) were regarded as suggestive of PIF.
Delineation: Sacral bone outer contour was delineated from S1 to S5.
Wilcoxon rank sum or Pearson's Chi2 tests were used for comparison between PIF vs. no PIF. A p-value ≤0.05 was considered statistically significant.

Results
27 patients were included, 81% female, median age 64 years (range 43-74). PIFs were identified in 52% (n=14). The most frequent site was alae of the sacral bone (L/R) n=20. RT dose to sacral bone was significantly higher in patients with PIF for: max and mean dose, V20Gy, V30Gy and V40 Gy, p=0.01, p=0.04, p=0.037, p=0.02, p=0.048 but not for V50Gy p=0.062.
Significantly more patients with PIF had pain (85% vs 23%), p=0.001. Seven (50%) patients had grade I bone pain, 7 (50%) patients grade II.

Conclusion
We found a very high incidence of PIFs on MRI 1 year after RT for AC. Importantly, a significant proportion had symptomatic PIF. Higher RT dose to sacral bone was associated to increased risk of PIF. Future studies could consider including specific constraints to pelvic bones.

Treatment morbidity and late effects

#188: Effect of dietary intervention on radiation-induced diarrhoea in patients with pelvic cancer, a systematic review

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Abstract
Introduction
Curative External radiation therapy (ERT) of cancer in the small pelvis often results in radiation-induced diarrhoea (RID). While nutrition and food additives may prevent diarrhoea via microbiota- and/or immune modulating mechanisms, the effectiveness of dietary interventions on RID remains unclear.
The aim of the study is to investigate current evidence of the effect of any kind of dietary interventions on RID in patients with pelvic cancer.

Material and Methods
A systematic literature search was conducted in PubMed, Embase, Cinahl and Cochrane Library from January 2005 to December 2020 for RCT's with dietary interventions and ≥20 patients with cancer in the pelvis, treated with curative ERT/concomitant chemotherapy. The review protocol was conducted according to the PRISMA guidelines (Prospero ID: CRD42020209499). Studies prior to 2005 were excluded due to outdated radiotherapy techniques. Two independent reviewers screened all abstracts and all authors assessed all articles included. According to the Cochrane Risk of Bias (RoB) tool the results were assessed as low, high and unclear RoB.

Results
Out of 3303 records, 18 full-text articles were included (n=1,400). Two of them showed low RoB, 12 high RoB and 4 unclear RoB. In all 6 interventions were investigated: prebiotics (2 high, 1 unclear RoB trials), probiotics (1 low, 3 high, 2 unclear RoB trials), glutamine (1 low, 1 high, 2 unclear RoB trials), dietary interventions (3 high RoB trials), others: selenium and green tea (2 high RoB trials). The probiotic trial of low RoB (n=54) showed significantly lower frequency of RID compared to the placebo group. The glutamine trial of low RoB (n=69) showed no impact on RID compared to the placebo group.

Conclusions
The effect of dietary interventions on prevention of RID remains inconclusive due to a low number of trials (2/18) of high quality. New intervention studies of high methodological quality are necessary in this field of RID.

Treatment morbidity and late effects

#189: Breast cancer and subsequent risk of hypothyroidism: a systematic review and meta-analysis

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Abstract
Introduction
Radiation therapy (RT) for breast cancer (BC) may increase the risk of late effects, such as hypothyroidism. We conducted a systematic review and meta-analysis to investigate the association between BC, focusing particularly on BC-directed RT, and the risk of hypothyroidism in BC survivors.

Methods and materials
Through February 2021, we searched PubMed and Embase, as well as references of relevant articles, to identify papers on BC, BC-directed RT and subsequent risk of hypothyroidism. We screened by title and abstract, and reviewed relevant articles for eligibility. We used a data extraction sheet, and evaluated the risk of bias using the STROBE guidelines. The main outcome was the confounder-adjusted relative risk (RR) of hypothyroidism. We used a random-effects model to calculate pooled RRs and associated 95% confidence intervals (95%CI). We used funnel plots to investigate publication bias.

Results
From 448 papers screened by title and/or abstract, 43 full-text papers were reviewed for eligibility. Nineteen studies conducted in 14 different countries, published between 1985 and 2021, were eligible for inclusion. All but five papers were cohort studies. The pooled RR of hypothyroidism in BC patients was 1.18 (95% CI= 1.11, 1.26). BC patients treated with RT had increased risk of hypothyroidism compared with BC patients without RT (RR=1.18, 95%CI=1.04, 1.32). Among BC patients treated with RT, highest risk of hypothyroidism was associated with RT to the supraclavicular region (RR=1.34, 95%CI=1.01, 1.67).

Conclusion
Our systematic review and meta-analysis suggested an elevated risk of hypothyroidism in BC patients, especially after RT to the supraclavicular field.
Oncologists should be aware of this and if possible, institute preventive measures like delineating and minimizing radiation dose to the thyroid gland and/or following the patients with thyroid blood tests.

Treatment morbidity and late effects

#190: Patient versus physician reported late gastro-intestinal morbidity after whole pelvic radiation therapy in high risk prostate cancer patients

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Abstract
Introduction
Whole pelvic irradiation is considered standard treatment for high-risk prostate cancer (PC) patients. Morbidity following pelvic radiotherapy (RT) is not well described. The aim of this study was to evaluate morbidity in high-risk PC patients receiving whole pelvic RT.

Material and Methods
A total of 88 patients with high-risk PC were enrolled and followed from 2011-2018. All patients received 39 fractions of RT delivering simultaneously 78 Gy to the prostate and 56 Gy to the seminal vesicles and pelvic lymph nodes. Radiotherapy was delivered with IMRT and daily image-guidance. Patients received three years of ADT starting three months before RT. The primary endpoint was late morbidity. Physician reported morbidity was scored by the CTCAE v.4.0 and patient reported outcomes (PROs) by the RT-ARD score.

Results
Median follow-up (FU) time was 4.6 years. CTCAE grade 2 or higher GI morbidities varied from 0-6.0% from baseline throughout FU time, except for diarrhoea which was reported in 19.3% of the patients post-RT, declining to 2.3% at three months and remaining low thereafter. Prevalence of GI PROs revealed a significant rise from baseline to 60 months: rectal urgency (12% vs.30%, p=0.016); blood in stool (2% vs. 11.5%, p=0.04); mucus in stool (5.5% vs. 18.3%, p=0.02); incomplete evacuation (13.5% vs. 33.9%, p=0.005); bowel function and its impact on quality of life (17.8% vs. 40%, p=0.006). No significant increases were found for diarrhoea; clustering; abdominal pain and tenesmus.

Conclusion
Whole pelvic RT in high-risk PC patients is associated with a moderate risk of late GI morbidity with impact on patients' QoL. Increased prevalence of GI morbidities was clearly demonstrated by PRO scoring systems and not by physician administrated scorings. This underlines the importance of using PROs for morbidity assessment following pelvic RT.

Treatment morbidity and late effects

#191: Treatments for lymphedema in breast cancer survivors: an overview of reviews

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Abstract
Introduction
Breast cancer is the most frequent cancer among women with lymphedema being a common complication after treatment. An overview of systematic reviews with meta-analysis was conducted to evaluate the current evidence on treatment of lymphedema in breast cancer survivors.

Materials and methods
The databases of PubMed, Cochrane, Embase, Cinahl, and Web of Science were searched independently by two authors, selecting studies using the following PICOS criteria: Population: Adults treated for breast cancer who developed lymphedema, Intervention: Surgical (e.g., liposuction, lymph vessel anastomosis, lymph node transfer), pharmacological (e.g., benzopyrones, anti-inflammatory agents, immunosuppressive agents), exercise (e.g., aerobic, resistance, yoga, aqua), conservative (e.g., skin care, compression, self-care), laser energy, and acupuncture. Outcome: Any measure of lymphedema severity (e.g., volume, L-dex stage/grade, self-reported symptoms, health- related quality of life, or upper extremity function). Study design: Only systematic reviews with meta-analyses of randomized controlled trials were included. The search included all published reports from the earliest date available in each database to March 2020. Two authors independently full-text screened the reports and rated the methodological quality of the included reviews with the AMSTAR 2 tool.

Results
Out of a total of 495 articles screened, 12 were found eligible for inclusion. Five lymphedema treatment types were identified: Conservative, exercise, acupuncture, laser, and kinesio taping. Data extraction and statistical analysis is currently ongoing and the results will be presented at the conference.

Conclusion
This overview will determine the current evidence base for the efficacy of different treatment modalities for lymphedema in breast cancer survivors.

Treatment morbidity and late effects

#192: The impact of time from surgery to radiotherapy on overall survival in patients with newly diagnosed glioblastoma.

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Abstract
Introduction
Newly suspected glioblastoma (WHO grade IV) is most often treated with surgery for cytoreduction and acquiring tissue samples for histological and molecular diagnosis. Concomitant chemoradiotherapy awaits pathological analysis. Previous studies have shown a detrimental effect, beneficial effect or no effect on median overall survival if radiotherapy is delayed.

Materials and Methods
Patient data from electronic medical records on patients who received surgical treatment for newly diagnosed glioblastoma at Odense University Hospital from January 1st 2013 till December 31st 2018 were extracted. Outcomes were evaluated with hazard ratio. Since non-linear relationships were expected, the data was also analyzed using generalized additive models (GAM) with Akaike's Information Criterion (AIC) to compare competing GAM models. Using GAM models, the probability of survival at month 6, 9, 12, 18 and 24 was tested.

Results
Preliminary data suggest an optimal timespan from surgery to radiation between 30 and 35 days for 9 months overall survival. The impact of days to radiation on overall survival and the impact of the type of surgery (biopsy, resection, excision), residual tumor on early postoperative control MRI and radiation dose will be analysed, and the data will be presented at the conference.

Conclusions
Preliminary data suggest an optimal timespan for radiation and an impact of surgery type, residual tumor on early postoperative control MRI and radiation dose.

Treatment morbidity and late effects

#193: Prevalence and clustering of general late effects among patients at the Department of Oncology, Rigshospitalet – a department wide cross-sectional screening study

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Abstract
Introduction
General somatic and psychological late effects are experienced by patients across cancer diagnoses. As part of the development of the new 'Clinic for Cancer rehabilitation and late effects' at the Department of Oncology, Rigshospitalet, we aimed to investigate the prevalence and clustering of late effects among all adult patients at the department.

Materials & Methods
Of 9533 patients with an open treatment or control-program at the Department, 8278 (87%) could be invited to participate and received a survey via e-Boks. Secretaries reminded patients of the survey in the clinic and handed out paper questionnaires to those unable to respond via e-Boks. Standardized scales and select single items were used to assess quality of life (EORTC-QLQ-C30), endocrine and cardiovascular late effects (single items), pain (BPI), neuropathic pain (S-LANSS), lymphedema (EORTC item bank), insomnia (ISI), fatigue (MFI-20), depression (MDI), and fear of recurrence (FCRI). Data will be analyzed to report the prevalence of late effects overall and by cancer site, time since diagnosis and sex, as well as to report the co-occurrence of late effects in cluster.

Results
When the survey closed on April 26th, a total of 5234 responses had been completed in the online survey and 39 patients had completed paper-based measures. Data analysis is now beginning and data on the prevalence and co- occurrence of late effects will be reported in August.

Conclusions and perspectives
Analyses are ongoing. This study will provide much-needed evidence on the prevalence of late effects among Danish cancer survivors. Specifically, results will inform the development of the 'Clinic for cancer rehabilitation and side effects' at Rigshospitalet, to ensure the new clinic meets patient needs. Further, the study will be expanded into a national survey, including patients from oncology departments across Denmark to create nationwide and population-based comprehensive data on general cancer late effects.

Treatment morbidity and late effects

#194: Surviving rectal cancer at the cost of a colostomy - a global survey of long-term HRQoL

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Abstract
Introduction
Colorectal cancer is the most common indication for ostomy formation. However, a stoma may negatively impact health-related quality of life (HRQoL). This study compares generic and stoma-specific HRQoL in 2557 patients with a permanent colostomy after rectal cancer surgery and investigates predictors of reduced HRQoL across ten countries.

Materials and methods
Cross-sectional cohorts of rectal cancer survivors with a colostomy in Denmark, Sweden, Spain, the Netherlands, China, Portugal, Australia, Lithuania, Egypt and Israel completed a questionnaire regarding demographic and socioeconomic factors and stoma care along with the Colostomy Impact (CI) score, EORTC QLQ-C30 and five anchor questions assessing colostomy impact on HRQoL. Response rates were 51-93%.

Results
A total of 2557 patients were included in the study and 25.8% reported that their colostomy impairs their HRQoL 'some' or 'a lot'. Patients reporting stoma related impairment of HRQoL had significantly unfavourable scores across all EORTC QLQ-C30 subscales compared to patients reporting no or little impairment on HRQoL, and compared to a reference population. Generic HRQoL differed significantly between countries, but resembled HRQoL of reference populations. Multivariate logistic regression showed that stoma dysfunction measured by the CI score (OR=3.22), financial burden of stoma care products (OR=1.78) and young age (OR=1.02) were the strongest predictors of reduced HRQoL.

Conclusions
Overall HRQoL is preserved in rectal cancer survivors with a colostomy compared to a reference population, but a minor proportion experiences impaired HRQoL due to their colostomy. To improve long-term QoL in this group, stoma dysfunction should be recognized and addressed, and awareness of age, financial difficulties and social/cultural norms should guide decision-making in stoma forming surgery.

Treatment morbidity and late effects

#195: Long-term gastrointestinal sequelae in colon cancer survivors: Prospective pilot study on identification, need for clinical evaluation and effect of treatment.

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Abstract
Introduction
The aim of the present pilot study was to describe the type and frequency of long-term gastrointestinal symptoms within a well-defined cohort of colon cancer survivors, their wish for clinical evaluation and outcomes of treatment.

Materials & Methods
A screening survey was sent to colon cancer survivors 12, 24 and 36 months after surgery. Based on their main symptoms, patients who wished to have a consultation were referred to the gastroenterological or surgical unit of our late cancer sequelae clinic. Treatment effect was monitored by questionnaires on bowel symptoms and the EuroQol five-dimensional (EQ-5D) quality-of-life score.

Results
Overall, 953 patients who had survived colon cancer received the screening survey, and 767 patients replied (response rate 80.5%). Of these, 76 (9.9% [7.9-12.2%]) were referred for algorithm-based clinical evaluation and treatment of bowel dysfunction. The majority were females (69.7%) who had undergone a right-sided colonic resection (65.8%). Patients reported various symptoms, mainly including urgency, fragmented defecation, loose stools and incontinence for liquid stools. Patients with emptying difficulties and low anterior resection syndrome-like symptoms were referred to the surgical unit and patients with diarrhoea were referred to the gastroenterological unit for clinical work-up. Our main endpoint, mean EQ-5D index after treatment, was improved compared to baseline (baseline: 0.809, after treatment: 0.846, p 0.049). After treatment, self-rated bowel function and several bowel symptoms were improved as well.

Conclusions
This study highlights the importance of identifying colon cancer survivors in need of treatment of late gastrointestinal sequelae and clinical management in a multidisciplinary team setting.

Treatment morbidity and late effects

#196: Diet and bowel symptoms among colon cancer survivors

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Abstract
Introduction
Bowel dysfunction is a late sequelae to treatment for colon cancer (CC). Many CC survivors make dietary changes. The present study aimed to describe the effects of diet on bowel function in a large, well-defined cohort of CC survivors and to compare the level of dietary information provided by clinicians with the patients´ perception of the information.

Methods
CC patients from four surgical departments in Denmark were invited to complete surveys regarding the effects of diet on bowel function, and dietary advice received. Data concerning sociodemographic characteristics and the surgical procedure were collected from the Danish Colorectal Cancer Group database. Forty-four clinicians specialized in treatment of CC completed a questionnaire about how they advise CC survivors about diet.

Results
Among 1544 patients invited, 1239 (80.4%) responded and 844 met the inclusion criteria (53% males, median age 72.6 years, median time since surgery 742 days). Among there, 267 (32%) reported that food affected their bowel function. Fat had a negative effect in 193 (25%), spices in 149 (19%), sweets in 101 (13%) and meat in 99 (13%). There was no association between tumour site and food categories affecting bowel function. Most clinicians (93%) stated that their unit gave advice about diet to CC survivors, but only 24% of patients remembered having received such information.

Conclusions
One third of CC survivors report that some food, especially fat and spices, has a negative impact on their bowel function. We found a major discrepancy between clinicians reporting that they provide dietary advice and the proportion of patients remembering this.

Treatment morbidity and late effects

#197: Treatment of bowel dysfunction after pelvic organ cancer

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Abstract
Introduction
As cancer survival improves so does awareness on functional outcomes and the impact of late sequelae on quality of life (QoL). This study aims to audit results on treatment of bowel dysfunction from our pelvic organ cancer late sequelae clinic.

Materials and methods
Patients with bowel dysfunction after pelvic organ cancer were offered treatment in a nurse- led clinic according to their symptoms. Patients completed validated electronic PROMs assessing bowel function and QoL. Information on treatment modalities was recorded. Data were prospectively registered in an online database in REDCap. The data collection is ongoing.

Results
To date, 326 cancer patients (49% rectal, 14% gynecological, 12% anal, 10% prostate, 10% colonic, 5% other cancers) have started treatment for bowel dysfunction in the late sequelae clinic and are included in this study. The mean age was 64 years (range; 27-93) with 55% women and 45% men. Patients primarily presented with faecal urgency (95%), fragmentation (93%), emptying difficulties (93%), flatus/faecal incontinence (80%) and obstructed defecation (80%). In total, 133 patients have completed treatment. Mean number of contacts were 1.5 (range; 1-4) and mean duration of the treatment course was 176 days (IQR; 84-234). At end of treatment, 53% were treated with fibre supplement, 40% with anti-diarrheal medication, 23% with rectal emptying aids, 20% with oral laxatives and 24% with transanal irrigation. Five patients had a stoma and one received Sacral Nerve Stimulation. Significant improvements in the most frequent symptoms ($p<0.05$) and QoL ($p<0.001$) were observed.

Conclusions
Treatment of bowel dysfunction after pelvic organ cancer in our nurse-led clinic significantly improved the most frequent symptoms and QoL. This encourages screening for- and treatment of late sequelae after pelvic organ cancer.

Treatment morbidity and late effects

#198: Development and validation of a delineation atlas of neurovascular structures

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Abstract
Introduction
Radiation-induced neurovascular late-effects in pediatric patients with brain tumor are currently being investigated in the HARMONIC prospective cohort study (https://harmonicproject.eu/). In this project, dose/volume effects to relevant neurovascular structures will be studied. We therefore developed an atlas for these structures, and explored if doses to the suprasellar cistern (SC) could be used as surrogate for the Circle of Willis (CW) doses.

Material and methods
Neuroradiologists developed an initial atlas of the CW, its 10 individual arteries and the SC. A single observer applied this atlas to thirty proton therapy plans from pediatric patients with brain tumors to delineate the neurovascular structures, and retrieved their associated dose metrics. The agreement between doses to the CW vs. SC was specifically investigated. The neurovascular structures were also contoured in three test patients by three independent observers, and the differences were assessed visually as well as dose-wise (Dmean/Dmax). This final step was used for refining the contouring guidelines.

Results
For the thirty validation patients, there was an excellent agreement between the Dmax/Dmean to the CW and the SC with a linear coefficient of determination R2 value of 0.99 for both metrics. Examining inter-observer variation, visual assessment showed good spatial correlation between all individual arteries for all three patients, especially in the cranio-caudal extent. This translated into similar doses to the CW, with a Dmean (in percent prescription dose) of 69.4%/68.1%/68.3% (patient 1), 19.8%/18.9%/17.8% (patient 2) and 4.7%/5%/3.7% (patient 3).

Conclusion
Our data indicate that the doses to the SC can be used as a surrogate for the dose to the CW. Following the atlas, all individual arteries could be located with high precision by the three independent observers. This knowledge could guide the treatment planning process in an effort to spare neurovascular structures.

Treatment morbidity and late effects

#199: No correlation between radiation dose to the cardiac substructures and coronary artery disease in early breast cancer patients based on CT-based treatment technique: A DBCG study

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Abstract
Background and purpose
Coronary artery disease (CAD) has been reported as a long-term side effect after radiation therapy (RT) for early breast cancer (BC). However, the relationship between RT dose to the heart and CAD is based on mean heart dose (MHD) estimated from outdated RT regimens before CT-based RT. This study aims to report individual RT doses to the heart and cardiac substructures in patients treated with CT-based RT and to investigate if a dose- response relationship is presented.

Material and methods
BC patients registered in the Danish Breast Cancer Group database from 2005 to 2016 and treated with CT-based RT were eligible. The study included 190 patients who developed CAD after irradiation (cases) and 380 controls. Individually planning CT scans and dose plans were retrieved and the heart and 24 cardiac substructures were delineated by an automatic atlas segmentation workflow developed in the MIM software system, version 7.0.4. Mean doses to the heart and cardiac substructures were extracted from the dose-volume histograms. The hypotheses of no difference in dose left vs right for the cases and case vs controls were tested by the Mann- Whitney test.

Results
The median follow-up time for the eligible patients was 7.3 years (IQR: 4.8-10.1). In 90% of all patients, the mean heart dose (MHD) was < 2.50Gy. For cases the median MHD was 1.50Gy (0.83-2.14) and 0.82Gy (0.58-1.18) for left and right-sided patients, respectively ($p < 0.001$). The highest RT dose was observed in the left ascending coronary artery for left-sided and in the right coronary artery in right-sided patients. However, no significant difference in the distribution of CAD by laterality was observed. For the controls, the mean RT doses to the heart and cardiac substructures was not significantly higher compared to the cases.

Conclusion
In a cohort of early BC patients treated with CT-based RT, no trend towards a dose-response relationship was observed during a median follow-up at 7 years.

Treatment morbidity and late effects

#200: DCCL-PRO: Udvikling og pilotafprøvning af en interaktiv mobil-baseret applikation til national registrering af symptomer og senfølger efter behandling for brystkræft

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Abstract
Introduktion
Overlevelse efter brystkræft er forbedret, men mange oplever fysiske og psykiske senfølger af betydning for livskvaliteten. Projektet sigter mod at udvikle og evaluere DCCL-PRO, en interaktiv mobil-applikation til systematisk monitorering af brystkræftsenfølger med individuelt tilpassede tilbagemeldinger og råd om håndtering af senfølgerne.

Materialer og metoder
Første version af DCCL-PRO blev afprøvet ved Brystkirurgisk klinik og Kræftafdelingen, Aarhus Universitetshospital, fra juli-september 2020. Patienternes oplevelse af procedurer og information samt deres tilfredshed med DCCL-PRO blev undersøgt med kvalitative semistrukturerede telefoninterviews ca. 4 uger efter inklusionen. Der anvendtes en interviewguide med 18 spørgsmål til funktionalitet, kvalitet og tilfredshed med mobil- applikationen og procedurerne for introduktion. Patienterne vurderede udvalgte aspekter med scores fra 1-10. De transskriberede interviews blev analyseret med induktiv tematisk analysemetode med henblik på at identificere relevante temaer og undertemaer.

Resultater
I alt 30 patienter med diagnosen primær brystkræft, alle kvinder i alderen 39-79 år, deltog. Af disse blev 22 inkluderet efter første konsultation i Brystklinikken, 6 halvvejs i deres planlagte primære adjuverende kemoterapiforløb og 2 efter afsluttet primær adjuverende kemoterapi. Patienterne evaluerede generelt DCCL-PRO positivt med gennemsnitscores på indhold 8,5 (SD: 1,3), tilbagemeldinger 9,0 (1,0), design 8,7 (1,4) og samlet vurdering 8,4 (1,3). Patienterne angav, at DCCL-PRO øgede deres sygdomsindsigt og oplevelsen af adgang til sundhedsvæsenet, med øget tryghed i behandlingsforløbet til følge. Alle inkluderede patienter ønskede at fortsætte med mobil-applikationen.

Konklusioner
Alle inkluderede patienter var positive ift. et øget fokus på senfølger efter brystkræft og vurderede, at den interaktive mobil-applikation ville styrke deres muligheder for at tage aktivt del i eget behandlingsforløb.